Original Article

Relationship Between Staging FDG PET/CT Findings and Distribution of Metastatic Sites in Metastatic Breast Cancer

Metastatik Meme Kanserinde Evreleme FDG PET/BT Bulgularının Metastatik Bölge Dağılımı ile İlişkisi

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ABSTRACT

Introduction: We aimed to investigate the relationship between staging FGD PET/CT findings and metastasis distribution and histopathological features of primary tumor in patients with metastatic breast cancer at diagnosis time.

Materials and Methods: Eighty patients with breast cancer who underwent F-18 FDG PET/CT for staging were included. The patients with newly diagnosed metastatic disease were included. Age and histopathological features of the primary tumor were recorded. The distant metastases sites, the numbers of metastasis and metastatic axillary/non-axillary lymph nodes were reviewed from PET/CT. The maximum standardized uptake(SUVmax) values were measured.

Results: All patients(n:80,mean age 58.0±14.4) had invasive breast carcinoma. Age was significantly related to the presence of lung metastases(p=0.006, mean ages 54y vs 64y).Only liver metastasis had a significant relationship with primary tumor SUVmax values and tumor molecular profile. The patients with HR+/HER2- (7/60 patients, 11.7%) had relatively less liver metastasis than with the other subtypes (9/20patients, 45%). There were significant associations between SUVmax of axillary lymph node(p=0.02), primary tumor(p=0.001), liver metastasis(p=0.02) and tumor subtypes. The numbers of distant metastasis were related with the numbers of axillary lymph node metastasis(p=0.02) and the highest SUVmax of distant metastasis(p=0.001).

Discussion: Accurate detection of distant metastases in breast cancer at the time of diagnosis is of great importance in terms of treatment planning and prognosis of the disease. FDG PET/CT is a very reliable modality in determining distant metastasis and their distribution, and as a result of our study, we suggest that PET/CT findings can predict factors with prognostic importance.

Keywords: breast cancer, metastasis, 18f fluorodeoxyglucose positron-emission tomography, cancer staging

ÖZET

Giriş: Tanı anında metastatik meme kanserinde evreleme FDG PET/BT bulgularının metastaz dağılımları ve tümör histopatolojik özellikleri ile ilişkisini araştırmayı amaçladık.

Gereç ve Yöntemler: Meme kanseri tanısıyla bölümümüzde evreleme FDG PET/BT görüntülemesi yapılan 80 hasta çalışmaya dahil edildi. Daha önce tedavi almamış hastalar çalışmaya alındı. Yaş, primer tümörün histopatolojik özellikleri geriye dönük olarak kaydedildi. Uzak metastaz alanları, metastaz odak sayıları, aksilla-aksilla dışı metastatik lenf nodlarıi PET/BT görüntülerinden tarandı. Standart maksimum tutulum (SUVmaks) değerleri hesaplandı.

Bulgular: Tüm hastalar (n:80, ort. Yaş 58.0±14.4) invaziv meme kanseri tanılı idi. Hasta yaşı akciğer metastazı ile ilişkiliydi (p=0.006, ort yaşlar 54, 64). Uzak metastaz alanlarından sadece karaciğer metastazının primer tümör SUVmaks değeri ve tümör moleküler profili ile ilişkisi olduğu gösterildi. Karaciğer metastaz sıklığı HR+/HER2- olan hastalarda (7/60, %11.7) diğer tümör subtipleri (9/20, %45) olanlara göre daha düşüktü. Primer tümör (p=0.001), aksilla lenf nodu(p=0.02) ve karaciğer metastaz(p=0.02) SUVmaks değerleri ile tümör subtipleri arasında anlamlı ilişki gözlendi. Uzak

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metastaz alan sayısı ile metastatik aksiller lenf nodu sayısı (p=0.02) ve en yüksek uzak metastaz SUVmaks değeri (p=0.001) arasında anlamlı ilişki gözlendi.
Tartışma: Meme kanserinde tanı anında metastaz varlığının doğru olarak saptanmasının tedavi planı ve hastalığın seyri açısından önemi büyüktür. FDG PET/BT uzak metastazı ve hatta dağılımını belirlemede oldukça güvenilir bir modalite olup, çalışamamız sonunda FDG PET/BT bulgularının prognostik öneme sahip faktörleri öngörebileceğini düşünmekteyiz.

