Review Article Open Access

Archives Of Breast Cancer

DOI: 10.19187/abc.20163377-82

Diagnostic Value of PET/CT in Comparison with Other Conventional Imaging Modalities for the Evaluation of Breast Cancer Recurrence: A Systematic Review of the Literature

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ARTICLE INFO

Received:
8 January 2016
Revised:
25 February 2016
Accepted:
20 August 2016

Keywords:
PET/CT,
recurrence,
breast cancer,
diagnostic value,
imaging modalities

ABSTRACT

Background: Despite developments in surgical treatment, radiation therapy, and chemotherapy protocols, tumor recurrence and metastasis are still major problems in breast cancer management. The aim of the present report was to review and compare the performance of PET/CT with some of the conventional imaging modalities in detection of breast cancer recurrence.

Methods: A literature search was performed in PubMed, Europe PMC and ScienceDirect databases with no search restriction for the date of publication but the search was limited to papers published in English.

Results: Twenty-two studies including a total of 1378 patients with prior breast cancer and clinical suspicion of recurrence that assessed the sensitivity, specificity, and accuracy of PET/CT and other conventional imaging methods in followed up by treated breast cancer and presented the results in systematic review format. The information extracted from each article included the first author, publication year, number of patients and their characteristics, index test(s), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy.

Conclusions: According to the literature, PET/CT seems to be a more useful modality than current techniques to assess the patients with suspected recurrent and metastatic breast cancer. If PET/CT is not applicable, MRI and also bone scintigraphy could also be performed as alternatives.

Introduction

Breast cancer is the most frequent malignancy among women, affecting 1 in 13 women in their lifetime.[1-3] Despite developments in surgical treatment, radiation therapy, and chemotherapy protocols, tumor recurrence has remained a major problem in breast cancer management.[4] The risk of recurrence in breast cancer patients is about 7–30% in the disease course.[5] A diagnosis of breast cancer recurrence is important to define appropriate therapeutic strategies and increase the odds of treatment. Cure options have developed over the past decade and have had an impact on survival.[1, 6, 7] Positron emission tomography/computed tomography (PET/CT) is increasingly used for oncologic imaging, and the utilization of PET/CT depends not only on their diagnostic accuracy, but also on their comparative advantage over available diagnostic methods.[1,8]

PET uses a radioactive tracer to produce three-dimensional (3D) images of body processes and is increasingly used for cancer diagnosis, staging, and restaging patient with breast cancer.[9] A commonly-

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used tracer is fluorodeoxyglucose (FDG) attached to the radioactive isotope fluorine-18 that can be used to detect tumor cells, which have a higher glucose uptake than normal cells.[10, 11] Metabolic tracers such as FDG-PET overcome the limitations of anatomical imaging modalities since functional changes assessed by PET or PET/CT imaging usually precede anatomical changes assessed by MRI or CT.[12] PET/CT scan allows for simultaneous visualization of the tissue anatomy and metabolic activities; moreover, it has been recently shown to have an increasing relevance in detection and management of breast cancer recurrence.

The aim of present study was to compare the performance of PET/CT with some conventional imaging modalities in the detection of breast cancer recurrence.

Methods

Search strategy

A literature search was performed in the following databases with "PET/CT AND Breast Cancer Recurrence" as key words: PubMed, Europe PubMed Central, and ScienceDirect. No search restriction was used for the date of publication, but the search was limited to papers published in English. Articles that cited related studies were also searched to find any related publication (using PubMed, and Europe PubMed Central citation tracking tools).

Selection of Studies

Titles and abstracts obtained from the literature search were examined for inclusion. If the information provided in the title and abstract suggested that the study included patients with a history of breast cancer, conducted PET/CT scans in those patients, and evaluated test values (sensitivity, specificity, and accuracy), full paper articles were retrieved for further assessment.

