ZKTB

ORIGINAL RESEARCH

Total Lesion Glycolysis on ^{18}F-FDG PET/CT of Women with Non-Locally Advanced Breast Cancer: Does it Correlate with CT Density of the Lesion?

Lokal Olarak İlerlememiş Meme Kanserli Kadınların ^{18}F-FDG PET/BT Tetkiklerinde Toplam Lezyon Glikolizi: Lezyonun BT Dansitesi ile Bağıntılı mı?

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ABSTRACT

Objective: *Breast cancer (BC) is the second most frequent malignancy in women. Fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET)/computed tomography (CT) has become a major diagnostic tool for staging of the disease and predicting the prognosis. We aimed to evaluate the correlation between main quantitative ^{18}F-FDG PET/CT parameters- primarily TLG (total lesion glycolysis), and CT density measurements as Hounsfield Unit (HU) of the primary BC masses in non-locally advanced BC (non-LABC) patients. And also we aimed to see whether there is a correlation between the volume and HU measurements of BC masses in non-LABC patients.*

Material and Methods: *In this retrospective study, we included 17 women with unilateral non-LABC having a mean age of 54.1±10.3 years who underwent ^{18}F-FDG PET/CT before any treatment between 2016−2017. The mean volume, HU, maximum standardized uptake value (SUVmax) and TLG of the primary BC masses with their standard deviations and 95% confidence intervals (CI)s were calculated. Of the BC masses, the correlations between their mean TLG and mean HU, their mean SUVmax and mean HU, their mean volume and mean HU were statistically calculated.*

Results: *The mean volume and HU of BC masses were 4.6±3.9 mL (95% CI: 2.6−6.6) and 42.5±4.1 HU (95% CI: 40.3−44.6), respectively. The mean SUVmax and TLG of BC masses were 6.4±5.6 g/mL (95% CI: 3.5−9.3) and 22.1±14.2 g/mLxmL (95% CI: 14.7−29.4), respectively. Of the BC masses, the correlations between their mean TLG and mean HU (r=-0.443, P=0.075), besides their mean SUVmax and mean HU (r=-0.368, P=0.146) were not statistically significant. The correlation between the mean volume and the mean HU of BC masses was also statistically insignificant (r=-0.214, P=0.410).*

Conclusion: *In women with non-LABC, ^{18}F-FDG PET/CT is a useful and reliable tool for obtaining the TLG of primary BC masses presenting with various CT densities.*

Keywords: *fluorodeoxyglucose F18, positron emission tomography computed tomography, carcinoma, ductal, breast, glycolysis*

ÖZET

Amaç: *Meme kanseri kadınlardaki ikinci en sık malign* tümördür*. Flor-18-florodeoksiglukoz pozitron emisyon tomografisi/ bilgisayarlı tomografi (18F-FDG PET/BT), hastalığın evrelemesi ve prognozun belirlenmesi için başlıca tanı aracı haline gelmiştir. Lokal olarak ilerlememiş meme kanseri olgularının primer kitlelerinde, başta toplam lezyon glikolizi (TLG) olmak üzere ana nicel 18F-FDG PET/BT değişkenleri ve Hounsfield ünitesi (HU)* şeklinde BT *dansite* ölçümleri *arasındaki bağıntıyı değerlendirmeyi ve ayrıca, bu kitlelerin hacimleri ile HU* ölçümleri *arasında bir bağıntı olup olmadığını görmeyi amaçladık.*

Gereç ve Yöntemler: *Bu retrospektif çalışmaya, 2016−2017 yıllarında tedavi öncesi 18F-FDG PET/BT tetkiki yapılan, yaş ortalaması 54.1±10.3 yıl olan ve tek taraflı, lokal olarak ilerlememiş meme kanseri bulunan 17 kadın olgu alınmıştır. Primer meme kanseri kitlelerinin hacim, HU, en yüksek standart tutulum değeri (SUVmaks) ve TLG ortalamaları, standart sapmalar ve %95 güven aralığı (GA) ile birlikte hesaplandı. Bu kitlelerin TLG ve HU, SUVmaks ve HU, hacim ve HU değerleri arasındaki bağıntı istatistiksel olarak hesaplandı.*