Anahtar kelimeler: meme kanseri, metastaz, f18 florodeoksiglukoz positron-emisyon tomografi, kanser evreleme

Introduction

Breast cancer is the most commonly diagnosed cancer accounting for 29% of all newly diagnosed cancers and the major cause for the death of women worldwide [1,2]. About 6% of breast cancer patients have metastatic disease at presentation [3]. The five-year relative survival rate of patients diagnosed with distant metastasis is significantly less than that of patients with early-stage disease at the time of diagnosis [4].The median five-year survival of metastatic breast cancer patients is only 33.8% [5].Despite advances in the current treatments for metastatic breast cancer that based on a strategy of systemic chemotherapy, endocrine or HER2-targeted therapy (depending on estrogen receptor [ER], progesterone receptor [PR], and human epidermal growth factor receptor type-2 [HER2]status), and palliative therapies, there are no specific standard-of-care therapeutic strategies indicated for patients with organ-specific metastases [6,7].

Precise evaluation of disease extent is quite essential for metastatic breast cancer patients before determining treatment strategy.18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography(PET/CT) has been widely used in various malignant diseases for initial stage, disease extent assessment, therapy response assessment, metastasis detection and prognosis prediction[8].FDG-PET/CT has shown high accuracy in detecting distant metastases and also, it allows on a single “whole-body” examination to assess for locoregional as well as distant metastases with a high positive predictive value [9,10].The maximum standardized uptake (SUVmax) value of 18F-FDG is useful for diagnosing high-grade malignancy and predicting the prognosis in breast cancer patients. It was reported that SUVmax and the HR status were useful for predicting malignancy grades and prognosis of patients with breast cancer [11].

We aimed to investigate whether pretreatment FDG PET/CT findings are related to metastatic sites distribution and histopathological features of the primary tumor, and whether SUVmax values may be associated with primary tumor molecular profile for breast cancer patients with metastatic disease at presentation.

Material and Methods

Eighty patients with breast cancer who underwent F-18 FDG PET/CT for staging in our department were included in the retrospective study. The inclusion criteria were newly diagnosed metastatic breast cancer that are not previously treated for metastatic disease and at least one visible lesion as metastatic with positive FDG uptake. Patients with prior excisional biopsy of breast, patients without distant metastasis and patients with second primary malign disease were excluded from the study.

This study adheres to the ethical principles of the Declaration of Helsinki and was approved by the ethics committee of our institution (2022-09/168).

Age and histopathological features of the primary tumor such as grade, hormone receptor (HR), human epidermal growth factor receptor type-2 (HER2) status and Ki-67 index were recorded from the institution patient information system, retrospectively.

PET/CT Acquisition and Imaging Analysis

Patients were imaged on an integrated PET/CT scanner (Siemens Biograph 6-True Point PET/CT systems). Patients were fasted for at least 6 hours prior to injection of 90μCi/kg 18F-FDG by using automatic infusion system (Intego PET Infusion System). The blood glucose levels were less than 150 mg/dl in all patients at the time of the FDG injection. Unenhanced CT images were acquired for attenuation correction from the vertex of the skull to distal thigh using 3 mm slice thickness and calculated effective mAs due to patient weight. The PET and CT images were reviewed on a workstation (Syngovia, Siemens Medical Solutions) in all standard planes along with maximum-intensity-projection images and were visually and quantitatively by two specialists experienced in interpreting PET/CT scans.

According to PET/CT findings; The sites of distant metastasis, the numbers of metastatic site, the numbers of metastatic axillary lymph node, the presence of retropectoral, internal mammarian and supraclavicular lymph nodes, T and N stages were recorded. The size of primary tumor and the size of enlarged axillary lymph node were measured. The maximum standardized uptake (SUVmax) values of primary tumor, axillary and non-axillary lymph nodes, each site of distant metastasis were measured by drawing of region of interest (ROI). To provide the most accurate measurement of SUV, voxels were created large enough to maintain tumor inside the boundaries.