Inclusion and Exclusion Criteria

Studies were included if they assessed the sensitivity, specificity, and accuracy of 18-F-FDG imaging in the follow-up of breast cancer. The included studies used PET/CT for a diagnosis of breast cancer recurrence. Recurrence could be local or distant, but the disease had to be a consequence of the originally diagnosed breast cancer. The diagnostic value was assessed in comparison with the gold standard of diagnosis, i.e. the results of pathological assessment. This review included both studies with and without comparator groups. Letters to the editor, case reports, and review articles was excluded.

Data Extraction

The information extracted from each article included the first author, publication year, number of patients and their characteristics, index test(s), sensitivity, specificity, positive predictive value, negative predictive value, and accuracy.

The patients were classified as true positive (TP) when both PET/CT scan and reference standard detected breast cancer recurrence, true negative (TN) when neither test detected recurrence, false negative (FN) when PET/CT scan failed to detect recurrence identified by the reference standard, and false positive (FP) when the PET/CT scan incorrectly suggested recurrence not detected by the reference standard.

Accuracy was defined as TN+TP / (TN + TP + FN + FP), sensitivity as TP / (TP + FN), and specificity as TN / (TN + FP).

Statistical Analysis

Twenty-two studies that assessed the sensitivity, specificity, and accuracy of PET/CT imaging in the follow-up of treated breast carcinoma and presented the results in a systematic review format were included.

SPSS version 16 was used for data analysis using descriptive statistics.

Results

Locoregional recurrence predominately affects the breast, supraclavicular nodes, skin, axillary, and the chest wall. Intrathoracic recurrence often occurs in internal mammary, mediastinal nodes, pleura, and lung parenchyma.

Brain, liver, and bone are the most frequent sites of extrathoracic recurrence. The correct identification of local and distant recurrence at the time of suggestive symptoms in the follow-up of breast cancer prompts clinical consideration for administration of different therapies. Thus, it is important and crucial to detect recurrences or metastases as soon as possible in patients with breast cancer.

This systematic review focused on evaluating the diagnostic value of PET, CT, MRI, bone scintigraphy (BS) and PET/CT, which are widely used non-invasive modalities for the detection of locally recurrent and metastatic breast cancer.

The results in Table 1 show the main characteristics of the six included studies for evaluating the diagnostic value of positron emission tomography-/computed tomography (PET/CT).

Four studies compared the diagnostic value of PET/CT with positron emission tomography (PET) (Table 2), 8 compared PET/CT with computed tomography (CT-scan) (Table 3), 2 compared PET/CT with magnetic resonance imaging (MRI) (Table 4), and 2 compared PET/CT with BS (Table 5).

Tables 1-5 show 22 studies including a total of 1378 patients with prior breast cancer and clinical suspicion of breast cancer recurrence.

Table 1. Main characteristics of the included studies for evaluating the diagnostic value of PET/CT

First author (Year)	Number of patients (Gender)	Mean age	Index test	FN (n)	TN (n)	FP (n)	TP (n)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Moon (1998) [13]	57 (Female)	55	PET/CT	2	22	6	27	79	93	82	92	86
Aukema (2009) [14]	56 (Female)	54	PET/CT	—	—	—	—	92	97	94	96	95
Palomar Monuz (2010) [15]	70 (Female)	—	PET/CT	4	32	5	29	86.4	87.8	85.2	88.8	87.1
Emad-Eldin (2013) [16]	34 (Female)	—	PET/CT	2	10	1	21	92.3	90.5	95	85.7	91.2
Manohar (2013) [17]	43 (Female)	—	PET/CT	—	—	—	—	96.8	100	91	100	—
Groheux (2014) [18]	15 (Male)	—	PET/CT	—	—	—	—	67	100	86	100	89

Abbreviations: PPV: Positive Predictive Value; NPV: Negative Predictive Value; PET/CT: Positron Emission Tomography/Computed Tomography

