Osteoporosis

**Keywords:** Bone diseases, Osteoporosis, Diagnostic tests

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**Background:** Bone turnover markers (BTM) reflect specific processes or aspects of bone (re)modeling. Their dynamic character provides additional information regarding the current status and balance of bone metabolism. Measurement of BTM is clinically relevant and common in patients with osteoporosis and other bone-related disease such as inflammatory rheumatic diseases as axial spondyloarthritis (axSpA). BTM can contribute to the diagnostic workup as well as treatment monitoring. Interpretation of absolute values is difficult as these are highly influenced by age and gender, which complicates data interpretation and comparison of studies involving BTM. In previous research, we used BTM Z-scores to study the effect of biological therapy on the course of BTM in patients with axSpA [1, 2].

**Objectives:** To establish BTM reference values based on widely used BTM assays and/or automated immunoassay platforms that can be used to calculate Z-scores to correct for the normal influence of age and gender.

**Methods:** Serum markers of collagen resorption, bone regulation, collagen formation and facilitator of bone mineralization (sCTX, OC, PINP and BALP respectively) were measured in volunteers without bone-related diseases/abnormalities. Assays were conducted in a ISO certified specialized routine diagnostic laboratory. Raw data was plotted, gender-specific age cohorts were established based on the distribution of the data and subsequently their respective means and standard deviations were calculated. Z-scores can be calculated using these reference values to correct for the normal influence of age and gender on BTM.

**Results:** In total, 856 individuals were included, of which 486 (57%) were female. Individuals were aged between 7 and 70 years. Highest serum levels of BTM were found in childhood and puberty. Peak levels are higher in boys than girls and prevail at later ages. In adults, BTM levels decrease before reaching stable nadir levels. For the calculation of Z-scores below the age of 20 years, intervals of one year were needed due to the change in BTM activity. In adults, 10-year reference cohorts could be established in order to calculate Z-scores (Figure 1). As example, a male of 40 years with a serum PINP level of 70.0 ng/mL has a Z-score of 1.56. At the age of 60, his PINP levels remained 70.0 ng/mL, which corresponds to a Z-score of 2.73. Despite the absence of change in absolute levels of PINP, Z-scores do indicate a large increase not only compared to the previous measurement but also compared to the reference population matched for age and gender.

**Conclusion:** With our data, Z-scores of sCTX, OC, PINP and BALP can be calculated using reference categories (for age and gender) of mainly Caucasian volunteers representative for the normal population. BTM Z-scores facilitate harmonization of data interpretation in both daily clinical practice and research. This is especially important in (rheumatic) diseases with known aberrant bone metabolism as axSpA or (secondary) osteoporosis.

**REFERENCES:**

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**SERUM LEVELS OF BONE TURNOVER MARKERS, ESTABLISHING Z-SCORES FOR USE IN RESEARCH AND DAILY CLINICAL PRACTICE: DATA FROM A DUTCH HEALTHY REFERENCE COHORT**

**Keywords:** Malignancy, interaction of cancer and bone disease

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**Background:** Bone loss is one of the major long-term side effects of adjuvant endocrine therapy for breast cancer. There is limited consensus on how to accurately assess fracture risk in this setting. Many trials showed the effectiveness of antiresorptive drugs in preventing the loss of bone mineral density (BMD) and, consequently, reducing fracture risk [1].

**Objectives:** Our study aims to investigate osteoporotic fractures prevalence and to assess the age adjusted fractures risk in breast cancer patients receiving AET and treated with antiresorptive drugs. Moreover, we analyzed differences in terms of clinical features and outcomes between patients treated with denosumab (DMAB) or bisphosphonates (BPs), and examined variations in biochemical markers of bone turnover and densitometric values to assess the effects of each antiresorptive medication.

**Methods:** In this monocentric, retrospective, non-randomized cohort study we enrolled patients with non-metastatic breast cancer who received at least 5 years of AET and were treated with DMABs or BPs. We retrieved demographic and clinical data pertaining to the cancer characteristics and the osteoporotic risk at the start of the antiresorptive therapy (baseline), as well as serum levels of C-terminal telopeptide of type I collagen (CTX), vitamin D, parathyroid hormone (PTH), and densitometric data (DXA) at baseline and at 24 months.

