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ORIGINAL RESEARCH ARTICLE

Extended field imaging in 2-[^{18}F]FDG PET/CT in multiple myeloma

Zehra Pınar Koç[1], Pelin Özcan[1], Aydan Akdeniz[2], Zeynep Selcan Sağlam[1]

[1]*Department of Nuclear Medicine, Faculty of Medicine, Mersin University, Mersin, Turkey*

[2]*Department of Hematology, Faculty of Medicine, Mersin University, Mersin, Turkey*

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*Corresponding Author:
Dr. Zehra Pınar Koç
Address: Department of Nuclear Medicine, Faculty of Medicine, Mersin University, Mersin, Turkey
Email: zehrapinarkoc@gmail.com

ABSTRACT

Introduction: Previous studies suggested the prognostic significance of the number of involvement sites in 2-[^{18}F]FDG PET/CT imaging in multiple myeloma. The aim of this study was to evaluate the significance of the findings that might be observed in case of whole body (extended field) imaging in the 2-[^{18}F]FDG PET/CT in multiple myeloma patients.

Methods: The imaging findings of 70 patients (33 female, 37 male; mean 66.3±10.2 years old) with the diagnosis of multiple myeloma 2-[^{18}F]FDG PET/CT were evaluated retrospectively. The patients were divided into two groups; Group 1; the patients with pathologic findings (lytic lesions with maximum standardized uptake value of >4) in extended field imaging and Group 2; the others respectively.

Results: The comparison of the two groups revealed no statistical significant difference between their index lesions uptake values (P>0.01). The time to progression of the groups were not significantly different (p=0.08) in the mean 27.2±32.5 months follow up. However, the ratio of disease specific mortality was higher (33% vs 5%) in the group of patients with extended field imaging findings.

Conclusion: Extended field imaging might point out higher disease specific mortality but this issue has to be evaluated by further studies in larger series.

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INTRODUCTION

Multiple myeloma is a hemotologic disease that is presented with both bone marrow involvement and solid lesions as well as lytic lesions of the bone. 2-[^{18}F]FDG PET/CT recently the test of choice in staging, restaging and treatment response evaluation in the workup of Multiple myeloma as presented in the guidelines [1]. The bone marrow involvement as well as soft tissue (extramedullary, paramedullary) involvements of the Multiple Mylema can be demonstrated precisely by 2-[^{18}F]FDG PET/CT. Recent studies usually compare WB-MR imaging with 2-[^{18}F]FDG PET/CT and 2-[^{18}F]FDG PET/MR imaging is considered a future direction in multiple myeloma [2-5]. The prognostic value of the 2-[^{18}F]FDG PET/CT is also well established with previous results; among these the SUVmax levels and as well as the number of focal lesions with significant 2-[^{18}F]FDG accumulation are considered the most important prognostic parameters [6, 7]. The imaging field in the routine 2-[^{18}F]FDG PET/CT imaging consists of the limited field (skull base to mid thigh) however there is a trend of extended field imaging in multiple myeloma. The aim of this study was to analyze the role of extended field imaging in multiple myeloma.

METHODS

Patients

The study was approved by Mersin University Ethics Committee (Date: 28/4/2021, Number: 2021/352) and the patients with the diagnosis of multiple myeloma (N: 70; 33F, 37M, mean: 66,3±10,2 years old) who were referred for staging /restaging/ treatment response evaluation to the 2-[^{18}F]FDG PET/CT were the subjects of this study. The patients were included in case of definite diagnosis of Multiple Myleoma. The patients with anamnesis of lactation/pregnancy and other malignancy and deniying the imaging were excluded.

Imaging study

The patients fasted at least 4 hours prior to the 2-[^{18}F]FDG PET/CT with restriction of physical activity for at least 24 hours. The imaging was performed after injection of the radiopharmaceutical (2-[^{18}F]FDG) (approximately 370 MBq/10 mCi according to the body weight) via venous line from vertex to the base of foot in craniocaudal direction with additional low dose CT scan for attenuation correction with oral contrast administration by the PET/CT scanner (Siemens MCT).

