Biological markers compound with dual-energy X-ray absorptiometry examination in the postoperative prediction of patients with postmenopausal osteoporotic fractures

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Abstract

Osteoporosis is a systemic bone mass loss, a deterioration of the bone microarchitecture, which causes the bone to become more fragile. The most common places of these types of fractures take place on the hip, spine and wrist, but other anatomical regions can be affected as well. The most cost-effective diagnostic method in osteoporosis is the bone mineral density (BMD) determination by dual-energy X-ray absorptiometry. Due to the poor sensitivity of this method, determination of biological markers of the bone turnover has an increasing importance; however, the clinical utility is still limited. The aim of this study is to compare the values of serum and urinary biochemical markers resulted from activities of bone tissue, that provide information of bone metabolism, with the BMD and also osteoporotic fracture predictive ability of the two methods. Between 2011-2013 in the orthopedic department of Bucharest Emergency University Hospital were selected a total of 60 women in postmenopausal that suffered fractures of the femoral neck, pertrochanteric fractures, compaction fractures of the lumbar spine and distal radius fractures. Of the 60 patients, we selected 10 patients considered the results to be representative of the analysis of the correlation between the outcome of BMD and bone metabolism biomarkers level. Assessing the biochemical markers of bone resorption was associated with increased risk of fractures of the hip, spine and fracture of distal radius, independent of BMD.
Keywords: *osteoporosis, fracture, biomarkers, bone mineral density*

Introduction

There has been a growing incidence of fractures in osteoporosis in the past decades, due to the number of postmenopausal women, the sedentary lifestyle and the overweight population. Osteoporosis is a systemic bone mass loss, a deterioration of the bone microarchitecture, which causes the bone to become more fragile. Fractures in these conditions may happen with minimal or even non-traumatic impact. The most common places of these types of fractures take place on the hip, spine and wrist, but other anatomical regions can be affected as well[(1)]. Most of the time, osteoporosis is diagnosed after a low-energy caused fracture. The most cost-effective diagnostic method in osteoporosis is the bone mineral density (BMD) determination by dual-energy X-ray absorptiometry (DXA). Low BMD was defined according to the World Health Organization guidelines by a value lower than 2.5 standard deviation (SD) below the young adult mean (T score less than - 2.5 SD). Due to the poor sensitivity of this method, determination of biological markers of the bone turnover has an increasing importance, however, the clinical utility is still limited[(2-4)]. Bone formation and bone resorption can be assessed by biochemical markers whose value depends on a number of factors, some of them controllable (physical activity, diet, circadian rhythm), other factors are hard to change (medication, associated diseases, nutritional status)[(5-9)]. Osteosynthesis in this condition is a major challenge for the orthopedic and trauma surgeons. The goal of the surgical treatment is to restore the pre-fracture status the functionality and the mobility of the affected region as soon as possible, even if the anatomical restoration is not perfect[(5)]. Several recent studies showed that ordinary fixation, like screw and plate techniques, are less useful[(6)]. A 30° angulated insertion of the screws can be used as an enhanced fixation. Canulated screws with side holes have the benefits of cement injection into bone, which increase the holding power of the screw[(7)]. Intramedullary nail fixation has the advantage of indirect reduction, lower blood loss, and better load sharing. Augmentation in osteoporotic fracture increases the hardness of the bone. However, material extraction in cemented areas is difficult and most of the time leads to a local bone loss[(8)]. Bioactive augmentation nowadays has a major interest in research.

Our aim is to compare the values of serum and urinary biochemical markers resulted from activities of bone tissue,

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that provide information of bone metabolism, with the BMD and also osteoporotic fracture predictive ability of the two methods.

Methods

Between 2011-2013 in the orthopedic Department of Bucharest Emergency University Hospital were selected a total of 60 postmenopausal women, aged between 60 and 85 years (mean: 68.46±6.61 SD), that suffered fractures of the femoral neck, pertrochanteric fractures, and distal radius fractures, without major traumatic impact (Figures 1 and 2).

