

The relationship between bone marrow involvement on ¹⁸F-FDG PET/CT and bone marrow biopsy in patients with multiple myeloma and other plasma cell neoplasms



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Background: Bone marrow biopsy (BMB) plays a crucial role in the diagnosis and assessment of treatment response in patients with multiple myeloma (MM). ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) has been shown to be a complimentary measure of marrow involvement in patients with Hodgkin and diffuse large B cell lymphomas. However, only limited information is available on its relationship with BMB in MM.

Aim: To assess the association between bone marrow involvement on ¹⁸F-FDG PET/CT, and BMB in patients with MM and other plasma cell neoplasms.

Setting: Cape Town, South Africa.

Methods: Hundred and three patients undergoing ¹⁸F-FDG PET/CT and BMB were included. Plasma cell infiltration (PCI) on BMB was compared for three visual patterns of ¹⁸F-FDG bone marrow uptake (irregular, diffuse less than or equal to the liver and diffuse greater than liver).

Results: Eighty-four patients had diffuse bone marrow uptake. Of these, 25/84 had uptake greater than liver, all having PCI $\geq 60\%$ and a median value of 85%. Of the 84 patients, the 59 patients with uptake less than or equal to liver had PCI $< 10\%$ in 57.6% (34/59), and $\geq 10\%$ in 42.4% (25/59) with a median value of 8%. Nineteen patients had irregular bone marrow uptake. Of these, 4/19 (21.1%) had PCI of $< 10\%$ and 15/19 (78.9%) had PCI $\geq 10\%$, with the median value of 23%. The median percentage of PCI across the three described patterns of FDG uptake was significantly different ($p = 0.0001$).

Conclusion: ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography might avoid the need of repeat BMB in most of the patients with diffuse and irregular patterns of ¹⁸F-FDG uptake.

Keywords: multiple myeloma; ¹⁸F-FDG PET/CT; bone marrow biopsy; patterns of ¹⁸F-FDG uptake; plasma cell neoplasms.

Introduction

Multiple myeloma (MM) is a plasma cell neoplasm characterised by unrestrained monoclonal proliferation of malignant plasma cells, which develop from B lymphocytes within the bone marrow.¹ As shown in Table 1, the diagnosis of MM is based on criteria that include plasma cell infiltration (PCI) of bone marrow, paraproteinaemia and the presence of end-organ damage, manifesting as hypercalcaemia, renal failure, anaemia and bone lesions (represented by the acronym CRAB).^{2,3} Most patients with MM progress from an asymptomatic pre-malignant stage called monoclonal gammopathy of undetermined significance (MGUS). In some patients, an intermediate asymptomatic but more advanced pre-malignant stage termed smouldering multiple myeloma (SMM) can be recognised. This progresses to myeloma at a rate of 10% per year over the first 5 years, 3.0% per year over the following 5 years and 1.5% per year subsequently.⁴ Now, MM can also progress from an underlying solitary plasmacytoma.²

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TABLE 1: Diagnostic criteria for plasma cell neoplasms according to the international myeloma working group.

