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REVIEW ARTICLE

The maximum standardized uptake value of metastatic site in 18 F-FDG PET/CT predicts molecular subtypes and survival in metastatic breast cancer: An Izmir Oncology Group study

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Summary

Purpose: *The purpose of this study was to analyse the association between the 18F-2-deoxy-2-fluorodeoxyglucose maximum standardized uptake value (SUVmax) of metastatic sites and molecular subtypes and survival in metastatic breast cancer (MBC) patients.*

Methods: *Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG-PET/CT) was performed in 176 MBC patients before any therapeutic intervention. The FDG uptakes of metastatic sites were evaluated using the SUVmax. Histopathological prognostic parameters, such as the tumor size, grade, lymph node involvement, lymphovascular invasion, estrogen (ER), progesterone receptors (PR), HER2 status and Ki67 were determined from the primary breast tumor tissue. The SUVmax of the metastatic sites was assessed in relation to the molecular subtypes and survival in univariate and multivariate analyses. Cox regression analysis was used to evaluate the associations between SUVmax measurements and overall survival (OS).*

Results: *The mean SUVmax of 176 tumors was 8.0. Among the subtypes 49 (28.8%) were luminal A, 51 (28.9%) luminal B, 35 (19.8%) HER2-overexpressing, and 41 (23.2%) triple-negative, and the corresponding means of SUVmax were 5.6, 7.4, 11.4, 11.0, respectively. A cut-off value of ≤8.4 yielded 80% sensitivity and 57.1% specificity with an area under the receiver operating characteristics curve (AUC) of 0.731 for predicting that a tumor was of the luminal A subtype. A cut-off value of SUVmax ≥10.05 yielded 62.9% sensitivity and 67.4% specificity with an AUC of 0.648 for predicting a HER2 overexpressing subtype. A cut-off value of SUVmax ≥9.25 yielded 61% sensitivity and 64.4% specificity with an AUC of 0.660 for predicting a triple-negative subtype. The SUVmax could not effectively differentiate patients with luminal B subtype. Cox regression analysis showed that in patients with MBC, a SUVmax ≤7.55 acted as an independent negative prognostic factor for OS (hazard ratio/HR = 1.552).*

Conclusion: *The SUVmax of metastatic sites on pretreatment 18F-FDG PET/CT may be an independent prognostic factor for the diagnosis of molecular phenotypes and survival in MBC patients.*

Key words: *breast cancer, molecular subtype, PET/CT, survival*

Introduction

The identification of 4 breast cancer subtypes with different molecular and biological features by gene expression analyses has become a milestone in the selection of treatment and prediction of prognosis for breast cancer. According to this, triple negative and HER2 overexpressing subgroups of breast cancer are tumors with higher proliferation rates and poor prognosis when compared to the luminal subgroup [1]. Gene expression analyses have limited use in daily clinical

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practice as they are expensive and require an extensive foundation, but they have revealed molecular subtypes of breast cancer; these subtypes can be predicted according to the features and receptor status identified in the histopathological evaluation of the tumor. In such a way, the St. Gallen expert panel determined breast cancer subtypes in 2011 as follows: luminal A as ER-positive and/or PR-positive, HER2-negative and Ki67 <14%; luminal B as ER-positive and/or PR-positive, HER2-negative and Ki67 ≥14 % ; or ER-positive and/or PR positive, HER2-positive, irrespective of Ki67 expression, HER2-positive as ER-negative, PR-negative and HER2-positive, and triple-negative as ER-negative, PR-negative and HER2-negative [2].

18F-FDG PET/CT imaging has been studied extensively in several cancers and is based on the principle of glucose metabolism in malignant cells [3]. The use of 18F-FDG PET/CT generally enables the visualization of the primary tumor and its distant metastases [3,4]. Several studies on the clinical value of FDG/PET in breast cancer have recently been performed and some of them have suggested that the level of 18F-FDG uptake in breast cancer is significantly correlated with tumor size, high histological grade, Ki67 labelling index, the number of mitotic figures, the abrogation of p53, and receptor status [5,12]. From this perspective, 18F-FDG PET/CT is a non-invasive procedure for evaluating the metabolism of tumor cells, which might be useful for the detection of subtypes in breast cancer. García Vicente et al. analyzed the correlation between the SUVmax value of primary breast tumors and their molecular subtypes and found that HER2-positive and basal tumors had significantly higher values of SUVmax than did other subtypes [13].

