A prospective comparison of 18F-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

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ABSTRACT

Background and Objectives

Bone lesions in multiple myeloma (MM) have been traditionally detected by whole body X-ray (WBXR) survey although magnetic resonance imaging (MRI) has become the gold standard for detecting MM involvement of the spine and pelvis. The aim of this study was to compare a new technique, positron emission tomography (PET) with 18F-fluorodeoxyglucose (FDG) integrated with computed tomography (18F-FDG PET-CT), with MRI and WBXR for baseline assessment of bone disease in MM.

Design and Methods

We prospectively compared 18F-FDG PET-CT, MRI of the spine-pelvis and WBXR for baseline assessment of bone disease in a series of 46 patients with newly diagnosed MM. In 23 patients who received up front autologous transplantation, we also compared post-treatment PET-CT scans with MR images of the spine and pelvis.

Results

Overall, PET-CT was superior to planar radiographs in 46% of patients, including 19% with negative WBXR. In 30% of patients, PET-CT scans of the spine and pelvis failed to show abnormal findings in areas in which MRI revealed an abnormal pattern of bone marrow involvement, more frequently of diffuse type. In contrast, in 35% of patients PET-CT enabled the detection of myelomatous lesions in areas which were out of the field of view of MRI. By combining MRI of the spine-pelvis and 18F-FDG PET-CT, the ability to detect sites of active MM, both medullary and extramedullary, was as high as 92%. Following transplantation, 15 patients had negative PET-CT scans (including 13 with a very good partial response or at least near complete response), but only 8 had normal MRI.

Interpretation and Conclusions

MRI of the spine and pelvis still remains the gold standard imaging technique for the detection of bone marrow involvement in MM. 18F-FDG PET-CT provides additional and valuable information for the assessment of myeloma bone disease in areas not covered by MRI.

Key words: 18F-fluorodeoxyglucose positron emission tomography-computed tomography, magnetic resonance imaging, whole-body planar radiographs, bone disease, multiple myeloma.

Multiple myeloma (MM) is a malignant plasma cell disorder which characteristically involves the skeleton as the result of a cytokine/chemokine-mediated imbalance between increased osteoclast activity and reduced osteoblast function. Clinically, patients suffer from bone pain due to osteoporosis and/or lytic bone lesions, are at increased risk of pathological fractures and may develop neurological complications or hypercalcemia.[1-5] For almost four decades, bone lesions in MM have traditionally been detected by means of whole body X-ray (WBXR) survey.[6] However, alternative techniques have been recently proposed, including magnetic resonance imaging (MRI),[7,8] bone scintigraphy with technetium-99m (99mTc) sestamibi[9] and positron emission tomography (PET) with the positron-emitting radionuclide 18F-fluorodeoxyglucose (18F-FDG).[10,11] 18F-FDG PET is a newer, non-invasive, total body imaging method which has been widely used to detect malignant cells and monitor treatment response in patients with solid tumors and lymphomas.[10,11] Preliminary observations suggest that FDG PET may also be useful in MM for detecting both medullary and extramedullary disease.[12-15] However, whether this newer imaging method may replace standard techniques in the staging work-up of newly diagnosed MM is still an unresolved issue which needs to be carefully addressed in the context of well-designed studies. The aim of the present study was a prospective comparison of 18F-FDG PET integrated with computed tomography (18F-DG PET-CT), MRI and WBXR for the assessment of bone involvement in a series of 46 consecutive patients with previously untreated MM.

Design and Methods

Forty-six patients entered this prospective study which was conducted at two hematology centers (Bologna and Udine) from March 2003 to December 2004. Of these 46 patients, 44 were referred with a diagnosis of MM, which was subsequently confirmed;[16] the last two patients had an initial diagnosis of solitary plasmacytoma of bone, which was subsequently changed to MM based on PET-CT findings. Once the diagnosis of symptomatic MM had been established, all patients were enrolled in the "Bologna 2002" clinical trial and received primary therapy with thalidomide-dexamethasone, as described elsewhere,[17] followed by double autologous transplantation to support two sequential courses of melphalan 200 mg/m^{2}. The clinical and hematologic characteristics at presentation of the 46 patients who form the basis of the present study are summarized in Table 1.