Type of PCN	Diagnostic criteria
MGUS	All three criteria must be met: <ul style="list-style-type: none"> • Serum IgM monoclonal protein concentration < 30 g/L • Bone marrow lymphoplasmacytic infiltration of < 10% • Absence of myeloma defining events and amyloidosis
SMM	Both criteria must be met: <ul style="list-style-type: none"> • Serum M protein (IgG or IgA) ≥ 30 g/L or urinary M protein ≥ 500 mg/24 h and/or clonal bone marrow plasma cell percentage of 10% – 60% • Absence of myeloma defining events or amyloidosis
MM	Clonal bone marrow plasma cell percentage ≥ 10% or biopsy-proven plasmacytoma and ≥ 1 of the following myeloma-defining events: <ul style="list-style-type: none"> • Hypercalcaemia: serum calcium > 0.25 mmol/L (> 1 mg/dL) higher than the upper limit of normal or > 2.75 mmol/L (> 11 mg/dL) • Renal insufficiency: creatinine clearance < 40 mL/min or serum creatinine > 177 μmol/L (> 2 mg/dL) • Anaemia: a haemoglobin value of > 2 g/dL below the lower limit of normal or a haemoglobin value < 10 g/dL • Bone lesions: ≥ 1 osteolytic lesion on skeletal radiography, CT or PET/CT • One or more of the following biomarkers of malignancy: <ul style="list-style-type: none"> • Clonal bone marrow plasma cell percentage ≥ 60% • An involved-to-uninvolved serum free light chain ratio ≥ 100 • Greater than 1 focal lesion on MRI
Plasmacytoma	All four criteria must be met: <ul style="list-style-type: none"> • Biopsy-proven solitary lesion of bone or soft tissue consisting of CPC. • Normal random bone marrow biopsy with no evidence of clonal plasma cells • Normal skeletal survey and MRI or CT (except for the primary solitary lesion) • Absence of end-organ damage, such as hypercalcaemia, renal insufficiency, anaemia and bone lesions (CRAB) attributable to a plasma cell proliferative disorder

Source: Adapted from Rajkumar SV. Updated diagnostic criteria and staging system for multiple myeloma. *Am Soc Clin Oncol Educ B.* 2016;36:e418–e423. https://doi.org/10.1200/EDBK_159009
MGUS, monoclonal gammopathy of undetermined significance; M protein, Monoclonal protein; IgM, immunoglobuline M; IgG, immunoglobuline G; CT, computed tomography; PET/CT, positron emission tomography/computed tomography; MRI, magnetic resonance imaging; CPC, clonal plasma cell; PCN, plasma cell neoplasm; MM, multiple myeloma; SMM, smouldering multiple myeloma.

Microscopic examination of the bone marrow plays a crucial role in the diagnosis of MM. In association with other clinical and laboratory parameters, bone marrow findings are used to differentiate patients with active MM from MGUS and SMM.⁵ It is also essential when evaluating response to therapy in patients with secretory and non-secretory myeloma. In non-secretory myeloma, the only way to assess myeloma tumour burden is with frequent bone marrow examination.⁶ The bone marrow biopsy (BMB) is also required for the definitive categorisation of a complete response to anti-MM therapy. Complete response includes disappearance of any soft tissue plasmacytomas and < 5% plasma cells in the bone marrow.^{7,8} However, BMB has a potential limitation with the risk of non-representative sampling because of the disease being unevenly distributed in the early stages. The pattern of distribution of plasma cells in MM varies from scattered interstitial plasma cells to small clusters or diffuse sheets.³

¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) is a surrogate measure of intracellular glucose metabolism and is a sensitive method for detecting, staging and monitoring therapy for various malignant tumours.⁹ The role of ¹⁸F-FDG PET/CT is well established in solid tumours, but also forms part of the evaluation of MM, being included in the Durie-Salmon plus staging system, as well as the international myeloma working group (IMWG) updated criteria for the diagnosis of MM.^{4,10} It is a useful tool to assess and monitor response to treatment because of its ability to differentiate between metabolically active and inactive sites of proliferating clonal plasma cells.¹¹ It is valuable for the work-up of patients with both newly diagnosed and relapsed or refractory MM, as it evaluates bone damage, and detects medullary and extramedullary sites of disease with relatively high sensitivity and specificity.¹² It also provides important prognostic information.^{11,13} The ¹⁸F-FDG PET/CT can also be combined with sensitive bone marrow-based techniques to detect minimal residual disease (MRD) inside and outside the bone marrow, helping to identify patients defined as being imaging MRD negative.^{8,12}

The ¹⁸F-FDG PET/CT has been shown to be a complimentary measure of bone marrow involvement in lymphomas, particularly in Hodgkin lymphoma and diffuse large B cell lymphoma.¹⁴ Only limited information is available on its potential role in the assessment of bone marrow involvement in plasma cell neoplasms. It is also unclear as to what extent bone marrow hypercellularity because of other comorbidities such as anaemia may affect this. Therefore, the purpose of this study was to assess the association between the visual assessment of ¹⁸F-FDG bone marrow uptake on PET/CT and BMB in assessing bone marrow involvement in patients with plasma cell neoplasms.

