The Accuracy of PET-CT Scan in Detecting Axillary Lymph Node Metastasis in Breast Cancer

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Objective: To evaluate the accuracy of positron emission tomography CT scan in detecting axillary lymph node metastases compared to the pathology results in patients with primary breast cancer.

Setting: Breast Surgery Unit, King Hamad University Hospital, Bahrain.

Design: A Retrospective Comparative Study.

Method: Twenty-one newly diagnosed females with invasive breast cancer and staged using FDG-PET-CT scan. Images were evaluated by two experienced radiologists for any abnormal increase in axillary FDG uptake. Imaging results were compared to axillary lymph node pathology, such as sentinel lymph node biopsy, FNA cytology from axilla or axillary clearance.

Result: All patients had histopathology results that matched the PET-CT finding except 2 (10%) patients who matched the CT scan alone but not the PET scan. The sensitivity of the PET-CT for detection of axillary lymph node metastasis in this series was 80% and the specificity was 100%. Both sensitivity and specificity were noted to be high compared to other published data.

Conclusion: PET-CT scan is highly sensitive and specific in detecting axillary lymph nodes metastases in breast cancer. The sensitivity reached 80% and the specificity was 100% in our study; this could be attributed to the small number of patients and the improvement in the new generation of the PET-CT scanners with high resolution, which led to further increase in the diagnostic value. Therefore, recent evidence does not support the use of PET-CT scan to replace clinically negative axillary lymph nodes as initial assessment.

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Breast cancer is the most common malignancy in women[1,2]. It is the second leading cause of death in females[1]. It is estimated that 1.38 million cases are detected worldwide per year and 458,000 deaths consequently[1].

Early detection of breast cancer is essential in managing patients with breast cancer; it is directly related to the type of therapy, outcome, prognosis and overall survivor[3]. Involvement of the axillary lymph nodes with malignant deposition is considered the most important prognostic element in recurrence and survival[4,5]. The number of the involved lymph nodes is directly proportionate to the ten-year survival of patients with breast cancer; survival reaches 90% if no lymph nodes were involved; 70% if one to three lymph nodes affected and as low as 30% if more than ten nodes affected[6,7]. For decades, any female diagnosed with breast cancer will be mandatory posted for axillary lymph node dissection (ALND) to achieve an accurate diagnosis.

Axillary clearance carried many surgical complications including wound hematoma, nerve paralysis, discomfort and lymphedema of the upper limb up to 20%; in addition to the cost and prolonged hospital stay[8-12]. Thus, alternative modalities were required to decrease the invasiveness of axillary procedures.

During staging process, an axillary ultrasound and biopsy of suspicious lymph nodes could detect up to 45% of metastases[13]. ALND is indicated if the ultrasound guided needle biopsy is positive for metastases to stage and not to treat the primary disease. In contrast, patients with impalpable axillary lymph

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nodes and negative ultrasounds are scheduled for sentinel lymph node biopsy (SLNB). It is the standard procedure to identify affected lymph nodes using a radioisotope, blue dye or both[8,10]. If metastases are proven with the SLNB, ALND is indicated during the same sitting[14].

Although SLNB carries fewer complications as opposed to ALND, it still requires experts, additional costs for the equipment and facilities. In addition, its sensitivity does not reach 100%[15]. Thus, the urge for safer, less invasive modalities to stage the axilla accurately became a necessity.

Recently positron emission tomography (PET) has been introduced in the diagnostic modalities of several malignant diseases including breast cancer[16]. PET produces three-dimensional images using radioactive tracer that can detect neoplastic cells. More advanced scanners add a computed tomography (CT) scan, known as PET-CT scan. This addition gives clearer data of the tissue anatomy[17].

The aim of this study is to evaluate the accuracy of PET-CT in assessing axillary nodes in patients with breast cancer.

METHOD

The study was performed between 1 January 2013 and 31 October 2015. Sixty-two patients were diagnosed with breast cancer. The clinical stage had been determined by using the triple assessment which includes: physical examination, mammography and ultrasound of the breast and the axilla and biopsy from the breast lesion. Twenty-one patients were diagnosed with breast cancer and had PET-CT prior to their surgery for initial staging. The PET-CT scans were interpreted by two nuclear medicine consultants.

The data was retrieved from the electronic hospital filing system (INDRA database) through the IT department and the histopathology department.

The data was analyzed using SPSS version 23. Categorical data was reported in percentages, diagnostic accuracy estimated using sensitivity and specificity analyses, and axillary involvement detection rates between PET-CT and Pathology were compared using Mc Nemar's test.

