Relationship Between Fluorine-18 Fluorodeoxyglucose PET/CT Uptake and the Plasma Cell Infiltration Rate in the Bone Marrow of Patients With Multiple Myeloma

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Abstract

Background: The present study investigated the relationship between maximum standardized uptake values (SUV_{max}) on Fluorine-18 Fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) and the plasma cell (PC) proliferation percentage in the bone marrow (BM) of patients with multiple myeloma (MM).

Material and methods: Patients clinically and pathologically diagnosed with MM between January 2012 and October 2019 were selected from the database of Dokkyo Medical University Hospital (DMU Hospital), Japan. Patients with other malignancies and those who received chemotherapy and radiation therapy or hematopoietic treatments in the previous 4 weeks and 2-3 months prior to PET/CT scans were excluded from the present study to avoid false uptake. We examined 60 patients (female: male; 27:33; 1:1.22) aged between 37 and 91 years; mean $\pm$ SD; 67.3 ± 10.2 years. Hematological and biochemical tests with results on hemoglobin (Hb), hematocrit (Ht), C reactive protein (CRP), beta-2 microglobulin (b2m), creatinine (Cre), albumin (Alb), calcium (Ca), white blood cells (WBC), and red blood cells (RBC) were recorded and evaluated. The percentage of PC in BM biopsy samples was calculated. On PET/CT images, the SUV_{max} of the region of interest (ROI) of the right anterior iliac crest, the biopsy site, was measured. Relationships were examined using Pearson's correlation coefficient with SPSS.

Results: The types of MM diagnosed were IgG κ in 31 patients (51.6%), IgG λ in 19 (31.6%), IgA λ in 5 (8.3%), IgA κ in 2 (3.3%), IgD λ in 2 (3.3%), and IgD κ in 1 (1.6%). According to the Durie-Salmon staging system, 4 patients had stage I, 6 stage II, and 33 stage III, while stages were not recorded in the remaining 17 patients. A positive correlation was observed between FDG uptake and the percentage of PC ($r=0.7$, $p<0.001$), but not between FDG uptake and hematological and biochemical parameters in all patients. However, a correlation was observed between FDG uptake and b2m ($r=0.596$, $p=0.004$) in 21 patients (35%).

Conclusion: Increased FDG uptake by BM correlated with the percentage of PC. PET/CT is crucial for the diagnosis, treatment evaluation, and follow-up of MM patients.

Background

Multiple myeloma (MM) is the second most common blood cancer worldwide, accounting for 1% of all cancers, and is characterized as a malignant hematological disorder with the uncontrollable monoclonal proliferation of malignant plasma cells (PC) [1,2]. According to Global cancer statistics 2018, MM represented 0.9% of all new malignancies as well 1.1% of the leading causes of cancer deaths worldwide [3].

Positron emission tomography/computed tomography (PET/CT) with the radiopharmaceutical Fluorine-18 Fluorodeoxyglucose (FDG), which is used as a glucose analog, accumulates in more metabolically active tissues, such as cancer and inflammatory lesions. It is a whole-body imaging technique that simultaneously provides morphological and functional information on the human body [4–9]. It is very

useful for detecting bone damage; more than 80-90% of MM patients have bone lesions [10,11], which is a myeloma-defining event. PET/CT also has the capacity to identify skeletal and extramedullary lesions with a sensitivity of approximately 80-90% and specificity of 70-100% [12–24].

The International Myeloma Working Group (IMWG) consensus recommend the mandatory use of FDG PET/CT to confirm a suspected diagnosis of solitary plasmacytoma and provide crucial prognostic information [25,26]. The European Society of Medical Oncology (ESMO) and European Myeloma Network (EMN) guidelines also recommend low-dose whole-body CT and FDG PET/CT based on their availability [5,8].