Statistical Analysis

The statistical analysis was performed using commercial software (SPSS 21.0, IBM SPSS Statistics for Windows, Version 21.0. Armonk NY: IBM Corp.). The variables were investigated using visual (histogram, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test) to determine whether or not they are normally distributed. Descriptive analyses were presented using frequencies for the ordinal/nominal variables and medians, minimum, and maximum values for the non-normally distributed variables. Kruskal-Wallis tests were conducted to compare the parameters and tumor molecular profiles, and metastatic sites distribution. The Mann-Whitney U test was performed to test the significance of pairwise differences using Bonferroni correction to adjust for multiple comparisons. The Chi-square test or exact method, where appropriate, was used to compare the proportions in different groups. An overall 5% type-1 error level was used to infer statistical significance.

Results

Patient characteristics are listed in Table 1.

The mean age of patients was 58.0±14.4 with a range of 23-90 years. All patients had invasive carcinoma.

Axillary lymph node metastasis was observed in 75 (93.8%) patients, followed by retro-pectoral lymph node metastasis in 58 (72.5%) patients.

Bone metastasis was seen as the most common distant metastasis site with a rate of 83.8% (n:67), followed by mediastinal lymph node (43.8%), lung (33.8%), and liver metastasis (20.0%), respectively.

The numbers of distant metastasis were>10 in 45 (56.2%) patients, and 5-10 in 15 (18.8%) patients and <5 in 20 (25%) patients.

We did not observe significant difference between the presence of bone metastasis and primary tumor SUVmax (p=0.55) and axillary lymph node SUVmax (p=0.75), the number of metastatic axillary lymph node (p=0.1). There was significant association between bone metastasis and the presence of retropectoral lymph node metastasis (p=0.03).Fifty-two (89.7%) of 58 patients with retropectoral lymph node metastasis had bone metastases.

We found that the patients with liver metastasis had a higher primary tumor size (median 33.0 mm vs 52.5 mm p=0.04), primary tumor SUVmax (median 10.1 vs 15.8 p=0.012), and Ki-67 index (median 30% vs 40% p=0.004) (Table 2). There was statistically significant difference between the presence of liver metastasis and the status of PR (p<0.001), ER (p=0.003), and HER2

Table 1. Patient Characteristics

Characteristics			
Age, years (mean)			58.0±1.6
Primary tumor size (mm) (median)			34 (9-134)
Primary tumor	Grade (N, %)	1	4 (5.2%)
		2	42 (54.5%)
		3	31 (40.3%)
	ER (N, %)	Positive	70 (87.5%)
		Negative	10 (12.5%)
	PR (N, %)	Positive	64 (80%)
		Negative	16 (20%)
	HER2 (N, %)	Positive	15 (18.8%)
		Negative	65 (81.3%)
	HR+/HER2- (N, %)		60 (75%)
	HR+/HER2+ (N, %)		10 (12.5%)
	HR-/HER2+ (N, %)		5 (6.3%)
	HR-/HER2- (N, %)		5 (6.3%)
	Ki-67 (%) (median)		30 (5-90)
Number of axillary metastatic lymph nodes (median)			6 (1-20)
Size of axillary metastatic lymph nodes (mm) (median)			13 (2-45)
Number of local metastatic lymph nodes (N, %)	Axillar lymph node		75 (93.8%)
	Inter-pectoral lymph node		27 (33.8%)
	Retro-pectoral lymph node		58 (72.5%)
	Internal mammarian lymph node		14 (17.5%)
	Infra-clavicular lymph node		14 (17.5%)
	Supra-clavicular lymph node		19 (23.8%)
T Stage (N, %)	T1		6 (7.5%)
	T2		27 (33.8%)
	T3		4 (5%)
	T4		43 (53.8%)
N Stage (N, %)	N0		5 (6.3%)
	N1		40 (50%)
	N2		6 (7.5%)
	N3		29 (36.3%)
Number of distant metastases (N, %)	<5		20 (25%)
	5-10		15 (18.8%)
	>10		45 (56.2%)
Sites of distant metastases (N, %)	Contralateral axillar and/cervical lymph node node		20 (25%)
	Mediastinal lymph node		35 (43.8%)
	Abdominal lymph node		10 (12.5%)
	Lung		27 (33.8%)
	Liver		16 (20%)
	Bone		67 (83.8%)
	Others (soft tissue, adrenal, pleura)		6 (7.5%)

ER, estrogene receptor; PR, progesterone receptor; HR, hormone receptor; HER2, human epidermal growth factor receptor type-2.