RESULT

Sixty-two patients were diagnosed with breast cancer. Twenty-one cases had axillary PET-CT scan and had been included in this study. Fourteen (66.6%) patients were Bahrainis, see table 1. Eighteen (85.7%) patients had invasive ductal carcinoma; the most common grade of tumor was G2, 11 (52.4%), see tables 2 and 3.

Table 1: Nationality

Nationality	n	%
Bahraini	14	66.6
Egyptian	2	9.5
Pakistani	2	9.5
Bangladeshi	1	4.8
Indian	1	4.8
Other	1	4.8
Total	**21**	**95.2**

Table 2: Type of Cancer

Type of Cancer	n	%
Invasive Ductal Carcinoma	18	85.7
Papillary Adenocarcinoma	1	4.8
Medullary Carcinoma	1	4.8
Mucinous Carcinoma	1	4.8
Total	**21**	**100**

Table 3: Grade

Grade of Cancer	n	%
G1	3	14.3
G2	11	52.4
G3	7	33.3
Total	**21**	**100**

Eight (38.1%) positive axillary PET-CT scans were confirmed by histopathology as positive axillary lymph nodes with tumor metastases. The number of lymph nodes retrieved at surgery ranged from 9 to 20 lymph nodes. Included were two cases where the histology was confirmed by tru-cut biopsies.

Thirteen (61.1%) patients had negative axillary PET-CT scans; five (23.8%) patients were histologically negative by axillary lymph node dissection and six (28.6%) patients had sentinel lymph node biopsy which were sent for frozen sections and confirmed subsequently by paraffin sections as negative nodes. However, 2 (9.5%) cases were negative PET-CT scan for axillary nodes but the lymph nodes removed surgically were positive for cancer; one (4.8%) patient had 11 lymph nodes removed surgically, 4 of which showed metastatic carcinoma. One case was negative PET-CT but positive sentinel nodes on histology.

On average, 14.5 lymph nodes per patient were surgically removed. Histologically, metastases were found in 38% of the patients. There was a progressive increase in metastases percentage with tumor size. The average tumor size tumor in the cases with lymph metastases was 42.5 mm, while the average tumor size for negative axillary lymph nodes was 25 mm.

The sensitivity of PET-CT in detecting axillary involvement compared to histopathology was computed to be 80% (95% CI: 0.55 – 1.047), with the negative predictive value being 85% (95% CI: 0.65 – 1.042). The overall accuracy of PET-CT in detecting axillary involvement was found to be 0.904 (95% CI: 0.779 – 1.0330), see table 4. A comparison of the percentage of subjects diagnosed as having axillary involvement through histopathology (47%) and PET-CT (38%), revealed no significant difference (Mc Nemar P-value = 0.500), indicating similar rate of diagnosis through both methods, see figure 1.

Table 4: PET-CT Compared to Pathology

Parameter	Measure	95% Confidence Intervals
Axillary Involvement Assessed by Pathology [n (%)]	10 (46.7%)	-
Axillary Involvement Assessed by PET-CT [n (%)]	8 (38.1%)	-
Sensitivity of PET CT	80%	0.55 - 1.047
Specificity	100%	1.00 - 1.00
Positive Predictive Value	100%	1.00 – 1.00
Negative Predictive Value	85%	0.65 – 1.042
Overall Accuracy	0.904	0.779 – 1.0330

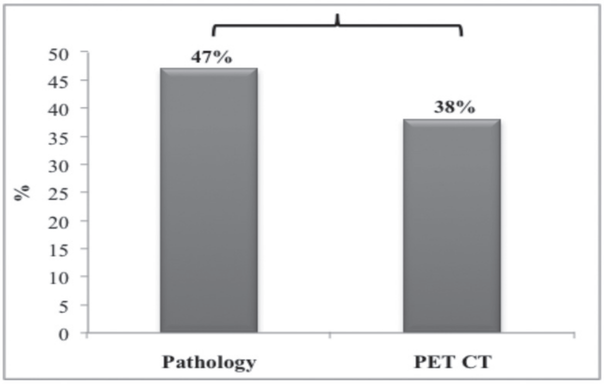

Figure 1: Comparison of PET-CT and Pathology in Detecting Axillary Involvement

DISCUSSION

Marco Greco et al evaluated the possibility of using PET-CT scan as a non-invasive procedure to detect axillary lymph node involvement rather than ALND in patients known to have breast cancer found that the sensitivity and specificity are 94.4% and 86.3% respectively, which were considered high compared to other studies[18].