The main objective of this study was to assess whether the SUVmax value of a metastatic lesion on PET-CT differs by the molecular subtype determined by ER, PR and HER2 status, and whether the SUVmax value of the metastasis can predict the molecular subtype of breast cancer when ER, PR and HER2 status is unknown. In the presence of metastatic disease, the correlation of the primary breast mass subtype was determined based on histopathological features and receptors, while the SUVmax value of the metastasis on PET/CT was investigated.

The second study objective was to explore the association between the SUVmax of metastasis and OS in MBC.

Methods

The study was approved by the Hospital's Ethics Committee, and was conducted according to the Declaration of Helsinki (1964) and its later amendments. All participants provided written informed consent.

Patients

In total, 246 MBC patients who underwent FDG-PET/CT at the Katip Celebi University, Department of Medical Oncology, between January 2010 and December 2014 were retrospectively evaluated, and 176 of them were eligible for this study. The inclusion criteria were newly diagnosed MBC (synchronous metastasis) with no treatment for metastatic disease and at least one visible metastatic lesion with abnormal FDG uptake. Patients diagnosed at early stages who had completed adjuvant chemoradiotherapy and patients with metastases that were detected during follow-up (metachronous metastasis) while they were on hormonal therapy were included in the study. The exclusion criteria were patients who had received radiotherapy or chemotherapy within one year prior to PET/CT, presence of brain metastasis confirmed by CT or MRI (because of low sensivitiy of PET/CT in detecting brain metastasis), history of diabetes mellitus, and active or uncontrolled infection. For patients who had multiple metastatic sites, the single lesion with the highest SUVmax was used. Medical records were used to collect data on standard prognostic variables and patient characteristics including age, tumor size and stage, grade, lymph node status, lymphovascular invasion, ER/PR and HER2 expression. The sites of the distant metastases were categorized as follows: bone, liver, lung and lymph nodes.

Follow-up and data collection

The median follow-up time was 40 months (range 20-312). The end date of the follow-up was 31st December 2014. The status of the recent follow-up was obtained from our prospective database. OS for synchronous MBC patients was defined as the time from breast cancer diagnosis to the date of death or last follow-up, and for metachronous MBC patients it was defined as the time from metastasis diagnosis to the date of death or last follow-up.

Acquisition of 18F-FDG PET/CT images

Combined FDG PET/CT was performed using a Siemens HI-REZ biograph 6 which provides an in-plane spatial resolution of 4.8 mm, an axial field view of 16.2 cm, and three-dimensional image acquisition. Patients were required to fast for 6 hrs prior to scanning, and whole-body PET scanning from the skull base to the upper thighs was performed approximately 1 hr after the intravenous injection of 555 MBq of F-18 FDG. Whole body CT scanning was performed in the cranio-caudal direction. Intravenous contrast was not used during CT scanning. Immediately after CT scanning, PET data were collected in the cranio-caudal direction with the arms down. FDG PET images were reconstructed using CT data for attenuation correction. One nuclear medi-

