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Evaluation of individual absolute fracture risk in obese perimenopausal women

Ocena indywidualnego bezwzględnego ryzyka złamania u otyłych kobiet w wieku okołomenopauzalnym

ABSTRACT

It is widely known that an elevated body weight correlates with increased bone mass and a lower rate of bone loss. However, some authors have suggested that excessive fat mass may not protect against a decrease in bone mass. As results of recent studies have diverged, and it is still unclear whether or not obesity has a beneficial effect on bone, we decided to evaluate the individual absolute fracture risk in obese perimenopausal women.

Sixty obese perimenopausal women were enrolled into the study. The control group consisted of 15 healthy women of comparable age. Dual energy X-ray absorptiometry (DXA) of the lumbar spine and femoral neck to measure bone mineral density (BMD) was performed using the Lunar DPXL apparatus. Absolute 10-year fracture risk was calculated as a multiplication of relative risk, according to the guidelines of the WHO/Polish Foundation of Osteoporosis.

Obese women have significantly a higher BMD both of the lumbar spine and the femoral neck and a significantly lower 10-year absolute fracture risk in comparison to healthy controls.

Key words: obesity, fracture risk, BMD

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STRESZCZENIE

Powszechnie uznaje się, że większa masa ciała wiąże się z większą gęstością mineralną kości oraz zmniejszonym tempem ubytku masy kostnej. Z drugiej strony, pojawiają się prace, w których autorzy donoszą, że nadmiar tkanki tłuszczowej nie wykazuje ochronnego wpływu na ubytek masy kostnej. Ponieważ wyniki dostępnych badań są rozbieżne i nie pozwalają na jednoznaczne wnioskowanie co do wpływu otyłości na tkankę kostną, autorzy pracy zdecydowali się ocenić 10-letnie bezwzględne ryzyko złamania u otyłych kobiet w wieku okołomenopauzalnym.

Badaniem objęto grupę 60 otyłych kobiet. Grupę kontrolną stanowiło 15 zdrowych kobiet w porównywalnym wieku. Badanie gęstości mineralnej kości w obrębie szyjki kości udowej oraz odcinka lędźwiowego kręgosłupa wykonano metodą absorpcjometrii podwójnej energii promieniowania rentgenowskiego przy użyciu aparatu Lunar DPXL. Dziesięcioletnie bezwzględne ryzyko złamania obliczono zgodnie z zaleceniami Światowej Organizacji Zdrowia/Polskiej Fundacji Osteoporozy. Otyłe kobiety charakteryzowały się większą gęstością mineralną kości w obrębie szyjki kości udowej oraz odcinka lędźwiowego kręgosłupa oraz mniejszym10-letnim bezwzględnym ryzykiem złamania w porównaniu z kobietami z prawidłową masą ciała.

Słowa kluczowe: otyłość, ryzyko złamania, BMD

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Introduction

Obesity and osteoporosis are two common complex diseases of multifactorial aetiologies. Both have

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Table 1. 10-year fracture risk of the proximal femur in a population of women of different ages (AR-10) [15]

Women (age)	45	50	55	60	65	70	75	80	85
Risk (PR-10)	0.4	0.6	1.2	2.3	3.9	7.3	11.7	15.5	16.1

Table 2. RR values of proximal femur fracture in relation to the value of BMI [11]

BMI	15	20	25	30	35
RR	4.48	1.95	1.0	0.83	0.75

Table 3. RR for given fracture risk factors [16–21]

Risk factors	RR
Prior fragility fracture after age 50	1.85
Parental history of hip fracture	2.27
Secondary osteoporosis	1.95
Use of corticosteroids at any time	2.07 — W 2.6 — M
Current cigarette smoking	1.84
Alcohol intake > units/day	1.68

Table 4. RR of proximal femur fracture with a decrease of Z-score in the proximal femur [22]

Z-score	–0.5	–1.0	–1.5	–2.0	–2.5	–3.0
RR	1.6	2.6	4.2	6.8	10.9	17.6

grown in prevalence over the past decade and both are associated with significant morbidity and mortality [1–3]. It is widely known that an elevated body weight is correlated with increased bone mass and a lower rate of bone loss [4, 5]. Additionally, a decrease in body weight may lead to bone loss [6, 7]. Some evidence does support the view that elevated fat mass has a beneficial effect on bone mass; in premenopausal and postmenopausal women body fat has been positively correlated to bone mineral density (BMD) through the skeleton [8, 9] The EPIC Study also showed that rapid bone losers are characterised by significantly lower fat mass than slow bone losers [10].

