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Diagnostic Performance of ^{18}F-FDG PET or PET-CT in Multiple Myeloma: A Systematic Review and Meta-analysis

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Abstract

Objectives: Conduct a systematic review and meta-analysis to assess the diagnostic performance of ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) or PET-computed tomography (PET-CT) in multiple myeloma (MM).

Methods: A comprehensive literature search about studies that published till July 2015 was performed. Methodological quality of each study was assessed. The meta-regression and subgroup analysis was applied to assess the heterogeneity of between-study. A meta-analysis was used to state sensitivity, specificity, diagnostic odds ratio (DOR), area under the curve (AUC), summary receiver operating characteristic (SROC) curve and Q* indexes with statistical software.

Results: Eleven studies met the inclusion criteria in this meta-analysis, which comprise a total of 492 patients. The pooled sensitivity and specificity of 18F-FDG PET or PET-CT in multiple myeloma were 0.870 (95% CI, 0.825-0.907), 0.937 (95% CI, 0.892-0.967), and the AUC and the Q* index were 0.9332, 0.869, respectively. The pooled sensitivity and specificity of PET in multiple myeloma were 0.94495% CI, 0.887-0.977) and 0.990 (95% CI, 0.947-1.000), and the AUC and the Q* index were 0.98, 0.95, respectively. The pooled sensitivity and specificity for PET-CT in multiple myeloma were 0.813 (95% CI, 0.743-0.870) and 0.875 (95% CI, 0.787-0.936), and the AUC and the Q* index were 0.88, 0.82, respectively. The funnel plots suggested the publication bias may exist.

Conclusions: The whole-body ^{18}F-FDG PET or PET-CT were imaging methods with high accuracy in differential diagnosis of multiple myeloma patients.

Keywords: 18F-FDG PET; PET-CT; Multiple meloma; Meta-analysis

Introduction

Multiple myeloma (MM) is a malignant hematologic disorder that is characterized by monoclonal proliferation of malignant plasma cells [1]. Furthermore, it can cause series of severe clinical features, such as extensive bone destruction, re-infection, anemia, hypercalcemia, high viscous syndrome and renal failure, etc. The incidence of multiple myeloma is increasing in recent years and it accounts for 1% in the entire malignant tumor and about 10% of malignant tumor in blood system which surpassed leukemia [2]. Therefore, it is early detection, diagnosis and treatment that play an important roles in improving patients' survival rate and quality of life.

However, traditional morphological imaging technologies, such as X-ray, Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), have some limitations in evaluating the curative effect and detecting early lesions [3]. While compared with traditional technologies, ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) or positron emission tomography-computed tomography (PET-CT) as a new imaging technique, can be applied in the diagnosis, stage and prognosis of tumor and the efficacy evaluation after the therapeutics [4,5].

Some researches believed that ^{18}F-FDG PET or PET-CT has a higher accuracy than traditional techniques in the diagnosis of multiple myeloma [2,6-9]. However, there is still controversy on the diversity of results because of the number of cases is generally insufficient. Besides, there is no uniform conclusion about the diagnostic accuracy of PET or PET-CT for multiple myeloma.

Two meta-analysis on the diagnostic performance of 18F-FDG PET or PET-CT for multiple myeloma had published [10,11]. The first paper analyzed that the ^{18}F-FDG PET or PET-CT detected intramedullary and extramedullary lesions of multiple myeloma, but it pooled only 5 articles to analyze.

The second paper reported the comparison of diagnostic performance about MRI, scintigraphy, FDG-PET and PET-CT in the diagnosis of multiple myeloma related to bone disease, and also discussed which one is the best.

However, both of the two papers only combined the assessment indexes and just used a monadic analytical method merely. What's

more, the number of selected studies were insufficient and the sample capacity were small. That is to say, their evidence of credibility is poor.

This paper aims to fully evaluate the diagnostic value of ^{18}F-FDG PET or PET-CT in multiple myeloma by proceeding a meta-analysis with larger database and more powerful statistical analysis methods for the published literature, and provide a reference to clinical further.