Table 1. Patient characteristics

Characteristics		
Follow-up (mo) (median, IQR)	40	57.8
Age, years (median, IQR)	49.5	18.8
Tumor size (cm) (median, IQR)	3.3	2.8
Initial stage (N, %)		
I	4	2.2
II	47	26.7
III	53	30.1
IV	72	40.9
Grade (N, %)		
I-II	98	55.7
III	78	44.3
Lymph node metastasis (N, %)		
0	37	21
1-4	55	31.3
5-9	39	22.2
≥10	45	25.6
Lymphovascular invasion (N, %)		
Absent	32	18.2
Present	144	81.8
Histology (N, %)		
Invasive ductal	162	92.0
Invasive lobular	14	8.0
Ki67 (median, IQR)	12.5	45.0
ER (N, %)		
Negative	86	48.9
Positive	90	51.1
PR (N, %)		
Negative	88	50.0
Positive	88	50.0
FISH (N, %)		
Negative	103	58.5
Positive	73	41.5
Kind of metastasis (N, %)		
Metachronous	104	59.1
Synchronous	72	40.9
Site of metastasis (N, %)		
Liver	31	17.6
Lung	28	15.9
Bone	55	31.3
Lymph node	62	35.2
Metastasis SUV max (median, IQR)	8	7.7
Biological subtypes (N, %)		
Luminal A	49	28.8
Luminal B	51	28.9
HER2 overexpressing	35	19.8
Triple negative	41	23.2
Final outcome (N, %)		
Alive	72	40.9
Dead	104	59.1

SUVmax: the maximum standardized uptake value; N.: number; IQR: interquartile range; ER:eostrogen receptor; PR: progesterone receptor; FISH: fluorescence in situ hybridization

Table 2. Associations between clinicopathological factors and SUVmax

Clinicopathological factors	*SUVmax*		*p value**
	Median	*IQR*	
Age (years)			
≤50	8.3	7.6	0.979
>50	7.6	7.8	
Tumor size (cm)			
≤5	8.0	7.4	0.314
>5	7.5	7.5	
Stage			
I-II	8.5	6.7	0.895
III-IV	7.8	7.7	
Grade			
I-II	7.6	6.7	0.393
III	8.2	7.8	
Lymph node metastasis			
Absent	6.7	7.4	0.134
Present	8.1	7.7	
Lymphovascular invasion			
Absent	6.8	8.4	0.292
Present	8.1	7.7	
Histology			
Invasive ductal	8.0	7.8	0.652
Invasive lobular	8.3	6.5	
ER			
Negative	10.9	7.7	<0.001
Positive	6.0	5.9	
PR			
Negative	10.5	8.2	<0.001
Positive	6.6	6.3	
FISH			
Negative	6.8	6.6	0.013
Positive	9.5	7.7	
Kind of metastasis			
Metachronous	8.7	6.6	0.283
Synchronous	6.8	8.0	
Site of metastasis			
Bone	7.5	6.6	0.344
Other	8.2	7.5	
Biological subtypes			
Luminal A	5.6	4.0	<0.001
Luminal B	7.4	8.2	
HER2 overexpressing	11.4	5.4	
Triple negative	11.0	9.1	

SUVmax: the maximum standardized uptake value, N: number, IQR: interquartile range, ER:estrogen receptor, PR: progesterone receptor, FISH: fluorescence in situ hybridization * Mann–Whitney U test (between 2 groups) or Kruskal-Wallis test (≥3 groups)

cine physician performed the visual assessment, image interpretation and data analysis. The SUVmax was defined as the SUV value on one pixel with the highest counts within the region of interest. A semi-quantitative measurement of the SUVmax was performed on the metastatic focus with the highest abnormal FDG uptake in PET/CT.