In contrast to these findings, other authors have suggested that excessive fat mass may not protect against a decrease in bone mass [11]. Therefore, when the mechanical loading effect of body weight is statistically removed, fat mass correlates negatively with bone mass [12].

Other authors have indicated that the relationship between obesity and the risk of fracture is related to age. Wearing et al. reported that elevated adiposity was considered to be associated with an increased risk of distal forearm fracture in children but turned out to be protective against hip fractures in the elderly [13].

As the results of recent studies have been divergent, and it is still unclear whether or not obesity has a beneficial effect on bone, we decided to evaluate individual absolute fracture risk in obese perimenopausal women.

Experimental procedures

Sixty obese perimenopausal women (BMI 36.4 ± ± 4.2 kg/m^2; age 50 ± 5.3 yrs) were enrolled into the study. All subjects gave their written informed consent before entering the study. Excluded from the study were subjects with diseases, undergoing treatments or with conditions that would be causes of abnormal bone mass or fat mass, such as smoking, consuming more than two drinks a week or hormonal disturbances. The control group consisted of 15 healthy, non-obese women of comparable age (BMI 23 ± 1.3 kg/m^2; 53.7 ± ± 5.6 yrs).

BMI was calculated as weight in kg divided by the square of the height (m^2).

Body composition was assessed using the impedance method (Bodystat).

Dual energy X-ray absorptiometry (DXA) of the lumbar spine and femoral neck to measure BMD was performed using the Lunar DPXL apparatus.

Absolute 10-year fracture risk (AR-10) was calculated according to the guidelines of the WHO and Polish Foundation of Osteoporosis [14, 23]. This was calculated by multiplying the population risk (in percentages) by relative risk (RR) values defined for consecutive unrelated independent factors of fracture risk and possibly also RR resulting from BMD.

The calculator for the AR-10 consisted of the following:

1. 10-year fracture risk of the proximal femur in a population of women of various ages (PR-10) (Table 1) [15].
2. RR values of proximal femur fracture in relation to the value of BMI (Table 2) [11].
3. RR for given fracture risk factors (Table 3) [16–21].
4. RR of proximal femur fracture with a decrease in the Z-score in the proximal femur (Table 4) [22].

$$\text{AR-10} = \text{PR-10} \times RR_{BMI} \times \text{Product}_{RR} \times RR_{\text{for a decrease in the Z-score in the proximal femur}}$$ [23]

All values presented in the text and tables are expressed as means ± S.D. All analyses were performed using the Statistica computer program. The normality of distribution was analysed using the Kołmogorov-Smirnov test. The Mann-Whitney pair-wise U test was used for com-

Table 5. BMD of the lumbar spine, femoral neck and body composition in obese perimenopausal women in comparison to controls (means ± SD)

	Subjects	Controls	Significancy
BMD of L_1-L_4 [g/cm^2]	1.26 ± 0.17	1.07 ± 0.12	$p < 0.0005$
BMD of femoral neck [g/cm^2]	1.09 ± 0.17	0.83 ± 0.10	$p = 0.000000$
Body fat (%)	48.69 ± 6.63	33.16 ± 4.77	$p = 0.000000$
Fat-free mass (%)	50.92 ± 6.31	66.82 ± 4.76	$p = 0.000000$

Table 6. 10-year absolute fracture risk (AR-10) (%) in obese perimenopausal women in comparison to controls (means ± SD)

	Subjects	Controls	Significancy
AR-10 for L_1-L_4	0.3 ± 0.56	2.27 ± 1.49	$p = 0.000000$
AR-10 for hip	0.28 ± 0.76	2.23 ± 2.69	$p = 0.000000$
AR-10 total	0.88 ± 0.77	2.20 ± 1.32	$p = 0.000000$

parison of independent samples. The results were analysed using Spearman's correlation analysis. P values < 0.05 were considered to be significant.

Results

Obese subjects had a significantly higher BMD both of the lumbar spine and the femoral neck and a lower AR-10 in comparison with the healthy controls (Tables 5 and 6). We observed a negative correlation between AR-10 and the BMD of both the femoral neck and the lumbar spine ($p = 0.000$ $r = -0.49$; $p = 0.0000$, $r = -0.45$; respectively). There was a negative correlation between body fat and the T-score of the lumbar spine ($r = -0.26$; $p < 0.05$). There were no significant correlations between body fat content and either BMD or the Z-score of the lumbar spine and the T and Z-scores of the femoral neck.

