FDG PET or PET/CT for Detecting Intramedullary and Extramedullary Lesions in Multiple Myeloma

A Systematic Review and Meta-analysis

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Aim: The purpose of the current study was to conduct a systematic review and meta-analysis of the published literature to evaluate the diagnostic accuracy of FDG PET or PET/CT for intramedullary and extramedullary lesions in multiple myeloma.

Methods: The authors conducted a systematic MEDLINE search of published articles. Two reviewers independently assessed the methodological quality of each study. We estimated pooled sensitivity, specificity, positive and negative likelihood ratios (LR+ and LR−), and summary receiver operating characteristic curves in the detection of intramedullary and extramedullary lesions in multiple myeloma.

Results: Fourteen studies with a total of 395 patients met the inclusion criteria. The pooled estimates of sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of FDG PET or PET/CT for the detection of extramedullary lesions in multiple myeloma were 96.0% [95% confidence interval (CI), 79.6%–99.9%], 77.8% (95% CI, 40.0%–97.2%), 3.28 (95% CI, 1.29–8.32), and 0.12 (95% CI, 0.03–0.42), respectively. The pooled estimates of sensitivity, specificity, LR+, and LR− of FDG PET or PET/CT for the detection of intramedullary lesions in multiple myeloma were 61.1% (95% CI, 43.5%–76.9%), 94.1% (95% CI, 71.3%–99.9%), 5.73 (95% CI, 1.53–21.40), and 0.43 (95% CI, 0.28–0.65), respectively.

Conclusions: Whole-body FDG PET or PET/CT is a valuable imaging tool for the assessment of patients with multiple myeloma, especially for the appraisal of extramedullary involvement.

Key Words: multiple myeloma, FDG PET, PET/CT, systematic review, meta-analysis

(*Clin Nucl Med* 2012;37: 833–837)

Multiple myeloma (MM) accounts for approximately 10% of all hematological cancers with a peak incidence during the seventh decade.[1] A proportion of patients with plasma cell myeloma have a different clinical presentation, such as plasmacytoma. Plasmacytoma can be confined to bone (solitary plasmacytoma of bone) or may occur in extramedullary sites (extramedullary plasmacytoma).[2–5] Approximately 5% to 10% of patients have a solitary bone plasmacytoma.[6] Extramedullary plasmacytoma is even less common than solitary bone plasmacytoma. Extramedullary plasmacytoma represents approximately 3% of all plasma cell neoplasms.[2,6,7] The clinical manifestation of MM results from increasing tumor burden in bones, bone marrow, and extraosseous sites, as well as production of excess monoclonal immunoglobulins. The diagnosis of MM is based on specific criteria that include paraproteinemia, plasma cell infiltration of bone marrow, and osteolytic bone destruction. The presence of extramedullary involvement and the exact number of lesions in patients with MM have a major impact on prognosis and clinical management.[2,8,9] The new Durie/Salmon PLUS staging system[9] is a refinement of the original 1975 Durie/Salmon system,[10] and advanced imaging studies have been added to the new staging systems to provide more precise staging.[9]

PET with ^{18}F-FDG is a whole-body metabolic imaging technique that is capable of detecting a wide range of tumors that exhibit higher accumulation of FDG than surrounding normal tissues. It has been reported that FDG PET can detect and distinguish between intramedullary and extramedullary lesions[11] and has been found useful for improving staging accuracy.[8]

Despite the increasing number of publications concerning FDG PET in the assessment of MM, patient population, study design, and results vary widely among studies, making it difficult to accurately assess the diagnostic value of FDG PET and PET/CT. In addition, differences between FDG PET and PET/CT in their ability to accurately detect intramedullary lesions and extramedullary involvement have not been clearly delineated. The purpose of the present study was to evaluate the diagnostic accuracy of FDG PET in MM by conducting a meta-analysis of the published literature.

METHODS

Literature Search

A comprehensive computer search for relevant articles was conducted using PubMed/MEDLINE and EBM Review search engines. The search included combinations of the following terms: (1) *PET, positron emission tomography*; (2) *FDG, fluorodeoxyglucose*; (3) *multiple myeloma*. Searches were limited to studies on human subjects. Although no language restrictions were used initially, the full-text review and final analysis were limited to articles published in English. Additional studies were manually searched using the references cited in the retrieved articles.