Table 2. Main characteristics of the included studies for evaluating the diagnostic value of PET/CT and PET in comparative studies

First author (Year)	Number of patients (Gender)	Mean age	Index test	FN (n)	TN (n)	FP (n)	TP (n)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Fueger (2005) [19]	58 (Female)	53.3	PET/CT PET	2 5	21 18	4 7	31 28	94 85	84 72	—	—	89.7 79.3
Veit-Haibach (2007) [20]	44 (Female)	—	PET/CT PET	0 2	19 17	4 6	21 19	100 89	84 76	—	—	90.9 81.8
Haug (2007) [21]	34 (Female)	—	PET/CT PET	1 3	8 7	1 1	24 23	96 88	89 78	—	—	94.1 88.2
Dirisamer (2010) [22]	52 (Female)	—	PET/CT PET	2 8	10 10	0 0	40 34	95 81	100 100	—	—	96.1 84.6

Abbreviations: PPV: Positive Predictive Value; NPV: Negative Predictive Value; PET/CT: Positron Emission Tomography/Computed Tomography; PET: Positron Emission Tomography

Table 3. Main characteristics of the included studies for evaluating the diagnostic value of PET/CT and CT in comparative studies

First author (Year)	Number of patients (Gender)	Mean age	Index test	FN (n)	TN (n)	FP (n)	TP (n)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Abo-Sheisha (2014) [23]	50 (Female)	50.85	PET/CT CT	1 5	14 19	1 6	34 18	97 75	93 73	97 72	93	96 74
Dirisamer (2010) [22]	52 (Female)	—	PET/CT CT	2 14	10 10	0 0	40 28	95 67	100 100	—	76 —	96.1 73
Radan (2006) [7]	37 (Female)	59.9	PET/CT CT	3 6	13 8	4 9	17 14	85 70	76 47	81 56	81 57	81 59
Haug (2007) [21]	34 (Female)	—	PET/CT CT	1 2	8 6	1 2	24 24	96 70	89 47	—	—	94.1
Piperkova (2007) [24]	48 (Female)	55.3	PET/CT CT	—	—	—	—	97.8 87.6	93.5 42	99.1 85.3	91.6 31.7	88.2 97.3
Evangelista (2011) [25]	111 (Female)	61	PET/CT CT	—	—	—	—	81 72	52 37	41 32	87 76	82.1 60
Niikura (2011) [26]	225 (Female)	53.4	PET/CT CT	1 12	162 128	7 21	55 38	97.4 85.9	91.2 67.3	—	—	47 —
Groheux (2013) [27]	117 (Female)	—	PET/CT CT	—	—	—	—	100 50	99.1 100	66.7 100	100 99.1	99.1 99.1

Abbreviations: PPV: Positive Predictive Value; NPV: Negative Predictive Value; PET/CT: Positron Emission Tomography/Computed Tomography; CT: Computed Tomography

Table 4. Main characteristics of the included studies for evaluating the diagnostic value of PET/CT compared to MRI

First author (Year)	Number of patients (Gender)	Mean age	Index test	FN (n)	TN (n)	FP (n)	TP (n)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Iagaru (2007) [28]	21 (Female)	52	PET/CT	—	—	—	—	75	92.3	—	—	—
			MRI	—	—	—	—	85.7	85.7	—	—	—
Schmidt (2008) [6]	33 (Female)	—	PET/CT	—	—	—	—	91	90	—	—	—
			MRI	—	—	—	—	93	86	—	—	—

Abbreviations: PPV: Positive Predictive Value; NPV: Negative Predictive Value; PET/CT: Positron Emission Tomography/Computed Tomography; MRI: Magnetic Resonance Imaging

Table 5. Main characteristics of the included studies for diagnostic value of PET/CT and BS in comparative studies