Methods

We conducted a retrospective cross-sectional audit of patients with plasma cell neoplasm who attended services at the Tygerberg Hospital Nuclear Medicine Division between January 2013 and July 2020. We screened 190 patients with plasma cell neoplasm for inclusion in our study. Patients who did not have a BMB and/or ¹⁸F-FDG PET/CT scans for the same indication, or whose medical records were incomplete or missing were excluded. The final sample size was 103 patients.

Data for the percentage of PCI of bone marrow biopsies and the pattern of ¹⁸F-FDG on PET/CT were collected. The percentage of plasma cells was based on bone marrow aspiration and biopsy. We also collected data for age, treatment status, haemoglobin level, human immunodeficiency virus (HIV) status and the time difference between ¹⁸F-FDG PET/CT and BMB.

¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography imaging protocol and image interpretation

The ¹⁸F-FDG PET/CT was performed following patient fasting (other than plain unflavoured water and permitted medications) for 4–6 h prior to the injection. In addition, to

prevent non-specific uptake because of treatment related inflammation, images were acquired 6–8 weeks after chemotherapy and/or at least 2 weeks discontinuation of the maintenance chemotherapy/steroid and at least 3 months following radiotherapy. Vertex to distal thigh images were acquired using a Philips Gemini TF PET/CT camera (Philips Medical Systems, Best, the Netherlands). This included a low-dose CT scan (16-slice; 0.5 s rotation; 120 kilovoltage peak (kVp); 80–165 milli-ampere-second (mAs) depending on the body mass index). The PET images were reconstructed with a standard iterative time-of-flight reconstruction algorithm (BLOB-OS-TF) with the CT data utilised for attenuation correction and image fusion.

Images were interpreted based on a proposed simple visual criterion for assessing bone marrow involvement in patients with plasma cell neoplasms. The ^{18}F -FDG PET/CT was reported by consensus by a nuclear medicine physician and radiologist. Criteria for defining the ^{18}F -FDG PET/CT positive studies for bone marrow involvement included diffuse uptake greater than liver or irregular uptake. A mixture of these two patterns of FDG uptake was categorised as irregular. The ^{18}F -FDG PET/CT was defined as negative if the bone marrow uptake was diffuse and less than or equal to liver.

Statistical analysis

Data were imported to STATA Statistical Software, version 15 (StataCorp. 2017, College Station, TX: StataCorp LLC). Bone marrow involvement expressed as % PCI was compared for different patterns of ^{18}F -FDG uptake using a Kruskal-Wallis test, and a quantile regression including an evaluation of the effects of treatment status, HIV status, haemoglobin level and the timing of the ^{18}F -FDG PET/CT relative to the BMB.

Bone marrow involvement on biopsy expressed as a binary categorisation (positive if $\geq 10\%$ or negative if $< 10\%$) was also compared for different patterns of ^{18}F -FDG uptake using logistic regression, including an evaluation of the effects of the biopsy site and treatment status. Based on this categorisation, the sensitivity, specificity, positive and negative predictive values of bone marrow patterns on ^{18}F -FDG PET/CT were also determined.

A secondary outcome was assessing the potential impact of any discrepancy between the BMB and ^{18}F -FDG PET/CT, on the categorisation of the plasma cell neoplasm, and therefore management of the patient. For this, simple descriptive analysis was used. Statistical significance was set at $p < 0.05$.

Ethical considerations

This retrospective study was granted institutional approval by the Health Research Ethics Committee at Stellenbosch University (reference number: S20/06/153).