Materials and Methods

Data sources and search strategies

A comprehensive search of abstracts was conducted to identify articles which focused on the diagnostic accuracy of ^{18}F-FDG PET or PET-CT for detecting the lesions of multiple myeloma. The PUBMED, MEDLINE, EMBASE and web of science databases were searched from January 1990 to June 2015 using the following keywords: ('multiple myeloma' OR 'MM'), ('positron emission tomography' OR 'PET' OR 'FDG' OR 'fluorodeoxyglucose' OR 'PET-CT' OR 'positron emission tomography-computed tomography') AND ('sensitivity' OR 'specificity' OR 'false negative' OR 'false positive' OR 'diagnosis' OR 'detection' OR 'accuracy'). Besides, the retrieved articles' accompanying references were also hand-searched.

Study selection

Two investigators independently reviewed all of the eligible articles according to the inclusion criteria for this study: (a) articles which were open access English scientific literature; (b) articles which used ^{18}F-FDG PET or PET-CT to identify as multiple myeloma; (c) studies which used histopathology or follow-up at least 6 months as the reference standard; (d) articles which presented sufficient datum to construct 2×2 tables; (e) sample capacity was not less than 10; (f) articles which used prospective or retrospective studies. In contrast, articles were excluded if: (a) articles which were unable to get the full-text; (b) articles that were duplicates, conferences, reviews or case reports.

Data extraction

Data abstracted from each eligible study were collected in homemade excel spread sheet included the following: title, authors, year of publication, study design, country, sample capacity, basic characteristics of the patients (gender, age, etc.), reference standard, use stand-alone ^{18}F-FDG PET or combined PET-CT technologies or not, use qualitative or semi-quantitative analysis or not.

The number of true-positive (TP), false-positive (FP), true-negative (TN) and false-negative (FP) results in the detection of multiple myeloma were extracted on a per-patient basis.

Quality assessment

The QUADAS (Quality Assessment of Diagnostic Accuracy Studies) checklist was used to assess independently the methodological quality by the same investigators [12]. This table is an evidence-based quality assessment tool which developed for systematic reviews about the diagnostic accuracy of studies [12].

Statistical methods

The χ2-based Q statistic test (Cochran's Q statistic) was used to test the heterogeneity, and the I2 statistic was calculated to quantify the proportion of total variation [13]. The I2 index was calculated to assess between-study heterogeneity. The values of I2 of 25, 50 and 75% were used as evidence of low, moderate, and high heterogeneity, respectively [14].

If the heterogeneity was low, the fixed-effects model was used to pool the results; otherwise, the random-effects model was used when I2 was more than 50%.

The pooled results included the items: sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR) and 95% confidence interval (95% CI).

The results of the individual studies were displayed in receiver operating characteristic (ROC) space, a weighted symmetric summary ROC curve SROC with 95% CI was computed with the Moses' constant of linear mode, and the value of area under the curve (AUC) and Q^* indexes (the point on the curve at which sensitivity and specificity are equal) as estimated [15].

The meta-regression analysis should be used to explore the sources of heterogeneity across studies, and it will be replaced by subgroup analysis if the sources can't be found. Besides, publication biases were assessed by using funnel plots [16].

Statistical analyses were performed with Meta-Disc (version 1.40) software [17] and STATA (version 12.0) for the eligible studies.

Results

Literature search and selection of studies

A total of 427 studies were searched by the computer-aided according to the key words. After reviewed the abstracts of each one, 48 studies were selected for further consideration. Of these articles, 32 were retrieved for full text review.

Furthermore, 21 articles were excluded because: (a) the data was unable to construct or calculate 2×2 tables (n = 12); (b) the studies were review articles or case reports (n = 6); (c) others (sample size was less than 10 or conferences) (n = 3). The remaining 11 articles, published between 2002 and 2015, met the inclusion criteria [18-28].

Research characteristics and quality assessment

Table 1 lists the principal characteristics of 11 studies comprising a total of sample size 474 patients with diagnosed in multiple myeloma, in which six studies[18-20,22,25-27] used blinding and five studies [19-21,23-28] were open trial. Of the 11 studies, three [20-28] took prospective designs and eight [18,19,22-27] studies used retrospective designs.

In terms of imaging device, three studies [18,19,27] used PET, all the rest [20-26,28] used PET-CT. In addition, 18F-FDG PET imaging was interpreted by a semi-quantitative method in five studies [20,21,23-27], qualitative method in six studies [18,19,21-24,25-28].