Assessment of bone involvement prior to the start of therapy was performed in all patients by means of

Table 1. Patients' baseline characteristics.

N° of patients	*46*
Male/female	30/16
Median age (range)	55 (42-65)
M protein isotype	
IgG	26
IgA	11
Bence Jones	7
Non-secretory	2
Durie & Salmon stage (%)	
I/SP	7
II	10
III	29
Median Hb (range) (g/dL)	12.2 (4.5-15.6)
Median β2M (range) (mg/L)	2.6 (1.4-13.3)
Median CRP (range) (mg/L)	0.3 (0.1-5)
Median LDH (range) (UI/L)	240 (124-578)
Median % bone marrow PC (range)	53 (10-100)
Median creatinine (range) (mg/dL)	1.16 (0.69-6.3)
No. of patients with ≥2 mg/dL	3
No. of patients with serum Ca ≥12	1
Cytogenetic abnormalities (%)	
Δ13 (FISH)	19 (47.5)
t(4;14)	9(22)

SP: solitary plasmacytoma; Hb: hemoglobin; β2M: β2 microglobulin; CRP: C reactive protein; LDH: lactate dehydrogenase; PC: plasma cells; Ca: calcium; FISH: interphase fluorescence, Δ: deletion, t: translocation. Note that data on cytogenetic abnormalities were available in 40 patients.

whole-body 18F-FDG PET-CT, MRI of the spine and pelvis and WBXR survey. In all patients, FDG PET-CT was performed within 2 weeks of WBXR and MRI.

Whole-body (including skull, upper limbs and femora) 18F-FDG PET-CT was carried out using standard procedures, as previously described.[15] PET-CT scans were independently and prospectively reviewed by two nuclear medicine physicians who were blinded to the patients' clinical characteristics at baseline, as well as to the results of the WBXR survey and MR images of the spine and pelvis. Non-physiologic areas of increased 18F-FDG uptake were considered positive for myelomatous bone involvement if the standard uptake volume (SUV) max based on body weight was >2.5 and a lytic bone lesion was recognized on the corresponding CT images. Areas of focal uptake of the tracer, in the absence of a correspondent lytic image on CT, were not considered positive for myelomatous bone involvement. By study design, no needle biopsy was performed in an attempt to confirm the diagnosis of MM histologically.

MRI was performed according to previously published methods;[18] T1-weighted images were repeated after the intravenous injection of gadolinium chelate. MR images were reviewed by two radiologists who were blinded to the WBXR images and PET-CT scans. They independently evaluated the bone marrow infiltration and, on the basis of previously reported criteria, identified the following patterns of bone marrow

involvement: normal, focal and diffuse.[18] In the case of focal pattern, the exact number and site of lesions were reported. WBXR survey included plain radiographs of the skull, spine, pelvis, ribs, femora and humeri.

As previously mentioned, another objective of our study was to compare the accuracy of PET-CT with that of MR of the spine and pelvis for the assessment of response to stem-cell-supported high-dose therapy. Response criteria were those proposed by Bladè et al.,[18] with the addition of a near complete response category, as identified by disappearance of M protein on routine electrophoresis, but positive immunofixation. Criteria used for evaluation of MRI following therapy were previously reported;[20] in particular, complete response included resolution of marrow abnormality or persistent abnormality without enhancement, whereas a decrease in the amount of marrow abnormality with persistent enhancement were considered a partial response. PET-CT was considered negative if every area of increased tracer uptake found at baseline disappeared following autologous transplantation, while it was defined as improved (partial response) if the number of sites of FDG uptake decreased and/or the SUV of the lesions decreased. According to previously published studies,[21] response was evaluated 3 months after transplantation.

Results

Comparison of 18F-FDG PET-CT with WBXR at baseline

Overall, the comparison of accuracy of FDG PET-CT with WBXR for assessment of myeloma bone disease at baseline showed the superiority of PET-CT over planar radiographs in 21/46 patients (46%), of whom nine were negative for bone osteolyses on planar radiographs and 12 had an extent and magnitude of bone involvement significantly underestimated by WBXR in comparison with PET-CT; $p<0.000$ (Tables 2 and 3). In particular, in a single patient the finding of multiple sites of increased tracer uptake in the skeleton (all of them out of the FOV of MRI) changed the diagnosis from solitary plasmacytoma of bone, as previously established on the basis of plain radiographs and MR scans of the spine and pelvis, to that of MM.