Bulgular: *Meme kanseri kitlelelerinin ortalama hacmi ve HU değeri sırasıyla 4.6±3.9 mL (%95 GA: 2.6−6.6) ve 42.5±4.1 HU (%95 GA: 40.3−44.6) bulundu. Bu kitlelerin ortalama SUVmaks ve TLG'si* sırasıyla 6.4±5.6 *g/mL (%95 GA: 3.5−9.3) ve 22.1±14.2 g/mLxmL (%95 GA: 14.7−29.4) bulundu. Meme kanseri kitlelerinin ortalama TLG'si ile HU değeri arasında (r=-0.443, P=0.075) ve ortalama SUVmaks'ı ile HU değeri arasında (r=-0.368, P=0.146) istatistiksel olarak anlamlı bağıntı saptanmadı. Bu kitlelerin ortalama hacmi ve HU değeri arasındaki bağıntı da istatistiksel olarak anlamlı bulunmadı (r=-0.214, P=0.410).*

Sonuç: *18F-FDG PET/BT lokal olarak ilerlememiş meme kanserli kadınlarda, değişik BT dansiteleri ile kendini gösteren primer meme kanseri kitlelerinin TLG'lerini hesaplamada yararlı ve güvenilir bir araçtır.*

Anahtar Kelimeler: *fluorodeoksiglukoz f18, pozitron emisyon tomografi bilgisayarlı tomografi; karsinoma, duktal, meme, glikoliz*

INTRODUCTION

Breast cancer (BC) was stated to be the second most frequent malignancy in women [1] and invasive ductal carcinoma is the most common type [2]. In current medical practice, fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET)/computed tomography (CT) has become a major diagnostic tool for evaluating the extent of BC and staging of the disease [3–5]. BC patients can preoperatively be grouped as locally advanced breast cancer (LABC) and non-LABC with regard to the existence or lack of locoregional LN metastasis, respectively [6]. There are two major quantitative ^{18}F-FDG PET/CT parameters which are directly related with ^{18}F-FDG uptake of tumor cells: standardized uptake value (SUV) and total lesion glycolysis (TLG). Maximum SUV (SUVmax) [7−10] and TLG [7, 11] not only reflect the aggressivity of the tumor mass but predict the prognosis, as well. It is well-known that the earlier BC is diagnosed, the better the survival is. Therefore, in order to obtain and present the mean SUVmax and TLG values at the early stages of BC in our study, we included the patients with non-LABC. Since BC masses can present with various CT densities (HU) and because the TLG is superior to SUVmax for its being able to reflect the whole tumoral metabolic activity,

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we primarily wanted to evaluate the correlation between TLG and HU measurements of these masses. And also, we aimed to see whether there is a correlation between the volume and HU measurements of BC masses in non-LABC patients.

MATERIAL AND METHOD

In this retrospective study we initially recruited 33 patients with known BC who underwent 18F-FDG PET/CT between 2016−2017. We excluded 16 patients who were demonstrated to have LABC or remote metastases, and also who received any surgical treatment, any chemotherapy and/or radiotherapy. We included the rest 17 women with a mean age of 54.1±10.3 years, who had unilateral invasive ductal carcinoma (IDC). None of the patients had multiofocal BC. All of the included women were non-LABC patients without any evidence of local lymph node metastases or remote metastases. They were also classified as Stage I (n=7/17) or Stage IIA (n=10/17) according to American Joint Committee on Cancer (AJCC) (edition 7) staging criteria [12]. All the procedures were performed according to the World Medical Association Declaration of Helsinki (revised in 2000, Edinburgh). The present study was conducted in accordance with ethics granted by the institution. All the patients were informed about ^{18}F-FDG PET/CT procedures and informed consent was taken.

^{18}F-FDG PET/CT was performed within one month of BC diagnosis before any treatment. The patients fasted 6 hours or more before ^{18}F-FDG PET/CT scan with a blood glucose under 150−200 mg/dL. Intravenous ^{18}F-FDG was given at a dosage of 262.7−425.5 MBq (7.1−11.5 mCi). Intravenous iodinated contrast material was not administered. Whole body emission scanning from head to the proximal thigh in supine position (7−8 bed positions; acquisition time, 3 min/bed position) was accomplished 50 minutes after the injection of ^{18}F-FDG. Hybrid imaging was done using a Discovery 610 PET/CT device (General Electric Medical Systems, LLC, Waukesha, WI, USA) device. CT images were taken while the patient was holding breath, with a detector row configuration of 16x1.25 mm, tube voltage of 120 kVp, maximum tube current of 200 mA, beam collimation of 20.0 mm, table speed of 27.5 mm/rotation, pitch of 1.375:1, helical thickness of 3.75 mm and with 512x512 matrix. Attenuation-correction and image reconstruction were accomplished.