Table 2. Association between primary tumor SUVmax, histopathological features of primary tumor and the presence of liver metastasis

	Liver metastasis		P value
	Negative	Positive	
Primary tumor size (mm)	39.7±21.7 33.0 (9.0-98.0)	57.2±33.1 52.5 (21.0-134.0)	p=0.04*
Primary tumor SUVmax	10.8±5.4 10.1 (1.09-33.3)	15.6±6.9 15.8 (5.6-27.2)	p=0.01*
Ki-67 index (%)	33.1±19.0 30.0 (5.0-90.0)	48.1±19.0 40.0 (25.0-80.0)	p=0.004*

*p value <0.05 was regarded as significant

(p=0.04) receptors and the presence of abdominal lymph node metastasis (p=0.003). The patients with HR+/HER2- (7 of 60 patients, 11.7%) had relatively less liver metastasis than with the other molecular profiles (9 of 20 patients, 45%). Also, it was demonstrated that there were significant associations between axillary lymph node SUVmax (p=0.02), primary tumor SUVmax (p=0.001), liver metastasis SUVmax (p=0.02) and tumor molecular profiles (Table 3). In the statistical sub-analysis, the primary tumor SUVmax of the patients with HR+/HER2- were significantly lower than patients with HR+/HER2+ (p=0.007), and patients with HR-/HER2+ or triple negative (p=0.006). Moreover, liver metastasis SUVmax values of patients with HR-/HER2+ or triple negative were higher than patients with HR+/HER2- (p=0.008).

As a result of the study, it was shown that the presence of lung metastases was significantly related to the patient age (p=0.006, mean ages 54.5 y vs 64.5 y). Moreover, there was a significant association between lung metastasis and mediastinal lymph node metastasis (p=0.02).

We observed that the numbers of distant metastasis related with the numbers of axillary lymph node metastasis (p=0.02) and the highest SUVmax of distant metastasis (p=0.001). In the statistical sub-analysis, in the patients with <5 distant metastases the highest SUVmax of distant metastasis was significantly lower than in the patients with >10 distant metastases (p<0.001, median 8.9 vs 13.9).

Discussion

FDGPET/CT has proven to be an effective imaging modality for detecting distant metastases in the initial staging of breast cancer [10,12]. In our study, we investigated the association of initial staging PET/CT findings and tumor histopathological features with metastatic sites distributions in newly diagnosed breast cancer patients with distant metastasis.

As stated in previous studies, PET/CT is more sensitive and more specific than conventional imaging modalities such as contrast-enhancement CT or bone scan to detect lytic or mixed bone metastases, or bone marrow involvement [13,14]; and by careful reading of the CT-scan data PET/CT can help to detect osteoblastic metastases because of variable FDG uptake [15]. Most recently, a National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database analysis indicated that specifically, the incidence of bone metastasis is highest inluminal subtypes. Furthermore, the study

Table 3. Association between tumor molecular subtypes and SUVmax

		SUVmax	
Primary tumor	HR+/HER2-	(10.5±5.8) 9.6 (1.1-33.3)	p=0.001*
	HR+/HER2+	(14.5±3.4) 15.5 (10.0-20.2)	
	HER2+ or triple negative	16.6±6.5 15.8 (7.6-27.2)	
Axillary lymph node metastasis	HR+/HER2-	8.5±5.6 7.2 (1.3-29.0)	p=0.02*
	HR+/HER2+	13.0±5.2 12.7 (6.3-21.0)	
	HER2+ or triple negative	12.0±5.9 13.2 (4.5-22.1)	
Liver metastasis	HR+/HER2-	8.0±2.4 8.0 (4.4-12.3)	p=0.02*
	HR+/HER2+	11.3±1.1 11.9 (10.1-12.0)	
	HER2+ or triple negative	13.7±4.5 12.3 (9.5-21.0)	

