A Systematic Review and Meta-analysis on the Diagnostic Accuracy of Whole-body PET/CT for Distant Metastases in Breast Cancers

Sagisag M. Dadap, MD, Michele D. Ogbac, MD and Dominic N. Velasco, MD
Nuclear Medicine Section, Department of Radiology, Cardinal Santos Medical Center

ABSTRACT

Background: *Breast cancer is the second most common malignancy globally. This study is a systematic review and meta-analysis assessing whole-body PET/CT using ^{18}F-FDG in detecting breast carcinoma distant metastases as an update to the study of Xu et al.*

Objective: To determine the diagnostic accuracy of whole-body PET/CT in distant metastasis detection among breast cancer patients

Methods: *The MEDLINE database was systematically searched for articles evaluating whole-body PET/CT in distant metastasis detection among breast cancer patients. Sensitivity, specificity, likelihood ratios and predictive values were derived by three independent readers. Summary receiver operating characteristic curves were plotted.*

Results: *Fifteen studies (n = 4175) were included with pooled sensitivities, specificities, positive and negative likelihood ratios, positive and negative predictive values (with 95% confidence intervals) of 0.98 (0.97–0.99), 0.98 (0.98–0.99), 86.6 (63.6–117.9), 0.01 (0.01–0.02), 0.94 (0.92–0.95) and 0.99 (0.995–0.998), respectively. Pooled positive and negative predictive values with a prevalence of 13.6% are 0.93 and 0.99, respectively.*

Conclusion: *Whole-body PET/CT with ^{18}F-FDG provides excellent detection of distant metastases in breast cancer and is recommended in assessing patients in earlier stages of the disease, not only in the later stages, especially in more aggressive tumors.*

Keywords: *Whole-body PET/CT, ^{18}F-FDG, breast cancer, carcinoma, distant metastasis, meta-analysis*

For correspondence:
Sagisag M. Dadap, MD
E-mail: sagolaman@gmail.com

INTRODUCTION

According to the World Health Organization (WHO), malignancy is the second highest cause of morbidity among non-communicable diseases [1], with the second highest incidence belonging to breast cancer [2]. Given its global magnitude, the importance of cancer detection cannot be overstated.

Once detected and established, cancers are staged as it is essential for management and prognostication. The presence of distant metastases drastically changes treatment strategies and outlook, from aggressive to palliative [3].

Conventional imaging modalities such as x-rays, ultrasonography, computed tomography (CT), magnetic resonance (MR) and bone scintigraphy are commonly used in the detection of metastases but have inherent limitations. Very small lesions may not be characterized or even cause abnormal anatomy to be detected. Even if lesions are detected, there may not be enough functional evidence to diagnose the lesion as benign or malignant [4].

Positron emission tomography with computed tomography (PET/CT) using ^{18}F-fluorodeoxyglucose (^{18}F-FDG) is a modality that combines the functional

sensitivity of PET to malignant tumors and the excellent spatial resolution of CT. PET alone with ^{18}F-FDG takes advantage of the high glucose uptake in many cancers but has poor anatomic localization, hence its invaluable fusion with CT [4].

Despite its apparent advantages, PET/CT has varying sensitivities and specificities with different tumors. With current National Comprehensive Cancer Network (NCCN) guidelines for breast cancer, whole-body FDG PET/CT is only recommended for Stage T4d, N0-N3, M0 in inflammatory breast cancer and optional even at stage IV [5], as compared to non-small-cell lung cancers, wherein FDG PET/CT is recommended in all stages of the disease [6]. Practice guidelines on breast cancer from other countries and specialty societies also regard ^{18}F-FDG PET/CT as useful to resolve inconclusive findings from conventional imaging modalities [7-10] but is not recommended as a procedure for routine surveillance [9]. Mettler and Guiberteau consider ^{18}F-FDG-PET/CT as moderately useful for breast cancers [11].

A retrospective study by Niikura et al. [12] comparing whole-body PET/CT to conventional imaging in detecting distant metastases in breast showed superiority over conventional imaging with a sensitivity and specificity of 97.4% and 91.2%, respectively. Choi et al. also extols whole-body PET/CT in detecting breast cancer distant metastases (100% sensitivity, 96.4% specificity) but does not recommend it as a primary study for detecting primary lesions [13]. In one study involving patients with locally advanced breast cancer, whole-body ^{18}F-FDG-PET/CT proved useful in detecting local regional lymph node and distal metastases with 100% accuracy [14]. Xu et al. concluded in a meta-analysis that ^{18}F-FDG-PET/CT was excellent for detecting distant metastasis and staging breast cancers with a pooled specificity of 0.96, sensitivity of 0.93, positive likelihood ratio of 20.8, and negative likelihood ratio of 0.08 [4].