Data Selection

Studies were eligible for inclusion in the analyses based on the following criteria: (1) they evaluated MM for staging and/or recurrence, (2) diagnosis was performed by ^{18}F-FDG PET or ^{18}F-FDG PET/CT, and (3) 2×2 tables could be derived from the provided data. Abstracts presented at congresses, unpublished data, case reports, meta-analyses, reviews, editorials, and comments were excluded. To avoid missing potentially useful articles for the present meta-analysis, the abstracts were double-checked by at least 2 authors to determine whether the reports fitted the inclusion criteria for this study.

Received for publication December 19, 2011; and revision accepted March 13, 2012.
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Conflicts of interest and sources of funding: This study was supported by grants (DMR-100-076 and DMR-100-110) from China Medical University Hospital and the Taiwan Department of Health Clinical Trial and Research Center and for Excellence (DOH101-TD-B-111-004) as well as the Taiwan Department of Health Cancer Research Center for Excellence (DOH101-TD-C-111-005). The authors declare that they have no conflict of interest.
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ISSN: 0363-9762/12/3709-0833

Quality Assessment and Data Extraction

Two reviewers independently assessed the methodological quality of the eligible studies. The criteria list recommended by the Cochrane Methods Working Group on Systematic Review of Screening and Diagnostic Tests was used modified by Chen et al.[12] Some items on the list were modified for this specific review. The complete criteria list used is presented in Table 1. Internal validity criteria (IV) were scored as "positive" (adequate methods) or "negative" (inadequate methods, potential bias, or insufficient information had been provided on a specific item). External validity criteria (EV) were assessed to evaluate generalizability. Standard performance of FDG PET or PET/CT was scored positive when the type of PET or PET/CT camera, the dose of FDG, the time between injection and scanning, and the method of reconstruction were described. The criteria for external validity were scored positive if sufficient information was provided to judge the generalizability of findings. Disagreements were resolved by consensus. Quality scores were expressed as a percentage of the maximum score. Subtotals were calculated for internal (maximum, 6) and external (maximum, 6) validity separately.

For each report, we recorded the number of true-positive, false-positive, true-negative, and false-negative findings for ^{18}F-FDG PET or PET/CT in detecting intramedullary or extramedullary lesions of MM.

Statistical Analysis

Data regarding the diagnostic performance of FDG PET or PET/CT in the detection of intramedullary or extramedullary lesions of MM were combined quantitatively across eligible studies. We gathered PET and PET/CT data to estimate the pooled sensitivities, specificities, LR+ (positive likelihood ratio), and LR− (negative likelihood ratio) in intramedullary and extramedullary lesions of MM, respectively. The I^2 index and χ^2 test would measure the heterogeneity of the included study. The I^2 would be less than 53% and P values of χ^2 test were not significant. We used the fixed-effect model to combine the pooled estimates. The steps were as follows. First, we combined sensitivities and specificities independently across studies. Second, we estimated the weighted LR+ and LR− across studies using the fixed-effects model. For diagnostic tests, the correlations between sensitivity and specificity did not exist. We showed the summary receiver operating characteristic (SROC) curve, which was the symmetrical by Mantel-Haenszel method. The SROC curve shows the trade-off between sensitivity and specificity across the included studies.[13]

Likelihood ratios are also metrics that combine sensitivity and specificity in the calculations. The ratio of sensitivity over 1 − specificity is defined as LR+. The ratio of 1 − sensitivity over specificity is defined as LR−. The discrimination ability is better with higher LR+ and lower LR−. In previous articles, a clinically useful test was defined when an LR+ was greater than 5.0 and LR− was less than 0.2.[14] Analyses were conducted using the free software Meta-DiSc (version 1.4).[15]

TABLE 1. Criteria List Used to Assess the Methodological Quality of the Studies

Criteria of Validity	Positive Score
Internal validity	
Valid reference test	Pathology from biopsy or surgery
Blind measurement of FDG PET without knowledge of reference test	
Blind measurement of reference test without knowledge of FDG PET	
Avoidance of verification bias	Assessment by reference test independent of FDG PET results
FDG PET interpreted independently of all clinical information	Mentioned in publication
Prospective study	Mentioned in publication
External validity	
Spectrum of disease	All stage of disease
Demographic information	Age and sex information given
Inclusion criteria	Mentioned in publication
Exclusion criteria	Mentioned in publication
Avoidance of selection bias	Consecutive series of patients
Standard execution of FDG PET	Type of camera, dose FDG, time interval, reconstruction