Discussion

BMD has been widely accepted as the criterion in the diagnosis or exclusion of osteoporosis. The WHO accepted the diagnostic threshold of a T-score of –2.5 as a value that qualifies patients for treatment for osteoporosis [24]. However, recent studies of fracture epidemiology have indicated that up to 75% of these fractures occur in persons with a T-score around –1.5, so with bone mass on the borderline between the norm and osteopoenia [25, 26]. Thus the majority of patients with fractures do not fulfil the densitometric criteria for osteoporosis set by the WHO in 1994, namely a decrease in bone mass with a deterioration in the microarchitecture. The conclusion to be drawn from these studies is that decreased bone mineral density increases fracture risk but normal values do not exclude it. The patients mentioned above were burdened with causes of lower bone strength other than low bone mass. Following on from these results, it emerges that a diagnosis based only on BMD and age reduces the possibility of determining fracture risk. This is why when evaluating risk fracture we have to take into consideration many other parameters that influence bone mass, including alcohol intake, smoking, BMI, fat mass and physical activity.

Obese subjects are known to have a decreased level of physical activity and sun exposure, an unbalanced diet, a higher serum level of parathormone and a lower serum level of vitamin D_3 in comparison with lean subjects [27]. Obese subjects also have a lower level of osteoprotegerin, supposed to be one of the factors protecting against bone loss [28]. All of these observed factors may lead to abnormal bone metabolism. Moreover, a recently published meta-analysis revealed that obesity is not a protective factor against osteoporosis [11].

In our study we have evaluated AR-10 using multiple clinical risk factors. We were able to exclude the influence of potential chronic disease, as our study group consisted of healthy obese subjects. Our obese subjects were characterised by statistically higher bone mineral density, both in the lumbar spine and femoral neck, and a significantly lower AR-10 in comparison to non-obese subjects. This would support the notion that obesity does have a protective influence on bone. In contrast to the results pre-

viously mentioned we did not find any correlation between body fat content and either BMD or T and Z-scores in the femoral neck. We found a negative relation between body fat and the T-score of the lumbar spine.

However, it is still unclear if fat body mass (FMB) or lean body mass (LBM) determines BMD, as authors have used different ways of measuring bone mass and have presented diverging results. Khosla et al. [29] suggested that the relationship between body composition and bone mass is strictly dependent on which bone mass parameter, whether bone mineral content (BMC) or BMD, is used in the analysis. The authors demonstrated that both LBM and FMB have important effects on bone mass, depending on the bone mass parameter used, skeletal site measured and menopausal status. In premenopausal and postmenopausal women both LBM and FBM predicted total BMC. LBM had a dominant effect on spine and forearm BMC in both groups and hip BMC in premenopausal women, whereas both LBM and FBM predicted hip BMC in postmenopausal women [29].

As mentioned in the introduction, studies demonstrate either a positive or negative effect of body fat mass on bone. Some suggest that fat mass, as a body mass component and direct index of obesity, has a protective effect on bone tissue, thereby reducing the risk of osteoporosis [8, 30]. Lau et al. [31] showed that males with vertebral deformities had a lower fat mass and BMD than controls. The other data provided evidence that excessive fat mass may not protect against a decrease in bone mass [11, 32]. Moreover, they documented a negative relation between fat mass and bone mineral density and suggested that fat mass has a detrimental effect on bone [12]. Consistent with these findings, Hsu et al. [33] observed a higher risk of osteopoenia, osteoporosis and non-spinal fractures in patients with a greater fat mass, independent of body weight. Other authors indicated that ethnicity may influence the effect of fat mass on bone metabolism. Castro et al. [34] reported that obesity was associated with a high BMD in white women but with a significant decrease in African American women. Wearing et al. [35] indicated that the relationship between risk of fracture and obesity is related to age; a high fat mass in children is associated with an increased risk of distal forearm in children but appears to be protective against hip fracture in the elderly.

These divergent findings suggest that the effect of fat mass on bone may be very complex and that results may be attributed to factors such as methods of analysis, menopausal status in women, study design, gender and age.