The methodological quality of the eligible 11 studies was assessed by the 'QUADAS' quality assessment tool (Table 2). A total of 14 questions were applied for each of the 11 studies. Scores for six of the 11 studies were greater than nine and less than nine for the other five studies, indicating moderate quality.

References	Country	Sex	Mean age	Type of study	Blinding	Type of imaging	FDG dose	Data assessment	TP	FP	FN	TN
		M/F	Yrs									
Durie et al. [18]	America	39/27	63	Retrospective	Yes	PET	222-444 MBq	Qualitative	52	0	0	14
Bredella et al. [19]	America	7-Oct	54	Retrospective	No	PET	3.7 MBq/kg	Qualitative	11	1	2	3
Zamagni et al. [21]	Italy	30/16	55	Prospective	No	PET-CT	NR	SUV2.5	37	2	3	4
Nanni et al. [20]	America	3-Jul	58	Prospective	Yes	PET-CT	5.3 MBq/kg	SUV≥1	6	0	0	4
Kim et al. [22]	Australian	NR	NR	Retrospective	Yes	PET-CT	NR	Qualitative	16	0	1	4
Nanni et al. [23]	America	3-Nov	55	Retrospective	No	PET-CT	5.3 MBq/kg	SUV3.0	6	2	0	6
Elliott et al. [24]	America	16/8	60.8	Retrospective	No	PET-CT	NR	Qualitative	6	2	4	12
Sager et al. [25]	Turkey	27/15	58.5	Retrospective	Yes	PET-CT	5.4 MBq/kg	Qualitative	35	0	5	2
Ho et al. [26]	Hong Kong	32/23	61.2	Retrospective	Yes	PET-CT	NR	SUV2.5	15	0	11	29
Park et al. [27]	Korea	NR	58	Retrospective	Yes	PET	NR	SUV2.5	54	0	5	84
Okasaki et al. [28]	Japan	NR	58.3	Prospective	NR	PET-CT	5MBq/kg	Qualitative	9	5	6	16

Table 1: Characteristics of studies included in the meta-analysis.
M: Man; F: Female; FDG: ^{18}F-Deoxyglucose; NR: Not Reported; TP: True-Positive; FP: False-Positive; FN: False-Negative; TN: True-Negative; PET: Positron Emission Tomography; PET-CT: Positron Emission Tomography-Computer Tomography; SUV: Standardized Uptake Value.

QUADAS criteria														
References	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Durie et al. [18]	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Bredella et al. [19]	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y
Zamagni et al. [21]	U	Y	Y	U	U	Y	Y	N	Y	U	Y	Y	Y	Y
Nanni et al. [20]	U	Y	Y	U	Y	N	Y	N	Y	U	Y	Y	Y	Y
Kim et al. [22]	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	Y	Y	Y	Y
Nanni et al. [23]	Y	Y	Y	U	Y	Y	Y	N	N	U	Y	Y	Y	U
Elliott et al. [24]	Y	Y	N	Y	Y	U	Y	N	N	Y	N	Y	Y	Y
Sager et al. [25]	Y	Y	Y	Y	U	N	Y	Y	Y	U	Y	Y	Y	U
Ho et al. [26]	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	U
Park et al. [27]	Y	Y	Y	U	Y	Y	Y	N	N	Y	Y	Y	Y	Y
Okasaki et al. [28]	U	Y	Y	Y	N	U	Y	N	Y	N	N	Y	Y	U
1. Was the spectrum of patients representative of the patients who will receive the test in practice?														
2. Were the selection criteria clearly described?														

3. Is the reference standard likely to correctly classify the target condition?
4. Is the time period between the reference standard and the index test short enough to be reasonably sure that the target condition did not change between the two tests?
5. Did the whole sample or a random selection of the sample receive verification using a reference standard of diagnosis?
6. Did patients receive the same reference standard regardless of the index test result?
7. Was the reference standard independent of the index test (i.e., the index test did not form part of the reference standard)?
8. Was the execution of the index test described in sufficient detail to permit replication of the test?
9. Was the execution of the reference standard described in sufficient detail to permit its replication?
10. Were the index test results interpreted without knowledge of the results of the reference standard?
11. Were the reference standard results interpreted without knowledge of the results of the index test?
12. Were the same clinical data available when the test results were interpreted as would be available when the test is used in practice?
13. Were uninterpretable/intermediate test results reported?
14. Were withdrawals from the study explained?
N: No; U: Unclear; Y: Yes.