The diagnosis and classification of MM previously required the presence of end-organ damage, known as the CRAB criteria, which include an elevated (C) calcium (Ca) level, (R) renal dysfunction, (A) anemia, and destructive (B) bone lesions. The Durie-Salmon Staging System (DSSS) shows the relationship between the extent of myeloma and associated damage, and the revised system in 2006 integrated new imaging techniques, such as FDG PET/CT and MRI. The International Staging System (ISS) is based on serum beta-2 microglobulin (b2m) and serum albumin (Alb) levels, and the 2015 revised system includes the chromosomal abnormality t(14;16), t(4,14), del17p and serum lactate dehydrogenase (LDH) levels.

The 5-year survival rate of MM in the United States (US) was 54%, approximately 75% among those diagnosed in the early stages, and 51% in those diagnosed at the late stage with metastasis to distant parts of the body. The survival rate of MM has steadily been increasing in the last few decades due to advances in treatment and management [27].

Increased PC infiltration rate brings higher FDG uptake in BM, hence in this retrospective study, we investigated this relationship based on our data. The result should be essential in the follow up evaluation of MM patients, where biopsy may not be necessary.

Materials And Methods

This retrospective study was approved by the Ethics Committee of Dokkyo Medical University. Between January 2012 and October 2019, all patients with biopsy-proven MM were retrospectively evaluated. We examined 60 patients (females:males; 27:33; 1:1.22) aged between 37 and 91 years; mean $\pm$ SD; 67.3 $\pm$ 10.2 years. We excluded patients with other malignancies and those who received hematopoietic treatments or chemotherapy and radiation therapy in the past 4 weeks and 2-3 months prior to PET/CT scans. Since this was a retrospective study, hematological and biochemical test results (hemoglobin (Hb), hematocrit (Ht), C reactive protein (CRP), b2m, creatinine (Cre), Alb, Ca, white blood cells (WBC), and red blood cells (RBC)) were obtained prior to or after 2 weeks, whichever was the nearest to the PET/CT scan date; however, some results had longer date gaps. The demographic and clinical properties of patients are shown in Table 1.

18F-FDG PET/CT imaging

Prior to PET/CT, all patients fasted overnight (for at least 6 hours) and were intravenously administered FDG based on their body mass. Blood glucose levels were measured before the FDG injection, it should be equal or less than 200 mg/dl. Patients rested in a warm room during the FDG uptake time of 1 hour. Whole-body imaging was performed using a Siemens Biograph mCT Flow PET/CT scanner or Siemens Biograph mCT Horizon PET/CT scanner at the PET Center, DMU Hospital, Tochigi prefecture, Japan. The PET acquisition time was 2.2 min per field of view. CT scan data were obtained with a peak voltage of 120 kV and tube current of 70 mAs.

Regarding the semi-quantitative evaluation, the SUV_{max} of the ROI, namely, the right anterior iliac crest, was calculated using semiautomatic image registration software package. The right anterior iliac crest was selected to standardize the calculation of FDG uptake by BM because it was the biopsy site and concordant with previous studies [12,28,29]. Figures 1 and 2 demonstrates the PET/CT scan image of MM patients.

PC counting

All H&E-stained specimens were examined under a light microscope (BX53 Olympus, Japan) and digital photos were taken using CellSens Standard imaging software. PC were counted using the application QuPath 0.2.2 [30]. The infiltration rate of PC represents the number relative to all nucleated hematopoietic cells in BM. PC biopsy samples are shown in Figures 3 and 4.

Statistical analysis

Statistical analyses were performed using SPSS 27 (SPSS Inc, Chicago, Ill., USA) [31]. The relationship between FDG uptake and PC infiltration as well other hematological and biochemical parameters was analyzed using Pearson's correlation coefficient. The results obtained were considered to be significant at a P value less than 0.05 ($p < 0.05$).