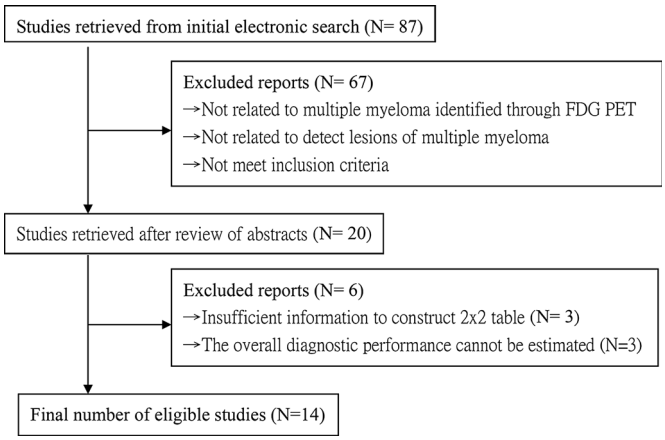

FIGURE 1. Flowchart of selection processes for eligible studies.

RESULTS

Literature Research

A total of 87 studies that investigated MM using FDG PET or PET/CT were found initially. After reviewing the titles and abstracts, 67 studies were excluded based on the criteria listed in the Data Selection subsection of the Materials and Methods.

We screened the full text of 20 articles. Three studies were excluded owing to insufficient information to construct a 2 × 2 table.[16–18] Three studies were excluded because the results of the diagnostic performance of FDG PET or PET/CT could not be estimated.[19–21] A total of 395 patients from fourteen eligible studies[8,11,22–33] were analyzed in the systematic review (Fig. 1).

Study Characteristics

The characteristics of the eligible studies are summarized in Table 2. Five of the studies were prospective,[23,26,27,29,31] and the others were retrospective. Ten of the studies that provided results of diagnostic performance were patient based and the others were lesion based.[24,25,29,30] Six of the studies were performed by FDG PET scan,[8,11,22–24,30] 7 studies were performed by FDG PET/CT scan, and the other was performed by FDG PET or PET/CT scan. Three of the studies provided results of the diagnostic performance for intramedullary lesions,[22,31,33] 4 studies showed results of the diagnostic performance for extramedullary lesions,[11,28,29,32] and the others described results of the diagnostic performance for both intramedullary and extramedullary lesions.

Quality Assessment

Methodological quality was assessed by 12 items for each of the 14 selected studies. The scores for internal and external validity of the 14 selected studies are presented in Table 3.

TABLE 2. Clinical Characteristics for Selected Studies

Author	Year	Design	No. Patients	Sex (M/F)	Age, y	PET or PET/CT	Reference Test	Type
Durie et al[8]	2002	Retrospective	66	39/27	Mean, 63 (range, 43–82)	PET	PA or FU	Intra + Extra
Jadvar et al[22]	2002	Retrospective	6	5/1	Range, 38–62	PET (Siemens, Knoxville, Tenn)	FU	Intra
Schirrmeister et al[23]	2002	Prospective	43	26/17	Median, 57 (range, 30–75)	PET (Siemens, CTI, Knoxville, Tenn)	FU	Intra + Extra
Hung et al[24]	2005	Retrospective	12	4/8	Mean, 49 (range, 30–74)	PET (Siemens)	FU	Intra + Extra
Bredella et al[11]	2005	Retrospective	13	10/3	Mean, 54 (range, 41–79)	PET (Siemens, CTI)	PA or FU	Extra alone
Breyer et al[25]	2006	Retrospective	16	12/4	Mean, 58 (range, 30–69)	PET/CT (Siemens or Philips [Cleveland, Ohio])	PA or FU	Intra + Extra
Zamagni et al[26]	2007	Prospective	46	30/16	Median, 55 (range, 42–65)	PET/CT	FU	Intra + Extra
Nanni et al[27]	2007	Prospective	10	7/3	Mean, 58	PET/CT (GE Discovery, Milwaukee, Wis)	FU	Intra + Extra
Nanni et al[28]	2008	Retrospective	14	11/3	Mean, 55 (range, 31–66)	PET/CT (GE Discovery)	FU	Extra (Solitary plasmacytoma of bone)
Salaun et al[29]	2008	Prospective	24	17/7	Median, 60 (range, 35–78)	PET/CT	PA or FU	Extra
Hur et al[30]	2008	Retrospective	67	15/7	Mean, 59 (range, 48–77)	PET (Philips)	PA or FU	Intra + Extra
Shortt et al[31]	2009	Prospective	24	11/13	Mean, 67.1 (range, 44–83)	PET/CT (Siemens)	PA	Intra
Kim et al[32]	2009	Retrospective	17	—	—	PET (UGM, Philadelphia, PA) or PET/CT (GE)	PA	Extra alone
Elliott et al[33]	2011	Retrospective	37	19/18	Mean, 60.8 (range, 43.9–78.9)	PET/CT (GE Discovery)	FU	Intra