Image interpretation

The images of the patients were evaluated with visual interpretation for reporting by two experienced nuclear medicine physician as well as second interpretation was performed by an experienced nuclear medicine physician for research purposes. The images were also semi-quantitatively evaluated with circular region of interests of the bone marrow (BM), from the most active lesion (Index lesion-IL), second lesion and thirdly the extremity lesion (EL) which could not possibly have determined in case of limited imaging. The SUVmax of a lesion above 4 was accepted as high according to this study. The patients were divided into two groups according to imaging findings; Group 1: patients without EL and Group 2: patients with EL. The paired samples T test and Kaplan Meier analysis were performed in order to compare groups with IBM SPSS statistics program. Follow up of the patients were considered by an experienced Hematology physician; the treatment history, time to progression and mortality of the patients were evaluated.

RESULTS

There were 39 patients in group 1 and 31 patients in group 2. The patients ages (68.8±9.8 vs 63.2±9.9) and bone marrow uptake values (4.04±1.6 vs 5.5±3.5) were significantly different but the SUVmax of the index lesion (8.5±6.2 vs 63.2±9.9) were not different. According to the paired samples T test the uptake values of the EL (SUVmax=8.2±8.8) compared to the BM (SUVmax=5.5±3.5) and IL (SUVmax=10.5±7.9) of the patients in group 2 were significantly different (p=0.05 and p=0.04, respectively).

Ten patients in group 2 and 5 patients in group 1 died in the 27.2±32.5 months follow up. Among these, 3/5 of the patients in group 1 died due to fungal infection, hearth failure and renal failure and only one patient died due to disease progression. The time to progression values were not significantly different (12.9±21.12 vs 8.2±8.8 months respectively; P=0.089).

The patients were analyzed according to the findings of the initial PET/CT image results and the patients imaging status was decided as more than five focal lesions, bone marrow uptake, lytic lesions, extramedullary involvement and paramedullary involvement or combination of these. (Table 1) The extended field imaging changed patients management by changing the group in 6 patients (Figures 1 & 2). Additionally the difference between the duration of life was significantly lower (p=0.0295) in the Group 2 according to the Kaplan Meier curves (Figure 3).

Table 1. The patients PET/CT results and mortality status according to the groups

Patients No	Group 1		Group 2	
	Mortality	PET/CT	Mortality	PET/CT
1	ex	>5FL	ex	EM
2	ex	BM	ex	BM, >5FL
3		BM		BM
4		BM, LL		BM, <5FL
5		>5FL		BM, <5FL
6		>5FL		BM
7		FL, BM		FL, EM
8		>5FL, PM		PM, <5FL
9		BM, LL		BM, EM
10		EM		BM, EM, FL
11		>5FL		>5FL, BM
12		>5FL	ex	>5FL, BM
13		FL, PM	ex	PM, EM
14		LL		BM, PM
15		>5FL		BM, FL
16		FL	ex	>5FL, EM
17		>5FL		LL
18		FL, LL		BM, FL
19		FL		BM, >5FL
20		BM		>5FL
21		BM, LL	ex	>5FL
22		BM, LL		BM, FL
23		BM		BM, LL, FL
24		BM, LL		>5FL
25		FL, LL	ex	>5FL, LL
26		>5FL		BM
27		FL, BM		>5FL
28	ex	2FL	ex	>5FL
29		LL	ex	BM, >5FL
30		BM, FL		BM, >5FL
31		>5FL	ex	>5FL
32	ex	2FL, EM		
33		>5FL		
34		EM, BM		
35		>5FL, LL		
36		EM		
37	ex	LL, FL		
38		LL		
39		LL, FL		