Results

The average SUV_{max} of ROI was between 1.34 and 7.76 (mean 2.72 ± 1.33) and the percentage of PC in the BM of the right anterior iliac crest was between 11.45 to 52 (mean 29.8 ± 9.7). The relationship between FDG uptake and PC infiltration in BM was positive ($r=0.7$, $p < 0.001$) (Figure 5). As a limitation of this retrospective study, hematological and biochemical parameter dates differed and, thus, FDG uptake and hematological and biochemical parameters did not correlate. However, we selected 21 cases in which PET/CT scans and parameter results occurred within one week and calculated the relationship between them. A positive correlation was observed between FDG uptake and b2m ($r=0.596$, $p=0.004$) (Figure 6).

Discussion

The present results revealed a correlation between FDG uptake by BM on PET/CT and PC proliferation in patients with MM.

MM is a PC proliferative disorder with high morbidity and mortality rates.

PET/CT exhibits high sensitivity and specificity (80-90%, 70-100%) [12–24] for the diagnosis of MM. This method also enables whole-body evaluations to be performed in one session and within a reasonable timeframe, while assuring high sensitivity and acceptable specificity for the detection of both medullary and extramedullary diseases [32,33]. The most important advantage of FDG PET/CT is its ability to distinguish between metabolically active and inactive lesions.

In comparisons among FDG PET/CT, ^{11}C -Methionine PET/CT, and ^{68}Ga -Pentixafor PET/CT, the latter two were found to be promising for the detection of intramedullary and extramedullary lesions in patients with MM [34–37]. Nanni et al. [22] compared whole-body X-rays (WBXR), magnetic resonance imaging (MRI), and FDG PET/CT in patients with MM. The findings obtained showed that the sensitivity of FDG PET/CT for detecting small lytic bone lesions was higher than that of WBXR, but similar to that of MRI for the detection of bone diseases in the spine and pelvis. However, MRI may be superior for diagnosing infiltrative patterns in the spine [19,20]. Another study reported that FDG PET/CT was superior to technetium sestamibi myocardial perfusion imaging (technetium-99m-MIBI) and MRI for the detection of focal lesions [16].

Chanty et al. [38] reported that for the initial diagnosis of MM, FDG PET/CT was 40-60% more accurate at detecting solitary plasmacytoma than plain X-rays. Ben S et al. retrospective study found that PET/CT scan results affected the planned management of two-thirds of patients with PC disorders including MM [7]. In a study by Dimitrakopoulou-Strauss, PET/CT prior to and after the first course of chemotherapy appeared to be useful for identifying patients who will respond to treatment [39], furthermore, studies have also shown that PET/CT scans are helpful in assessing responses to treatment [40] and allow for better management of patients with MM [41].

Previous studies reported a correlation between FDG uptake by BM and PC infiltration [12,20,28,29,42–45], while others showed that FDG uptake correlated with b2m [28,29] and CRP (29) and negatively correlated with Hb and HT [29] as well as Alb [28].

In the present study, a positive correlation was observed between PET/CT FDG uptake and the PC infiltration rate ($r=0.7$, $p<0.001$). As a limitation of this retrospective study, hematological and biochemical parameter dates differed and, thus, no correlation was observed between FDG uptake and hematological and biochemical parameters. However, we selected 21 cases in which PET/CT scans and parameter results occurred within one week and calculated the relationship between them. A positive correlation was observed between FDG uptake and b2m ($r=0.596$, $p=0.004$). Therefore, the time gap between PET/CT and hematological and biochemical parameter tests is crucial for assessing the significance of this relationship.

Significant prognostic laboratory parameters, such as b2m, CRP, and LDH, correlated with the number of focal FDG-avid lesions on PET/CT. Furthermore, the suppression of FDG prior to transplantation was previously identified as an independent favorable prognostic factor [46]. In newly diagnosed MM patients,

the presence of at least 3 focal lesions and SUV>4.2 or extramedullary disease predicted poor progression-free survival [47]. PET/CT may be used to predict the outcomes of patients with new, relapsed, or refractory MM [44,46–51]

Based on these findings, increased FDG uptake on PET scan indicates a higher percentage of PC in BM; therefore, BM biopsy may not be necessary in the follow-up period because SUV_{max} values in the BM of MM patients with recurrence will be elevated.