All postmenopausal women included in this study, were not receiving estrogen therapy or other systemic treatment like calcium or vitamin D that could influence BMD and bone turnover. Fixation was performed according to every case apart, given the fragility of the bone and trying as possible to get a firm fixation of the fracture to begin a rapid mobilization thus improving the prognosis of fracture healing. We further avoided the fixation with plates and screws due to low mechanical strength associated with poor bone quality. In 25 cases of fractures, osteosynthesis were made by centro-medullary fixation by Gamma nail (Figure 3), AO type external fixation in fractures of the wrist (in 11 cases) (Figure 4) and prosthetic implants (18 cemented total hip arthroplasties, and 6 hemiarthroplasties) were used in femoral neck fractures (Figures 5 and 6).

At 6 weeks postoperative control patients are investigated using the following methods:

a) X-ray exam for the affected segment

b) BMD determination for the lumbar spine (L1–L4), total hip, and mid-distal radius and ulna using DXA

c) Biological samples from blood and urine to determine the biological markers of the BTM that fall into two categories:

- products of osteoblastic activity evaluated by determining serum levels of osteocalcin (OC), Alkaline Phosphatase (ALP) serum bone-specific and intact N-terminal propeptide of type 1 serum collagen.
- products of osteoclastic activity such as urine N-telopeptide of type I collagen (NTX) scores and deoxipiridinoline (DPD). Bone resorption was evaluated by measurement of serum levels of NTX in 24-h urine collections by an ELISA kit.

We had the possibility to measure the biological markers in 10 cases. For these cases a multiple regression model was run using the biological markers as independent variables and the T score as dependent variable.

Processing technology of these biomarkers analyze directly a broad array of proteins of different physical properties in patient samples. Using this technology it was possible to identify biomarkers in serum samples without the need to know before their existence or relevance in a disease known. For the determination of the OC, NTX and DPD we used the following assays: CIS-ELISA-Osteo assay in case of OC, for

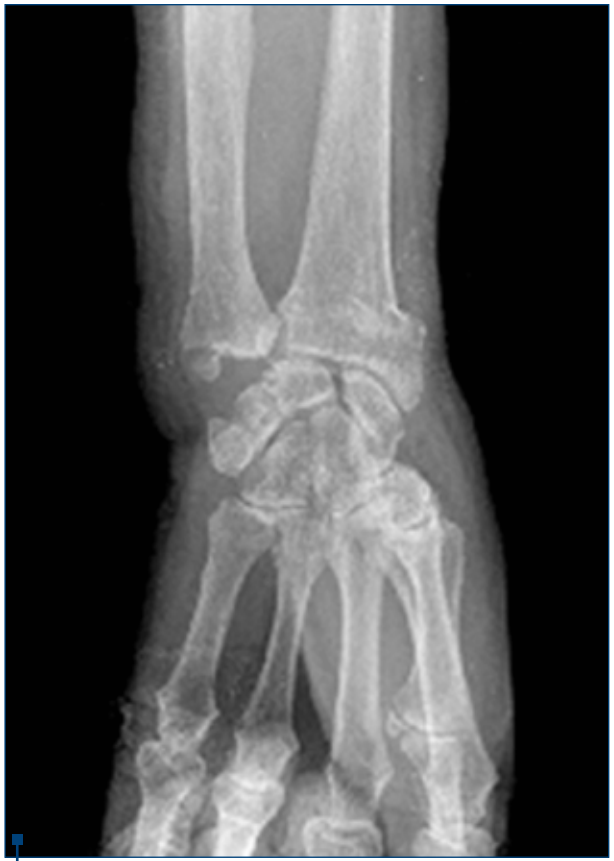

Figure 1. X-ray of a left wrist, with distal epiphiseal fracture of the radius and of the ulnar styloid process