Results

The median participants' age was 60 years with an interquartile range of 53 to 67 years. Of the patients analysed, myeloma accounted for 68.9% ($n = 71$), plasmacytoma 21.4% ($n = 22$), MGUS 2.9% ($n = 3$) and smouldering myeloma 6.8% ($n = 7$).

Of all participants, 47.6% ($n = 49$) had received treatment and 52.4% ($n = 54$) were treatment naive (Table 2). Of the treated patients, only 6.1% ($n = 3$) had ^{18}F -FDG uptake diffusely greater than liver, 67.4% ($n = 33$) had uptake diffusely less than or equal to liver and 26.5% ($n = 13$) had irregular uptake. Of the untreated patients, uptake diffusely less than or equal to liver accounted for 48.2% ($n = 26$), uptake diffusely greater than liver was found in 40.7% ($n = 22$) and 11.1% ($n = 6$) of patients had irregular uptake. The median percentage of plasma cell bone marrow infiltration in the untreated patients was 25% and in the treated patients, it was 10%. Seven patients were positive for HIV, 81 negative and in 15 patients, HIV status was unknown (Table 2). The median time difference between BMB and ^{18}F -FDG PET/CT study was 0.97 months with an interquartile range of 0.33 to 1.87 months. The median haemoglobin (Hb) level of all participants was 11.6 g/dL with the interquartile range of 4.3 g/dL. The median haemoglobin level was lowest in the patients with high degree of PCI and positive on ^{18}F -FDG PET/CT for bone marrow involvement (Table 2).

Based on the BMB and aspiration results, the median percentage of plasma cell bone marrow infiltration of all patients was 15% with the interquartile range of 8% to 65%. A binarised classification of BMB found BMB to be positive ($\geq 10\%$ PCI) in 63.1% ($n = 65$) of patients and negative ($< 10\%$ PCI) in 36.9% ($n = 38$) of patients. The majority of untreated patients 74.1% ($n = 40$) had PCI of $\geq 10\%$ and 25.9% ($n = 14$) was with PCI of $< 10\%$. Of the treated patients, 51% ($n = 25$) had PCI of $< 10\%$ and 49% ($n = 24$) had PCI of $\geq 10\%$.

The ^{18}F -FDG PET/CT assessment found that 25 patients had diffuse bone marrow uptake greater than liver, 19 patients with irregular uptake and 59 patients with diffuse uptake less than or equal to liver (Table 2). The ^{18}F -FDG PET/CT was thus positive for marrow involvement in 42.7% patients

TABLE 2: Summary of results.

BM FDG Uptake patterns	n	PCI (Median) %	Hb (g/dL) (Median)	HIV status						PPT†			
				Negative		Positive		Unknown		No		Yes	
				n	%	n	%	n	%	n	%	n	%
Diffuse > liver	25	85.00	8.8	20	24.7	2	28.6	3	20.0	22	40.7	3	6.1
Diffuse \leq liver	59	8.00	12.7	45	55.6	5	71.4	9	60.0	26	48.1	33	67.3
Irregular	19	23.00	10.6	16	19.8	0	0.0	3	20.0	6	11.1	13	26.5

PPT; patient previous treated; %PCI; percentage of bone marrow plasma cell infiltration, Hb; haemoglobin, BM FDG; bone marrow fluorodeoxyglucose uptake.

†, Treatment includes radiotherapy and/or chemotherapy.

($n = 44$) and negative in 57.3% ($n = 59$) patients. All patients with smouldering myeloma and MGUS demonstrated uptake diffusely less than or equal to liver with a median PCI of 10% and 5%, respectively. Most of the patients with plasmacytoma (86.4%, $n = 19$) showed diffuse uptake less than or equal to liver and 13.6% ($n = 3$) demonstrated irregular uptake, with a median PCI of 5%. In patients with myeloma, 42.3% ($n = 30$) of patients showed diffuse uptake less than or equal to liver, 22.5% ($n = 16$) demonstrated irregular uptake and 35.2% ($n = 25$) showed diffuse uptake greater than liver. The median PCI for MM was 30%. Eighty-eight per cent ($n = 22$) of the patients with uptake diffusely greater than liver were untreated and only 12% ($n = 3$) had received treatment. On the other patients with uptake diffuse less than or equal to liver, 56% ($n = 33$) of patients were treated and 44% ($n = 26$) of them were untreated. Sixty-four per cent ($n = 13$) of the patients with irregular uptake were treated, while 36.6% ($n = 6$) of patients were untreated. Of the patients with false negative imaging using a PCI threshold of 10% as gold standard, 52% ($n = 13$) patients had received treatment including maintenance therapy and the remaining 40% ($n = 12$) of patients were untreated.