BM: Bone marrow, FL: Focal lesions, EM: Extramedullary, PM: Paramedullary

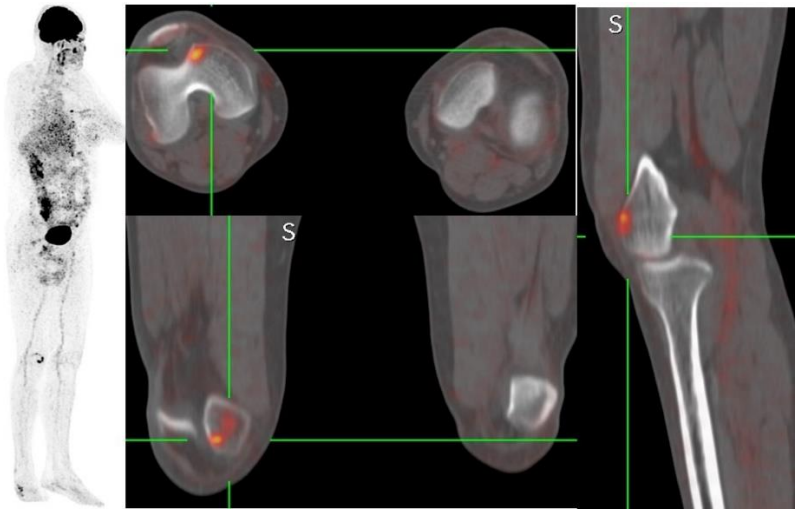

Fig 1. The patient with single pathologic lesion at the distal diaphysis of right femur (outside the routine imaging field); 68 years old male patient referred for restaging; Multiple intensity projection, transaxial, sagittal and horizontal slices of fusion PET/CT images, respectively

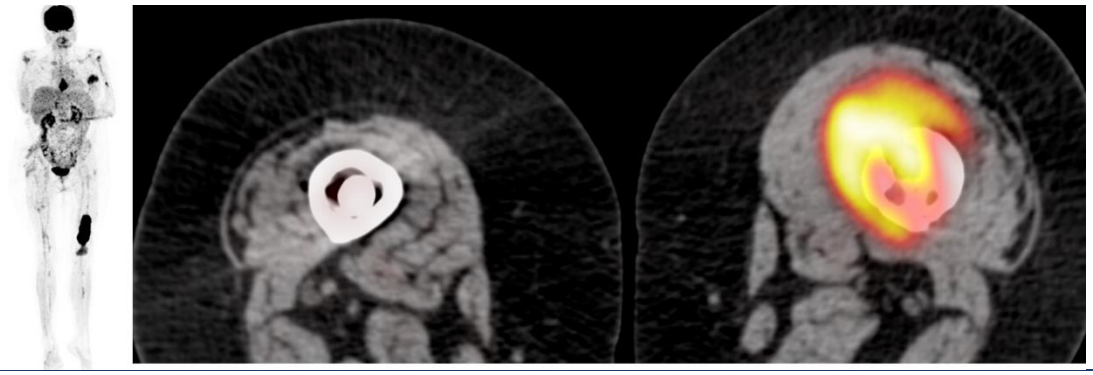

Fig 2. The patient presented with progressive right distal femoral lesion as well as thoracic plasmocytoma; multiple intensity projection and transaxial fusion PET/CT images of a female patient at 53 years of age

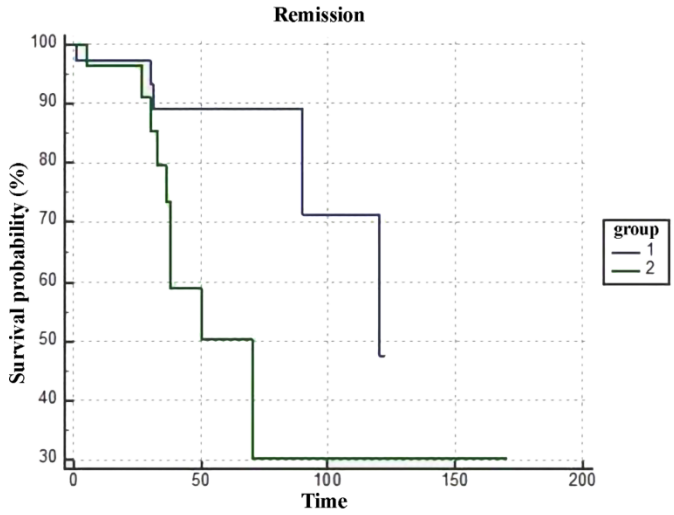

Fig 3. The Kaplan-Meier survival curves

DISCUSSION

The extended field imaging changed the patients management in 6 among the 70 patients included in the analysis. Additionally the disease spesific mortality was higher (33% vs 5%) compared with the Group 1 patients. However time to progression and other parameters (index lesion uptake) were not significantly different among groups.