The size and HU measurements of the BC mass were done on axial plain CT images. The SUV (including SUVmax and SUVmean) and metabolic tumour volume (MTV) measurements beside TLG calculations were performed by utilizing the reciprocal ^{18}F-FDG PET/CT fusion images. Circular regions of interests (ROI)s were utilized. The SUVmax was computed as follows: The maximum activity in ROI (MBq/mL) / [injected dose (MBq)/body weight (g)] [6, 13]. The HU measurements were performed from the corresponding parts of BC mass where SUVmax measurements were done. The TLG was computed for BC mass as metabolic tumor volume (MTV)xSUV-mean [14]. A board-certified nuclear medicine specialist with 15 years of experience interpreted the images and accomplished the measurements. At least three measurements regarding the parameters mentioned above were performed in each patient and the average value was taken into consideration.

STATISTICAL ANALYSIS

The mean values, their standard deviations and 95% confidence intervals (CI)s were calculated for all the quantitative variables. The correlation between the mean TLG and the mean HU density of BC masses, the correlation between the mean SUVmax and the mean HU density of BC masses, besides the correlation between the mean volume and the mean HU density of BC masses in non-LABC patients were assessed by Spearman correlation test. P values <0.05 were accepted as statistically significant. All analyses were done with SPSS software (version 16.0; SPSS Inc; Chicago, IL, USA).

RESULTS

The mean volume, HU density (Fig. 1), SUVmax and TLG of BC masses (Fig. 2) with their 95% confidence intervals (CI)s in non-LABC patients were given in Table 1.

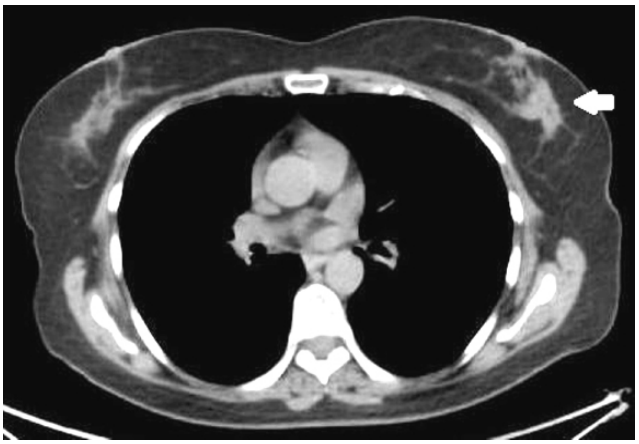

Figure 1: Axial plain CT image of a breast cancer mass (arrow) in the left breast of a non-LABC patient. The volume of the lesion was 6.3 mL and its CT density was 46 HU.

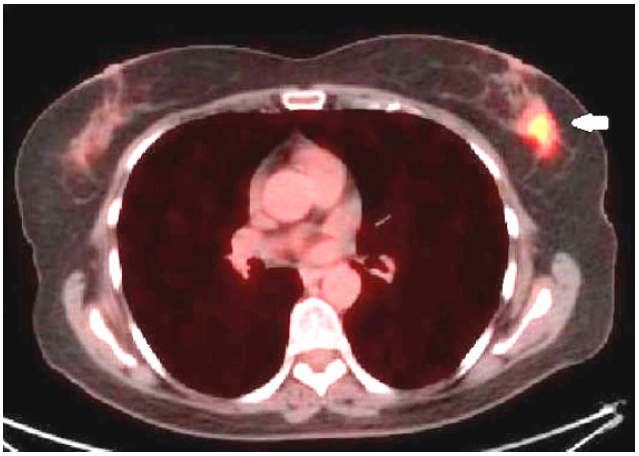

Figure 2: Axial ^{18}F-FDG PET/CT fusion image of the same breast cancer mass (arrow) given in Fig. 1. The SUVmax and TLG were 6.6 and 24.3, respectively.

There was no significant correlation between the mean TLG and the mean HU density of BC masses (r=-0.443, P=0.075). There was no significant correlation between the mean SUVmax and the mean HU density of BC masses (r=-0.368, P=0.146). The correlation between the mean volume and the mean HU density of BC masses was also statistically insignificant (r=-0.214, P=0.410).

Table 1: The mean volume, HU density, SUVmax and TLG of breast cancer masses with their 95% confidence intervals (CI)s in non-LABC patients.