Patients with diffuse uptake greater than liver, irregular uptake and diffuse uptake less than or equal to liver had a median percentage and interquartile range bone marrow infiltration of 85% (60% – 90%), 23% (10% – 40%) and 8% (5% – 15%), respectively (Figure 1). Of the 59 patients with diffuse bone marrow uptake less than or equal to liver, 42.4% ($n = 25$) showed a PCI of 10% to 60% and the majority of these patients, 57.6% ($n = 34$) showed a PCI of < 10%. All patients with uptake diffusely greater than liver showed a PCI of $\geq 60\%$. However, the PCI in patients with an irregular pattern of ^{18}F -FDG uptake was highly variable, ranging from < 10% to > 60%. Of all the patients with irregular pattern of ^{18}F -FDG uptake, 21.1% ($n = 4$) had a PCI of < 10% and 78.9% ($n = 15$) patients demonstrated PCI of $\geq 10\%$. The BMB sites were positive in most of the patients with irregular ^{18}F -FDG uptake, with only 4 of 19 patients demonstrating a negative or inadequate BMB result.

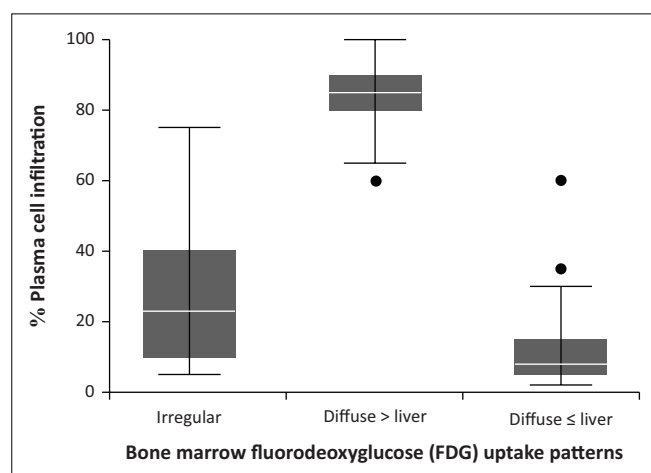


FIGURE 1: A box plot showing median and interquartile percentage of bone marrow plasma cell infiltration for the three patterns of ^{18}F -FDG uptake.

Analysis using Kruskal-Wallis rank testing found the median percentage of PCI differed across all three patterns of bone marrow ^{18}F -FDG uptake ($p = 0.0001$). Significant differences were also found comparing diffuse uptake greater than liver versus irregular uptake ($p < 0.001$), diffuse uptake greater than liver versus diffuse uptake less than or equal to liver ($p = 0.0001$) and diffuse uptake less than or equal to liver versus irregular uptake ($p = 0.001$).

Using a quintal regression analysis, patient treatment status and time difference between ^{18}F -FDG PET/CT and BMB had no statistically significant effect on the percentage of PCI across the described patterns of bone marrow uptake ($p = 0.821$ and $p = 0.094$, respectively). Quintal regression also showed that the patients with diffuse uptake greater than liver showed a median PCI 77% higher than in patients with diffuse uptake less than or equal to liver ($p < 0.001$). The patients with diffuse uptake greater than liver also showed a 62% higher median PCI than the patients with an irregular pattern of FDG uptake ($p < 0.001$). The percentage of plasma cell bone marrow infiltration in patients with an irregular pattern of uptake showed 15% higher median tumour burden when compared to patients with uptake less than or equal to liver ($p < 0.001$). The HIV status of the patients did not show a statistically significant effect on the percentage of plasma cell bone marrow infiltration across the three described patterns of FDG uptake ($p = 0.66$). Similarly, Hb level did not show statistically significant effect on the degree of ^{18}F -FDG uptake in comparison with PCI ($p = 0.134$).