HR, Hormone receptor; HER2, human epidermal growth factor receptor type-2
*p<0.05 was regarded as significant

revealed that all breast cancers regardless of subtype, were prone to metastasize to bone over other locations [16]. A recent study which examined HER2+ patient data deposited within the SEER database, uncovered that breast cancers which are HR+/HER2+ are significantly more likely to metastasize to the bone when compared to HR−/HER2+ disease, and that patients with HR−/HER2+ disease have a worse overall prognosis than those with HR+, HER2+ malignancy [16]. At the current study, bone metastasis was the most common distant metastasis detected by PET/CT. We did not find association with bone metastasis and findings derived from PET/CT and tumor histopathological features. We observed that bone metastasis is more common in those with only the presence of retropectoral lymph node metastasis.

We defined that lung metastasis as the third most common distant metastasis site is associated with the presence of second most common site mediastinal lymph node metastasis and advanced age. The mean age of patients without lung metastases was 54 years, while the mean age of patients with lung metastases was 64 years. To the results of studies, triple-negative and basal-like disease is more likely than other types of breast cancer to metastasize to the lungs [18], and patients with triple negative, especially basal-like type, primarily presented with lung metastasis. However, there was no difference in the total probability of lung metastasis across all subtypes [16]. We also did not find any relationship between lung metastasis and primary tumor histopathological features and PET/CT findings (such as primary tumor SUVmax, axillary lymph node SUVmax) in our study. The reason for this result may be due to the fact that the number of triple negative patients is less than the patients with HR+/HER2-.

Prognosis is poor in breast cancer with liver metastasis, with median survival time being 2 to 3 years [19]. In the analysis based on SEER database, it was reported that 1.4% of breast

cancer patients assessed harbored liver metastasis at the time of diagnosis, and that the presence of liver metastasis significantly reduced patient overall survival compared to patients without liver metastasis (HR 1.94 [1.86, 2.02]) [20]. In the present study, liver metastasis was the fourth most common distant metastasis site and it is the only distant metastasis site found to be associated with PET/CT findings and tumor molecular profile. Liver metastasis was associated with hormone [progesterone (PR) and estrogen (ER)] status and HER2. Patients with HR+/HER2- had less liver metastasis than HR+/HER2+, HR-/HER2+ and triple negative subtypes. Patients with liver metastasis had higher primary tumor size, higher primary tumor SUVmax and higher Ki-67 index.

In a prospective study which was performed with luminal type breast cancer patients with newly diagnosed metastases, baseline (maximum one of SUVmax of metastatic lesions) SUVmax was found significantly related to the number of metastatic sites and presence of visceral metastasis but could not effectively differentiate patients with luminal A from luminal B subtype. Baseline SUVmax as determined on PET//CT was predictive of both progression-free survival and overall survival. In multivariate analysis, the baseline SUVmax, relapse-free interval, and number of metastatic sites were independent prognostic factors for progression-free survival. For overall survival, the significant predictors were only baseline SUVmax and relapse-free interval [21].

In a recent study, the authors suggested that SUVmax of metastatic site would be useful biomarker of molecular subtypes in patients with metastatic breast cancer while yet with unknown HR and HER2 status and SUVmax also an independent prognostic factor on overall survival [22]. In our study, we demonstrated the association with the presence of synchronal liver metastasis and high SUVmax of primary tumor, and also the relation with primary tumor subtypes and primary tumor SUVmax, axillary lymph node SUVmax, liver metastasis SUVmax values. It was observed that SUVmax values of primary tumor, axillary lymph node and also liver metastasis were significantly lower in HR+/HER2- subtype compared to other subtypes. Although there is no survival data in our study as a limitation, we think that defining on staging PET/CT that liver metastasis is more common in patients with high primary tumor SUVmax, regardless of tumor subtypes, may be an important prognostic indicator and may predict the tumor subtype in patients whose tumor histopathological characteristics are not clearly known.