This paper is a systematic review and meta-analysis after that of Xu et al. but focuses on breast cancer distant metastasis detection. It assesses the diagnostic accuracy of whole-body PET/CT with ^{18}F-FDG in detecting distant metastases in patients with breast cancer by systematic review of studies from May 1, 2012 to September 30, 2016 and serves as an update to the meta-analysis by Xu et al. [4] with the following measures: sensitivity and specificity, and positive and negative likelihood ratios and positive and negative predictive values.

METHODOLOGY

The study is an updated systematic review and meta-analysis of the diagnostic accuracy of whole-body PET/CT using ^{18}F-FDG in the detection of metastases in breast cancers. This adopted a methodology similar to the methodology used by Xu et al. [4].

Search Strategy

The MEDLINE database was searched for articles assessing the diagnostic performance of whole-body ^{18}F-FDG PET/CT in evaluating distant metastasis in breast cancers. Articles from May 1, 2012 to September 30, 2016 were included, based on the following search words: (CT OR "computed tomography") AND (PET OR "positron emission tomography") AND breast AND (neoplasm OR cancer OR carcinoma) AND (staging OR "distant metastases"). Only articles with English texts were considered.

Study Selection

Studies with whole-body ^{18}F-FDG PET/CT in the overall assessment of distant metastases in breast cancer patients were considered. Distant metastasis is defined as tumor spread beyond the regional lymph nodes of a primary malignancy. In the case of breast cancer, it is spread of tumor cells beyond the ipsilateral axillary, supraclavicular, infraclavicular and internal mammary lymph nodes [5]. Quantitatively, metastasis is suspected in a lesion having a standard uptake value (SUV) > 2.0 in PET/CT [15].

Inclusion criteria:

a. Whole-body ^{18}F-FDG PET/CT was used as a diagnostic tool in breast cancer patients regardless of age or sex;

b. A table with true-positive, false-positive, true-negative, and false-negative results can be plotted;

c. Minimum sample size of 10 cancer patients, with and without distant metastases;

d. Analysis was done at the patient level;

e. Retrospective or prospective designs;

f. Histopathology, clinical and/or imaging follow-up was used as reference standard

Exclusion criterion: studies wherein the reference standard was used based only on positive PET/CT findings.

Data Extraction

Authors, publication date, country where published, patient size, tumor histology, study type (prospective or retrospective), and criteria for a positive PET/CT result {i.e., if they were determined by qualitative (QL), qualitative and quantitative (QL+QN), or unclear} were derived from each study. Two readers gleaned the following data from each article: patients that are true-positive, false-positive, true-negative, and false-negative with whole-body PET/CT, based on the reference standard (histopathologic analysis, clinical and/or imaging follow-up). A third reader settled any discrepancy between the previous two readers.

Quality Assessment

Studies were assessed using the quality assessment of diagnostic accuracy studies (QUADAS) [16] tool (see Appendix). The tool includes 14 items, each of which is assessed as "yes," "no" or "unclear." Studies with less than 12 "yes" were considered low in quality while those with 12 or more "yes" were considered high-quality. Again, two readers made the quality assessment independently with a third reader settling any discrepancy.

Statistical Analysis

Bivariate regression models determined the weighted overall estimates of sensitivity and specificity with construction of summary receiver operating characteristic (SROC) curves using the Moses-Littenberg model. Overall sensitivity and specificity, positive and negative likelihood ratios (PLRs and LRs), positive and negative predictive values (PPVs and NPVs) were calculated with 95% confidence intervals.

Analysis of the covariates were as follows: quantitative and qualitative vs. qualitative imaging analysis, high-quality vs low-quality studies and prospective vs. retrospective study designs. Analyses were conducted with RevMan v 5.3 (Nordic Cochrane Center) and MedCalc© [17].

RESULTS

Selection of studies

The database search yielded 417 titles, 301 of which were excluded because they apparently did not fit the inclusion criteria. Of the 116 titles, 89 were excluded since their abstracts yielded no diagnostic data. Of the 27 abstracts with full-text articles, 12 articles were excluded as 6 had no 2 x 2 tables that could be plotted, 1 had no patient-level analysis, 2 had incomplete data, 1 assessed for bone metastases only, and no distant metastases were recorded in 2 (Figure 1). Fifteen (15) studies were finally included in the meta-analysis (Table 1).