Wahl et al concluded that ALND is more accurate than PET-CT scan in detecting lymph node metastasis, as the sensitivity of PET scan is 61% while it is 80% specific; he concluded that PET-CT scan is not suitable to replace the histological evaluation of axillary lymph nodes[19]. Veronesi et al found that PET scan sensitivity rate is 70% and specificity rates were noted to be 37% and 96% respectively[20]. Fuster et al concluded that SLB is better than PET scan in detecting axillary LN metastasis, as PET scan sensitivity rate is 70%[21].

Groves et al found that PET-CT scan be 62.5% sensitive and 91.3% specific in detecting axillary lymph node involvement[22].

Pritchard et al concluded that a positive PET-CT scan results indicate axillary nodes disease as it carries high positive predictive value (96%). However PET-CT scan is neither sensitive nor specific to detect positive axillary lymph nodes and identify distant metastases[23].

Till et al concluded that PET-CT could not replace invasive methods to stage the axilla but PET-CT could assist in deciding what invasive method to start with SLNB versus ALND[24].

Meta-analysis and systematic review by Cooper et al reached a conclusion that SLNB is more sensitive and specific than PET scan[25].

PET is superior to bone scan in detecting lytic bone lesions and less in detecting sclerotic[26-27]. However, adding CT imaging could detect the sclerotic bone lesions.

PET-CT has showed significant sensitivity and specificity in detecting, staging, evaluating the residual or recurrence of tumors and monitoring treatment response in breast cancer cases[28].

The radiation dose from the PET-CT using non-diagnostic CT and ten mCi FDG dose is approximately 15 mSv from the CT radiation and eight from the PET radiotracer injection[28,29].

CONCLUSION

PET-CT scan is highly sensitive and specific in detecting axillary lymph nodes metastases in breast cancer. The 80% sensitivity and 100% specificity in our study could be attributed to the small number of patients and the improvement in the new generation of the PET-CT scanners with high resolution, which led to further increase in diagnostic value.

However, the literature review revealed that PET and PET-CT scans had lower sensitivity in detecting axillary metastasis compared to open biopsy. Therefore, current evidence does not support the use of PET-CT scan to replace clinically negative axilla as an initial assessment.

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REFERENCES

1. Ferlay J, Shin HR, Bray F, et al. Estimates of Worldwide Burden of Cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010; 127(12):2893-917.
2. Jemal A, Siegel R, Ward E, et al. Cancer Statistics, 2007. CA Cancer J Clin 2007; 57(1):43-66.
3. Iagaru A, Masamed R, Keesara S, et al. Breast MRI and 18F FDG PET-CT in the Management of Breast Cancer. Ann Nucl Med 2007; 21(1):33-8.
4. Honkoop AH, van Diest PJ, de Jong JS, et al. Prognostic Role of Clinical, Pathological and Biological Characteristics in Patients with Locally Advanced Breast Cancer. Br J Cancer 1998; 77(4):621-6.
5. Fisher B, Bryant J, Wolmark N, et al. Effect of Preoperative Chemotherapy on the Outcome of Women with Operable Breast Cancer. J Clin Oncol 1998; 16(8):2672-85.
6. Ranaboldo CJ, Mitchel A, Royle GT, et al. Axillary Nodal Status in Women with Screen-Detected Breast Cancer. Eur J Surg Oncol 1993; 19(2):130-3.
7. Walls J, Boggis CR, Wilson M, et al. Treatment of the Axilla in Patients with Screen-Detected Breast Cancer. Br J Surg 1993; 80(4):436-8.