Conclusion

An increased uptake of FDG on PET/CT correlated with the percentage of PC in BM. Therefore, the percentage of PC in BM and FDG PET/CT are crucial for the diagnosis, staging, treatment evaluation, and follow-up of MM patients.

Abbreviations

SUV_{max}: standardized uptake value; FDG: Fluorine-18 Fluorodeoxyglucose; PET/CT: positron emission tomography/ computed tomography; PC: plasma cell; BM: bone marrow; MM: multiple myeloma; Hb: hemoglobin; Ht: hematocrit; CRP: C reactive protein; b2m: beta-2 microglobulin; Cre: creatinine; Alb: albumin; Ca: calcium; WBC: white blood cells; RBC: red blood cells; ROI: region of interest; LDH: Ig: immunoglobulin; serum lactate dehydrogenase; WBXR: whole body X rays; MRI: magnetic resonance imaging; technetium-99m-MIBI: technetium sestamibi myocardial perfusion imaging; DSSS: Durie-Salmon staging system; MIP image: maximal intensity projection image.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of Dokkyo Medical University, Tochigi, Japan.

Consent of publication

Not applicable.

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Competing interest

The authors declare that they have no competing interests.

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Authors' contribution

TG, YN, YK develop the concept and design the study. YN supervised the study. TG, KI, YM acquired data. TG, YN, YK, HA analyzed and interpreted the data. KI advised on the plasma cell counting. DK, SH advised on statistical analysis. All authors read and approved the final manuscript.

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References

1. Kyle RA, Rajkumar SV. Multiple Myeloma. 2004;1860–73. <https://doi.org/10.1056/nejmra041875>
2. Genadieva-stavric S, Cavallo F, Palumbo A. New Approaches to Management of Multiple Myeloma. 2014;157–70. <https://doi.org/10.1007/s11864-014-0276-6>
3. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancer.pdf. <https://doi.org/10.3322/caac.21492>
4. Jamet B, Bailly C, Carlier T, Touzeau C, Nanni C, Zamagni E, et al. Interest of Pet Imaging in Multiple Myeloma. 2019;6(April):1–9. <https://doi.org/10.3389/fmed.2019.00069>
5. Caers J, Garderet L, Kortüm KM, Dwyer MEO, Donk WCJ Van De, Binder M, et al. European Myeloma Network recommendations on tools for the diagnosis and monitoring of Correspondence: 2018;103(11):1772–84. <https://doi.org/10.3324/haematol.2018.189159>
6. Kosmala A, Bley T, Petritsch B. Imaging of Multiple Myeloma Bildgebende Diagnostik des Multiplen Myeloms Authors Imaging for diagnosing MM Conventional radiography. 2019; <https://doi.org/10.1055/a-0864-2084>
7. Shachar B, Prica A, Anconina R, Hawsawy A, Maccrostie P, Langer D, et al. Impact of 18 F-fluorodeoxyglucose PET / CT in the management of patients with plasma cell disorders. 2020; <https://doi.org/10.1097/mnm.0000000000001113>
8. Dimopoulos MA, Ludwig H, Einsele H, Zweegman S, Facon T, Cavo M, et al. Multiple myeloma: ESMO Clinical Practice Guidelines for diagnosis , treatment and follow-up † Clinical Practice Guidelines. ESMO Updat Clin Pract Guidel [Internet]. 2017;28(April):iv52–61. Available from: <http://dx.doi.org/10.1093/annonc/mdx096>
9. Messiou C, Kaiser M. Whole-Body Imaging in Multiple Myeloma. Magn Reson Imaging Clin NA [Internet]. 2018;26(4):509–25. Available from: <https://doi.org/10.1016/j.mric.2018.06.006>
10. Article O. Review of 1027 Patients With Newly Diagnosed Multiple Myeloma. 2003;78(January):21–33. <https://doi.org/10.4065/78.1.21>