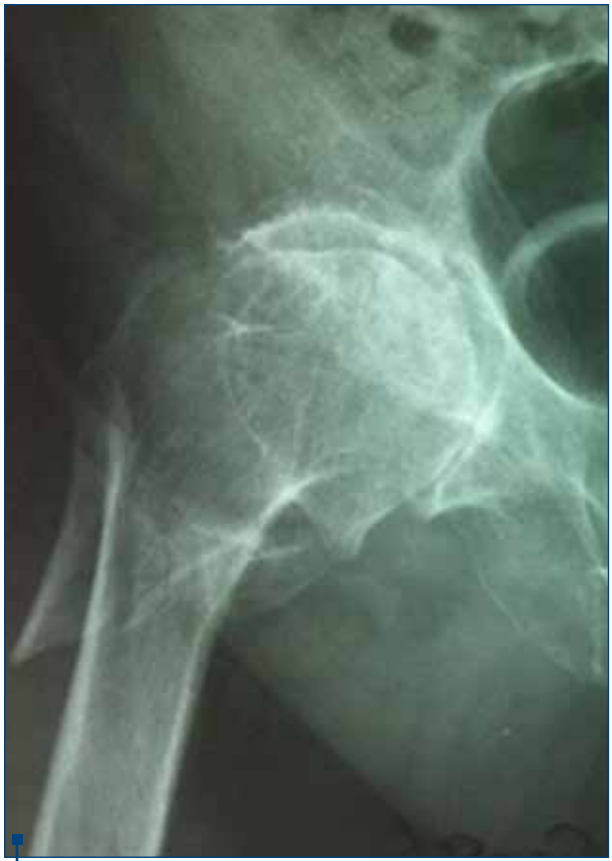

Figure 2. X-ray of a right hip joint, with a subtrochanteric fracture and arthrosis of the joint