The former imaging methods in the follow up of multiple myeloma included Skeletal Survey which showed lytic lesions of the disease. However recent developments in the multiple myeloma imaging is providing activity of the bone lesions and the soft tissue lesions as well as bone marrow involvement. Whole body MR imaging and 2-[^{18}F]FDG PET/CT are recently the tests of choice for multiple myeloma due to the high resolution and superiority of showing the bone and soft tissue lesions in a single imaging modality. A recent study comparing these modalities with Skeletal survey strongly suggest the inclusion of one of these modalities in the workup of the patients with multiple myeloma [2]. In that study the diagnostic parameters were concordant in medullary and extramedullary involvement of the patients but the bone marrow findings after treatment might suggest false positive results in MR thus PET/CT is superior in the treatment response decision [8, 9]. Another study about the detection of minimal residual disease by PET/CT and MR showed that concordant negativity might point out the disease outcome [10]. However there are some reports about the higher sensitivity of MR at initial staging for bone marrow involvement [11]. A recent study have suggested that the MR is superior to the 2-[^{18}F]FDG PET/CT in both lesion and bone marrow involvement detection [12]. However that study included non extended field approach.

The previous studies in the evaluation of multiple myeloma by PET/CT suggested the classification of the lesions into groups of focal lesions, bone marrow uptake, and extramedullary-paramedullary disease thus we performed this discrimination in this study. According to a previous study >3 focal lesions is a independent prognostic factor associated with PF and OS [13]. Additionally high risk associated with six [14] and ten [15] focal lesions have been determined previously. Since the number of focal lesions is a major concern to predict survival the extended field imaging can be suggested in the workup of multiple myeloma. In our series nearly half of the patients (31/70) had lesions beyond the routine imaging field.

Considering the lesion positivity 'SUVmax cutoff value'; a previous study including 172 patients at first diagnosis were analyzed and the bone marrow uptake higher than the liver background activity was accepted as positive and it was suggested that the mixed uptake pattern (diffuse and focal) is associated with worse PFS and OS [16]. . Extramedullary disease is another independent prognotic factor. In this presented study we demonstrated the importance of the extended field imaging. A recent article also have demonstrated the high extremity involvement of the disease (25%) might contribute to the fragility and fractures of lung bone and PET/CT can determine fracture risk [17] among 21% of the patients with long bone lesions were determined by PET/CT and 8% of patients experienced fracture. The MR findings of 67 patients who has pain were examined and the change in management was shown in 58.5% due to the appendicular skeleton involvement [18]. Similarly, Abe et al. have shown the prognostic significance of the appendicular focal lesions detected by pretreatment PET/CT also [19].

Another recent prognostic index; heterogeneity factor was used in multiple myeloma in a research study and concluded that this index is an independent prognostic factor [20]. 2-[^{18}F]FDG PET/CT also could be prefered for soft tissue involvements (paramedullary and extramedullary) of the disease with better diagnostic performance compared to MR [21]. A quantative index in the PET/CT and its difference during treatment (ΔIBI) was shown to be in a good indicator of the disease progression and regression [22].

[^{68}Ga] DOTA FAPI-04 PET/CT which is a recent modality has shown to be superior compared to 2-[^{18}F]FDG in some certain tumors. Multiple myeloma and lymphoma were not among these group of tumors according to a recent study [23].

Recent studies also indicate the prognostic value of SUVmax and number of focal lesions with 2-[^{18}F]FDG uptake [24] as well as total lesion glicolysis and metabolic tumor volume [25]. Additionally, multiple myeloma imaging by means of PET/CT with other radiopharmaceuticals are presented as case report or pilot studies with radioabeled choline/methionine analogs [26, 27].

Limitation

The limitation of this study was the retrospective nature of this study.

CONCLUSION

Extended field imaging might be a necessity in the patients with diagnosis of multiple myeloma due to the disseminated nature of the disease. Furthermore this study showed prognostic value by predicting disease related death.

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