Table 2: QUADAS (appraisal) tool results.

Heterogeneity assessment of studies and ^{18}F-FDG PET/PET-CT performance in the diagnosis of multiple myeloma.

For the 11, 18F-FDG PET or PET-CT studies that we evaluated, the test of homogeneity indicated the present of statistical heterogeneity (Q value for sensitivity = 46.23, P = 0.000, I2 = 78.4%; Q value for specificity = 33.85, P = 0.000, I2 = 70.5%). Thus, it is necessary that meta-regression and subgroup analysis to be carried out for analysis of potential sources.

Consequently, the results of meta-regression analysis showed there were significant differences with blinding (regression coefficient, 3.288; P = 0.006) (Table 3).

The pooled sensitivity and specificity of PET or PET-CT were 0.870 (95% CI, 0.825-0.907) and 0.937 (95% CI, 0.892-0.967), respectively (Figure 1).

Covariates	Regression coefficient	RDOR (95% CI)	P value
Type of study (prospective vs. respective)	-0.294	0.75 (0.06-8.68)	0.7707
Data assessment (qualitative vs. semi-quantitative)	1.017	2.77 (0.38-20.22)	0.2659
Blinding (yes vs. no)	3.288	26.78 (3.52-203.44)	0.0057
Type of imaging (PET vs. PET-CT)	-2.030	0.13 (0.01-1.68)	0.0993

Table 3: Meta-regression analysis for possible sources of heterogeneity between studies of patients with multiple myeloma.
PET: Positron Emission Tomography; PET-CT: PET-Computed Tomography; RDOR: Relative Diagnostic Odds Ratio; CI: Confidence Interval.

The pooled sensitivity and specificity of using PET were 0.94495% CI, 0.887-0.977) and 0.990 (95% CI, 0.947-1.000), respectively (Figure 2).

The pooled sensitivity and specificity for PET-CT were 0.813 (95% CI, 0.743-0.870) and 0.875 (95% CI, 0.787-0.936), respectively (Figure 3). The overall PLR, NLR and DOR were 9.442 (95% CI, 5.849-15.243), 0.194 (95% CI, 0.145-0.260) and 42.405 (95% CI, 22.355-80.437), respectively.

Figure 1 shows the distribution of diagnostic performance in studies with a hierarchical SROC graph, the AUC was 0.9332 and Q^* index estimate was 0.869. The more the curve approaches to the upper left corner, the higher the diagnostic efficacy is.

In subgroup analysis, the pooled sensitivity and specificity of PET or PET-CT for multiple myeloma with blinding were 0.890 (95% CI, 0.838-0.930) and 1.000 (95% CI, 0.973-1.000), respectively.

The pooled sensitivity and specificity of PET or PET-CT for multiple myeloma with non-blinding were 0.821 (95% CI, 0.723-0.896) and 0.744 (95% CI, 0.638-0.877), respectively (Table 4).

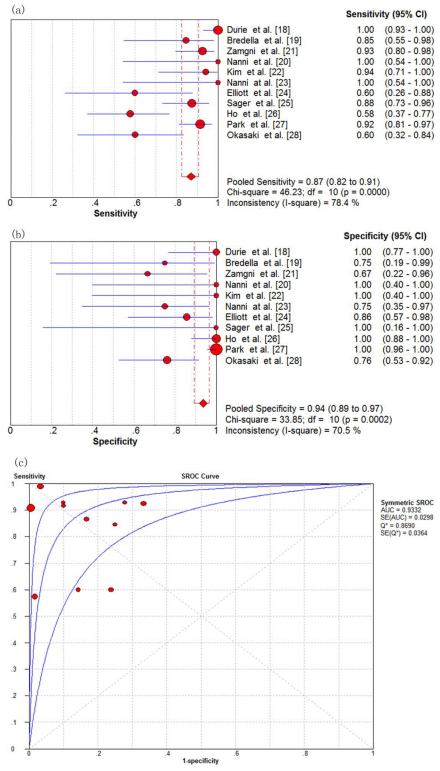

Figure 1: (a) Sensitivities, (b) specificities and (c) summary receiver-operating characteristic (SROC) curves for studies assessing the diagnostic accuracy of PET/PET-CT in patients with multiple myeloma.
PET: Positron Emission Tomography; PET-CT: PET-Computed Tomography; CI: Confidence Intervals.