It is known that high SUVmax values are an indicator of tumor aggressiveness in many malignancies including breast cancer and the number of metastatic axillary lymph nodes is predicting poor prognosis in breast cancer [11,23,24]. In compatibility with this knowledge, in this study, we defined that the numbers of distant metastasis is related with the number of metastatic axillary lymph nodes and the highest SUVmax of distant metastasis. The highest SUVmax of distant metastasis was significantly elevated in the patients with >10 distant metastasis sites than in patient with <5 distant metastasis sites. To our results, we predict that further prospective studies can support the thesis that higher distant metastasis SUVmax value may be a worse prognostic indicator.

Primary tumors of breast cancer have high structural and molecular heterogeneity and may present with minor components of differing tumor cell types, in example, cells with differing molecular profiles [25]. To the authors, when a cancer spreads to other tissues, the metastases can be of a different type to the primary cancer, and sometimes the metastases are even different to each other [26,27]. This may be due to heterogeneity in the primary tumor that comprises more than one cell clone [26]. This heterogeneity of metastatic breast cancer has stimulated the development of new treatment approaches such as estrogen- and HER2-receptor targeting therapies. Survival with metastatic breast cancer is improving along with the

rapid development of new treatments [28]. In clinical practice, treatment planning of metastatic breast cancer is based on the histopathological molecular profile of the disease dominant cell type [29]. Despite all these treatment improvements, insufficient therapy response in some patients is maybe due to the cellular differences between primary tumor and metastases. Although treatment is based on primary tumor histopathological features, due to hetero-geneity of tumor and also metastasis we believe that a more aggressive treatment approach can be initiated in patients with high SUVmax of distant metastasis especially with high SUVmax of liver metastasis in order to increase the treatment response. The limitation of our study is that it is a retrospective study without patient follow-up information. More prospective studies with larger series and with follow-up data may be required to support our suggestions.

In conclusion, accurate detection of distant metastases in breast cancer at the time of diagnosis is of great importance in terms of treatment planning and prognosis of the disease. FDG PET/CT is a very reliable modality due to superiority in determining distant metastasis and their distribution, and it can lead to alter treatment approach in newly diagnosed metastatic breast cancer patients. As a result of our study, we suggest that PET/CT findings can predict factors with prognostic importance in breast cancer patients with metastasis at time of diagnosis.

REFERENCES

1- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016, CA Cancer. J. Clin. 2016; 66(1): 7-30.

2- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018; 68(6): 394-424.

3- Brewster AM, Hortobagyi GN, Broglio KR et al. Residual risk of breast cancer recurrence 5 years after adjuvant therapy. J Natl Cancer Inst. 2008; 100(16): 1179-1183.

4- Howlader NN, Noone AM, Krapcho M et al. SEER cancer statistics review, 1975-2013. 2016. Avaliable from: http://seer.cancer. gov/csr /1975_2013/.

5- Deluche E, Antoine A, Bachelot T, et al. Contemporary outcomes of metastatic breast cancer among 22,000 women from the multicentre ESME cohort 2008-2016. Eur J Cancer. 2020; 129: 60-70.

6- Grinda T, Antoine A, Jacot W, et al. Evolution of overall survival and receipt of new therapies by subtype among 20 446 metastatic breast cancer patients in the 2008-2017 ESME cohort. ESMO Open. 2021; 6(3): 100114.

7- Hortobagyi GN. Trastuzumab in the treatment of breast cancer. N Engl J Med. 2005; 353(16): 1734–6.

8- Kitajima K, Miyoshi Y. Present and future role of FDG-PET/CT imaging in the management of breast cancer. Jpn. J. Radiol. 2016; 34(3): 167-180.

9- Koolen BB, VranckenPeeters M-JTFD, Aukema TS, et al. 18F-FDG PET/CT as a staging procedure in primary stage II and III breast cancer: comparison with conventional imaging techniques. Breast Cancer Res Treat. 2012; 131: 117–126.

10- Groheux D, Hindié E, Delord M, et al. Prognostic impact of 18FDG-PET-CT findings in clinical stage III and IIB breast cancer. J Natl Cancer Inst. 2012; 104: 1879–1887.