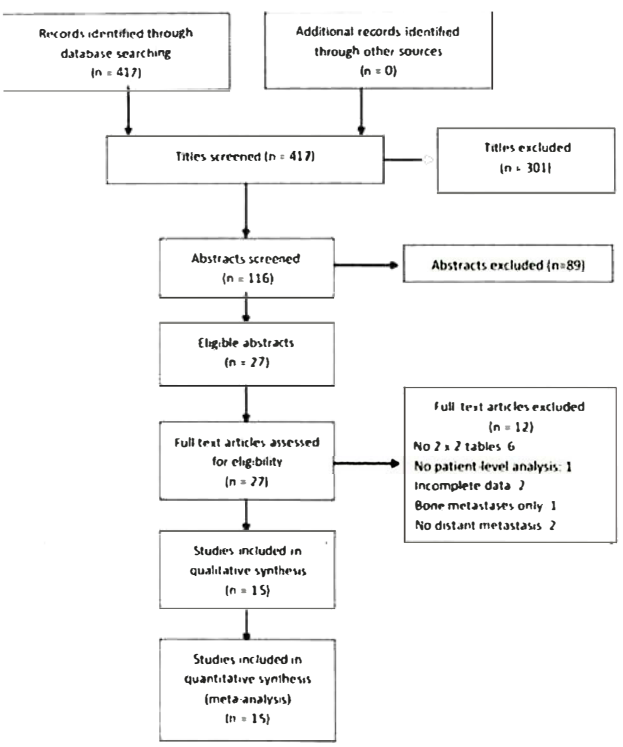

Figure 1. Flow-chart of the database search leading to the included studies

Quality assessment

Assessment of the articles using the QUADAS tool showed that all articles scored "Yes" in 6 items: well-defined selection criteria (item 2), good reference standard (item 3), verification using a reference standard (item 5), no differential verification (item 6), and detailed index test and reference standards (items 8 and 9). Two studies [18, 19] were not scored in item 1 (representative spectrum) as they dealt with a small subgroup of the population (male patients and patients with suspected recurrences). Item 4 was not scored in 2 studies [20, 21] as there was no mention of any interval between the performance of the standard reference and index test. Item 7 (incorporation bias) was not scored in 4 studies [20-23] as PET/CT formed part of the reference standard. Interpretation of the index test without blinding to the reference standard (item 10) and vice versa (item 11) was noted in 6 [18–20, 22, 23] and 7 [18–24] studies, respectively. Interpretation of the reference standard, particularly by imaging, often requires comparison with the index test and conversely. Item 12 (availability of the same clinical data during the study and in actual practice) was lacking in 2 studies [21,22]. Seven studies [13, 15, 18–20, 23, 25] did not report uninterpretable cases (item 13) while 5 studies did not report any case of withdrawal [19, 20, 23, 25, 26] (item 14). Of the 15 articles assessed, 9 (60%) were considered of high quality (≥ 12 "Yes") [13, 15, 24–30].

Analysis of diagnostic accuracy

Data from the 15 studies yielded highly remarkable overall sensitivity (0.98, 95% CI: 0.97–0.99), specificity (0.98, 0.98–0.99), positive likelihood ratio (86.6, 63.6–117.9), negative likelihood ratio (0.01, 0.01–0.02), positive predictive value (0.94,

Table 1. Characteristics of studies of Whole-body PET/CT in detecting breast cancer distant metastases included in the meta-analysis

Author (Year)	Country Of Origin	Design	Sample Size	Stage	Tumor type	Age* (years)	% Male	Follow-up time*	QUADAS Score	Imaging Analysis	Reference Standard
Aliyev, A *et al.* (2016) [20]	Turkey	Retrospective	254	I-IV	Var.	54.3	2.3	NR	8	QL+QN	H+I+C
Chang H-T, *et al.* (2014) [18]	Taiwan	Retrospective	140	I-III	Var.	29-84	NR	4-73 mos.	10	QL+QN	H+I+C
Choi, YJ *et al.* (2012) [13]	S. Korea	Retrospective	154	I-IV	Var.	30-81	NR	NR	13	QL+QN	H+I+C
Groheux, D. *et al.* (2012) [25]	France	Prospective	117	III	LABC/IBC	NR	NR	10 d	14	QL+QN	H+I+C
Groheux, D. *et al.* (2014) [19]	France	Retrospective	14	NR	Var.	NR	100	<4 wks.	9	QL+QN	H+I
Hogan, MP *et al.* (2015) [23]	USA	Retrospective	235	I-III	ILC/IDC	33-92	0	[PT]	12	QL+QN	H+I
Hulikal, N *et al.* (2015) [22]	India	Prospective	38	III	LABC	27-73	0	[PT]	9	QL	H+I
Jung, NY *et al.* (2014) [21]	S. Korea	Retrospective	1,161	II-IV	Var.	22-88	0.99	1 mo.	10	QL+QN	I+C
Koolen, BB *et al.* (2012) [27]	Netherlands	Prospective	311	II-IV	Var.	49.3	0	2 wks.	14	QL+QN	I+C
Krammer, J *et al.* (2015) [29]	Germany	Prospective	101	II-IV	Var.	54	0	[PT]	14	QL+QN	H+I+C
Manohar, K *et al.* (2013) [21]	India	Prospective	43	IIB-IIIB	LABC	49.2	0	6 mos	10	QL	H+I
Nursal *et al.* (2016) [28]	Turkey	Retrospective	419	I-II	Var.	51.5	0	[PT]	12	QL	H+I
Riedl, CC *et al.* (2014) [15]	USA	Retrospective	134	I-IIIC	Var.	36	0	21.5 d	13	QL+QN	H+I
Ulaner, GA *et al.* (2016) [26]	USA	Retrospective	232	I-IIIC	TNBC	21-93	NR	[PT]	14	QL	H+I
Zhang, X, Wu, F and Han, P (2014) [24]	China	Retrospective	164	I-IV	ILC/IDC	21-70	0	2-5 d	13	QL+QN	H+I