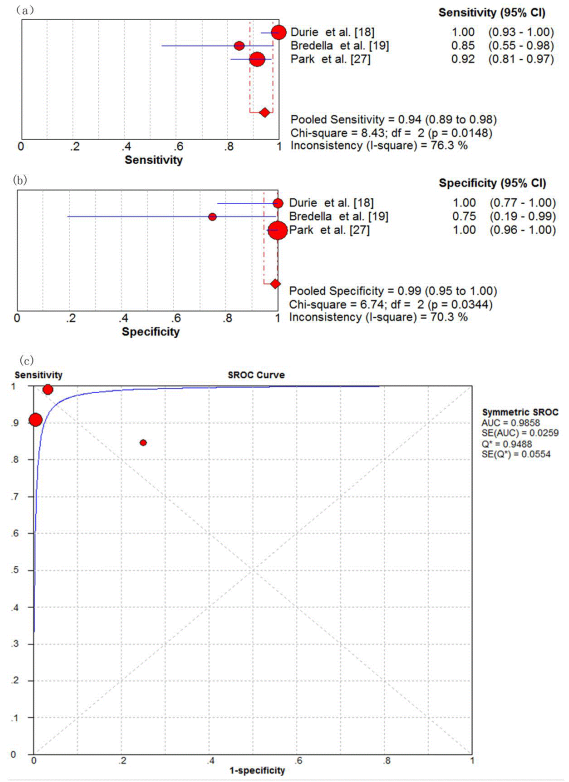

Figure 2: (a) Sensitivities, (b) specificities and (c) summary receiver-operating characteristic (SROC) curves for studies assessing the diagnostic accuracy of PET in patients with multiple myeloma.
PET: Positron Emission Tomography; CI: Confidence Intervals.

Characteristic	Studies, n	Sensitivity % (95% CI)	Specificity % (95% CI)	DOR (95% CI)
Type of study				
Prospective	3	0.852 (0.738-0.930)	0.774 (0.589-0.904)	12.932 (2.655-62.997)
Respective	8	0.874 (0.824-0.915)	0.969 (0.928-0.990)	75.012 (16.999-331.010)
Data assessment				
Qualitative	6	0.878 (0.813-0.926)	0.864 (0.750-0.940)	25.377 (5.313-121.220)
Semi-quantitative	5	0.861 (0.792-0.914)	0.969 (0.924-0.992)	93.999 (18.092-488.390)
Blinding				
Yes	6	0.890 (0.838-0.930)	1.000 (0.973-1.000)	215.46 (50.058-927.400)
No	5	0.821 (0.723-0.896)	0.744 (0.638-0.877)	10.129 (4.078-25.159)
Pooled results	11	0.870 (0.825-0.907)	0.937 (0.892- 0.967)	46.130 (13.496-157.68)

Table 4: Subgroup analysis of the diagnostic performance of 18F-FDG PET/PET-CT on a per-patient.
18F-FDG PET: 18F-Fluorodeoxyglucose Positron Emission Tomography; PET-CT: Positron Emission Tomography-Computed Tomography; CI: Confidence Interval; DOR: Diagnostic Odds Ratio.

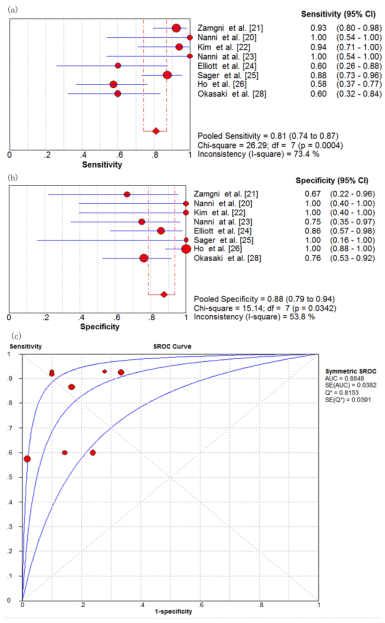

Figure 3: (a) Sensitivities, (b) specificities and (c) summary receiver-operating characteristic (SROC) curves for studies assessing the diagnostic accuracy of PET-CT in patients with multiple myeloma. PET: Positron Emission Tomography; CI: Confidence Intervals.

