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FDG PET/CT Findings in Breast Cancer Patients for the Purpose of Initial Staging Versus Restaging and Its Impact on Clinical Management

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Abstract

Introduction: Breast cancer is one of the most prevalent malignancies in the world and a major problem that cancer patients struggle with is the failure in timely and early diagnosis. The present study is an attempt to survey EDG PET/CT findings in breast cancer patients for the purpose of initial staging versus restaging and its impact on clinical management. Methodology: In this descriptive-analytical study all breast cancer patients referred to Masih Daneshvari Hospital for the purpose of initial staging or restaging were included. All patients' medical record information including CT scan and MRI findings, FDG PET/CT results and treatment protocols were reviewed. Findings: The mean age of the patients was 52.73±11.90 years. The most common reason for patient referral was metastatic evaluation (43.1%) and least common reason was initial staging (5.2%). Interestingly extremities involvements were more frequently diagnosed on PET/CT (74.9%) comparing to the imaging modalities (41.6%). Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of PET/CT to detect lesions were 96.98%, 40.81%, 53.82%, 95%, 64.16% respectively. Conclusion: Using PET/CT imaging is a reliable method for evaluating breast cancer. This method is also helpful to direct the biopsy site and further treatment planning.

Key words: Breast Cancer, MRI/CT scan, PET/CT, initial stating, restating.

Introduction

Breast cancer is the most prevalent women malignancy in the world and the number of cases is growing. (Asgarian et al., 2016) According to the national statistics in Iran, among cancer cases, breast cancer in women is at the top and with age-standardized incidence rate of 33.2 it is more prevalent than skin cancer. (Jazayeri et al., 2015) It is notable that 76% of cancers in women are pertinent to the breast and there are 41 thousand women in Iran with breast cancer. This figure is growing by 7 thousand every year. (Enayatrad and Salehiniya, 2015) The average age of incidence in the West is 55< and for Iranian, this rate is 10 years lower. (Key et al., 2001) Although, breast cancer incidence in Iranian women is one-fifth of the incidence rate in the West, the mortality rate in Iran is notably higher and creates a considerable economic and medical load for the health system of the country. (Matthews et al., 2012)

One of the fundamental and unresolved problems in cancer treatment is absence of a method for timely and early diagnosis. Diagnosis of breast cancer at the early stages has a notable effect on lowering the mortality rate in women. (Løberg et al., 2015) Studies have shown that higher mortality rate in these patients is due to late diagnosis. Five years survival rate in the women whose breast cancer is diagnosed at early stages is 90%, while this figure is 60% for women with advanced cancer. (Sheikhpour and Mohiti Ardekani, 2014 ; Fentiman, 2001) Therefore, there is a need for an accurate and reliable system for timely diagnosis and determine if the tumor is benign or malignant. (Charkazi et al., 2013)

The new molecular imaging technologies have been widely used for understanding the diverse and complicated behavior of cancers. (Pysz et al., 2010) The recent years have witnessed an increase in using a combination of PET and CT technologies. The reason for this is to combine the unique functional information from PET technology and SC Scan technology to fill the anatomical information gap in

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PET and accurate localization of the lesion. (Burger et al., 2002; Emad-Eldin et al., 2013) Using CT and PET at the same time not only adds greatly to diagnosis power, but also improves sensitivity of tumor diagnosis process. (Razak et al., 2011) The FDG-PET technique is usually a more efficient way to determine if the lesion is benign or malignant. For tumor staging, the PET/CT imaging is typically performed from the head to the bottom of pelvis, while contrast CT might be only notable in a subregion. (Radan et al., 2006) With EDG PET/CT, it is possible to obtain notable information about staging and assessing the treatment process of several types of tumors like pulmonary carcinoma, colorectal cancer, lymphoma, head and neck tumors, melanoma, and so on. (Sachelarie et al., 2005)

Among different types of cancers, breast cancer is clinically more important given its higher prevalence. On the other hand, given the key role that women play in the family and human society growth, their health is highly effective in productivity of family and society. Staging cancer is helpful to determine the best treatment. It is an accurate attempt to find out if the tumor has attacked the adjacent tissues and what limbs are affected by metastasis if any. The PET/CT imaging is more accurate and faster than other imaging techniques like MRI for tumor staging so that using this technology, it is possible to diagnose cancer at early stages. (Emad-Eldin et al., 2013) Therefore, the present study surveys the PET/CT findings in patients with breast cancer visiting PET/CT center of Masih Hospital for restaging. The findings were also compared with CT and MRI results.

Methodology

The study was carried out as an analytical study in Masih Daneshvari Hospital in 2018. The study population consisted of women with breast cancer referred to the PET/CT ward of hospital for staging or restaging. The subjects were selected from the breast cancer patients visited the hospital from 2013 to 2017 who met the inclusion criteria. The inclusion criteria were older than 18 years old, breast cancer patient visiting the hospital for primary staging or already received treatment, patients with higher marker tumor or clinical symptoms, and no lesion revealed by CT or MRI. Exclusion criteria included pregnant or breast feeding women, lake of interest to participant, and failure to do follow up after being discharged from the hospital.