QUADAS: quality assessment of diagnostic accuracy studies, QL: qualitative, QN: quantitative, I: imaging, H: histopathology, C: clinical, NR: not reported, Var.: varied, LABC: locally advanced breast cancer, IBC: inflammatory breast cancer, ILC: invasive lobular cancer, IDC: invasive ductal cancer, TNBC: triple-negative breast cancer, PT: pre-treatment

*range or mean

Table 2. Summary of diagnostic performance of whole-body PET/CT with ^{18}FDG in the detection of breast cancer distant metastasis.

STUDY	NO. OF STUDIES (PATIENTS)	SENSITIVITY (95% CI)	SPECIFICITY (95% CI)	LR+	LR-	PPV	NPV
ALL	15 (4175)	0.98 (0.97-0.99)	0.98 (0.98-0.99)	86.6 (63.6-117.9)	0.01 (0.01-.02)	0.94 (0.92-0.95)	0.99 (0.99-1.0)
QUALITY							
HIGH	8(1713)	1.0 (0.98-1.0)	0.98 (0.97-0.99)	64.43 (42.95-96.6)	0	0.90 (0.87-0.93)	1.0
LOW	7(2462)	0.98 (0.96-0.99)	0.99 (0.98-0.99)	116.94 (72.83-187.76)	0	0.96 (0.94-0.97)	0.99 (0.992-1.0)
DESIGN							
RETRO-SPECTIVE	10 (3565)	0.98 (0.97-0.99)	0.98 (0.98-0.99)	82.4 (59.5-114.0)	0.01 (0.01-0.03)	0.93 (0.91-0.95)	0.99 (0.99-1.0)
PROSPECT-IVE	5 (610)	1.0 (0.96-1.0)	0.99 (0.97-0.99)	124.75 (47-331.1)	0	0.96 (0.91-0.98)	1.0
IMAGING ANALYSIS							
QL	4 (732)	1.0 (0.96-1.0)	0.96 (0.95-0.98)	32 (20.8-49.2)	0	0.82 (0.75-0.87)	1.0
QL+QN	11 (3443)	0.98 (0.97-0.99)	0.99 (0.98-0.99)	141.4 (91.4-218.9)	0.01 (0.01-0.03)	0.96 (0.95-0.98)	0.99 (0.99-1.0)

CI: confidence interval, QL: qualitative, QN: quantitative, LR+: positive likelihood ratio, LR-: negative likelihood ratio, PPV: positive predictive value, NPV: negative predictive value

92.45–95.78) and negative predictive value (0.99, 0.995–0.998) with a given global prevalence of 13.6% (Table 2). Covariate analyses show that differences in study design, imaging analysis, or study quality had no significant effect in the values of the aforementioned parameters. The biggest difference between covariates is within the method of analysis (QL vs QL+QN) in terms of specificity (0.96 vs. 0.99). This may indicate that quantitative and qualitative methods of analysis should go hand-in-hand in detecting distant metastases, though the differences are not wide.

The plotted summary receiver operating curve (SROC) showed high overall diagnostic accuracy (Figure 3) with the curve placed closely to the upper left corner. The study by Groheux et al. [19] is an outlier with its relatively low specificity of 0.8 and wide confidence intervals. Being the only study included with an all-male population and consequent small sample size, the calculated sensitivity, specificity and corresponding confidence intervals are expected.