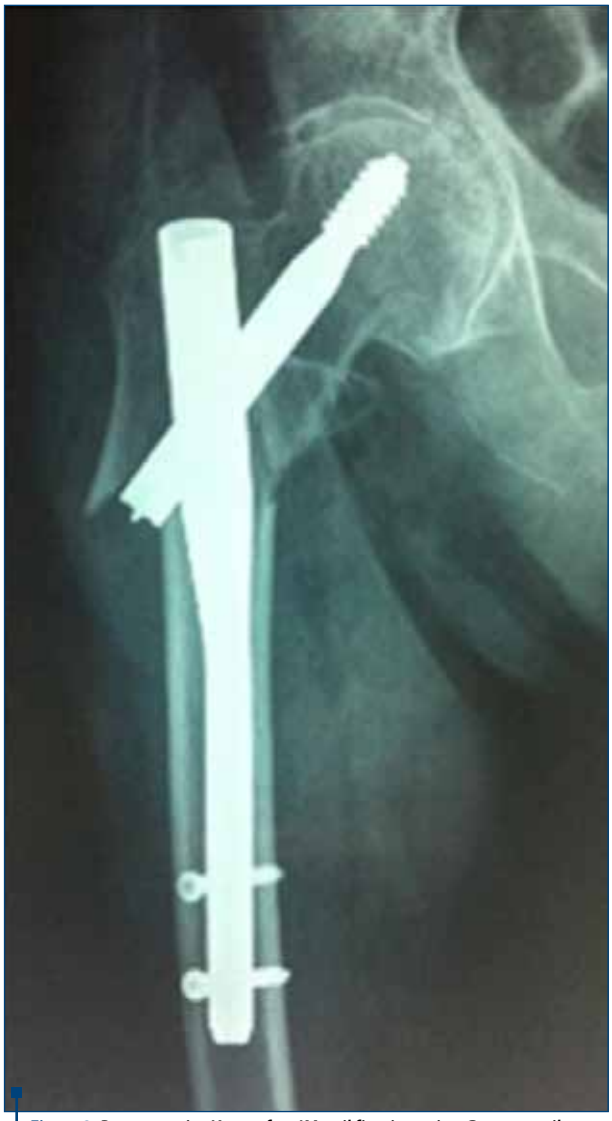

Figure 3. **Postoperative X-ray of an IM nail fixation using Gamma nail**

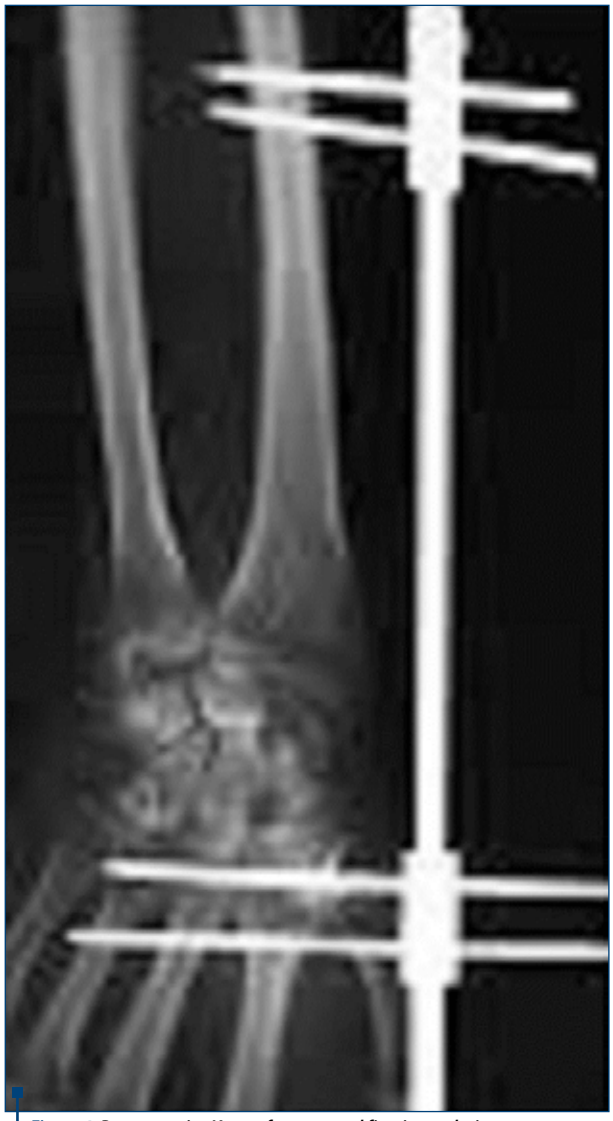

Figure 4. **Postoperative X-ray of an external fixation technique**

N-telopeptid ELISA and high-performance liquid chromatography for DPD.

Results

The second day after surgery patients begin recovery by active and passive maneuvers conducted by physiotherapist. Six weeks postoperatively, the patients came back for control and they had X-ray examination of the affected segment BMD determination by examining the lumbar spine and coxofemoral and wrist joint of the opposite hip or wrist fracture (Table 1) and the determination of biological markers of the bone turnover (Table 2). Based on the DXA results, the mean values of T-scores, in the evaluated ages, were below -2.5 SD as shown in Table 1.

Table 1 Average values of T-score, BMD, bone mineral concentration (BMC) and affected area of the examined region

	T-Score	BMD (g/cm^2)	BMC (g)	Area (cm^2)	Region
Femur	-2,81	0,55	1,37	2,72	Wards
ALP spine	-2,83	0,54	1,38	2,79	L2-L4