When categorised as negative or positive, BMB results did not differ for the pattern of the ^{18}F -FDG uptake. Using multiple logistic regression, differences in bone marrow positivity across the patterns of ^{18}F -FDG uptake did not reach statistical significance ($p = 0.108$). Based on this categorisation, the sensitivity and specificity of ^{18}F -FDG PET/CT were 61.5% and 89.5%, respectively. The positive and negative predictive values were 90.9% and 57.6%, respectively.

Discrepancies in characterisation of bone marrow involvement between ^{18}F -FDG PET/CT and BMB were assessed. The ^{18}F -FDG PET/CT was found to provide additional information in 3/22 (13.6%) patients known with plasmacytoma, showing positive results, whereas the BMB was negative. In the remaining patients, PET/CT was either concordant with BMB or failed to detect bone marrow involvement detected on biopsy (in 6/34 newly diagnosed MM patients with PCI of 10% – 60%, and in 7/7 patients with SMM with low grade PCI).

Discussion

In this study, we evaluated the relationship between a simple three-way visual categorisation of bone marrow uptake on ^{18}F -FDG PET/CT and BMB in patients with plasma cell neoplasms.

Our results showed that the median percentage of plasma cell bone marrow infiltration across the three described

patterns of ^{18}F -FDG uptake was significantly different. Consistent with the findings of this study, several previous studies based on bone marrow standard uptake values showed a strong positive correlation between ^{18}F -FDG PET/CT and BMB.^{15,16,17}

Patients with normal appearing (diffuse non-hypermetabolic) bone marrow on ^{18}F -FDG PET/CT (Figure 2c) had the lowest PCI, although in a significant proportion PCI still exceeded 10% but was not greater than 20%. This is consistent with the concentration of malignant plasma cells not being high enough and/or metabolically active to create a detectable signal on PET/CT. The low sensitivity of PET/CT for low grade PCI has also been reported in a previous study.¹⁸

Conversely, diffuse hypermetabolic bone marrow on ^{18}F -FDG PET/CT (Figure 2a) correlates with a high degree of bone marrow PCI. These patients invariably had a high PCI, typically > 60%. Similar result has been reported in a recent study.¹⁹ This is consistent with diffuse hypermetabolism on ^{18}F -FDG PET/CT because of a diffusely high concentration of malignant plasma cells. Interestingly in this study population, none of the cases were found to be because of hypercellularity related to secondary anaemia or

inflammation. Therefore, diffuse uptake greater than liver on ^{18}F -FDG PET/CT was found to be highly predictive of bone marrow infiltration with high tumour burden in patients with MM.

An irregular pattern on ^{18}F -FDG PET/CT (Figure 2b) showed greater variability in percentage of plasma cell bone marrow infiltration. This is probably because of variability of bone marrow sampling. The percentage of plasma cell bone marrow infiltration was generally greater than those with normal appearing bone marrow and less than those with diffuse hypermetabolic bone marrow. It is likely that in the majority of these patients have significant bone marrow infiltration in some areas, but in many of these cases, BMB was poorly representative.

Patterns of ^{18}F -FDG uptake had no statistically significant effect on the negativity or positivity of the BMB result based on a 10% threshold. At the same time, the sensitivity and negative predictive value of ^{18}F -FDG PET/CT was relatively low using BMB as gold standard for bone marrow involvement assessment. Thus, whilst one is unable to use PET/CT alone to assess bone marrow, it can complement BMB particularly in patients with irregular bone marrow infiltration.