First author (Year)	Number of patients (Gender)	Mean age	Index test	FN (n)	TN (n)	FP (n)	TP (n)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Withofs (2011) [29]	24 (Female)	60.2	PET/CT	—	—	—	—	73.9	79.3	86.1	63.7	76
			BS	—	—	—	—	43	76.8	76.3	43.8	55
Balci (2012) [30]	158 (Female) 4 (Male)	50.6	PET/CT	—	—	—	—	83	100	100	90	100
			BS	—	—	—	—	96	100	100	98	100

Abbreviations: PPV: Positive Predictive Value; NPV: Negative Predictive Value; PET/CT: Positron Emission Tomography/Computed Tomography; BS: Bone Scintigraphy

Diagnostic Value of PET/CT for Detection of BC Recurrence

Analysis of the 22 included studies showed that the sensitivity, specificity, PPV, NPV, and accuracy of PET/CT for detection of recurrence ranged from 73.9%-100%, 52%-100%, 41%-100%, 63.7%-100%, and 60%-99.1%, respectively.

Diagnostic Value of PET for Detection of BC Recurrence

Four included studies showed that the sensitivity, specificity, and accuracy of PET for detection of recurrence ranged from 81%-89%, 72%-100%, and 79.3%-88.2%, respectively.

Diagnostic Value of CT-scan for Detection of BC Recurrence

Eight included studies showed that the sensitivity, specificity, PPV, NPV, and accuracy of CT-scan for detection of recurrence ranged from 50%-87.6%, 37%-100%, 32%-100%, 31.7%-99.1%, and 47%-99.1%, respectively.

Diagnostic Value of MRI for Detection of BC Recurrence

Based on the two included studies, the sensitivity and specificity of MRI technology for detection of recurrence ranged from 85.7%-93% and 85.7%-86%, respectively.

Diagnostic Value of PET for Detection of BC Recurrence

According to the findings of two included studies, the sensitivity, specificity, PPV, NPV, and accuracy of BS for detection of recurrence ranged from 43%-96%, 76.8%-100%, 76.3%-100%, 43.8%-98%, and 55%-100%, respectively.

Discussion

Sixteen out of 22 included studies compared PET/CT with conventional imaging modalities such as PET, CT scan, MRI, and BS. Four studies compared PET/CT with PET (marked in Table 2) and found it had a high sensitivity, specificity, and accuracy as compared with PET. The rate of the detection of recurrence and metastasis was significantly higher with PET/CT than with PET. Table 3 shows eight studies that compared PET/CT with CT scan for detection of BC recurrence and reported that the sensitivity, specificity, and accuracy of PET/CT were higher than CT scan. In six studies of combined PET/CT (marked in Table 1), the mean sensitivity and specificity for the detection of recurrence was higher than PET and CT scan, indicating a marginally increased diagnostic value or diagnostic precision. It has been reported that PET/CT is superior for the detection of BC recurrence with a mean accuracy of 89.33% versus 83.1% and 74.62% for PET and CT, respectively. Two studies compared PET/CT with MRI (marked in Table 4) and reported a high sensitivity and specificity as compared with MRI.

Table 5 shows two studies that compared PET/CT with BS for the detection of BC recurrence and bone metastases. The PET/CT sensitivity ranged from 73.9%-100% (43-96% using BS) and the PET/CT specificity ranged from 52%-100% (76.8-100% using BS). Data analysis showed a high sensitivity and a low specificity for PET/CT as compared with BS. In twenty-two included studies, PET/CT and MRI had the highest sensitivity (0.920 and 0.893, respectively), and BS and PET/CT had the highest specificity (0.884 and 0.875, respectively).

In conclusion, according to the results, PET/CT seems to be a more useful modality than the existing

techniques to assess the patients with suspected recurrent and metastatic breast cancer. However, uncertainty remains around the use of PET/CT as a substitute for current imaging technologies. If PET/CT is not applicable, MRI and also BS could also be used as alternatives.

Conflict of Interest

The authors have no potential conflict of interest concerning the content of this article.

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