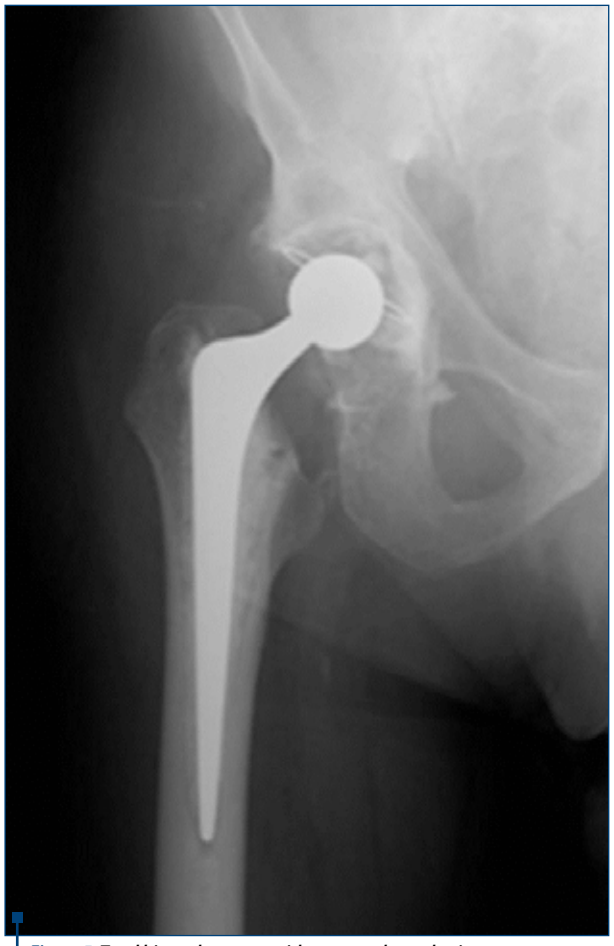

Figure 5. Total hip replacement with cemented prosthesis

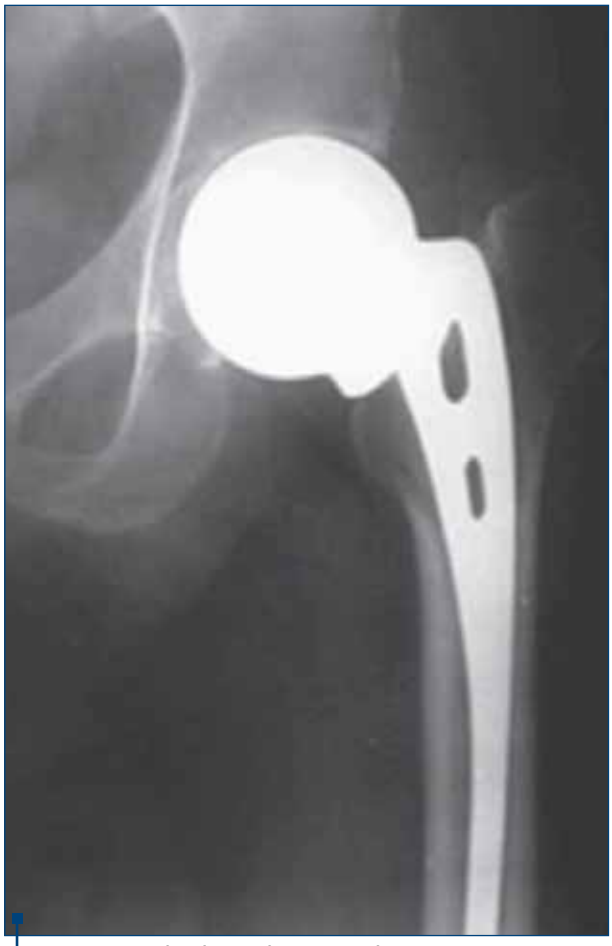

Figure 6. Hemiarthroplasty with Moore prosthesis

Table 2 Results of BMD and biomarkers of bone turnover; OC, DPD, NTX

Femur			APSpine			Biological markers		
T-score	BMD g/cm²	Area cm²	T-score	BMD g/cm²	Area cm²	OC (ng/mL)	DPD (nM/mM)	NTX (nM/mM creat.)
-3,3	0,481	2,73	-3,1	0,804	5,12	14,3	10,4	131,5
-2,6	0,542	2,01	-2,8	0,867	3,36	10,8	7,2	118,2
-2,4	0,595	2,61	-2,7	0,874	17,15	8,4	5,6	121,1
-3	0,608	5,1	-3,3	0,807	36,02	11,2	9,1	122,9
-3,1	0,459	2,89	-3,4	0,801	9,12	12,1	9,4	117,2
-2,3	0,613	2,97	-2,5	0,905	3,15	6,2	4,6	111,2
-2,9	0,537	2,91	-2,6	0,884	3,26	11,4	7,3	124,3
-3,1	0,505	2,78	-2,1	0,918	5,99	13,3	11,5	132,1
-2,7	0,564	2,27	-3,7	0,759	3,26	10,4	6,2	112,4
-2,6	0,512	2,73	-3,2	0,814	3,15	8,7	5,1	109,2

