Baseline bone involvement in multiple myeloma – a prospective comparison of conventional X-ray, low-dose computed tomography, and ^{18}flourodeoxyglucose positron emission tomography in previously untreated patients

Maja Hinge,[1] Kristian T. Andersen,[1] Thomas Lund,[2] Henrik B. Jørgensen,[3] Paw C. Holdgaard,[3] Tina E. Ormstrup,[4] Lone L. Østergaard,[4] and Torben Plesner[1]

[1]Department of Internal Medicine, Division of Hematology, Vejle Hospital, Institute of Regional Health Research, University of Southern Denmark; [2]Department of Hematology, Odense University Hospital; [3]Department of Nuclear Medicine, Vejle Hospital; [4]Department of Radiology, Vejle Hospital, Denmark

Correspondence: maja.hinge@rsyd.dk
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Supplementary material

Supplementary methods

Thirty-five previously untreated MM patients were enrolled in a prospective single centre phase-II study evaluating the safety and efficacy of the five drug combination of doxorubicin, cyclophosphamide, bortezomib, dexamethasone and lenalidomide as first-line treatment. All patients had biopsy proven MM that required therapy according to the CRAB criteria.[1]

Bone involvement at baseline was assessed by a set of imaging methods and serum markers of bone turnover as a secondary end point of this study. The imaging procedures encompassed conventional X-ray, low-dose CT, ^{18}FDG-PET and dual energy absorptiometry scan. The serum markers of bone turnover were C-terminal cross-linking telopeptide of type I collagen (CTX) for bone resorption and N-terminal propeptide of procollagen I (P1NP) for bone formation. The examinations were performed at Vejle Hospital, Denmark between November 2011 and May 2014.With no minimum restriction on the size of osteolytic lesions, decisions about the significance of the findings were left to a dedicated team of radiology experts.

This clinical trial was approved by The Regional Scientific Ethical Committees for Southern Denmark (id: 2011-0123), registered at clinicaltrials.gov (NCT01481194) and by EUDRACT number 2011-002751-34. All patients provided written informed consent. The study was conducted in accordance with the Declaration of Helsinki.

Imaging

Conventional X-ray: Included plain anterior-posterior radiographs of pelvis and anterior-posterior and lateral views of the total spine. Pelvis and spine were evaluated separately, and X-rays of the anatomic areas were assessed positive if at least one osteolytic lesion or malignant fractures was present and negative if not. The X-rays were reviewed by a team of five experienced radiographers certified to evaluate spine and pelvis X-rays. X-ray reviews were performed blinded to the results of the other imaging techniques.

Low-dose CT: CT-examinations were conducted as low-dose scans (120 KV, dose modulation) without the use of contrast medium, and with a reconstructed slice thickness of 3 mm on bone algorithm. Low-dose CT imaging was conducted in combination with PET or using a16-slices Philips Precedence scanner. The CT images were first assessed according to the standard procedure by two physician-specialists from the radiologic department with the aim to reach a consensus, and then reviewed by a radiologist with a specific expertise in bone examination by CT-scan. The

anatomical areas of the spine and pelvis were considered as either positive or negative respectively for osteolytic lesions. Additional findings of soft tissues lesions by CT were also noted.
^{18}FDG-PET: After fasting for at least six hours the patients received an injection of ^{18}FDG with an activity of 4 MBq/kg (minimum 300 MBq), before resting for one hour prior the scan. Imaging was performed on one of two scanners: Philips Gemini TF 16 slices or Philips Gemini TF 64 slices and reconstructed with the Philips manufactory reconstruction protocol: Body-CTAC-NAC. The images were reviewed by two nuclear medicine physicians with the aim to reach a consensus. The anatomical areas of the spine and pelvis were either considered positive or negative for focal PET-activity based on the standard uptake volume (SUV) activity. A focal SUV activity above 2.5 was considered to be positive. Increased activity in tissue outside of the bone was also noted.
DXA: The hip and the lumbar spine (L1-L4) were scanned with dual X-ray technology on Hologic Discovery W equipment. While the left hip was the preferred choice, the right was scanned in case a patient had undergone hip replacement surgery. Those vertebrae that had either collapsed, received irradiation treatment or had been treated with vertebroplasty were excluded and the calculation was then carried out on the remaining vertebrae. Bone mineral density, the Z-values and the T-values were calculated.