^{18}F-FDG PET/CT parameters regarding the BC mass	Mean±SD with 95% CI
Volume (mL)	4.6±3.9 mL (95% CI: 2.6−6.6)
HU	42.5±4.1 HU (95% CI: 40.3−44.6)
SUVmax (g/mL)	6.4±5.6 g/mL (95% CI: 3.5−9.3)
TLG (g/mL x mL)	22.1±14.2 (95% CI: 14.7−29.4)

BC: Breast cancer; SD: Standard deviation; SUVmax: Maximum standardized uptake value; HU: Hounsfield unit (CT density); CI: confidence interval. TLG: total lesion glycolysis.

DISCUSSION

The relationship between mammographic tissue density of breast which is virtually obtained utilizing the physical principles similar to CT by means of x-ray attenuation, and its ^{18}F-FDG uptake has long been investigated by many authors [15−17]. Regarding their early study on this topic which included 45 women with a median age of 54 years, Vranjesevic et al. [17] reported that mammographic breast density correlated significantly with breast ^{18}F-FDG uptake. It was also reported by Kumar et al. [15] that the SUV of normal breast tissue is directly proportional to its mammographic density which means that mammographic density of normal breast tissue affects its ^{18}F-FDG uptake. Additionally, Lakhani et al. [16] reported a positive correlation between quantified breast density on digital mammography and ^{18}F-FDG uptake. Our study differs from the above mentioned ones by means of target tissue and the imaging method. In the present study, our goal was to investigate the relationship between ^{18}F-FDG PET/CT parameters and CT density of primary BC masses, not those of normal breast tissue. While doing this we also wanted to quantify the density of the lesions by CT which is an irreplaceable component of ^{18}F-FDG PET/CT, instead of digital mammography. So it would not be proper to compare our study which already demonstrated no correlation between ^{18}F-FDG PET/CT parameters and CT density of BC, with the above mentioned ones.

The CT density measurements in patients who undergo ^{18}F-FDG PET/CT imaging have been found to be useful in differentiating and defining malignant lesions such as lymphoma [18], lung cancer [19], head and neck squamous cell carcinoma [20], and lymph node metastases in lung cancer, malignant melanoma, gastroenteropancreatic neuroendocrine tumors and prostate cancer [21]. In a recent ^{18}F-FDG PET/CT study, malignant lymph nodes were reported to display higher HU compared to the benign ones in lung cancer [22]. In another ^{18}F-FDG PET/CT study, the CT density in primary thyroid lymphoma was found to be lower than that measured in chronic thyroiditis [23]. All the above mentioned studies demonstrate that CT density measurements are irreplaceable components of ^{18}F-FDG PET/CT imaging and the threshold or mean HU values differ significantly from one malignant tumor type to the other. CT density measurements on ^{18}F-FDG PET/CT images were also stated to be useful in making a decision about tumor response to treatment, such as decrease in CT density indicated a response and lack of change in HU demonstrated no change [24]. Nevertheless, we considered that the relationship between CT density of BC masses and ^{18}F-FDG PET/CT parameters including SUVmax and TLG needed to be further investigated. Therefore we designed our study according to these needs, at least at a basic level. In the present study we have found that neither SUVmax nor TLG of the lesions in our patients did not show any significant correlation with their CT densities. This serves an advantage for the interpreter in ^{18}F-FDG PET/CT evaluation of BC masses possessing any HU values, which also adds more evidence to strengthen the independency and reliability of SUVmax and TLG. However, the difference between these two major quantative parameters should always be taken into consideration during ^{18}F-FDG PET/CT practice. The SUV of a tumour, including the ones under treatment does not demonstrate the whole tumoral metabolic activity and in these situations TLG can more precisely reflect the response to treatment, because it is directly proportional to metabolic tumor volume [24]. Nevertheless, since we included the patients whose treatments were not yet initiated, and also because we found no correlation between size (volume) and CT density of BC masses, we consider that SUVmax and TLG acted similarly with regard to their relationship with CT density in our patient group. It was also interesting to see that the volumes and HU values of the lesions did not show any significant correlation, which contributed to standardization of HU measurements of BC masses presenting with any size.

The present study possesses some limitations largely because of its relatively small sample size and its being retrospective. Firstly, our findings were confined to the patients with IDC. So ^{18}F-FDG PET/CT properties of IDC in non-LABC patients could not be compared with those of other invasive BC types in the similar patient groups. Secondly, since we did not have any satellite lesions in our patient population, we could not compare their TLG and CT densities with those of the primary lesions. Thirdly, we included only the patients with non-LABC and could not compare the results with those of the patients having LABC. However we consider that our results maintained a basic data for future studies with different patient groups and larger patient populations.

In conclusion, ^{18}F-FDG PET/CT is a useful and reliable tool for obtaining the TLG of primary BC masses presenting with various CT densities in women with non-LABC.

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