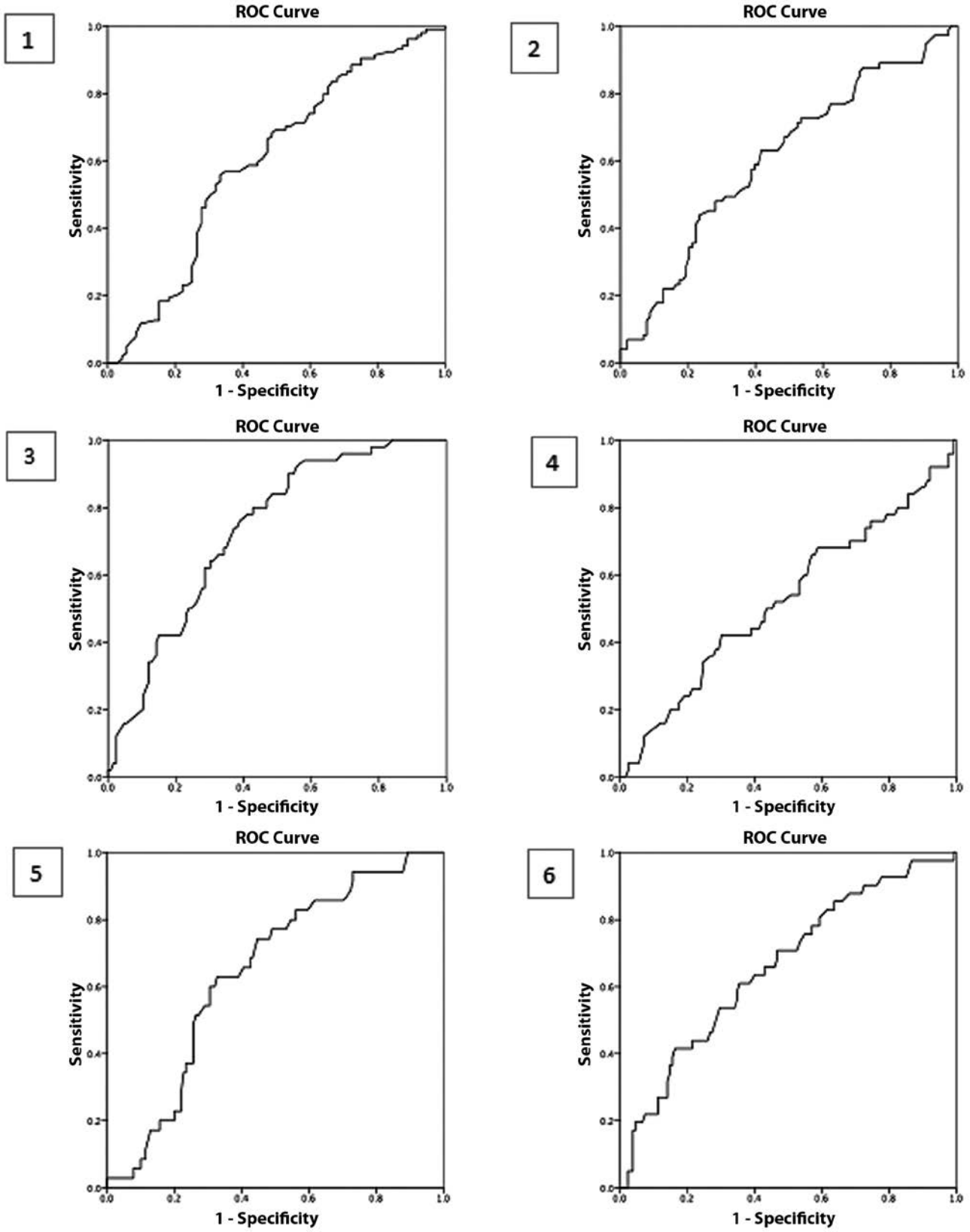

Figure 1. ROC curves. 1: Mortality; 2: FISH positive; 3: Luminal A; 4: Luminal B; 5: HER2 overexpressing; 6: Triple negative.

Histology, immunohistochemistry and biological subtypes

All the information on the molecular phenotype was obtained from the primary breast tumor sample. The determination of tumor type and the histopathological grading were performed on formalin-fixed, paraffin-embedded tumor tissue, cut into 5-μm sections and stained with haematoxylin and eosin. Immunohistochemistry (IHC) was performed on paraffin-embedded

material using primary antibodies for ER, PR and HER2, and the proliferation index was assessed using the Ki67 antibody. Samples were scored as positive for ER and PR by IHC, when at least 1% of tumor cells showed staining. HER2 status was scored as positive when strong IHC membrane staining (3+) was present in more than 30% of tumor cells. When membrane staining was less than 30% (2+) fluorescence in situ hybridization (FISH) was performed for clarifying HER2 gene amplification. The molecular subtypes of breast cancer were categorized according to ER, PR, and HER2 status. Tumors that were ER or PR positive, HER2 negative and had a Ki67 index <14% were categorized as luminal A, tumors that were ER and PR positive, HER2 positive and had a Ki67 index ≥14% were categorized as luminal B, and tumors that were ER and PR negative with HER2 positive as HER2 overexpressing, and tumors that were negative for both ER and PR and without HER2 overexpression were categorized as triple negative breast cancer subtype.