Publication bias

In this meta-analysis, the Begg's test (z = 2.02, P = 0.043) and Egger's test (t = 1.58, P = 0.149) showed an asymmetric funnel plots, indicating the publication bias may exist (Figure 4).

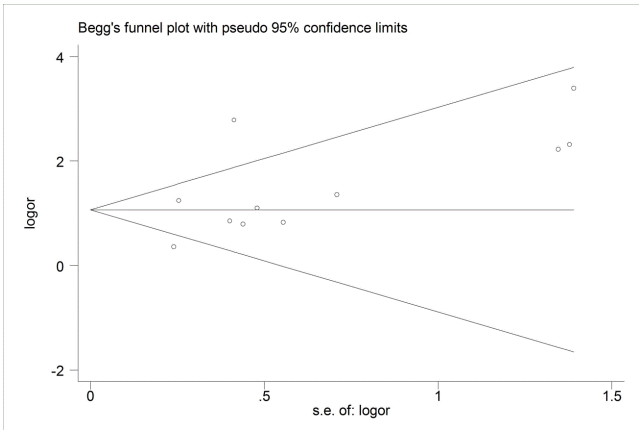

Figure 4: Begg's funnel plots for assessing the publication bias (PEgger = 0.149). OR: Odds Ratio.

Discussion

CT can provide precise anatomic localization for lesions, and can also show more information of bone destruction and soft tissue structures. While PET, using 18F-FDG as a tracer, can show the distribution of glucose in cell of body and detect the early metabolic changes of lesions at the gene molecular level before the anatomical structure became abnormal. Whereas, the greatest disadvantage of ^{18}F-FDG PET is that the anatomical structures display unclearly [29]. While PET-CT, an image fusion technology, combining the advantage of CT and PET, can provide a high resolution imaging. Besides, once PET-CT scanning can obtain whole body images with PET and CT at the same time, and thus can save patients' time and costs. Multiple myeloma cells have a high metabolic characteristic and they absorb glucose more significantly than normal cells [30]. Therefore, the tumor cells can accumulate a large number of ^{18}F-FDG and make the PET images more active than non-tumor cells.

This meta-analysis demonstrated that ^{18}F-FDG PET or PET-CT has superior diagnostic performance for multiple myeloma. Studies basis on patients, there is a big difference between individual studies of the pre-pooled sensitivity is 58-100% and the pre-pooled specificity is 67-100%, respectively. After being analyzed, the pooled sensitivity and specificity of ^{18}F-FDG PET or PET-CT were 87% and 93.7%, respectively. This result indicated that the probability of diagnosing in multiple myeloma patients and excluding non-MM patients for 18F-FDG PET was 87% and 94%, respectively. In addition, this result also shows a 13% of misdiagnosis rate or a false negative rate, which may be concerned with the lower metabolism activity of osseous tissue destroyed tumor cells. Diagnosis ratio rate reflects the strength of association between diagnostic test and the disease itself. The greater its value is, the greater effect of the diagnostic test in differential diagnosis benign and malignant lesions there is, when the value is more than 1. In this study, diagnosis ratio rate is 46.13, indicating that the ^{18}F-FDG PET or PET-CT has stronger ability in diagnosing multiple myeloma than others imaging technique. Additionally, the SROC AUC is 0.933, further supporting the conclusion. Wang et al. [11] reported that the pooled sensitivity and specificity of MRI for multiple myeloma were 88% and 68%, while the PET or PET-CT were 90.6% and 68.9%, respectively. Fonti et al. [31] believed that the PET-CT can detect more focal lesions than MRI, while the MRI has the superiority in detecting diffuse pattern lesions, especially soft tissue lesions.