8. Purushotham AD, Upponi S, Klevesath MB, et al. Morbidity after Sentinel Lymph Node Biopsy in Primary Breast Cancer: Results from a Randomized Controlled Trial. J Clin Oncol 2005; 23(19):4312-21.
9. Blanchard DK, Donohue JH, Reynolds C, et al. Relapse and Morbidity in Patients Undergoing Sentinel Lymph Node Biopsy Alone or with Axillary Dissection for Breast Cancer. Arch Surg 2003; 138(5):482-7; discussion 487-8.
10. Mansel RE, Fallowfield L, Kissin M, et al. Randomized Multicenter Trial of Sentinel Node Biopsy versus Standard Axillary Treatment in Operable Breast Cancer: The ALMANAC Trial. J Natl Cancer Inst 2006; 98(9):599-609.
11. Crane-Okada R, Wascher RA, Elashoff D, et al. Long-Term Morbidity of Sentinel Node Biopsy versus Complete Axillary Dissection for Unilateral Breast Cancer. Ann Surg Oncol 2008; 15(7):1996-2005.
12. McLaughlin SA, Wright MJ, Morris KT, et al. Prevalence of Lymphedema in Women with Breast Cancer 5 Years after Sentinel Lymph Node Biopsy or Axillary Dissection: Patient Perceptions and Precautionary Behaviors. J Clin Oncol 2008; 26(32):5220-6.
13. Alvarez S, Añorbe E, Alcorta P, et al. Role of Sonography in the Diagnosis of Axillary Lymph Node Metastases in Breast Cancer: A Systematic Review. AJR Am J Roentgenol 2006; 186(5):1342-8.
14. National Collaborating Centre for Cancer (UK). Early and Locally Advanced Breast Cancer: Diagnosis and Treatment. National Collaborating Centre for Cancer (UK); 2009.
15. Benson JR, Wishart GC. Is Intra-Operative Nodal Assessment Essential in a Modern Breast Practice? Eur J Surg Oncol 2010; 36(12):1162-4.
16. Vercher-Conejero JL, Pelegrí-Martinez L, Lopez-Aznar D, et al. Positron Emission Tomography in Breast Cancer. Diagnostics (Basel) 2015; 5(1):61-83.
17. Facey K, Bradbury I, Laking G, et al. Overview of the Clinical Effectiveness of Positron Emission Tomography Imaging in Selected Cancers. Health Technol Assess. 2007; 11(44):iii-iv, xi-267.
18. Greco M, Crippa F, Agresti R, et al. Axillary Lymph Node Staging in Breast Cancer by 2-Fluoro-2-deoxy-D-glucose–Positron Emission Tomography: Clinical Evaluation and Alternative Management. Jnl of National Cancer Institute 2001; 93(8): 630-5.
19. Wahl RL, Siegel BA, Coleman RE, et al. Prospective Multicenter Study of Axillary Nodal Staging by Positron Emission Tomography in Breast Cancer: A Report of the Staging Breast Cancer with PET Study Group. J Clin Oncol 2004; 22(2):277-85.
20. Veronesi U, De Cicco C, Galimberti VE, et al. A Comparative Study on the Value of FDG-PET and Sentinel Node Biopsy to Identify Occult Axillary Metastases. Ann Oncol 2007; 18(3):473-8.
21. Fuster D, Duch J, Paredes P, et al. Preoperative Staging of Large Primary Breast Cancer with Fluorodeoxyglucose Positron Emission Tomography/ Computed Tomography Compared with Conventional Imaging Procedures. J Clin Oncol 2008; 26:4746-4751.
22. Groves AM, Shastry M, Ben-Haim S, et al. Defining the Role of PET-CT in Staging Early Breast Cancer. Oncologist 2012; 17(5):613-9.
23. Pritchard KI, Julian JA, Holloway CM, et al. Prospective Study of 2-Fluorodeoxyglucose Positron Emission Tomography in the Assessment of Regional Nodal Spread of Disease in Patients with Breast Cancer: An Ontario Clinical Oncology Group Study. J Clin Oncol 2012; 30(12):1274-9.
24. Heusner TA, Kuemmel S, Hahn S, et al. Diagnostic Value of Full-Dose FDG PET-CT for Axillary Lymph Node Staging in Breast Cancer Patients. Eur J Nucl Med Mol Imaging 2009; 36(10):1543-50.
25. KL Cooper, Y Meng, S Harnan, et al. Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI) for the Assessment of Axillary Lymph Node Metastases in Early Breast Cancer: Systematic Review and Economic Evaluation. Southampton (UK): NIHR Journals Library; 2011: 187.
26. Cook GJ1, Houston S, Rubens R, et al. Detection of Bone Metastases in Breast Cancer by 18FDG PET: Differing Metabolic Activity in Osteoblastic and Osteolytic Lesions. J Clin Oncol 1998; 16(10):3375-9.
27. Radan L1, Ben-Haim S, Bar-Shalom R, et al. The Role of FDG-PET-CT in Suspected Recurrence of Breast Cancer. Cancer 2006; 107(11):2545-51.
28. Rosen EL, Eubank WB, Mankoff DA. FDG PET, PET/CT, and Breast Cancer Imaging. Radiographics 2007; 27 Suppl 1:S215-29.
29. Boellaard R, O'Doherty MJ, Weber WA, et al. Eur J Nucl Med Mol Imaging 2010; 37:181.