Extra indicates extramedullary; FU, follow-up; Intra, intramedullary; PA, pathology.

Nine studies had a valid reference test (IV1). The readers were blinded to the results of the reference standard in 5 of the selected studies (IV2). All studies had verification bias (IV4) because patients were selected for assessment by the reference test but this not performed independently of FDG PET results. Five studies were prospective (IV6), and in the other 9 studies, patients were enrolled in the studies consecutively (EV5).

In 13 of the 14 studies, all staging of disease was included (EV1). In 7 studies, the inclusion criteria (EV3) were described, and in 3 studies, the exclusion criteria (EV4) were described. The type of camera, the FDG dosage, the uptake period, the time interval, and reconstruction were reported in 11 of the studies (EV6). The total score for the combined internal and external validity, expressed as a fraction of the maximum score, ranged from 33% to 75%.

Performance

The diagnostic performance between PET and PET/CT for MM was not significantly different ($P = 0.7458$) in meta-regression. The pooled estimated results of FDG PET or PET/CT in the detection of intramedullary and extramedullary lesions in MM were patient based. The pooled estimates of sensitivity, specificity, LR+, and LR− of FDG PET or PET/CT in the detection of extramedullary lesions in MM were 96.0% [95% confidence interval (CI), 79.6%–99.9%], 77.8% (95% CI, 40.0%–97.2%), 3.28 (95% CI, 1.29–8.32), and 0.12

TABLE 3. Quality Assessment of the Selected Studies

		IV						EV								
Study	Year	IV1	IV2	IV3	IV4	IV5	IV6	EV1	EV2	EV3	EV4	EV5	EV6	Total IV Score	Total EV Score	% of Maximum Score
Durie et al[8]	2002	+	−	+	−	−	−	+	+	−	−	+	+	2	4	50
Jadvar et al[22]	2002	−	−	−	−	−	−	+	+	−	−	+	+	0	4	33
Schirrmeister et al[23]	2002	−	+	+	−	+	+	+	+	+	−	+	+	4	5	75
Hung et al[24]	2005	+	+	−	−	+	−	+	+	−	−	+	+	3	4	58
Bredella et al[11]	2005	+	−	−	−	−	−	+	+	−	−	+	+	1	4	42
Breyer et al[25]	2006	−	−	−	−	−	−	+	+	+	−	+	+	0	5	42
Zamagni et al[26]	2007	−	+	−	−	+	+	+	+	+	−	+	−	3	4	58
Nanni et al[27]	2007	−	−	−	−	−	+	−	+	−	−	+	+	1	3	33
Nanni et al[28]	2008	+	−	−	−	−	−	+	+	+	−	+	+	1	5	50
Salaun et al[29]	2008	+	+	−	−	−	+	+	+	−	−	+	−	3	3	50
Hur et al[30]	2008	+	−	−	−	+	−	+	+	+	+	+	+	2	6	67
Shortt et al[31]	2009	+	−	−	−	−	+	+	+	+	+	+	+	2	6	67
Kim et al[32]	2009	+	−	−	−	−	−	+	−	−	−	+	+	1	3	33
Elliott et al[33]	2011	+	+	−	−	+	−	+	+	+	+	+	−	3	5	67

EV1 to EV6 indicates 6 criteria for external validity (EV; Table 1); IV1 to IV6, 6 criteria for internal validity (IV; Table 1).