With the calculated pooled sensitivity and specificity, whole-body PET/CT with ^{18}F-FDG has exceptional accuracy. No significant difference is seen even withanalysis of covariates with the SROCs showing consistently high sensitivity and specificity values (Figures 2 to 4). Also, with a summarized PLR of 86.6 and NLR of 0.01, this study submits that whole-body PET/CT can reliably determine if a patient has distant metastasis or not.

DISCUSSION

Whole-body PET/CT with ^{18}F-FDG has consistently exceptional sensitivity, specificity, likelihood ratios

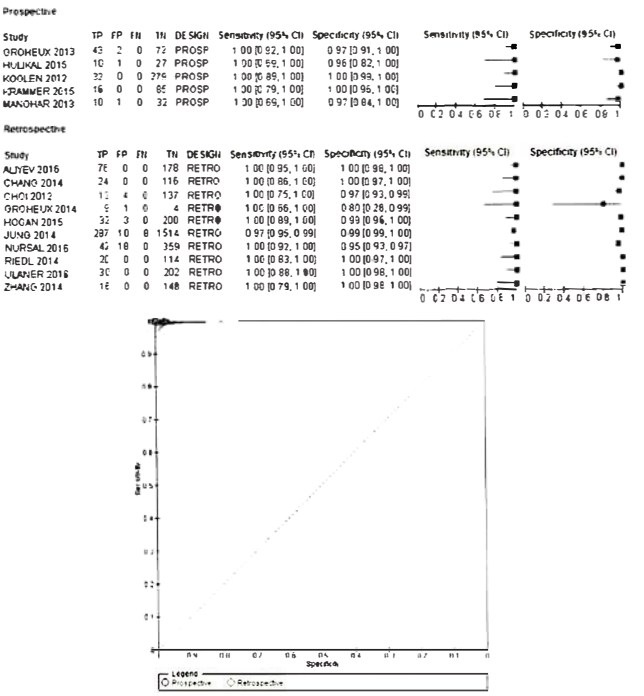

Figure 2. Summary of sensitivity and specificity with SROC curve for detecting distant metastasis in breast cancer using whole-body PET/CT with ^{18}F-FDG comparing study designs

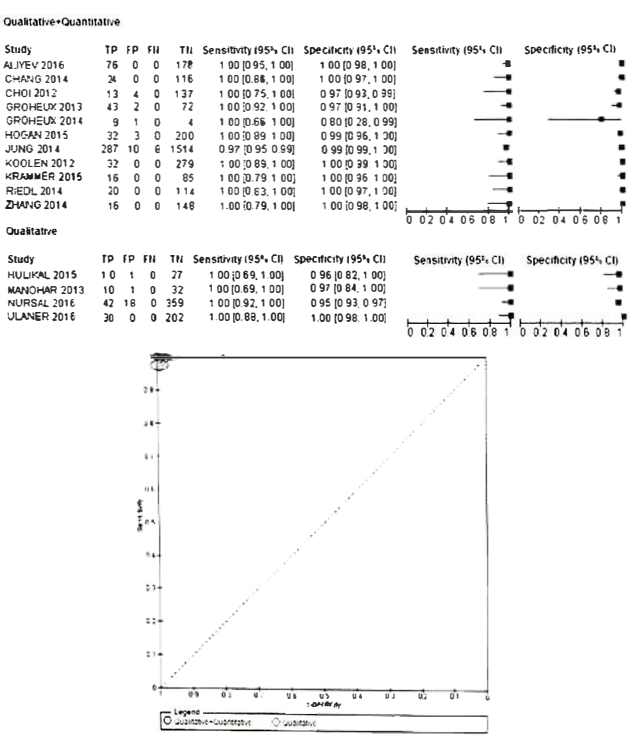

Figure 3. Summary of sensitivity and specificity with SROC curve for detecting distant metastasis in breast cancer using whole-body PET/CT with ^{18}FDG comparing image analysis.