Statistics

All statistical analyses were performed using SPSS 17.0 software. Compliance with the normal distribution of numerical variables was tested by Kolmogorov-Smirnov test. Categorical variables were expressed as frequencies and percentages, and numerical variables were expressed using medians and interquartile range (IQR) values. Independent more than two-sample medians were analyzed by Kruskal-Wallis test and *post-hoc* analysis was performed by Dunn's test. Independent two-sample medians were compared using the Mann-Whitney U test. In survival analysis, all factors have been firstly investigated by univariate analysis and those with p<0.150 entered multivariate Cox regression analysis. Receiver operating characteristics (ROC) analyses of the SUVmax values were performed and the Youden Index Method was used to determine the cut-off values. The findings were presented with 95% confidence intervals (CI). A p value <0.05 was defined as statistically significant.

Results

The patient characteristics are shown in Table 1. The mean patient age was 49.5±11.8 years. The sites of metastases on FDG PET/CT at the time of metastatic diagnosis were lymph nodes (N=62), bone (N=55), liver (N=31), and lung (N=28). Of the 176 patients, 104 (59.1%) had stage I-II or III, and had completed adjuvant treatment (chemotherapy and/or radiotherapy). These patients had been followed-up with examinations for at least 1 year without chemotherapy or radiotherapy. Of the 176 patients, 72 (40.9%) were diagnosed with stage IV, and had not received any prior treatment for breast cancer. The observed molecular subtypes were as follows: 49 (28.8%) were luminal A, 51 (28.9%) were luminal B, 35 (19.8.%) were HER2 overexpressing, and 41 (23.2 %) were triple negative.

The median SUVmax values were determined for patients grouped according to age, tumor size, lymph node status, nuclear grade, lymphovascular invasion, and ER, PR, and HER2 status. The SUVmax was associated with ER, PR and HER2 status (Table 2). The relationship between SUVmax and the breast cancer molecular subtypes was investigated and differed significantly among the 4 subgroups (p<0.001). The median SUVmax value of the patients in the luminal A group was 5.6 which was significantly lower than the mean SUVmax of all other groups. The median SUVmax value of the patients in the luminal B group was 7.4, which was significantly lower than the mean SUVmax of the HER2 positive and triple negative groups. The median SUVmax value of the patients in the HER2 positive group was 11.4 and the median SUVmax value of the patients in the triple negative group was 11.0 (Table 2).

The ability of the SUVmax to predict various features was tested using ROC analysis. There was evidence that SUVmax was able to predict mortality, FISH positive, luminal A, HER2 overexpressing and triple negative tumors, however, there was no evidence that SUVmax could predict luminal B (Figure 1). The AUC and the cut-off

Table 3. Results of ROC (AUC) analysis of the efficacy of the SUVmax for predicting mortality, FISH positive, luminal A, luminal B, HER2 overexpressing, and triple negative

	AUC	*p*	*Cutt-off*	*Sensitivity (%)*	*Spesificity (%)*
Mortality	0.598	0.027	≤7.55	55.8	66.7
FISH positive	0.611	0.013	≥7.95	63.0	58.3
Luminal A	0.731	<0.001	≤8.4	80.0	57.1
Luminal B	0.525	0.601	NA	NA	NA
HER2 (+)	0.648	0.007	≥10.05	62.9	67.4
Triple (-)	0.660	0.002	≥9.25	61.0	64.4