(95% CI, 0.03–0.42), respectively. The SROC curves for extramedullary lesions in MM are presented in Figure 2. The Q* index presents maximum joint sensitivity and specificity, calculated as a global measure of diagnostic accuracy. The Q* index was 0.84 for FDG PET or PET/CT in extramedullary lesions in MM.

The pooled estimates of sensitivity, specificity, LR+, and LR− of FDG PET (PET/CT) in the detection of intramedullary lesions in MM were 61.1% (95% CI, 43.5%–76.9%), 94.1% (95% CI, 71.3%–99.9%), 5.73 (95% CI, 1.53–21.40), and 0.43 (95% CI, 0.28–0.65), respectively. The SROC curves for intramedullary lesions in MM are presented in Figure 3. The Q* index was 0.79 for FDG PET or PET/CT for intramedullary lesions in MM.

The diagnostic performances in the 4 studies that analyzed lesion-based data could not be assessed by meta-analysis because the numbers of true-negative results were not provided. In the other 4 reports, the numbers of true-positive, false-positive, true-negative, and false-negative findings between FDG PET and PET/CT for detection of intramedullary and extramedullary lesions could not be clearly separated into individual 2 × 2 tables. Therefore, the data from these studies could not be pooled into individual results for intramedullary or extramedullary lesions.

DISCUSSION

The use of FDG PET or PET/CT in the assessment of MM continues to be a topic of considerable debate in the literature. However, to date, FDG PET and PET/CT have not been compared with regard to diagnostic accuracy of MM. In our meta-analysis study, the differences in diagnostic performances between FDG PET and PET/CT for MM were not significantly different ($P = 0.7458$). This result indicates that neither FDG PET nor PET/CT was a primary factor in the heterogeneity found among studies.

The pooled estimates of sensitivity, specificity, LR+, and LR− of FDG PET or PET/CT in the detection of extramedullary lesions of MM were 96.0% (95% CI, 79.6%–99.9%), 77.8% (95% CI, 40.0%–97.2%), 3.28 (95% CI, 1.29–8.32), and 0.12 (95% CI, 0.03–0.42), respectively.

The pooled estimates of sensitivity, specificity, LR+, and LR− of FDG PET (PET/CT) in the detection of intramedullary

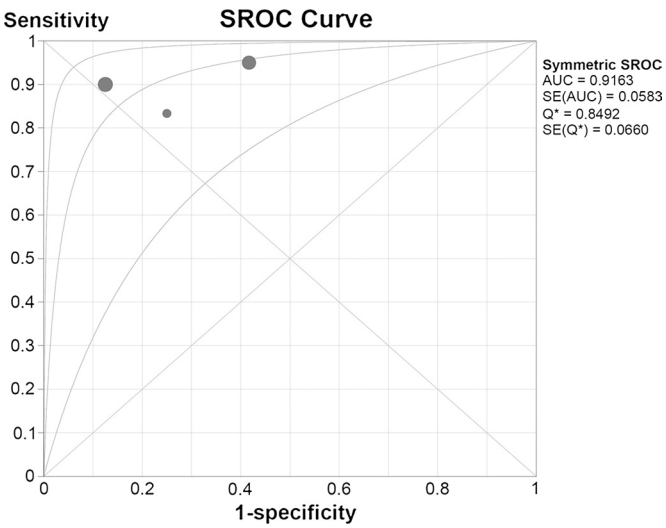

FIGURE 2. Summary ROC curves of diagnostic performance of ^{18}F-FDG PET or PET/CT in the assessment of extramedullary lesions of MM. The 3 data points are from the results of these studies of Bredella et al,[11] Nanni et al,[28] and Kim et al.[32] The area under the symmetric SROC curve is 0.9163, and the Q* index (overall diagnostic accuracy) is 0.8492.