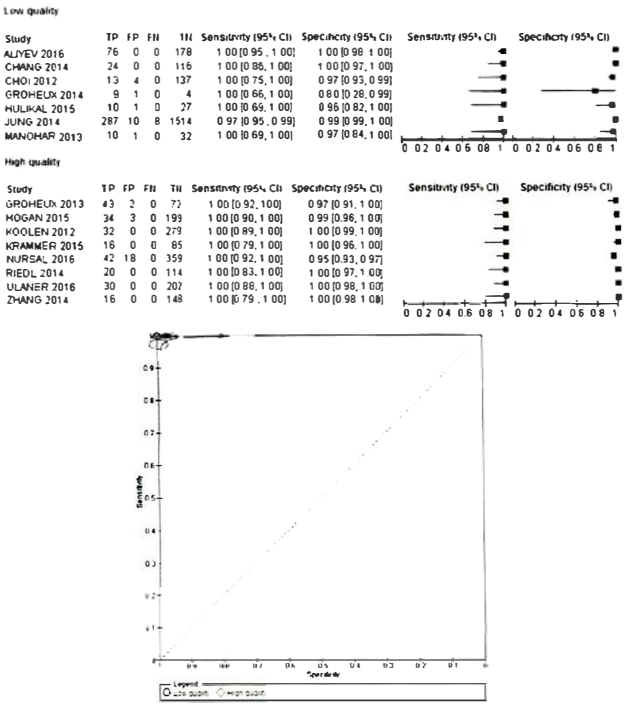

Figure 4. Summary of sensitivity and specificity with SROC curve for detecting distant metastasis in breast cancer using whole-body PET/CT with ^{18}FDG comparing study quality

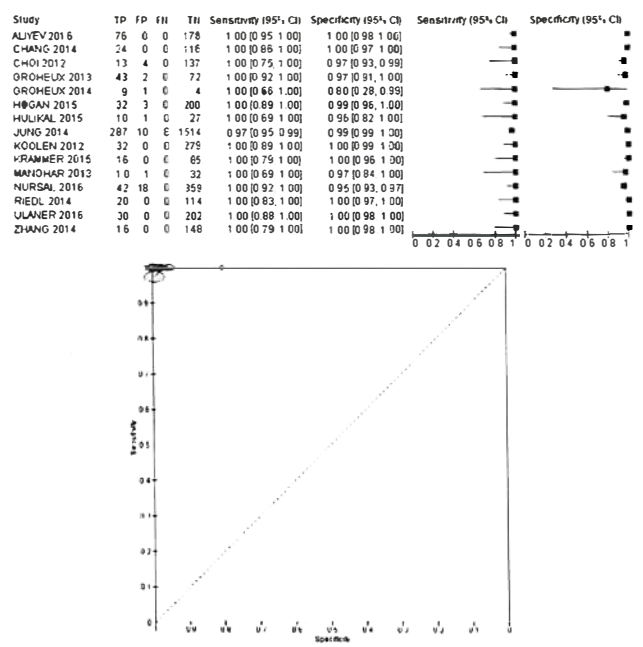

Figure 5. Summary of sensitivity and specificity with SROC curve for detecting distant metastasis in breast cancer using whole-body PET/CT with ^{18}FDG comparing all studies

and predictive values. Compared to the meta-analysis of Xu et al. on breast cancer distant metastasis detection with whole-body PET/CT, this study reports a slightly higher sensitivity (98.8% vs 97%) and specificity (98.8% vs 95%), positive likelihood ratio (86.6 vs 18.5), and negative likelihood ratio (0.01 vs 0.03). Five studies were included in Xu et al. while this study included 15 within a shorter period (12 years vs. 4 years). Staging cancers is imperative in guiding their subsequent management and determining the presence of distant metastasis may drastically change treatment strategies, especially in women with breast cancer younger than 40 years [5]. Whole-body PET/CT may prove to be highly sensitive in the detection of distant metastasis and more accurate in staging. This meta-analysis has included 15 studies, involving 4,715 patients, to evaluate the diagnostic accuracy of whole-body PET/CT with ^{18}F-FDG in detecting distant metastases in breast cancer patients.

Despite several existing guidelines that advise against using whole-body PET/CT for initial staging in breast cancer or limit it to resolution of equivocal findings in conventional imaging, there are studies that recommend otherwise. Riedl et al. [15] confirmed distant metastases in young women (< 40) even from clinical stage I to IIIC. Aliyev et al. [20] also detected distant metastases with whole-body PET/CT in patients with breast cancer at initial staging and in all stages. This will significantly impact management, particularly if surgery is contemplated, and may do away with unnecessary morbidity.

The limitations of the study are as follows:

First, publication bias is probable, as only one database was searched (MEDLINE) and not all

languages were considered. Unpublished studies of a similar nature, for whatever reason, cannot be discounted. But this is, in principle, an inherent weakness of systematic reviews as not all relevant studies are accessible. There is no hard and fast rule as to how many databases are needed to be searched, but EMBASE and MEDLINE are recommended databases [31].

Second, only patient-level analysis of the presence of distant metastases was considered and data or studies concerning lesion-level analysis were disregarded. Lesion-level analysis of metastases will likely alter the sensitivity and specificity of whole-body PET/CT as some of the studies report cases with false-positive and false-negative results at this level [18, 25, 28].