In an additional 21/46 patients (46% of cases) results of both techniques were comparable (Table 2). Notably, all the 9 patients with negative WBXR and PET-CT findings had an abnormal bone marrow pattern on MRI of the spine. Finally, in the last four patients (8%), no areas of increased 18F-FDG uptake were found on PET-CT, whereas WBXR showed small lytic bone lesions of sub-centimeter size in the skull. Of note, all these patients showed an abnormal spinal bone marrow pattern on MRI (Table 2). In conclusion, in the whole patient population the sensitivity of 18F-FDG PET-CT for assessment of myeloma bone disease was 92%. The specifici-

ty of the hybrid PET-CT technique was directly demonstrated in all the patients by the morphologic appearance of a lytic lesion on the correspondent CT image of each area of increased bone marrow uptake of 18F-FDG.

Comparison of 18F-FDG PET-CT with MRI at baseline

Overall, comparison of the accuracy of MRI and FDG PET-CT for the detection of bone lesions in the spine and pelvis showed concordant findings in 32/46 patients (70%) and discordant results (e.g. negative PET-CT, but positive MRI) in the remaining 30% of cases (14/46, of whom 10 had a diffuse pattern and 4 had a focal pattern of bone marrow involvement on MRI) (Table 2).

Finally, in 16/46 patients (35%), PET-CT scans enabled detection of myelomatous lesions in sites (medullary: 15 patients; extramedullary: 1 patient) which were out of the FOV of MRI, thus contributing to a more careful assessment of myeloma bone disease. It is worthy of note that in the single patient with extramedullary increased tracer uptake in the liver, a biopsy to confirm the diagnosis of MM was not performed for anatomical reasons. Nevertheless, the SUV of tracer uptake was almost comparable to that seen in the skeleton; moreover, complete resolution of 18F-FDG uptake was observed at re-evaluation following autologous transplantation. In addition, in another patient, the finding of

Table 2. Comparative imagings of 18F-FDG PET-CT, MRI and WBXR at baseline.

Comparative imagings	Concordant results		Discordant results	
	N. of pts (%) with negative findings	N. of pts (%) with positive findings	N. of pts (%) with superiority of PET-CT	N. of pts (%) with inferiority of PET-CT
PET-CT WB vs WBXR	9/46 (19)	12/46 (26)	21/46 (46)	4/46 (8)
PET-CT SP vs MRI SP	4/46 (8)	28/46 (61)	0/46	14/46 (30)
PET-CT WB vs MRI SP	4/46 (8)	15/46 (34)	13/46 (28)	14/46 (30)

WBXR: whole body X Ray; MRI S-P: magnetic resonance imaging of spine-pelvis; PET-CT: positron emission tomography-computed tomography; SP: spine-pelvis; WB: whole body; Pts: patients, vs: versus.

Table 3. Comparison of the accuracy of different imaging methods in the assessment of myelomatous lesions at baseline.

	N. of patients (%) with negative findings	N. of patients (%) with positive findings	N. of lesions	
			Median (range)	Mean±SD
WBXR	18/46 (39)	28/46 (61)	2 (0-10)	2.2±2.8*
MRI S-P	4/46 (8)	42/46 (92)	3 (0-10)	5.0±4.0
PET-CT S-P	19/46 (41)	27/46 (59)	2 (0-10)	3.5±4.2
PET-CT WB	13/46 (28)	33/46 (72)	10 (0-10)	5.4±4.7*

WBXR: whole body X Ray; MRI S-P: magnetic resonance imaging of spine-pelvis; PET-CT: positron emission tomography-computed tomography; SP: spine-pelvis; WB: whole body, *p<0.000.

multiple sites of FDG uptake out of the FOV of MRI corrected the diagnosis from solitary plasmacytoma of bone, as previously established on the basis of MRI survey, to that of MM.