11. Zamagni E, Tacchetti P, Cavo M. Imaging in multiple myeloma : How ? When ? 2019;133(7):644–51. <https://doi.org/10.1182/blood-2018-08-825356>
12. Sager S, Ergül N, Ciftci H. The value of FDG PET / CT in the initial staging and bone marrow involvement of patients with multiple myeloma. 2019;(November). <https://doi.org/10.1007/s00256-010-1088-9>
13. Hur J, Ryu YH, Yun MJ. 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. 2009;49(4):427–35. <https://doi.org/10.1007/s00256-010-1088-9>
14. Spinnato P, Bazzocchi A, Brioli A, Nanni C, Zamagni E, Albisinni U, et al. Contrast enhanced MRI and 18 F-FDG PET-CT in the assessment of multiple myeloma : A comparison of results in different phases of the disease. *Eur J Radiol* [Internet]. 2012;81(12):4013–8. Available from: <http://dx.doi.org/10.1016/j.ejrad.2012.06.028>
15. Waheed S, Mitchell A, Usmani S, Epstein J, Yaccoby S, Nair B, et al. Standard and novel imaging methods for multiple myeloma : correlates with prognostic laboratory variables including gene expression profiling data. 2013;98(1):71–8. <https://doi.org/10.3324/haematol.2012.066555>
16. Weng W, Dong M, Zhang J, Yang J, Xu Q, Liu N. RESEARCH ARTICLE A Systematic Review of MRI , Scintigraphy , FDG-PET and PET / CT for Diagnosis of Multiple Myeloma Related Bone Disease - Which is Best ? 2014;15:9879–84. <https://doi.org/10.7314/apjcp.2014.15.22.9879>
17. Tsai S, Kao C. FDG PET or PET / CT for Detecting Intramedullary and Extramedullary Lesions in Multiple Myeloma A Systematic Review and Meta-analysis. 2012;37(9):833–7. <https://doi.org/10.1097/rlu.0b013e31825b2071>
18. Mesguich C, Fardanesh R, Tanenbaum L, Chari A, Jagannath S, Kostakoglu L. State of the art imaging of multiple myeloma : Comparative review of FDG PET / CT imaging in various clinical settings. *Eur J Radiol* [Internet]. 2014;83(12):2203–23. Available from: <http://dx.doi.org/10.1016/j.ejrad.2014.09.012>
19. Fonti R, Salvatore B, Quarantelli M, Sirignano C, Segreto S, Petruzzello F, et al. Evaluation of Patients with Multiple Myeloma. :195–200. <https://doi.org/10.2967/jnumed.107.045641>
20. Sachpekidis C, Mai EK, Goldschmidt H, Hillengass J, Hose D, Pan L, et al. F-FDG Dynamic PET / CT in Patients with Multiple Myeloma Patterns of Tracer Uptake and Correlation With Bone Marrow. 2015;40(6). <https://doi.org/10.1097/rlu.0000000000000773>
21. Moreau P, Attal M, Karlin L, Garderet L, Facon T, Macro M. Prospective Evaluation of MRI and PET-CT at Diagnosis and before Maintenance Therapy in Symptomatic Patients with Multiple Myeloma Included in the IFM / DFCI 2009 Trial. 2015; <https://doi.org/10.1200/jco.2017.72.2975>
22. Nanni C, Zamagni E, Farsad M, Castellucci P, Tosi P, Cangini D, et al. Role of 18F-FDG PET/CT in the assessment of bone involvement in newly diagnosed multiple myeloma: Preliminary results. *Eur J Nucl Med Mol Imaging*. 2006;33(5):525–31. <https://doi.org/10.1007/s00259-005-0004-3>
23. Iii RJB, Mulligan ME, Smith SE, Line BR. Comparison of imaging with FDG PET / CT with other imaging modalities in myeloma. 2006;632–40. <https://doi.org/10.1007/s00256-006-0127-z>