In this sense, ^{18}F-FDG PET or PET-CT would theoretically reduce the amount of unnecessary invasive procedures in patients with benign lesions. Meanwhile, PET or PET-CT images is capable of guiding clinicians to perform puncturing biopsy in obvious osteodynia and metabolic activity area, and then can minimize the operational error and increase success probability [32].

The results of subgroup analysis showed that the specificity of semi-quantitative analysis was better than that of the qualitative one. This may be associated with the PET-CT used semi-quantitative analysis, because the morphology advantages of CT was ability to distinguish benign between malignant lesions than PET. In terms of identifying lesions, however, Procel et al. [33] believed that the visual interpretations of PET are more sensitive than the semi-quantitative of PET-CT. This conclusion due to the biotechnology factors, which limited the semi-quantitative analysis based on standardized uptake value (SUV). For instance, SUV usually can measure a small area of the region of interest, which may be not suitable for the scattered or diffuse lesions. In the clinical practice, visual sensation can perceive the lesions metabolic uptake while the SUV doesn't meet the diagnostic threshold regarded as negative. As a consequence, the positive rate of using semi-quantitative analysis methods is lower than qualitative analysis.

Besides, the current study also found that the sensitivity and specificity of PET are higher than those of PET-CT, that is to say, the PET can detect more lesions than PET-CT under the same condition. Wang et al. [11] found that the specificity and specificity of PET for multiple myeloma was 0.947, 0.955, respectively, whereas 0.896, 0.538 for PET-CT. This is, perhaps, because the PET just take visual analysis for lesions, as long as the lesions appear higher metabolism than background can be considered to be positive. But the PET-CT can identify the real lesions with the help of CT which can judge by morphology. In fact, PET scan may get more false positivity, on the contrary, the PET-CT can offer a more accurate diagnostic capability.

Two meta-analysis on the diagnostic performance of ^{18}F-FDG PET for multiple myeloma, had published by others [10,11]. In the first article [10], comprising five articles [19,22-24,33] total 87 patients, the pooled results for FDG PET or PET-CT in detection of extramedullary and intramedullary lesions of multiple myeloma were 96.0% and 61.1% in sensitivity, 77.8% and 94.1% in specificity, respectively. In another article [11], selected five articles [18,20,21,25-35] which included 157 patients with confirmed multiple myeloma. Under the same assumptions, that is, pooled results for FDG PET or PET-CT in diagnosis of multiple myeloma, the test yielded sensitivity was 90.6%, and specificity was 68.9%, respectively. In both articles, the authors concluded that ^{18}F-FDG PET or PET-CT is an accurate imaging method for the differential diagnosis of multiple myeloma. However, these previous meta-analysis were flawed due to a number of methodological limitations, which made their encouraging conclusions questionable. Heterogeneity was absented in both of the two papers. Larger database, more sample capacity and used more powerful and scientific statistical analysis methods such as subgroup analysis, mete-regression analysis and publication bias make our study more credibility and convincing than the previous studies.

The quality of our study is limited by heterogeneity and publication bias. In this study, using the QUADAS tool, the methodological quality was found to be moderate. The heterogeneity test indicated presenting heterogeneity among each study. Meanwhile, meta-regression analysis suggested that the blinding may be the source of heterogeneity. In additions, the pooled results of sensitivity and specificity were found better for blinding assessment than non-blinding, which may be due to a more rigorous and more scientific methods of blinding, but the non-blinding method could target exclusion. That is, the result of blinding methods is more reliable than non blinding. Besides, subgroup analysis showed that other characteristics among studies have no significantly influence on the diagnostic performance of FDG-PEF or PET-CT for multiple myeloma.

Additionally, the current study reveals an asymmetric funnel plots, indicating the publication bias may existwhich implied more unpublished negative results articles were needed to offset this condition. There might be several reasons. First, some writers didn't submit to internationally renowned medical journal but to local magazine when they get negative results, which made us unable to get their research results. Second, this study only included English-language literature, however, non-English literatures did not include. Third, there are many research papers which unpublished or privacy in the postgraduates' academic dissertation. Last, some researchers against the interests of supporters, lead to the failure of publishing.

Conclusions

The results of the present meta-analysis suggested that whole-body ^{18}F-FDG PET or PET-CT were imaging methods with high accuracy in differential diagnosis of multiple myeloma patients.

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