Comparison of 18F-FDG PET-CT with MRI according to treatment response at 3 months after autologous transplantation

In 23 patients, bone marrow involvement was re-evaluated 3 months after autologous transplantation. PET-CT scans and MR images at re-evaluation were compared with those at baseline and both findings were analyzed in relationship to response to high-dose therapy (Table 4). In 15 patients (65%), 18F-FDG PET-CT scans at re-evaluation were negative and in 12 of these patients a ≥90% decrease in M protein concentration was documented. Of these 15 patients, eight had a normal MR bone marrow pattern of the spine and pelvis, whereas in the remaining seven patients MRI was either unchanged or showed a reduced number of lesions. In the remaining eight patients, 18F-FDG PET-CT was considered to be improved, according to the criteria above mentioned. Of these eight patients, six had an unmodified MRI, whereas two patients had an improvement in the MR pattern.

Discussion

Studies aimed at comparing FDG-PET with conventional techniques for the detection of bone disease at the onset of MM have been limited and incomplete, due to the small number of patients analyzed, most frequently in a retrospective fashion, and, more importantly, to the lack of data confirming the diagnosis of MM.[9,12,13,14,15,22] To the best of our knowledge, the present study is the first designed to prospectively compare 18F-FDG PET-CT, MRI and WBXR in a relatively large series of newly diagnosed MM patients who were homogeneously treated and for whom all correlative data were available in all the cases analyzed. Although preliminary results of this study were previously reported,[15] in the current analysis we nearly doubled the sample size by including another 18 patients, thus improving the accuracy of the results and reporting one of the largest prospective series so far evaluated at diagnosis with three different imaging techniques. In addition, in this series of patients who were homogeneously treated with autologous stem-cell transplantation, we compared the role of PET-CT and MRI of the spine and pelvis in the assessment of treatment response. Furthermore, we also analyzed the results in relationship to the quality of response to autologous transplantation. For this purpose, we used a hybrid system of 18F-FDG PET integrated with CT which allowed exact detection of small and/or slightly active lesions that could not been easily recognized, or differentiated

Table 4. Post-transplant comparison of PET-CT vs MR imagings and treatment response in 23 patients.

Pts.	18F-FDG PET results	MRI results	Clinical response
2	Pos multiple ribs (PR) (↓SUV and number of sites)	Pos D9, D11, D12, L3 (no change)	nCR
6	Pos 3 ribs (PR)	Pos D9, D11, L2, L5 (no change)	nCR
7	Pos D2, D8, D12, L1-L5, sacrus, sternum, ribs, pelvis (↓SUV) (PR)	Pos D2, D8, L1, L5 (no change)	PR
8	Pos scapula, D5, D7 (PR)	Pos C3, C7, D4, D7, D9, L3, L5 (no change)	CR
9	Neg	Pos D2 (PR)	VGPR
10	Pos ribs (PR) (↓SUV and number of sites)	Pos multiple vertebrae (PR)	PR
19	Neg	Pos C2, D4, D12, S1, S2 (no change)	VGPR
21	Neg	Neg	VGPR
22	Pos right pelvis (PR)	Pos D7, D8 (no change)	nCR
23	Pos II left rib (PR)	Pos L3 (PR)	nCR
25	Neg	Pos L4, L5 (PR)	CR
26	Neg	Neg	CR
27	Neg	Diffuse infiltrative pattern of the spine (no change)	CR
30	Pos right rib, right femur (PR)	Pos D5, D11, L1, L4, L5 (no change)	CR
31	Neg	Pos D11, D12, right pelvis (PR)	PR
36	Neg	D6, D8, L2 (no change)	nCR
37	Neg	Neg	CR
38	Neg	Neg	VGPR
39	Neg	Neg	CR
40	Neg	Neg	PR
41	Neg	Neg	CR
42	Neg	Pos multiple vertebrae (PR)	VGPR
43	Neg	Neg	N.V.