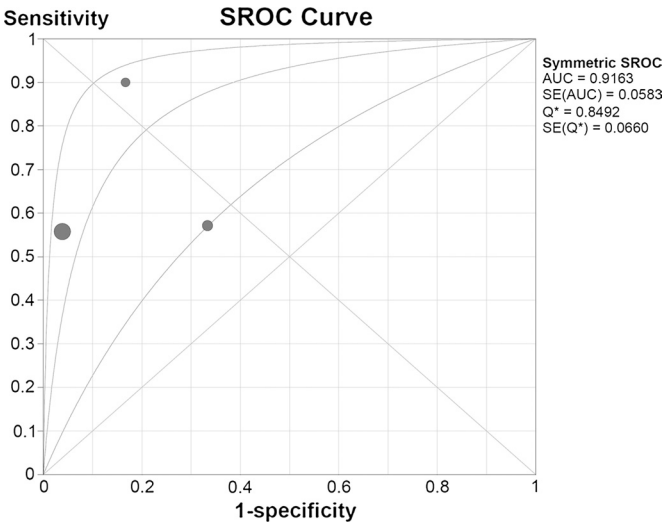

FIGURE 3. Summary ROC curves of diagnostic performance of ^{18}F-FDG PET or PET/CT in the assessment of intramedullary lesions of MM. The 3 data points are from the results from these studies of Bredella et al,[11] Jadvar et al,[22] and Elliott et al.[33] The area under the symmetric SROC curve is 0.8602, and the Q* index (overall diagnostic accuracy) is 0.7910.

lesions of MM were 61.1% (95% CI, 43.5%–76.9%), 94.1% (95% CI, 71.3%–99.9%), 5.73 (95% CI, 1.53–21.40), and 0.43 (95% CI, 0.28–0.65), respectively. A high LR+ (>5.0) is clinically useful for determining a change that indicates a person has a disease. For patients who had negative results, LR− of less than 0.2 can rule out or decrease the probability of disease.[14] In addition, there was significantly higher sensitivity of FDG PET or PET/CT for the detection of extramedullary than for intramedullary lesions (95% CI, 79.6%–99.9% vs 43.5%–76.9%). The results of our meta-analysis study suggest that both FDG PET and PET/CT can each provide a good diagnostic performance in the evaluation of MM, especially for extramedullary involvement.

In 4 studies, the diagnostic performances of FDG PET and PET/CT for intramedullary lesions and extramedullary involvement could not be clearly separated into individual 2 × 2 tables. The pooled estimates of sensitivity, specificity, LR+, and LR− of FDG PET or PET/CT for the detection of a mixture of intramedullary and extramedullary lesions in MM were 86.7% (95% CI, 79.6%–92.1%), 96.4% (95% CI, 81.7%–99.9%), 10.8 (95% CI, 3.36–35.24), and 0.09 (95% CI, 0.01–0.73), respectively. In general, the results indicated that FDG PET and PET/CT had a good diagnostic accuracy for the detection of MM.

Six studies compared the diagnostic performances of FDG PET with those of PET/CT with MRI for the detection of MM. Salaun et al[29] reported that the performance of FDG PET/CT seemed to be equivalent to that of MRI in spine and pelvic bone. However, MRI missed 18 lesions located outside the areas covered by MRI. They suggested that FDG PET/CT provides additional information for the assessment of MM in areas not covered by MRI.

Fonti et al[16] showed that FDG PET/CT visualized more focal lesions than MRI ($P < 0.005$). MRI performed better than FDG PET/CT in the detection of a diffuse pattern. Breyer et al[25] showed that FDG PET/CT was superior to MRI in 7 of 16 patients, and that MRI was superior to FDG PET/CT in 4 of 16 patients, of whom 4 had diffuse bone marrow involvement. Shortt et al[31] found that whole body MRI had a higher sensitivity (68% vs 59%) and specificity (83% vs 75%) than those of FDG PET/CT for the assessment of MM. Hur et al[30] demonstrated that MRI had a higher detection

rate of bone lesions (92% vs 80%) than that of FDG PET. Zamagni et al[26] showed MRI was superior to FDG PET/CT in 14 of 46 patients, of whom 10 had a diffuse pattern and 4 had a focal pattern of bone marrow involvement on MRI, which was in agreement with the findings of Shortt et al[31] and Hur et al.[30] These results indicated that FDG PET or PET/CT can contribute to an accurate whole-body evaluation in patients with MM, whereas MRI is better suited to the evaluation of bone marrow involvement.