11- Kadoya T, Aogi K, Kiyoto S, Masumoto N, Sugawara Y, Okada M. Role of maximum standardized uptake value in fluorodeoxyglucose positron emission tomography/computed tomography predicts malignancy grade and prognosis of operable breast cancer: a multi-institute study. Breast Cancer Res Treat. 2013; 141: 269–275.

12- Mahner S, Schirrmacher S, Brenner W, et al. Comparison between positron emission tomography using 2-[fluorine-18] fluoro-2-deoxy-D-glucose, conventional imaging and computed tomography for staging of breast cancer. Ann Oncol. 2008; 19(7): 1249-1254.

13- Groheux D, Giacchetti S, Delord M, et al. 18F-FDG PET/CT in staging patients with locally advanced or inflammatory breast cancer: comparison to conventional staging. J Nucl Med. 2013; 54(1): 5-11.
14- Morris PG, Lynch C, Feeney JN, et al. Integrated positron emission tomography/ computed tomography may render bone scintigraphy unnecessary to investigate suspected metastatic breast cancer. J Clin Oncol. 2010; 28: 3154–3159.
15- Groheux D, Espié M, Giacchetti S, Hindié E. Performance of FDG PET/CT in the clinical management of breast cancer. Radiology. 2013; 266: 388–405.
16- Wu Q, Li J, Zhu S, et al. Breast cancer subtypes predict the preferential site of distant metastases: a SEER based study. Oncotarget. 2017. 8(17): 27990–6.
17- Arciero CA, Guo Y, Jiang R, et al. ER+/HER2+ breast cancer has different metastatic patterns and better survival than ER−/HER2+ breast cancer. Clin Breast Cancer. 2019; 19(4): 236–245.
18- Smid M, Zhang Y, Sieuwerts AM, et al. Subtypes of breast cancer show preferential site of relapse.Cancer Res. 2008; 68(9): 3108–14.
19- Zhao HY, Gong Y, Ye FG, Ling H, Hu X. Incidence and prognostic factors of patients with synchronous liver metastases upon initial diagnosis of breast cancer: a population-based study. Cancer Manag Res. 2018; 10: 5937–5950.
20- Horn SR, Stoltzfus KC, Lehrer EJ, et al. Epidemiology of liver metastases. Cancer Epidemiol. 2020; 67: 101760.
21- Zhang J, Jia Z, Ragaz J, et al. The maximum standardized uptake value of 18 F-FDG PET scan to determine prognosis of hormone-receptor positive metastatic breast cancer. BMC Cancer. 2013; 13: 42.
22- Cokmert S, Tanriverdi O, Karapolat I, et al. The maximum standardized uptake value of metastatic site in 18F-FDG PET/CT predicts molecular subtypes and survival in metastatic breast cancer: An Izmir Oncology Group study. JBUON. 2016; 21(6): 1410-1418.
23- Buck A, Schirrmeister H, Kuhn T, et al. FDG uptake in breast cancer: correlation with biological and clinical prognostic parameters. Eur. J. Nucl. Med. Mol. Imaging. 2002; 29(10): 1317-1323.
24- Jatoi I, Hilsenbeck SG, Clark GM, Osborne CK. Significance of axillary lymph node metastasis in primary breast cancer. J Clin Oncol. 1999; 17(8):2334-40.
25- Alimirzaie S., Bagherzadeh M., Akbari M.R. Liquid Biopsy in Breast Cancer: A Comprehensive Review. Clin. Genet. 2019; 95: 643–660.
26- Kroigard A.B., Larsen M.J., Thomassen M., Kruse T.A. Molecular Concordance between Primary Breast Cancer and Matched Metastases. Breast J. 2016; 22: 420–430.
27- Gundem G., Van Loo P., Kremeyer B., et al. The Evolutionary History of Lethal Metastatic Prostate Cancer. Nature. 2015; 520: 353–357.
28- Swain S.M., Baselga J., Kim S.B., et al. Pertuzumab, Trastuzumab, and Docetaxel in Her2-Positive Metastatic Breast Cancer. N. Engl. J. Med. 2015; 372: 724–734.
29- Cardoso F., Kyriakides S., Ohno S., et al. Early Breast Cancer: ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. Ann. Oncol. 2019: 30: 1194-1220.

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