FISH: fluorescence in situ hybridization, NA: not applicable, AUC: area under the curve

Table 4. Univariate analysis

Prognostic factors	*Median*	*SE*	*95% CI*		*p value**
			Lower	*Upper*	
Age (years)					
≤50	70	9.6	51.1	88.9	0.167
>50	62	12.4	37.8	86.2	
Tumor size (cm)					
≤5	70	10.4	49.5	90.5	0.635
>5	62	15.1	32.5	91.5	
Stage					
I-II	111	11.9	87.6	134.4	<0.001
III-IV	50	5.5	39.2	60.8	
Grade					
I-II	81	9.3	62.8	99.2	0.066
III	50	5.9	38.4	61.6	
Lymph node metastasis					
Absent	81	14.6	52.4	109.6	0.314
Present	62	8.4	45.5	78.5	
Lymphovascular invasion					
Absent	106	17.9	70.9	141.1	0.103
Present	57	8.0	41.2	72.8	
Histology					
Invasive ductal	70	8.5	53.3	86.7	0.497
Invasive lobular	109	57.1	0.0	220.9	
ER					
Negative	83	9.4	64.6	101.4	0.453
Positive	57	6.1	45.0	69.0	
PR					
Negative	83	5.5	72.3	93.7	0.433
Positive	57	6.4	44.5	69.5	
FISH					
Negative	92	11.3	69.8	114.2	<0.001
Positive	48	6.7	35.0	61.0	
Kind of metastasis					
Metachronous	94	8.5	77.3	110.7	<0.001
Synchronous	30	3.8	22.6	37.4	
Site of metastasis					
Bone	57	11.7	34.1	79.9	0.258
Other	82	10.4	61.7	102.3	
Metastasis SUVmax					
≤7.55	62	8.4	45.6	78.4	0.113
>7.55	82	12.6	57.4	106.6	
Biological subtypes					
Luminal A	94	20.0	54.7	133.3	
Luminal B	45	6.5	32.3	57.7	<0.001
HER2 overexpressing	66	20.9	25.1	106.9	
Triple negative	110	25.2	60.6	159.4	

SUVmax: maximum standardized uptake value, N: number, IQR: interquartile range, ER: estrogen receptor, PR:progesterone receptor, FISH: fluorescence in situ hybridization, CI: confidence interval.*p: log- rank test

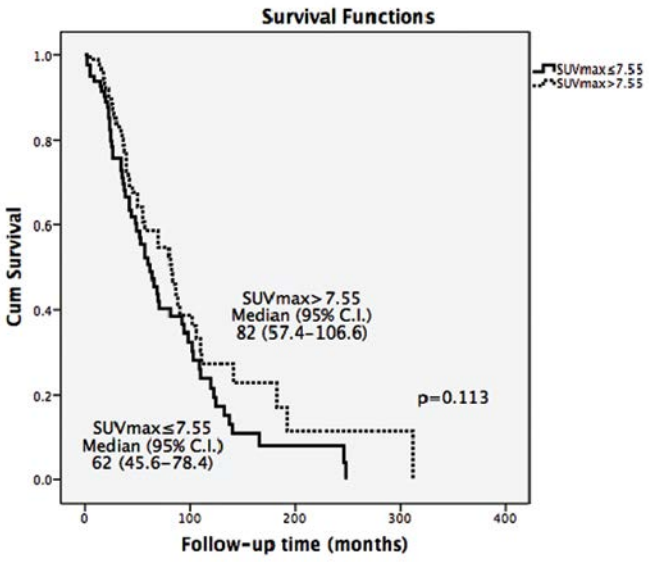

Figure 2. Overall survival.

values and the sensitivity and specificity of these values are presented in Table 3. A cut-off value of ≤8.4 yielded 80% sensitivity and 57.1% specificity with an AUC ROC of 0.731 for predicting that a tumor was of the luminal A subtype. A cut-off value of SUVmax ≥10.05 yielded 62.9% sensitivity and 67.4% specificity with an AUC of 0.648 for predicting a HER2 overexpressing subtype. A cut-off value of SUVmax ≥9.25 yielded 61% sensitivity and 64.4% specificity with an AUC of 0.660 for predicting a triple negative subtype. In the threshold value analysis it has been detected that SUVmax ≤ 7.55 value had the ability of predict mortality with 56% sensitivity and 67% specificity (Table 3).