There were some potential limitations in this study. First, the clinical heterogeneity may affect the generalizability of the results. Second, it was not possible to detect precisely all lesions in patients with MM (the number of true-negatives was not available), and therefore, the pooled meta-analysis for studies with lesion-based data could not be calculated. Third, 4 studies had results comprising a mixture of intramedullary and extramedullary lesions. Thus, we could not determine the number of true-positive, false-positive, true-negative, and false-negative findings based on the type of lesion, that is, intramedullary or extramedullary. The data could therefore not be pooled into individual intramedullary or extramedullary results. Fourth, pathology findings were available for some lesions, whereas results for other lesions depended on the clinical follow-up, which may have involved a variety of imaging modalities and clinical examinations. Finally, 5 studies[11,22,25,27,32] have the total score for the combined internal and external validity less than 50%. In our current meta-analysis, the *P* value of heterogeneity test in the detection of extramedullary or intramedullary lesions was larger than 0.1 and the number of patients conducted into the individual extramedullary and intramedullary group was not large. If we excluded the studies, which have the total score for the combined internal and external validity less than 50%, only 1 study[28] kept in the detection of extramedullary lesions and 2 studies[31,33] kept in the detection of intramedullary lesions. The outputs were not very different from meta-analysis results. Therefore, we did not present the data after excluding these 5 studies, which have the total score for the combined internal and external validity less than 50%.

CONCLUSIONS

The results of this systematic review and meta-analysis suggest that whole-body FDG PET and PET/CT are both valuable imaging tools for the assessment of patients with MM, especially for the appraisal of extramedullary involvement. The use of FDG PET (PET/CT) with MRI provides complementary information for evaluation of bone marrow involvement.