Third, given the relatively small number of studies, many of which reported no false-negative result, it was not possible to construct a hierarchical SROC (HSROC) that can allow assessment of sources of heterogeneity between studies [32]. These kinds of results are often encountered in drafting meta-analyses with studies that report 100% sensitivities or specificities, or 2 x 2 tables with values of "0" in any of the boxes, requiring different statistical techniques that are not readily available to the author [33].

Fourth, seven of the included articles [18-24] have readers who interpreted the index test without blinding of the reference standard, and vice versa. This will much likely reduce objectivity and be a source of bias.

CONCLUSION

All of the studies in this systematic review conclude that whole-body PET/CT with ^{18}F-FDG is an excellent modality in detecting distant metastases, at least at the patient level. It can be used not only to resolve equivocal findings [7–10] but also as a modality to assess breast cancer in earlier stages of the disease, if not in the initial staging. Its consistently high accuracy in detecting distant metastases may preclude unnecessary treatment measures, particularly in tumors with more aggressive histologic types.

Given the small population of this study and the aforementioned biases, larger studies with standardized protocols are needed to come up with a more statistically significant performance evaluation of the modality. Prospective recruitment of subjects with consistent and more reliable reference standards, coupled with appropriate blinding of readers, will minimize confounders and perhaps enable lesion-level analysis. These may further establish whole-body PET/CT with ^{18}F-FDG as a well-recommended diagnostic tool for detecting and monitoring distant metastases. Being relatively new, its overall impact on patient survival has yet to be defined [27].

ACKNOWLEDGMENT

Much gratitude is given to Dr. Maria Luz Joanna B. Soria, FPCP, FPCC and Ms. Kristine Joy S. Calvario for their invaluable support and wisdom.

REFERENCES

1 Non-communicable diseases. World Health Organization. 2016 [cited 15 September 2016]. Available from: http://www.who.int/mediacentre/factsheets/fs355/en/

2. Stewart B, Wild C. World cancer report 2014. 1st ed.

3. Fauci A, Harrison T. Harrison's Manual of Medicine. 1st ed. New York: McGraw-Hill Medical; 2009.

4. Xu G, Zhao L, He Z. Performance of whole-body PET/CT for the detection of distant malignancies in various cancers: a systematic review and meta-analysis. Journal of Nuclear Medicine. 2012;53(12):1847–1854.

5. National Comprehensive Cancer Network. Breast Cancer. Version 2.2016. Available at http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf (accessed 26 October 2016).