Univariate analysis indicated that stage (p<0.001), FISH (p<0.001), kind of metastasis (p<0.001), metastasis SUVmax (p=0.003), and biological subtypes (p<0.001) were significantly associated with OS (Table 4). Cox multivariate analysis showed that synchronous metastasis, stage III-IV, SUVmax ≤ 7.55 luminal B and HER2 overexpressing subtypes, and FISH positive were independent prognostic factors that negatively affected prognosis. The probability of death was approximately 7-fold higher in patients with synchronous metastasis. (HR=6.790, 95%CI 3.738-12.334) and the probability of death was approximately 2-fold higher in FISH positive patients (HR=2.075, 95%CI 1.362-3.159). The probability of death was approximately 2-fold higher in stages III-IV patients (HR=2.010, 95% CI 1.211-3.335). The probability of death was approximately 2-fold higher in SUVmax ≤ 7.55 patients (HR=1.552, 95%CI 1.027-2.345) (Figure 2). The probability of dying in patients with luminal B compared to patients with luminal A was more than 2-fold (HR=2.030, 95%CI 1.204-3.420). The probability of dying in patients with HER2 overexpressing compared to patients with luminal A was more than 2-fold higher (HR=2.223, 95%CI 1.188-4.160) (Table 5).

When we analyzed the patients who had metastases on diagnosis (synchronous) and patients who developed metastases during follow-up (metachronous) in relation to luminal A, luminal B, HER2 overexpressing or triple negative to assess the correlation with SUVmax, we found a statistically significant association between SUVmax and the biological subtypes in patients with either synchronous or metachronous metastases. There was statistically significant relationship between SUVmax and the FISH status in patients with metachronous metastasis but not in those with synchronous metastasis (Table 6).

Discussion

In this study, we investigated the correlation between SUVmax of metastatic sites and molecular subtypes based on hormone receptors and

Table 5. Multivariate analysis

Factors	*p*	*HR*	*95.0% CI for HR*	
			Lower	*Upper*
Synchronous	<0.001	6.790	3.738	12.334
FISH (+)	0.001	2.075	1.362	3.159
Stage III-IV	0.007	2.010	1.211	3.335
SUVmax ≤7.55	0.037	1.552	1.027	2.345
Biological subtypes	0.005			
Luminal B	0.008	2.030	1.204	3.420
HER2 overexpressing	0.012	2.223	1.188	4.160
Triple negative	0.775	0.910	0.478	1.734

SUVmax: the maximum standardized uptake value, CI: confidence interval, FISH: fluorescence in situ hybridization.
The procedure was carried out with the method of ''forward: LR.''

Table 6. Associations between biological subtypes or FISH status and SUVmax according to kind of metastasis

Subtypes and FISH	*SUVmax*					
	Metachronous			*Synchronous*		
	Median	*IQR*	*p*	*Median*	*IQR*	*p*
Biological subtypes						
Luminal A	6.5	4.7	0.001	5.3	2.0	0.003
Luminal B	8.8	10.3		6.6	7.5	
HER2 overexpressing	10.8	4.9		12.1	6.6	
Triple negative	11.0	7.7		13.0	15.3	
FISH						
Negative	7.8	6.7	0.019	5.8	5.7	0.177
Positive	10.5	8.3		8.0	7.8	

SUVmax: maximum standardized uptake value, IQR: interquartile range, FISH: fluorescence in situ hybridization

HER2 status in MBC. We hypothesized that SUVmax of a metastatic site would be a useful biomarker of molecular subtypes in patients with MBC while yet with unknown hormone receptors and HER2 status. The results showed that SUVmax of the metastatic site could be used as a predictor of molecular subtypes. SUVmax also had a significant impact on OS of MBC patients. Cox regression analysis showed that a SUVmax ≤7.55 was an independent negative prognostic factor for OS. Our data also indicated that the SUVmax value of the metastatic site may be a surrogate for the presence of HER2 amplification in metachronous MBC patients.