REFERENCES

1. Landis SH, Murray T, Bolden S, et al. Cancer statistics, 1998. *CA Cancer J Clin*. 1998;48:6–29.
2. Dimopoulos MA, Kiamouris C, Moulopoulos LA. Solitary plasmacytoma of bone and extramedullary plasmacytoma. *Hematol Oncol Clin North Am*. 1999;13:1249–1257.
3. Moulopoulos LA, Dimopoulos MA, Weber D, et al. Magnetic resonance imaging in the staging of solitary plasmacytoma of bone. *J Clin Oncol*. 1993;11:1311–1315.
4. Rajkumar SV, Dispenzieri A, Kyle RA. Monoclonal gammopathy of undetermined significance, Waldenström macroglobulinemia, AL amyloidosis, and related plasma cell disorders: diagnosis and treatment. *Mayo Clin Proc*. 2006;81:693–703.
5. Wilder RB, Ha CS, Cox JD, et al. Persistence of myeloma protein for more than one year after radiotherapy is an adverse prognostic factor in solitary plasmacytoma of bone. *Cancer*. 2002;94:1532–1537.
6. Knowling MA, Harwood AR, Bersagel DE. Comparison of extramedullary plasmacytoma with solitary and multiple plasma cell tumors of bone. *J Clin Oncol*. 1983;1:255–262.
7. Shih LY, Dunn P, Leung WM, et al. Localised plasmacytomas in Taiwan: comparison between extramedullary plasmacytoma and solitary plasmacytoma of bone. *Br J Cancer*. 1995;71:128–133.
8. Durie BG, Waxman AD, D'Agnolo A, et al. Whole-body (18)F-FDG PET identifies high risk myeloma. *J Nucl Med*. 2002;43:1457–1463.
9. Durie BG, Kyle RA, Belch A, et al. Myeloma management guidelines: a consensus report from the Scientific Advisors of the International Myeloma Foundation. *Hematol J*. 2003;4:379–398.
10. Durie BG, Salmon SE. A clinical staging system for multiple myeloma. Correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. *Cancer*. 1975;36:842–854.
11. Bredella MA, Steinbach L, Caputo G, et al. Value of FDG PET in the assessment of patients with multiple myeloma. *AJR Am J Roentgenol*. 2005;184:1199–1204.
12. Chen YK, Yeh CL, Tsui CC, et al. ^{18}F FDG PET for evaluation of bone marrow involvement in non–Hodgkin lymphoma: a meta-analysis. *Clin Nucl Med*. 2011;36:553–559.
13. Moses LE, Shapiro D, Littenberg B. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations. *Stat Med*. 1993;12:1293–1316.
14. Kang S, Kim SK, Chung DC, et al. Diagnostic value of (18)F-FDG PET for evaluation of para-aortic nodal metastasis in patients with cervical carcinoma: a meta-analysis. *J Nucl Med*. 2010;51:360–367.
15. Zamora J, Abraira V, Muriel A, et al. Meta-DiSc: a software for meta-analysis of test accuracy data. *BMC Med Res Methodol*. 2006;6:31.
16. Fonti R, Salvatore B, Quarantelli M, et al. ^{18}F-FDG PET/CT, ^{99m}Tc-MIBI, and MRI in evaluation of patients with multiple myeloma. *J Nucl Med*. 2008;49:195–200.
17. Castellani M, Carletto M, Baldini L, et al. The prognostic value of F-18 fluorodeoxyglucose bone marrow uptake in patients with recent diagnosis of multiple myeloma: a comparative study with Tc-99m sestamibi. *Clin Nucl Med*. 2010;35:1–5.
18. Mileshkin L, Blum R, Seymour JF, et al. A comparison of fluorine-18 fluorodeoxyglucose PET and technetium-99m sestamibi in assessing patients with multiple myeloma. *Eur J Haematol*. 2004;72:32–37.
19. Hur J, Yoon CS, Ryu YH, et al. Efficacy of multidetector row computed tomography of the spine in patients with multiple myeloma: comparison with magnetic resonance imaging and fluorodeoxyglucose—positron emission tomography. *J Comput Assist Tomogr*. 2007;31:342–347.
20. Adam Z, Bolcak K, Stanicek J, et al. Fluorodeoxyglucose positron emission tomography in multiple myeloma, solitary plasmocytoma and monoclonal gammapathy of unknown significance. *Neoplasma*. 2007;54:536–540.
21. Schirrmeister H, Buck AK, Bergmann L, et al. Positron emission tomography (PET) for staging of solitary plasmacytoma. *Cancer Biother Radiopharm*. 2003;18:841–845.
22. Jadvar H, Conti PS. Diagnostic utility of FDG PET in multiple myeloma. *Skeletal Radiol*. 2002;31:690–694.
23. Schirrmeister H, Bommer M, Buck AK, et al. Initial results in the assessment of multiple myeloma using ^{18}F-FDG PET. *Eur J Nucl Med Mol Imaging*. 2002;29:361–366.
24. Hung GU, Tsai CC, Tsai SC, et al. Comparison of Tc-99m sestamibi and F-18 FDG-PET in the assessment of multiple myeloma. *Anticancer Res*. 2005;25:4737–4741.
25. Breyer RJ 3rd, Mulligan ME, Smith SE, et al. Comparison of imaging with FDG PET/CT with other imaging modalities in myeloma. *Skeletal Radiol*. 2006;35:632–640.
26. Zamagni E, Nanni C, Patriarca F, et al. A prospective comparison of ^{18}F-fluorodeoxyglucose positron emission tomography—computed tomography, magnetic resonance imaging and whole-body planar radiographs in the assessment of bone disease in newly diagnosed multiple myeloma. *Haematologica*. 2007;92:50–55.
27. Nanni C, Zamagni E, Cavo M, et al. ^{11}C-choline vs. ^{18}F-FDG PET/CT in assessing bone involvement in patients with multiple myeloma. *World J Surg Oncol*. 2007;20:68.
28. Nanni C, Rubello D, Zamagni E, et al. ^{18}F-FDG PET/CT in myeloma with presumed solitary plasmocytoma of bone. *In Vivo*. 2008;22:513–517.
29. Salaun PY, Gastinne T, Frampas E, et al. FDG–positron-emission tomography for staging and therapeutic assessment in patients with plasmacytoma. *Haematologica*. 2008;93:1269–1271.
30. Hur J, Yoon CS, Ryu YH, et al. Comparative study of fluorodeoxyglucose positron emission tomography and magnetic resonance imaging for the detection of spinal bone marrow infiltration in untreated patients with multiple myeloma. *Acta Radiol*. 2008;49:427–435.
31. Shortt CP, Gleeson TG, Breen KA, et al. Whole-Body MRI versus PET in assessment of multiple myeloma disease activity. *AJR Am J Roentgenol*. 2009;192:980–986.
32. Kim PJ, Hicks RJ, Wirth A, et al. Impact of ^{18}F-fluorodeoxyglucose positron emission tomography before and after definitive radiation therapy in patients with apparently solitary plasmacytoma. *Int J Radiat Oncol Biol Phys*. 2009;74:740–746.
33. Elliott BM, Peti S, Osman K, et al. Combining FDG-PET/CT with laboratory data yields superior results for prediction of relapse in multiple myeloma. *Eur J Haematol*. 2011;86:289–298.