The imaging process was performed in Masih Daneshvari PET/CT center. The images were examined by two radiology and nuclear medicine specialists. The positive and negative results of the scans and the percentages were determined. The study was examined and approved by Ethics Committee, Shahid Beheshti University. The data was analyzed in SPSS 18. Diagnosis accuracy of FDG PET/CT, sensitivity, specification, positive predictive value, and negative predictive value in staging breast cancer were determined.

Results

The mean age of the participants in the study was 52.73±11.90 years. Data analysis on the type of examination of the individuals showed that metastasis with 43.1% and initial staging with 5.2% had the highest and lowest frequencies respectively (Table 1).

Table 1. Reason for PET/CT referral in breast cancer patients

Reason for referral	Frequency	%
Metastatic evaluation	309	43.1
Restating	199	27.8
Treatment response assessment	172	24
Initial stating	37	5.2

In terms of limbs involvement, 74.9% had limb involvement based on PET/CT, while only 41.6% had limb involvement based on MRI/CT (Table 2).

Table 2. Comparison of PET/CT and MRI / CT findings in patients with breast cancer

Limb Involvement	MRI/CT		PET/CT	
	Frequency	%	Frequency	%
Positive	298	41.6	537	74.9
Negative	419	58.4	180	25.1

The data about limb involvement based on PET/CT method showed that 9.5% of the individuals had topical involvement, 22.6% had bone involvement, 15.1% had pulmonary involvement, 10.3% had abdominal involvement, 5.4% had abdominal lymphadenopathy, 17.8% had pulmonary lymphadenopathy, 9.2% had cervical lymphadenopathy, 6.4% had topical recurrent, 0.4% had peritoneum involvement, 1.1% had cerebral involvement, 1.8% plural-effusion, and 0.4% had pericardial effusion (Table 3).

Table 3. Distribution of PET Scan findings based on organ involvement

Location	Frequency	%
Bone involvement	256	22.6
Lung lymphadenopathy	203	17.8
Lung involvement	172	15.1
Abdominal involvement	117	10.3
Local involvement	108	9.5
Neck lymphadenopathy	103	9.2
Local recurrence	73	6.4
Abdominal lymphadenopathy	61	5.4
Pleural-effusion	21	1.8
Brain involvement	13	1.1
Peritoneal involvement	5	0.4
Pericardial -effusion	5	0.4

Data analyses were performed to determine sensitivity, specification, positive predictive value, negative predictive value, and accuracy of PET/CT. As the results showed, 289 patients had involvement at different parts of the body as shown by PET/CT findings (confirmed positive). Moreover, 171 cases had no involvement according to the two diagnosis technique (confirmed negative). Based on PET/CT method, 248 cases had involvement, which was not diagnosed in MRI/CT method (false positive) and nine patients had no involvement in PET/CT method, while according MRI/CT method, they had limb involvement (false negative). Sensitivity, specification, positive predictive value, negative predictive value, and accuracy of PET/CT were 96.98%, 40.81%, 53.82%, 95%, 64.16% respectively (Table 4 and 5).

Table 4. An agreement between PET/CT and MRI / CT in detecting metastatic cases

		MRI/CT	
		Positive	**Negative**
PET/CT	**Positive**	289	248
	Negative	9	171

Table 5. Diagnostic value of PET/CT in Breast cancer staging and restaging

Sensitivity	96.98	95% CI 94.34-98.6%
Specificity	40.81	95% CI 36.07-45.69%
Positive Predictive value	53.82	95% CI 51.77-55.85%
Negative Predictive value	95	95% CI 90.81-97.34%
Accuracy	64.16	95% CI 60.52-67.67%

Discussion

The findings based on EDG PET/CT in breast cancer patients referred to Masih Daneshvari Hospital between 2013-2017 for primary staging or restaging were examined. In addition, the effect of these findings on clinical governance of the patients was examined. The results showed that 289 cases of the patients who had different involvements were diagnosed based on PET/CT (confirmed positive). Moreover, 171 cases (confirmed negative) who had no involvement were diagnosed by the two techniques (i.e. PET/CT and MRI/CT). There were 248 cases (false positive) diagnosed based on PET/CT technique, who were not diagnosed based on MRI/CT method. Moreover, nine patients had no involvement based on PET/CT (negative involvement), while their limb involvement was confirmed by MRI/CT technique. Eventually, sensitivity, specification, positive predictive value, negative predictive value and accuracy of PET/CT were obtained equal to 96.98%, 40.81%, 53.82%, 95%, 46.16% respectively.