Serum markers of bone turnover

Fasting blood tests were collected in the morning for measurement of the bone resorption marker C-terminal cross-linking telopeptide of type I collagen (CTX) (β-CrossLaps, Roche Diagnostics) and the bone formation marker N-terminal propeptide of procollagen I (P1NP) (Total P1NP, Roche Diagnostics).

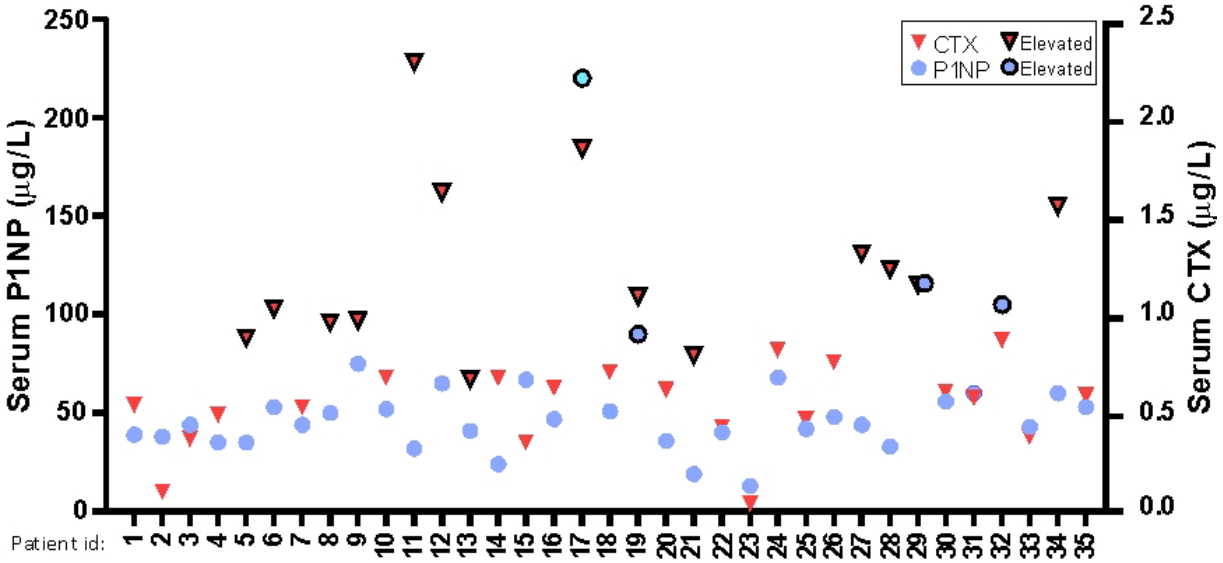
Statistics

The statistical difference between the number of patients diagnosed with osteolysis by X-ray or low-dose CT-scan was calculated using Fishers exact test. P-values < 0.05 were considered statistically significant. Statistical analyses and graphical illustrations were performed using GraphPad Prism version 5.

Reference List

1. Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol. 2014;15(12):e538-e548.

Supplementary figure, S1.



Supplementary figure:

Baseline levels of serum markers of bone turnover in 35 previously untreated multiple myeloma patients. Levels above the reference limits are marked with a black border. CTX reference values: Male 50-70 years < 0.84 µg/L; Male > 70 years < 1.05 µg/L; Females pre-menopausal < 0.59 µg/L; Females post-menopausal < 0.83 µg/L. P1NP reference values: Males 14-86 µg/L; Females pre-menopausal 15-59 µg/L, Females post-menopausal 16-74 µg/L. CTX: C-terminal cross-linking telopeptide of type I collagen. P1NP: N-terminal propeptide of procollagen I.