SUMMARY

INTRODUCTION: Osteoporosis (OP) is the most common metabolic bone disease characterized by low skeletal mass and deteriorated bone microarchitecture, leading to fractures. Globally, this chronic disease primarily affects postmenopausal women. One of the most important non-invasive methods used in the diagnostic approach to OP and fragility is bone densitometry with dual-energy X-ray absorptiometry (DXA) providing measurement of bone mineral density (BMD) in the femoral neck (FN) and lumbar spine region, whereas individual results are referenced to the normative data for peak bone mass, and are expressed as T-scores. Based on published reports, about 55-75% of low-energy fractures may occur in women and men with BMD within normal range (T-score above -2.0) i.e. in osteopenia. Due to several discrepancies between the DXA results and comprehensive clinical diagnosis of OP, there is a need to incorporate also alternative methods or paradigm in the evaluation of osteoporotic fractures and risk factors, particularly in postmenopausal women. Importantly, fracture risk assessment is essential not only to identify individuals at high risk, but also for therapeutic decision. Over the last two decades, the FRAX calculator (the algorithm including both BMD and BMI) has been regarded an effective tool for estimating the absolute risk (AR) of osteoporotic fractures after menopause. The role of anthropometric characteristics in bone mass accrual and age-related bone loss has been largely studied, and evidence has been shown for extremely low body mass index (BMI) less than 18.5 as a well-proven risk factor for postmenopausal OP. On the other hand, the impact of overweight and obesity, as well as body composition pattern (fat mass, lean tissue) on osteoporotic fractures, still remains unclear, while published data vary across populations, ethnic groups, research design and methodology. Large body of evidence has yet demonstrated a significant role of adipose tissue in skeletal health. Therefore, elucidation of relationships between anthropometry, obesity and the risk of fractures in postmenopausal women may contribute to clinical practice, and may potentially support the diagnosis of OP. The rationale of such research is to determine diagnostic potential of anthropometry or its predictive value in fracture risk assessment.

AIM OF THE STUDY: The main objective was to examine the relationships between anthropometric features, bone and body composition measured by DXA, and the risk of osteoporotic fractures in postmenopausal women, with regard to selected demographic characteristics, clinical risk factors (CRF) and lifestyle. Specific objectives included assessment of the prevalence, location of fragility (osteoporotic) fractures, and the risk of fractures using FRAX, in relation to BMD, body composition with regional fat and lean tissue distribution, and

anthropometric characteristics (Wt, Ht, BMI, waist circumference, waist-to-hip ratio [WHR]). Furthermore, the aim was to investigate associations between BMD and anthropometric features in relation to fracture history, and to assess potential usefulness of the FRAX method in combination with body composition in estimating fracture risk among postmenopausal women.

PARTICIPANTS AND METHODS: This cross-sectional observational study included 300 Caucasian postmenopausal women aged 42-88 years (mean 66.1 ± 8.2) followed in outpatient clinic of osteoporosis in Białystok. Secondary osteoporosis, chronic diseases and iatrogenic factors deleterious to the skeleton were excluded. A review of medical records and a direct questionnaire-based survey were carried out, including items on lifestyle, physical activity, history of fractures (circumstances and mechanism of bone fractures), family history of OP, smoking and alcohol history, falls, chronic comorbidities and pharmacological treatment. History of fractures was confirmed by X-ray examination. Densitometric scan (DXA) was performed using Hologic Discovery equipment in two standard locations: femoral neck (Femur), Lumbar Spine (L1-L4 AP), and additionally in the Total Body, providing the measurement of bone mineral density (Total BMD), area, and Bone Mineral Content (Total BMC), and also fat tissue mass (Fat) and lean body mass. At the same time, anthropometric procedures were carried out using standard methods: height, body weight, body mass index (BMI), waist and hip circumferences with the calculation of the waist-to-hip ratio (WHR) considered as an approximation of visceral fat. Using the DXA, an individual 10-year fracture risk (AR-10) was determined based on the Polish version of the FRAX® (Kanis J. et al. 2006). The data were subjected to basic (descriptive, Student's t-test, Spearman's correlation coefficients), and then to multivariate statistical analysis with stepwise elimination and logistic regression. Statistical models were subsequently created with a level of 0.1 defined as the threshold for leaving the variables in the models. The diagnostic value of the models was assessed using area under curve (AUC) values in the ROC analysis. Association of statistically significant factors with fracture probability was expressed using Odds Ratio (OR) and 95% Confidence Interval (95%CI), in order to determine factors being significantly associated with the prevalence of fractures (significance level $p<0.05$).