6. NCCN clinical practice guidelines: Non-small cell lung cancer version 3. 2016. [Internet]. 1st ed. 2016 [cited 1 September 2016]. Available from: http://nccn.org
7. Senkus E, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rutgers E et al. Primary breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2015;26 (suppl 5): v8-v30.
8. Katcheressian JL, Hurley P, Bantug E, Esserman LJ, Grunfeld E, Halberg F et al. Breast cancer follow-up and management after primary treatment: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 31:961–965.
9. Saskatchewan Cancer Agency Breast Cancer Guidelines. 1st ed. 2012. [cited 23 November 2016]. Available from: http://www.saskcancer.ca/
10. Management of Breast Cancer. 2nd ed. [Internet]. 1st ed. 2010 [cited 23 November 2016]. Available from: http://www.moh.gov.my/
11. Mettler F, Guiberteau M. Essentials of nuclear medicine imaging. 1st ed. Philadelphia, PA: Elsevier/Saunders; 2012.
12. Niikura N, Costelloe C, Madewell J, Hayashi N, Yu T, Liu J et al. FDG-PET/CT compared with conventional imaging in the detection of distant metastases of primary breast cancer. The Oncologist. 2011;16(8):1111-1119.
13. Choi Y, Shin Y, Kang Y, Lee M, Lee M, Cho B et al. The effects of preoperative ^{18}F-FDG PET/CT in breast cancer patients in comparison to the conventional imaging study. J Breast Cancer. 2012;15(4):441.
14. Mittal BR, Manohar K, Battacharya A, Singh B, Singh G. The role of ^{18}F-FDG PET/CT in initial staging of patients with locally advanced breast carcinoma with an emphasis on M staging. Hell J Nucl Med 2011;14(2).
15. Riedl C, Slobod E, Jochelson M, Morrow M, Goldman D, Gonen M et al. Retrospective analysis of ^{18}F-FDG PET/CT for staging asymptomatic breast cancer patients younger than 40 years. Journal of Nuclear Medicine. 2014;55(10):1578–1583.
16. Whiting P, Rutjes A, Reitsma J, Bossuyt P, Kleijnen J. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. BMC Med Res Methodol. 2003;3(1).
17. Schoonjans F. Diagnostic test evaluation calculator. MedCalc. 2016 [cited 15 November 2016]. Available from: http://www.medcalc.org/calc/diagnostic_test.php
18. Chang H, Hu C, Chiu Y, Peng N, Liu R. Role of 2-[^{18}F] fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography in the post-therapy surveillance of breast cancer. PLoS ONE. 2014;9(12):e115–127.
19. Groheux D, Hindié E, Marty M, Espié M, Rubello D, Vercellino L et al. 18F-FDG-PET/CT in staging, restaging, and treatment response assessment of male breast cancer. European Journal of Radiology. 2014;83(10):1925–1933.
20. Aliyev A, Yilmaz AS, Özhan M, Ekmekçioğlu Ö, Vatankulu B, Kocael P et al. The role of FDG PET/CT in detection of distant metastasis in the initial staging of breast cancer. Turkish Journal of Medical Sciences. 2016; 46:349–360.
21. Jung N, Yoo I, Kang B, Kim S, Chae B, Seo Y. Clinical significance of FDG-PET/CT at the postoperative surveillance in the breast cancer patients. Breast Cancer. 2014;23(1):141–148.
22. Manohar K, Mittal B, Bhoil A, Bhattacharya A, Singh G. Role of ^{18}F-FDG PET/CT in identifying distant metastatic disease missed by conventional imaging in patients with locally advanced breast cancer. Nuclear Medicine Communications. 2013;34(6):557–561.
23. Hulikal N, Gajjala S, Kalawat T, Kottu R, Amancharla Yadagiri L. Utility of [^{18}F] fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) in the initial staging and response assessment of locally advanced breast cancer patients receiving neoadjuvant chemotherapy. Indian Journal of Surgical Oncology. 2015;6(4):330–336.
24. Nursal G, Nursal T, Aytac H, Hasbay B, Torun N, Reyhan M et al. Is PET/CT necessary in the management of early breast cancer? Clinical Nuclear Medicine. 2016;41(5):362–365.
25. Hogan M, Goldman D, Dashevsky B, Riedl C, Gonen M, Osborne J et al. Comparison of ^{18}F-FDG PET/CT for systemic staging of newly diagnosed invasive lobular carcinoma versus invasive ductal carcinoma. Journal of Nuclear Medicine. 2015;56(11):1674–1680.
26. Zhang X, Wu F, Han P. The role of (^{18}) F-FDG PET/CT in the diagnosis of breast cancer and lymph nodes metastases and micrometastases may be limited. Hell J Nucl Med 2014 Sep-Dec;17(3):17783. 2014;17(3): 177–183.
27. Groheux D, Giacchetti S, Delord M, Hindie E, Vercellino L, Cuvier C et al. ^{18}F-FDG PET/CT in staging patients with locally advanced or inflammatory breast cancer: comparison to conventional staging. Journal of Nuclear Medicine. 2012;54(1):5–11.
28. Ulaner G, Castillo R, Goldman D, Wills J, Riedl C, Pinker-Domenig K et al. ^{18}F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. European Journal of Nuclear Medicine and Molecular Imaging. 2016;43(11):1937–1944.
29. Koolen B, Valdés Olmos R, Elkhuizen P, Vogel W, Vrancken Peeters M, Rodenhuis S et al. Locoregional lymph node involvement on ^{18}F-FDG PET/CT in breast cancer patients scheduled for neoadjuvant chemotherapy. Breast Cancer Research and Treatment. 2012;135(1):231–240.
30. Krammer J, Schnitzer A, Kaiser C, Buesing K, Sperk E, Brade J et al. ^{18}F-FDG PET/CT for initial staging in breast cancer patients – is there a relevant impact on treatment planning compared to conventional staging modalities? European Radiology. 2015;25(8):2460–2469.
31. Lee J, Kim K, Choi S, Huh J, Park S. Systematic review and meta-analysis of studies evaluating diagnostic test accuracy: a practical review for clinical researchers–part I. general guidance and tips. Korean J Radiol 2015;16(6):1175–1187.
32. Lee J, Kim K, Choi S, Huh J, Park S. Systematic review and meta-analysis of studies evaluating diagnostic test accuracy: a practical review for clinical researchers-part II. statistical methods of meta-analysis. Korean Journal of Radiology. 2015;16(6):1188.
33. Takwoingi Y, Guo B, Riley R, Deeks J. Performance of methods for meta-analysis of diagnostic test accuracy with few studies or sparse data. Statistical Methods in Medical Research. 2015;.0 (0):1–19.