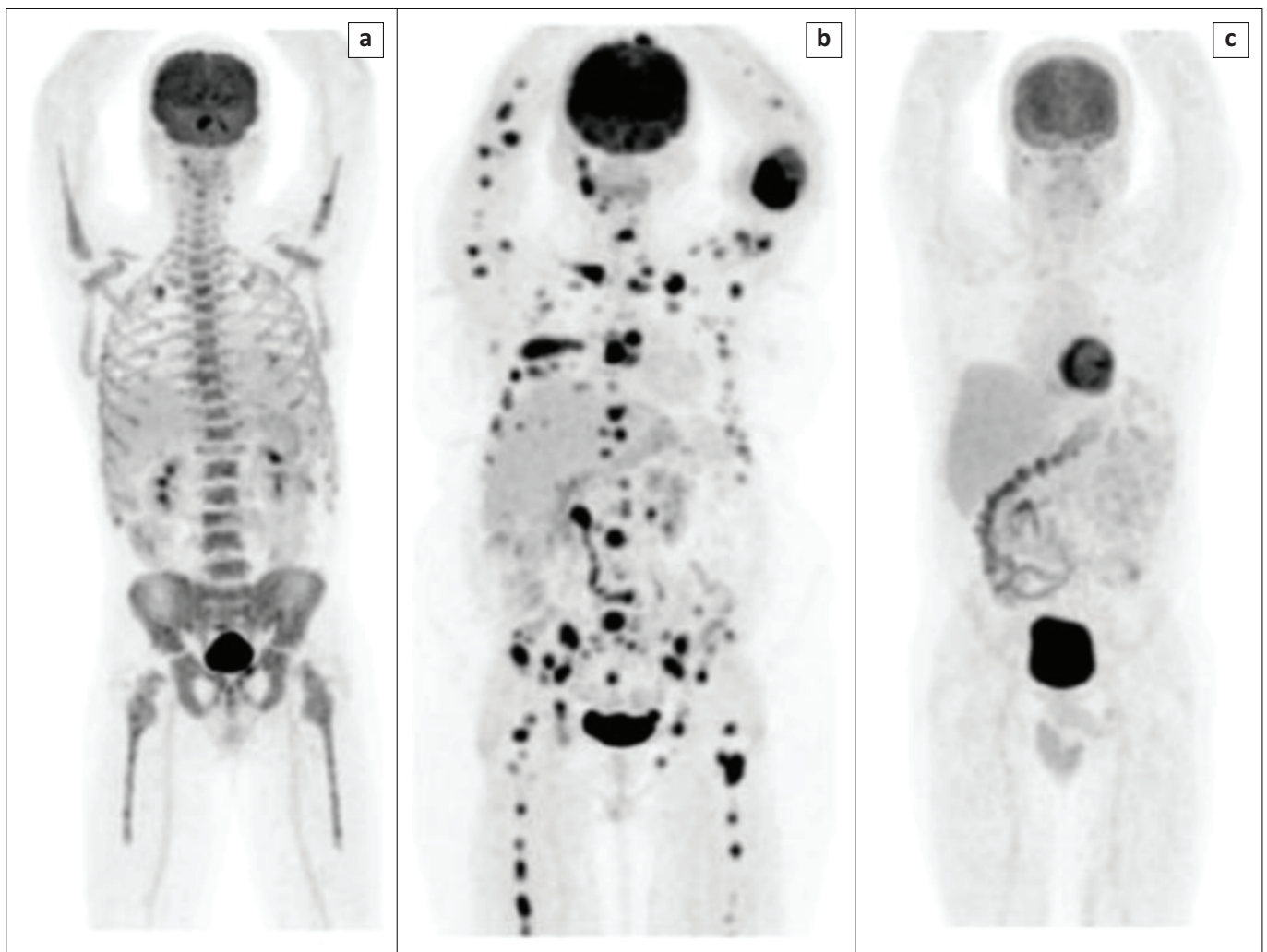


FIGURE 2: The three patterns of ^{18}F -FDG uptake in three of the study patients. (a) Diffuse greater than liver; (b) irregular and (c) diffuse less than or equal to liver.