24. Healy CF, Murray JG, Eustace SJ, Madewell J, O'Gorman PJ, O'Sullivan P. Multiple myeloma: a review of imaging features and radiological techniques. *Bone Marrow Res.* 2011;2011:583439. <https://doi.org/10.1155/2011/583439>
25. Cavo M, Terpos E, Nanni C, Moreau P, Lentzsch S, Zweegman S, et al. Review Role of ¹⁸F-FDG PET / CT in the diagnosis and management of multiple myeloma and other plasma cell disorders: a consensus statement by the International Myeloma Working Group. *Lancet Oncol* [Internet]. 18(4):e206–17. Available from: [http://dx.doi.org/10.1016/S1470-2045\(17\)30189-4](http://dx.doi.org/10.1016/S1470-2045(17)30189-4)
26. Deng S, Zhang B, Zhou Y, Xu X, Li J, Sang S. The Role of 18 F-FDG PET / CT in Multiple Myeloma Staging according to IMPeTUs: Comparison of the Durie – Salmon Plus and Other Staging Systems. 2018;2018. <https://doi.org/10.1155/2018/4198673>
27. Multiple Myeloma: Statistics | Cancer.Net [Internet]. [cited 2020 Dec 25]. Available from: <https://www.cancer.net/cancer-types/multiple-myeloma/statistics>
28. Ak I, Gulbas Z. F-18 FDG uptake of bone marrow on PET/CT scan: It's correlation with CD38/CD138 expressing myeloma cells in bone marrow of patients with multiple myeloma. *Ann Hematol.* 2011;90(1):81–7. <https://doi.org/10.1007/s00277-010-1037-7>
29. Myelom M, Kemik H, Pet İ, Bulguları BT, Cd H, Ekspresyonu CD, et al. Correlation Between Baseline 18F-FDG PET / CT Findings and CD38- and CD138-Expressing Myeloma Cells in Bone Marrow and Clinical Parameters in Patients with Multiple Myeloma. 2018;(March 2017):175–80. <https://doi.org/10.4274/tjh.2017.0372>
30. Bankhead, P. et al. (2017). QuPath: Open source software for digital pathology image analysis. *Scientific Reports.* <https://doi.org/10.1038/s41598-017-17204-5>.
31. IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk NIC. No Title.
32. Van Lammeren-Venema D, Regelink JC, Riphagen II, Zweegman S, Hoekstra OS, Zijlstra JM. 18F-fluoro-deoxyglucose positron emission tomography in assessment of myeloma-related bone disease: A systematic review. *Cancer.* 2012;118(8):1971–81. <https://doi.org/10.1002/cncr.26467>
33. Zamagni E, Nanni C, Patriarca F, Englaro E, Castellucci P, Geatti O, et al. emission tomography-computed tomography , magnetic. 2007;92(01):50–5. <https://doi.org/10.3324/haematol.10554>
34. Lapa C, Garcia-veloso MJ, Lückerrath K, Samnick S, Schreder M, Otero PR, et al. T h e r a n o s t i c s C-Methionine-PET in Multiple Myeloma: A Combined Study from Two Different Institutions. 2017;7(11). <https://doi.org/10.7150/thno.20491>
35. Lapa C, Knop S, Schreder M, Rudelius M, Knott M, Samnick S, et al. T h e r a n o s t i c s C-Methionine-PET in Multiple Myeloma: Correlation with Clinical Parameters and Bone Marrow Involvement. 2016;6(2). <https://doi.org/10.7150/thno.13921>
36. Lapa C, Schreder M, Schirbel A, Samnick S, Kortüm KM, Kropf S, et al. T h e r a n o s t i c s [68 Ga] Pentixafor-PET / CT for imaging of chemokine receptor CXCR4 expression in multiple myeloma – Comparison to [18 F] FDG and laboratory values. 2017;7(1). <https://doi.org/10.7150/thno.16576>
37. Qingqing Pan, Xinxin Cao, Yaping Luo, Jian Li, Jun Feng3, Fang Li1 2. Chemokine receptor-4 targeted PET / CT with 68 Ga-Pentixafor in assessment of newly diagnosed multiple myeloma: comparison.