Pts: patients; Pos: positive; Neg: negative; SUV: standard uptake volume; PR: partial response; nCR: near complete response; CR: complete response; VGPR: very good partial response; N.V.: not evaluable.

from soft tissue lesions, on the basis of PET alone. In addition, due to the generation of fused images on which each hypermetabolic lesion was concordant with the morphology of a lytic bone lesion on the corresponding CT image, we were able to directly confirm the reliability and specificity of our PET-CT findings in all the patients who were analyzed. Thus, the diagnostic accuracy of PET-CT used in the present study is likely to

be superior to that of all other studies of PET alone so far reported in the literature.[23]

Overall, skeletal involvement was documented by WBXR in 61% of newly diagnosed MM patients and by PET-CT in 72% of patients (Table 3). By combining these two imaging methods, the ability to detect myelomatous lesions, both medullary and extramedullary, increased up to 80%. In 46% of patients, PET-CT was superior to WBXR in terms of the ability to reveal small bone lesions which, albeit included in the FOV of planar radiographs, were under the spatial resolution limit of the plain film. Notably, in 19% of these patients WBXR failed to detect bone lytic lesions. No false-positive results were documented in any of the patients with PET-CT positive scans. In contrast, false negative PET-CT scans were found in 8% of patients in whom planar radiographs showed subcentimeter lytic lesions of the skull, a finding consistent with the known difficulty of 18F-FDG PET to reveal skull lesions due to the high, physiologic uptake of the tracer in the adjacent brain.[11] It is worthy of note that in all these patients MRI revealed an abnormal pattern of bone marrow in the spine and pelvis.

The comparison between PET-CT scans and MR images with respect to the assessment of bone disease in the spine and pelvis showed that the sensitivity of MRI was as high as 92%, whereas increased uptake of 18F-FDG was documented in only 59% of patients (Table 3). Careful analysis of 30% of patients with false-negative PET-CT scans and positive MR images, revealed an abnormal, diffuse pattern of the bone marrow in ten out of 14 patients. Thus, MRI of the spine and pelvis was more sensitive and specific than PET-CT, particularly among patients lacking a focal MR bone marrow pattern. On the basis of these results, which resemble those of previously published studies,[22,24] and in the light of the adverse prognostic relevance of an abnormal diffuse MR pattern of the spine,[18] it can be concluded that MRI still remains the gold standard technique for the detection of bone marrow involvement of the spine and pelvis.

Another objective of our analysis was to assess the complementary role of PET-CT for the assessment of whole-body bone disease, particularly in the light of the FOV of MRI which was limited to the spine and pelvis. In 35% of patients, PET-CT allowed the detection of myelomatous lesions which were out of the FOV of MRI, and were thus missed by this technique (Table 2 and 3). By combining MRI of the spine-pelvis and 18F-FDG PET-CT, the ability to detect medullary and, albeit occasionally, extramedullary myelomatous lesions increased up to 92%. As a result of this work, only four patients with damage to organs other than the skeleton

(e.g. the bone marrow with related anemia or the kidney with related renal failure) were found to have negative whole body PET-CT scans and MR imagings of the spine and pelvis.

Even now, uncertainties still exist concerning the optimal imaging method to be used for the assessment and monitoring of response to therapy in patients with MM. 18F-FDG PET-CT may be of value given that response can be carefully assessed by recording changes in 18F-FDG uptake. Preliminary results of our study showed that in 65% of patients PET-CT scans normalized following autologous transplantation and that this finding closely followed the achievement of a marked (e.g ≥90%) degree of tumor response. In contrast, normalization of MRI was seen in only 35% of patients. However, a 3-month evaluation of post-transplant response, although based on a previously reported analysis of M protein changes,[21] may not be an adequate period for MRI reassessment.

In conclusion, PET-CT proved to be a technique that can be used in clinical practice for widespread screening of myelomatous lesions, both medullary and extramedullary, at the onset of MM. MRI was superior to PET-CT in the assessment of bone marrow involvement of the spine and pelvis. On the basis of these results, which need to be confirmed in larger and independent series of patients, 18F-FDG PET-CT and MRI of the spine and pelvis, with eventual addition of plain X ray of the skull, could be proposed as standard methods for the detection of myeloma bone disease in the routine work-up of patients with newly diagnosed MM. More data and longer follow-up are needed for a better definition of the role of 18 F-FDG PET-CT in assessment and monitoring of response to therapy.