As far as the authors are aware, there are no published studies to assess the relationship between BMB and ^{18}F -FDG bone marrow uptake which use PET interpretation criteria directly comparable to those used here. A dynamic ^{18}F -FDG PET/CT study over the pelvis and lower lumbar spine of the PCI in four described patterns of ^{18}F -FDG uptake found that the highest PCI was in patients with mixed pattern of ^{18}F -FDG uptake.²⁰ The comparability of these two studies is questionable.

While it cannot replace BMB for diagnosis, classification of bone marrow involvement on ^{18}F -FDG PET/CT using the three categories described here may augment biopsy information. In patients with diffuse marrow involvement, we can accept that BMB is representative, and that marrow intensity is related to PCI. However, in patients with a lower grade bone marrow infiltration, this may not be visually detectable. In this study, in some patients with irregular ^{18}F -FDG uptake, BMB was not representative. Used in isolation, this may result in underestimation of PCI and potentially even a false negative BMB result. Consequently, there is a potential for mis-categorisation and/or undertreatment of the patient.

The Italian Myeloma criteria for PET Use (IMPeTUs) provide comprehensive visual interpretation criteria for ^{18}F -FDG PET/CT image interpretation in order to make clinical trial results more consistent and reproducible.²¹ The system used in this study consolidates this more comprehensive classification into three broad categories based on the potential effect on the BMB results. This provides the advantage of simplicity but does not rule out the possibility that more information may be obtainable using a more detailed classification. Similarly in a recent study aimed on standardisation of ^{18}F -FDG PET/CT according to Deauville Criteria (DC) for metabolic complete response definition in newly diagnosed MM patients, FDG PET/CT was confirmed to be a reliable predictor of outcomes using the DC.²² Given the simplicity of the three-way categorisation used here, it is likely to have a low inter-observer variability, although this was not measured in this work. Several previous studies reported comparable patterns of plasma cell bone marrow infiltration on ^{18}F -FDG PET/CT.^{19,23,24,25}

Inherent limitations of this study were its retrospective nature and the heterogeneity of the study population. Potential consequences of these are the confounding effects of treatment status, haemoglobin level, HIV status and time of difference between ^{18}F -FDG PET/CT and BMB. However, analysis showed no statistically significant effect for any of these in this study sample. The non-significant effect of therapy status may in part be because of the two measurements (^{18}F -FDG PET/CT and BMB) being performed for the same treatment status (new/untreated or treated) in all patients.

Conclusion

The ^{18}F -FDG PET/CT and BMB showed a good concordance in patients with representative BMB samples. Diffusely hypermetabolic bone marrow on ^{18}F -FDG PET/CT

corresponds to PCI of > 60%. Diffuse marrow that is not hypermetabolic corresponds to a significantly lower PCI, but it does not reliably predict PCI of < 10%. In a minority of patients with irregular bone marrow infiltration, reliance on BMB alone may result in underestimation of PCI with potential undertreatment of the patient. Therefore, although ^{18}F -FDG PET/CT may not replace BMB for diagnosis in MM, it can provide complementary information. However, ^{18}F -FDG PET/CT may avoid the need of repeat bone marrow biopsies in most of the patients with diffuse and irregular bone marrow ^{18}F -FDG uptake although its sensitivity is low for low grade PCI. A properly designed prospective study is suggested to support this finding.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

K.S.G. was responsible for study design, data collection, analysis, interpretation and manuscript writing. F.C.B. was responsible for study design, data collection, interpretation and manuscript editing. Z.C.C. was responsible for data collection, interpretation and manuscript editing. J.M.W. was responsible for study design, analysis, interpretation and manuscript editing.

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Data availability

Derived data supporting the findings of this study are available from the corresponding author, K.S.G., on request.

Disclaimer

The views and opinions expressed in this research article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

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