RESULTS: The mean body mass index was 26.8 ± 4.4, and the mean value of waist-to-hip ratio (WHR) was 0.9 ± 0.1. The DXA scan of femoral neck (BMD FN) showed T-score -1.9, and Z-score = -0.24, while Spine BMD T-score was -2.27, and Spine BMD Z-score -0.47. Out

of all women, 121 individuals (40.3% of the population) had a total of 145 fracture episodes during adulthood, Sixty-five women had sustained one fracture (64.4%) and 32 had 2 fractures (31.7%), In the studied group, 61 women (20.3%) reported a family history of low-energy fracture. The predominant location of fractures was wrist (109 episodes; 75% of all fractures). There were also 19 vertebral fractures found (13% of fractures). Based on the FRAX calculation, the 10-year risk (AR-10) for hip fracture was 4.1%, whereas 14.5% for all major fracture sites. Strong positive linear and interrelated correlations were found between BMD, BMC in different locations and anthropometric features, as well as links between anthropometric measurements of body fat (weight, BMI, WHR) and DXA fat measurement (Fat%), although no association was observed between body fat and BMD or BMC either. There was also no relationship between fracture occurrence or number and CRF, lifestyle factors, smoking, parity or history of falls. The BMI >25.9 was not associated with fractures either. Low bone mass (BMD in Total Body and FN, but not Spine BMD) was significantly associated with the risk of fracture. Women with fractures were shown to have significantly lower crude and relative values of Femoral Neck BMD (T-score -2.2 *vs.* -1.8, p=0.001), and a lower Total Body BMD/BMC than those without fractures. Women with Total BMD T-score > median demonstrated half the risk for any fracture, compared to those with Total BMD T-score < median (OR=0.5; 95%CI = 0.26-0.94, p=0.03). Among the anthropometric characteristics, only the WHR was an independent factor associated with any fracture: more specifically, women with a WHR above the median had approximately two-fold higher fracture risk in comparison to those with a WHR below the median (OR=1.8; 95%CI = 0,96-3.5, p=0.065), though this result did not reach statistical significance. No other anthropometric or DXA-related indicators of body fat or obesity were associated with fractures.

SUMMARY AND CONCLUSIONS: The prevalence of clinically significant fractures in postmenopausal women is high as the fragility fractures affect a large proportion of this population, with the dominant location in the wrist (75% of all fractures), and these finding is consistent with literature data published elsewhere, reflecting an important and serious public health problem. No significant association between body composition (extraskeletal soft tissues measured by DXA) and postmenopausal fracture risk could be unequivocally confirmed based on our study, however, the limitations and cross-sectional nature of this study implicate a cautious interpretation. Contrastingly, the significant association between decreased bone mineral density (BMD) and postmenopausal osteoporotic fractures, found in the study, is consistent with a number of evidence-based data, and thereby highlights the importance and

value of measuring DXA in individuals at risk. Postmenopausal women with a waist-to-hip ratio (WHR) higher than median may have a higher risk of fracture, particularly wrist fracture, regardless of their BMI, Total Fat, and Lean Body Mass. This association may indicate, at least partly, a negative role for abdominal fat in skeletal health and bone quality. The WHR assessment in postmenopausal women provides certain important information, independently of the BMI, bone densitometry or FRAX. Thus, this simple measurement can become a practical element of a routine anthropometry supplementing the diagnosis of osteoporosis in women. However, larger well-designed prospective studies are necessary to assess the predictive value of WHR for estimation of fracture risk after menopause.