References

1. Terpos E, Politou M, Rahemtulla A. New insights into the pathophysiology and management of bone disease in multiple myeloma. Br J Haematol 2003;123:758-69.
2. Mitsiades CS, Mitsiades N, Munshi NC, Anderson KC. Focus on multiple myeloma. Cancer Cell 2004;6:439-44.
3. Kyle RA., Rajkumar V. Multiple myeloma. N Engl J Med 2004; 351:1860-73.
4. Sezer O. Myeloma bone disease. Hematology 2005;1:19-24.
5. Berenson JR. Advances in the biology and treatment of myeloma bone disease. Semin Oncol 2002;29 Suppl 17:11-6.
6. 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;36:842-54.
7. Lecouvet FE, Malghem J, Michaux L, Maldague B, Ferrant A, Michaux JL, et al. Skeletal survey in advanced multiple myeloma: radiographic versus MR imaging survey. Br J Haematol 1999;106:35-9.
8. Angtuaco EJ, Fassas AB, Walker R, Sethi R, Barlogie B. Multiple myeloma: clinical review and diagnostic imaging. Radiology 2004;231:11-23.
9. Mileshkin L, Blum R, Seymour JF, Patrikeos A, Hicks RJ, Prince HM. A comparison of fluorine-18 fluorodeoxyglucose PET and technetium-99m sestamibi in assessing patients with multiple myeloma. Eur J Haematol 2004;72:32-7.
10. Juweid ME, Cheson BD. Role of positron emission tomography in lymphoma. J Clin Oncol 2005;23: 4577-80.
11. Einat Even-Sapir. Imaging of malignant bone involvement by morphologic, scintigraphic and hybrid modalities. J Nucl Med 2005; 46: 1356-67.
12. Jadvar H, Conti PS. Diagnostic utility of FDG PET in multiple myeloma. Skel Radiol 2002;31:690-4.
13. Schirmeister H, Bommer M, Buck AK, Miller S, Messer P, et al. Initial results in the assessment of multiple myeloma using FDG-PET. Eur J Haematol Med 2002;29:361-6.
14. Durie GM, Waxman AD, D'Agnolo A, Williams CM. Whole body 18F-FDG-PET identifies high-risk myeloma. J Nucl Med 2002;43:1457-63.
15. Nanni C, Zamagni E, Farsad M, Castellucci P, Tosi P, Cangini D, et al. Role of (18)F-FDG PET/CT in the assessment of bone involvement in newly diagnosed multiple myeloma: preliminary results. Eur J Nucl Med Mol Imaging 2006;33:525-31.
16. International Myeloma Working Group. Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: a report of the International Myeloma. Br J Haematol 2001;121:749-57.
17. Cavo M, Zamagni E, Tosi P, Tacchetti P, Cellini C, Cangini D, et al. Superiority of thalidomide and dexamethasone over vincristine-doxorubicine-dexamethasone (VAD) as primary therapy in preparation for autologous transplantation for multiple myeloma. Blood 2005;106:35-9.
18. Moulopoulos LA, Varma DG, Dimopoulos MA, Leeds NE, Kim EE, Johnston DA, et al. Multiple myeloma: spinal MR imaging in patients with untreated newly diagnosed disease. Radiology 1992;185:833-40.
19. BladèJ, Samson D, Reece D, Apperley J, Bjorkstrand B, Gahrton G, et al. Criteria for evaluating disease response and progression in patients with multiple myeloma treated with high-dose therapy and haematopoietic stem cell transplantation. Br J Haematol 1998;102:1115-23.
20. Moulopolous LA, Dimopoulos MA, Alexanian R, Leeds NE, Libshitz HI. Multiple myeloma: MR patterns of response to treatment. Radiol 1994; 193:441-6.
21. Attal M, Harousseau Jl, Facon T, Guilhot F, Doyen C, Fuzibet JG, et al. Single versus double autologous stem-cell transplantation for multiple myeloma. N Engl J Med 2003;349: 2495-502.
22. Bredella MA, Steinbach L, Caputo G, Segall G, Hawkins R. Value of FDG PET in the assessment of patients with multiple myeloma. Am J Radiol 2005;184:1199-204.
23. Ell PJ. The contribution of PET/CT to improved patient management. Br J Radiol 2006;79:32-6.
24. Baur A, Stäbler A, Nagel A, Lamerz R, Bartl R, Hiller E, et al. Magnetic resonance imaging as a supplement for the clinical staging of Durie and Salmon. Cancer 2002;95:1334-45.