**Results:** We enrolled 120 patients, 38 on DMABs and 82 on BPs. During a median follow-up of 32 months (24-38), 16 (13.3%) fractured at least once. At baseline, the latter had lower BMI [22 kg/m2 (21-27) vs 24 kg/m2 (20-26), p=0.043], higher prevalence of osteoporosis (12/16 vs 35/104, p=0.002), higher prevalence of prior fractures (8/16 vs 15/104, p=0.003), and lower AET exposure time [2.7 years (1.2-3.7) vs 3.8 years (2.4-5.8), p=0.008]. In age-adjusted Cox-proportional model, a history of previous fractures and BMD at the femoral neck < -2 at baseline were associated with higher fracture risk [HR 7.8 (2.7-22.9), p=0.001, and HR 3.4 (1.1-10.4), p=0.033, respectively], whereas higher levels of vitamin D resulted protective [HR 0.7 (0.5-0.9), p=0.010]. AET exposure time and the type of antiresorptive drug, instead, had no impact on the fracture risk. Patients who received DMAB had significantly lower levels of vitamin D, age and AET exposure time [33 ng/ml (26-39) vs 36 ng/ml (30-41), p=0.022, 55 years (10.2) vs 60 years (9.1), p=0.008, and 2.9 years (2.0-4.4) vs 3.9 years (2.6-5.9), p=0.014, correspondingly]. At 24 months, both medications were successful in reducing serum levels of bone resorption markers and increasing densitometric values. The DMAB group experienced substantially larger BMD increases in the lumbar spine and femoral neck [respectively, +9.0% (+4.2/+19.8) vs +3.3% (-1.3/+6.6), p<0.001, and +6.1% (+2.2/+15.5) vs +0.7% (-3.5/+4.4), p=0.001].

**Conclusion:** The frequency of fractures tends to stay high in women receiving AET even if on antiresorptive drugs despite biochemical and instrumental improvements, indicating the existence of other concurrent processes of bone damage. To enable quick management of bone health-related issues, a thorough

**REFERENCES:**
Objective: We aimed to evaluate the prevalence and incidence of osteoporotic vertebral fractures (OVF) and the risk factors for incident OVF in patients with prostate cancer (PCa).

Methods: We included 289 patients: 162 males (56%), mean age 66.4 years old. Eighty-two percent of patients were current or past smokers (42 ± 22 number of year smoking) and 22% consumed alcohol regularly. The mean BMI was 24.7 ± 5.0 kg/m². Seventy-eight percent had an adenocarcinoma and 18% a squamous cell carcinoma. Sixty one percent of patients had a metastatic cancer, including 25% of bone metastasis. The mean follow-up time was 36.3 ± 29.4 months. At inclusion, 31 of the 289 had an OFV, for 40 OFV (24 thoracic, 16 lumbar, mean 1.3 ± 0.6 OFV per patient). The prevalence at inclusion was therefore 10.7%. At end of follow-up, 23.2% of patients (67/289) had an OVF. During the follow-up of 36 ± 29 months: 36 patients had an incident OFV. The incidence of OFV was 12.5%. Ninety-seven OFV occurred (68 thoracic, 29 lumbar). Median time to incident OFV was 13 months (6.7; 21.2). In univariate analysis (Table 1), the risk factor of OFV were: age (p=0.036), BMI <19 kg/m² (p < 0.001), steroid use (p=0.001), and radiotherapy (p = 0.036). In multivariate analysis, BMI <19 kg/m² (p=0.01), steroid use (p<0.001), and L1 at inclusion (HR 0.986, p < 0.001) were independent risk factors of incident OFV. Median survival was 80 months in the incident OFV group and was not reached in the patients without incident OFV (p = 0.074, Image 1).

Conclusion: In our population, prevalence of OFV at inclusion was 10.7%. Incidence was 12.5% during a mean follow-up of 36 months. Occurrence of a new OFV may have an impact on survival. Presence of OFV and UH in L1 should be evaluated systematically during NSCLC follow-up. We should pay more attention to this population, in order to prescribe preventive anti-resorptive drugs if needed.