- Eur J Nucl Med Mol Imaging. 2020;47(3):537–46. <https://doi.org/10.1007/s00259-019-04605-z>
38. Chantry A, Kazmi M, Barrington S, Goh V, Mulholland N, Streetly M, et al. Guidelines for the use of imaging in the management of patients with myeloma. *Br J Haematol*. 2017;178(3):380–93. <https://doi.org/10.1111/bjh.14827>
 39. Fdg-pet D, Dimitrakopoulou-strauss A, Hoffmann M, Bergner R. Prediction of Progression-Free Survival in Patients With Multiple Myeloma Following Anthracycline-Based Chemotherapy Based on. 2009;34(9). <https://doi.org/10.1097/rlu.0b013e3181b06bc5>
 40. Caldarella C, Treglia G, Antonietta M, Treglia I, Giordano A. The Role of Fluorine-18-Fluorodeoxyglucose Positron Emission Tomography in Evaluating the Response to Treatment in Patients with Multiple Myeloma. 2012;2012. <https://doi.org/10.1155/2012/175803>
 41. Hillner BE, Siegel BA, Shields AF, Liu D, Gareen IF, Hunt E, et al. Relationship between cancer type and impact of PET and PET/CT on intended management: Findings of the national oncologic PET registry. *J Nucl Med*. 2008;49(12):1928–35. <https://doi.org/10.2967/jnumed.108.056713>
 42. Li Y, Liu J, Huang B, Chen M, Diao X, Li J. Application of PET / CT in treatment response evaluation and recurrence prediction in patients with newly-diagnosed multiple myeloma. 2017;8(15):25637–49. <https://doi.org/10.18632/oncotarget.11418>
 43. Pace L, Catalano L, Pinto A, Renzo A De, Gennaro F Di, Califano C. Original article Different patterns of technetium-99m sestamibi uptake in multiple myeloma. 1998;(August). <https://doi.org/10.1007/s002590050274>
 44. Haznedar R, Akı SZ, Akdemir ÖU, Özkurt ZN, Çeneli Ö, Yağcı M, et al. Value of 18 F-fluorodeoxyglucose uptake in positron emission tomography/computed tomography in predicting survival in multiple myeloma. *Eur J Nucl Med Mol Imaging*. 2011;38(6):1046–53. <https://doi.org/10.1007/s00259-011-1738-8>
 45. Subramanian R, Basu D, Dutta TK. Prognostic significance of bone marrow histology in multiple myeloma. *Indian J Cancer*. 2009;46(1):40–5. <https://doi.org/10.4103/0019-509x.48594>
 46. Bartel TB, Haessler J, Brown TLY, Shaughnessy JD, Rhee F Van, Anaissie E. F18-fluorodeoxyglucose positron emission tomography in the context of other imaging techniques and prognostic factors in multiple myeloma. 2009;114(10):2068–76. <https://doi.org/10.1182/blood-2009-03-213280>
 47. Zamagni E, Patriarca F, Nanni C, Zannetti B, Englaro E, Pezzi A, et al. Prognostic relevance of 18-F FDG PET/CT in newly diagnosed multiple myeloma patients treated with up-front autologous transplantation. *Blood*. 2011;118(23):5989–95. <https://doi.org/10.1182/blood-2011-06-361386>
 48. Fonti R, Larobina M, Del Vecchio S, De Luca S, Fabbricini R, Catalano L, et al. Metabolic tumor volume assessed by 18F-FDG PET/CT for the prediction of outcome in patients with multiple myeloma. *J Nucl Med*. 2012;53(12):1829–35. <https://doi.org/10.2967/jnumed.112.106500>
 49. Zamagni E, Nanni C, Mancuso K, Tacchetti P, Pezzi A, Pantani L, et al. PET / CT Improves the Definition of Complete Response and Allows to Detect Otherwise Unidentifiable Skeletal Progression in Multiple Myeloma. 2015;21(19):4384–91. <https://doi.org/10.1158/1078-0432.ccr-15-0396>

