

Original Article

Prognostic significance of ^{18}F -sodium fluoride in newly diagnosed multiple myeloma patients

Mahdi Zirakchian Zadeh^{1,2}, Siavash Mehdizadeh Seraji¹, Brian Østergaard³, Stephanie Mimms⁴, William Y Raynor^{1,5}, Mahmoud Aly¹, Austin J Borja¹, Leila S Arani¹, Oke Gerke⁶, Thomas J Werner¹, Hongming Zhuang⁷, Mona-Elisabeth Revheim^{8,9}, Niels Abildgaard^{3,10}, Poul Flemming Højlund-Carlsen⁶, Abass Alavi¹

¹Department of Radiology, Hospital of The University of Pennsylvania, PA, USA; ²Penn Dental School of Medicine, University of Pennsylvania, PA, USA; ³Department of Hematology, Odense University Hospital, Odense, Denmark; ⁴MMRC, Jackson, MS, USA; ⁵Drexel University College of Medicine, Philadelphia, PA, USA; ⁶Department of Nuclear Medicine, Odense University Hospital, Odense, Denmark; ⁷Children's Hospital of Philadelphia, Division of Nuclear Medicine, Department of Radiology, PA, USA; ⁸Division of Radiology and Nuclear Medicine, Oslo University Hospital, Oslo, Norway; ⁹Faculty of Medicine, University of Oslo, Norway; ¹⁰Hematology Research Unit, Department of Clinical Research, University of Southern, Denmark

Received June 12, 2020; Accepted August 22, 2020; Epub August 25, 2020; Published August 30, 2020

Abstract: Focal bone lesions and fractures due to weakened bone are associated with higher morbidity and mortality of multiple myeloma (MM) patients. ^{18}F -sodium fluoride (^{18}F -NaF) is a sensitive PET radiotracer for detection of abnormal bone metabolism and, therefore, is particularly suited to assess the degree of bone involvement in MM patients. We aimed to investigate the prognostic significance of metabolic active volume (MAV) of ^{18}F -NaF-avid lesions in MM patients. In addition to MAV, conventional methods of PET quantification, namely SUVmean and SUVmax, were measured in each patient for the purpose of comparison. Thirty-seven newly diagnosed MM patients were included. PET imaging was performed after intravenous administration of 200 MBq NaF. Active bone lesions and fractures on whole-body ^{18}F -NaF-PET/CT scans were identified. An adaptive thresholding algorithm automatically calculated the total MAV, SUVmean and SUVmax for each patient (ROVER, ABX, Radeberg, Germany). The patients were followed for a median of 39.8 months after treatment (range: 17.8-55.4). The overall survival (OS) of patients with ^{18}F -NaF-MAV value > 38.65 (36.36% [N of Events/Total N: 4/11]) was significantly shorter than that of patients with ^{18}F -NaF-MAV value < 38.65 (3.85% [1/26]; $P = 0.002$). In multivariate forward stepwise (conditional LR) Cox regression analysis of prognostic factors of OS (including ^{18}F -NaF-MAV (> 38.65 or < 38.65), age, gender, beta-2 microglobulin, and revised international staging system), ^{18}F -NaF-MAV remained the only significant factor (HR: 14.39, $P = 0.02$). The results for PFS were not significant. Moreover, Kaplan-Meier analyses of conventional methods of PET quantification did not reveal any statistically significant log-rank p -values. MM patients with high ^{18}F -NaF-MAV had shorter overall survival, compared to those with low ^{18}F -NaF-MAV levels (NCT02187731).

Keywords: ^{18}F -sodium fluoride, multiple myeloma, PET/CT, survival, metabolic active volume, myeloma bone disease, osteolytic lesion, fracture

Introduction

The majority of multiple myeloma (MM) patients will have bone lesions and/or fracture due to weakened bone over the course of the disease [1]. Lytic bone lesions are the hallmark of myeloma bone disease that are marked by local areas of increased osteolysis in areas adjacent to MM cells [2]. In addition to lytic lesions, pathological fractures can occur in patients, which result not only from the malignant plasma infiltration of the bone, but also from overexpression of signaling factors such

as the receptor activator of nuclear factor-kappa B ligand [RANK ligand (RANK-L)] that constitutively activate osteoclasts and stimulate bone resorption [3]. The combination of enhanced weakened bone due to bone lesions and fractures is associated with higher morbidity and mortality of the patients, as a result increase the cost of the management [2].

According to the International Myeloma Working Group, due to the low sensitivity and specificity of X-ray, which was the standard modality for detecting lesions in MM patients, there is a dire