Dose et al. reported that the sensitivity and specification of FDG PET were 86% and 90% respectively, while these figures for the routine techniques were 36% and 95% respectively. (Dose et al., 2002) Aukema et al. studied 56 patients using PET/CT method and found new tumors in 32 patients (57%). Moreover, while the routine techniques diagnosed 11 patients with metastasis, 23 were diagnosed with metastasis with PET/CT. There were also undiagnosed lesions based on routine methods in 25 patients (45%), which were found by

PET/CT method. With more accurate diagnosis comparing with routine methods, PET/CT was more effective in clinical governance of 27 patients (48%). Sensitivity, specification, and positive/negative predictive values of FDG PET/CT were 97%, 92%, 95%, 94%, and 96% respectively. (Aukema et al., 2010) Garami et al. reported that the sensitivity of PET/CT to diagnose primary tumor was 93%. In addition, sensitivity and specification of sonography technique in assessing armpit lymph nodes were 30% and 95% respectively; these figures for PET/CT were 72% and 96% respectively. (Garami et al., 2012)

The PET imaging system is a powerful and non-invasive tool that yields information needed to diagnose and treat diseases by showing metabolic and functional changes of tumors. Such information might not be obtained using CT Scan and MRI, as these methods only give anatomic information and generate not metabolic and functional information. (Tatsumi et al., 2006)

The PET and CT are two standard methods to examine malignant diseases before adopting therapeutic strategies and during and after implementation of treatment. (Scheidhauer et al., 2004) Studies have supported higher sensitivity and specification for FDG-PET in diagnosing large and palpable breast tumors. However, the sensitivity is lower when the lesions are small or not palpable with low degree and or non-invasive neoplasm. (Hodgson and Gulenchyn, 2008 ;Groheux et al., 2015)

Imaging plays a key role in screening, diagnosing, staging, restaging, and determining treatment protocol in cancer patients. Although, mammography is a diagnostic method that is generally used, its low specification makes using other methods essential for special cases (Jacobs et al., 2015; Lebron et al., 2015)

Standard imaging methods like sonography, CT Scan, and MRI are used for staging, assessing response to treatment, and checking recurrence in suspicious cases. However, CT Scan and MRI might not be effective in diagnosing diseases in a large group of patients. Such methods only demonstrate morphological and anatomic changes at the primary tumor sites and far metastasis. Molecular imaging methods are superior in diagnosing response to treatment and recurrent especially in the case of anatomic changes caused by treatment/surgery. Studies have supported the advantages of PET/CT imaging. (Pritchard et al., 2012) According to the results, sensitivity and specification of PET/CT for breast cancer are at 48-96 and 73-100 ranges respectively. (Groheux et al., 2011)

The mean age of the participants was 52.73±11.90 years and data analysis showed 43.1% of metastasis, 27.8% of restaging, 24% of response to the treatment, and 5.2% of primary staging in the patients.

In terms of limbs involvement, PET/CT showed that 74.9% had limbs involvement; while MRI/CT showed limb involvement in only 41.6% of the subjects. The data about limb involvement generated by PET/CT was analyzed. The results showed that 9.5% of the individuals had topical involvement, 22.6% had bone involvement, 15.1% had pulmonary involvement, 10.3% had abdominal involvement, 5.4% had abdominal lymphadenopathy, 17.8% had pulmonary lymphadenopathy, 9.2% had cervical lymphadenopathy, 6.4% had topical recurrent, 0.4 peritoneum involvement, 1.1% had cerebral involvement, 1.8% plural-effusion, and 0.4% had pericardial effusion.

Staging breast cancer patients is essential to choose the right treatment for patients. The findings reported by several studies have shown that PET/CT imaging can be beneficial for primary staging of the patients with high risk of metastasis. (Baba et al., 2014)

Diagnosis accuracy of PET/CT for metastasis have been surveyed by several studies. A meta-analysis showed that PET/CT is a worthy replacement for standard MRI. The study showed a significant difference in diagnosing performance of PET/CT and MRI. (Aukema et al., 2010) Another meta-analysis reported sensitivity, specification, positive predictive value, and negative predictive value of PET/CT equal to 99%, 95%, 21%, and 2% respectively, while these figures for the standard imaging techniques were 57%, 88%, 4.8%, and 49% respectively. (Manohar et al., 2018)

These show that using PET/CT imaging to diagnose breast cancer metastasis should be accepted as a new method. (Niikura et al., 2011; Teke et al., 2015) Prognosis plays a key role in selecting the effective treatment in patients with breast cancer. Research results play a key role in adaptation of PET/CT imaging for breast cancer prognosis. (Teke et al., 2015 ;Cochet et al., 2014) The results in this study are consistent with those of other studies.

Conclusion

Using PET/CT can be an alternative way to diagnose breast cancer. This method can decrease the need for invasive therapeutic measures to determine the breadth of the disease. Capability to exactly spot the lesion for biopsy and further therapeutic measures like surgery and radiotherapy are other advantages of PET/CT imaging.

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