50. Patriarca F, Carobolante F, Zamagni E, Montefusco V, Bruno B, Englari E, et al. Biology of Blood and Marrow Transplantation The Role of Positron Emission Tomography with 18F-Fluorodeoxyglucose Integrated with Computed Tomography in the Evaluation of Patients with Multiple Myeloma Undergoing Allogeneic Stem Cell Transplantation. Biol Blood Marrow Transplant [Internet]. 2015;21(6):1068–73. Available from: <http://dx.doi.org/10.1016/j.bbmt.2015.03.001>

51. Lapa C, Lückerrath K, Malzahn U, Samnick S, Einsele H, Buck AK, et al. FDG-PET / CT for prognostic stratification of patients with multiple myeloma relapse after stem cell transplantation. 2014;5(17). <https://doi.org/10.18632/oncotarget.2290>

Tables

Table 1 Demographic and clinical properties of patients.

N	60 (100%)
Age (mean ± SD)	67.3 ± 10.2
Sex (females:males)	27:33; 1:1.22; 45%:55%
Monoclonality type	
· IgG <i>k</i>	· 31 patients (51.6%)
· IgGλ	· 19 patients (31.6%)
· IgAλ	· 5 patients (8.3%)
· IgA <i>k</i>	· 2 patients (3.3%)
· IgDλ	· 2 patients (3.3%)
· IgD <i>k</i>	· 1 patient (1.6%)
Durie-Salmon staging	
· stage I	
· stage II	· 4 (6.66%)
· stage III	· 6 (10%)
· NA	· 33(55%)
	· 17 (28.33%)

Figures

Figure 1

60 y/o male, DSSS (Durie-Salmon staging system) III a) Transaxial FDG PET/CT scan image demonstrates active myeloma lesion in the right anterior iliac crest level with strong FDG uptake, SUVmax of 7,76. (white arrow) b) Sagittal FDG PET/CT scan image show high metabolic active areas. c) Whole body FDG PET/ CT Maximal Intensity Projection (MIP) image shows significant myelomatous involvement areas.

Figure 2

71 y/o female, SUVmax of ROI 1.34, DSSS N/A a) Transaxial FDG PET/CT scan image shows iliac crest level with low FDG uptake, SUVmax of 1,34. b, c) Sagittal FDG PET/CT scan image and whole body FDG PET/CT MIP image shows non-FDG avid myeloma area.

Figure 3

Plasma cell biopsy sample, HE-stained, $\times 400$ under a light microscope (BX53 Olympus, Japan). PC infiltration rate, 41.5%. Corresponds to the patient in Figure 1

Figure 4

Plasma cell biopsy sample, HE-stained, $\times 400$ under a light microscope (BX53 Olympus, Japan). PC infiltration rate, 11.45%. Corresponds to the patient in Figure 2

Figure 5

Scatter plot of the relationship between FDG uptake and the PC infiltration rate, derived from PET/CT scan and bone marrow biopsy sample ($r=0.7$, $p<0.001$).

Figure 6

Scatter plot of the relationship between FDG uptake and b2m, derived from PET/CT scan and hematological test sample (21 cases) ($r=0.596$, $p=0.004$)