Several trials have demonstrated a correlation between 18F-FDG uptake denoted as the SUVmax and molecular subtypes [12-16]. These studies have been mainly composed of non-metastatic patients. García Vicente et al. prospectively evaluated 168 patients with FDG PET/CT before neoadjuvant therapy for locally advanced breast cancer and demostrated a significant correlation between the SUVmax value of primary breast tumors and molecular subtypes [13]. The predictive value of 18F-FDG uptake for the estimation of molecular subtypes in MBC has not been fully clarified. The first study conducted by Zhang and colleagues [14] in MBC determined that the SUVmax could not distinguish between the molecular types of luminal A and luminal B; the second study by the same authors [15] found a correlation between SUVmax value of the metastases and the molecular subtypes of MBC. In our study, SUVmax of the metastatic site was significantly correlated with the molecular subtype of the primary breast tumor (Table 2). Similarly to both studies of Zhang et al, we also identified the SUVmax as an independent factor for predicting survival; SUVmax ≤7.55 was an independent negative prognostic factor for OS in MBC patients. Based on the fact that SUVmax value is considered an indirect indicator of the tumor metabolism, and also because chemotherapy is more effective on the rapidly growing cells which have higher metabolic rate, low tumor metabolism rate and low response to chemotherapy in metastatic patients with SUVmax ≤7.55 could negatively affect survival. Synchronous metastases containing much more stem cells compared to metachronous metastases and therefore being more resistant to chemotherapy could also be a factor for unfavorable survival than metachronous metastases. Unlike the previously mentioned 2 studies, our study had a retrospective design and evaluated both patients with synchronous and metachronous metastases. Therefore, heterogeneity, which is a limitation of this study, could have affected the results.

When the patients were grouped as having synchronous and metachronous metastasis, a statistically significant association was found between SUVmax of metastatic site and the biological subtypes in patients of both groups (Table 6). There was no statistically significant relationship between SUVmax and FISH in patients with synchronous metastasis, but a statistically significant relationship was detected in patients with metachronous metastases (Table 6). This meaningful result may suggest that HER2 overexpression as a result of the change in the genetic properties of the primary tumor, can change in metachronous metastasis, while HER2 amplification is negative in early stages of disease, and high SUVmax values may direct the clinician towards making a biopsy from the metastasis to identify changes in HER2 expression.

There are several limitations in our study. First, because of its retrospective nature, the patient population was heterogeneous in terms of

synchronous and metachronous metastases and treatment. Second, biopsies were not performed in metastatic lesions and molecular types were determined according to the receptor status information obtained from biopsies of the primary mass as in the trials of Zhang et al. [14,15]. Therefore, we were unable to evaluate changes in the receptor status of metastatic lesions caused by potential genetic changes and their relationship with SUVmax values. We were also unable to exclude the effects of endocrine treatment in patients receiving hormonotherapy (approximately half of the patients). Nevertheless, we believe that our preliminary results, which are in concordance with the tumor biology, are encouraging for conducting prospective studies.

Conclusion

Significant association was found between SUVmax and molecular subtypes. This study also demonstrated that a correlation exists between SUVmax of metastases and OS. Prospective studies that will compare gene expression status in materials obtained from the primary tumor and its metastasis with the SUVmax values of the primary tumor and metastasis will help provide new information in this field.

Authors' contributions

SC designed the study. PET/CT examinations were performed by IK. VB, MA, AC, SC and OT collected the clinical data. OT, SC, MOT and LD performed the statistical analyses. All authors contributed to the final analysis and writing of the manuscript.

Conflict of interest

All authors declare that they have no conflict of interest.

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