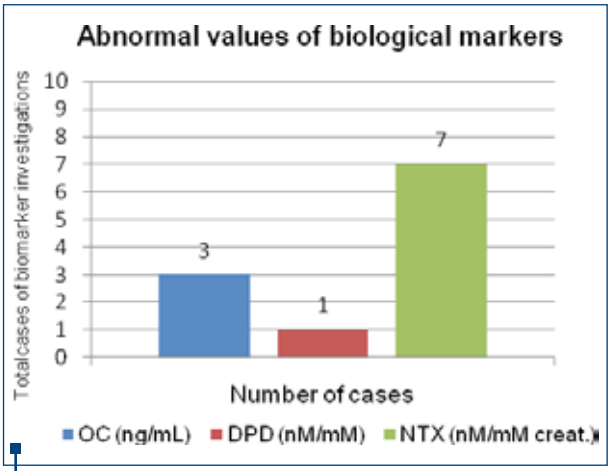

Figure 7. Abnormal values of biological markers of bone turnover

Near the determination of BMD, in 10 cases we were able to determine the aforementioned biological markers of bone turnover: OC (normal value in adult woman 3.1- 14.4ng/mL), DPD (normal value in woman: 15.3-33.6 nM/mM), urine NTX (normal value in postmenopausal woman: 26-124 nM-mMcreat) (Figure 7).

Discussion

It is well known that the main issue in menopause reduced bone mass due to an imbalance between bone formation and bone resorption process as a result of decreasing ovarian activity. Thus the loss of ovarian function is the primary factor in the development of osteoporosis in postmenopausal women[8,9]. Biochemical markers provide a dynamic view of the remodeling process, which covers rate of turnover and pathogenesis, and should improve fracture risk prediction[10]. The clinical significance of any marker for bone remodeling depends on two fundamental characteristics: specificity and variability. Interestingly, increased levels of DPD in urine are associated with an increased risk of fracture in older postmenopausal women who have a bone mineral density close to normal[11-13]. The mean urinary excretion of DPD crosslinks, a marker of bone resorption is up to 100 percent higher in patients with osteoporosis than its normal value[14-17].

The T score concept considered a screening analysis, was originally developed to assess the probability of fragility fractures in postmenopausal women. It has been useful knowing the increased risk of fracture in this group of patients. However, the use of this single score is not enough to formulate a diagnosis of osteoporosis and to determine fracture risk prediction due to the low incidence of this disease in patients younger postmenopausal.

In agreement with the notion that the biomarker signature reflects specific skeletal changes, the individual components of the identified fingerprint are also significantly correlated with clinical BMD measurements[18-19]. A significant correlation between serum osteocalcin concentrations (a marker of bone formation) and BMD of the spine was described in a research by Sherman and contributors[20-23].

Conclusions

The selected group for this study underlines the importance of the prevention of non-traumatic fractures in postmenopausal osteoporosis, and the importance of the early diagnosis. The biological markers of bone turnover seem to be an effective screening method, and it has the benefit of not irradiating the patients. The findings of our study and of other research papers in the literature showed that the level of BMD is a strong indicator of fracture risk in postmenopausal women. Assessing the biochemical markers of bone resorption was associated with increased risk of fractures of the hip, spine and fracture of distal radius, independent of BMD. The mean values for biochemical markers of bone turnover are high in patients with postmenopausal osteoporosis. The findings are consistent with the concept that osteoporosis is characterized by a decrease in bone formation and an increase in bone resorption. ■

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