Following our results we conclude that even though obesity is associated with significant mortality and morbidity, its influence on bone is beneficial.

Conclusion

Obese perimenopausal women are characterised by a significantly lower 10-year absolute fracture risk in comparison to healthy women of normal body weight.

References

1. Seidel J.C.: Obesity: a growing problem. Acta Paediatr. 1999; 88: (suppl.) 46–50.
2. Kopelman P.: Obesity as a medical problem. Nature 2000; 404: 635–643.
3. Ray N.F., Chan J.K., Thamer M., Melton L.J 3rd.: Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: report from the National Osteoporosis Foundation. J. Bone. Miner. Res. 1997; 12: 24–35.
4. Jones G., Nguyen T., Sambrook P., Kelly P., Eisman J.: Progressive loss of bone in the femoral neck in elderly people: longitudinal findings from the Dubbo osteoporosis epidemiology study. BMJ 1994; 309: 691–695.
5. Ensrud K., Palermo L., Black D. et al.: Hip and calcaneal bone loss increase with advancing age: longitudinal results from the study of osteoporotic fractures. J. Bone. Miner. Res. 1995; 10: 1778–1787.
6. Radak T.: Caloric restriction and calcium's effect on bone metabolism and body composition in overweight and obese premenopausal women. Nutr. Rev. 2004; 62: 468–481.
7. Wardlaw G.: Putting body weight and osteoporosis into perspective. Am. J. Clin. Nutr. 1996; 63: 433–436.
8. Reid I.R., Plank L.D., Evans M.C.: Fat mass is an important determinant of whole body bone density in premenopausal women but not in men. J. Clin. Endocrinol. Metab. 1992; 75: 779–782.
9. Reid IR., Ames R., Evans MC. et al.: Determinants of total body and regional bone mineral density in normal postmenopausal women Ż a key role for fat mass. Clin. Endocrinol. Metab. 1992; 75: 45–51.
10. Riis B.J., Rodbro P., Christiansen C.: The role of serum concentrations of sex steroids and bone turnover in the development and occurrence of postmenopausal osteoporosis. Calcif. Tissue Int. 1986; 38: 318–322.
11. De Laet C., Kanis J.A., Oden A. et al.: Body mass index as a predictor of fracture risk: a meta-analysis. Osteoporos Int. 2005; 16: 1330–1338.
12. Zhao L.J., Liu Y.J., Liu P.Y., Hamilton J., Recker R.R., Deng H.W.: Relationship of obesity with osteoporosis. J. Clin. Endocrinol. Metab. 2007; 92: 1640–1646.
13. Wearing S.C., Hennig E.M., Byrne N.M., Steele J.R., Hills A.P.: The impact of childhood obesity on musculoskeletal form. Obes. Rev. 2006; 7: 209–218.
14. Czerwiński E., Badurski J., Marcinowska-Suchowierska E., Osiedleniec J.: Current understanding of osteoporosis according to the position of the World Health Organization (WHO) and International Osteoporosis Foundation. Ortop. Traumatol. Rehabil. 2007; 9: 337–356.
15. Kanis J.A., Johnell O., Oden A., Dawson A., De Laet C., Jonsson B.: Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds. Osteoporos Int. 2001; 12: 989–995.
16. Kanis J.A., Johnell O., De Laet C. et al.: A meta-analysis of previous fractu-

re and subsequent fracture risk. Bone 2004; 35: 375–382.
17. Kanis J.A., Johansson H., Oden A. et al.: A family history of fracture and fracture risk: a meta-analysis. Bone 2004; 35: 1029–1037.
18. Kanis J.A., Johansson H., Oden A. et al.: A meta-analysis of prior corticosteroid use and fracture risk. J. Bone. Miner. Res. 2004; 19: 893–899.
19. Kanis J.A., Johnell O., Oden A. et al.: Smoking and fracture risk: a meta-analysis. Osteoporos. Int. 2005; 16: 155–162.
20. Kanis J.A., Johansson H., Johnell O. et al.: Alcohol intake as a risk factor for fracture. Osteoporos. Int. 2005; 16: 737–742.
21. Kanis J.A., Borgstrom F., De Laet C. et al.: Assessment of fracture risk. Osteoporos. Int. 2005; 16: 581–589.
22. Marshall D., Johnell O., Wedel H.: Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ 1996; 312: 1254–1259.
23. Badurski J., Czerwiński E., Marcinowska-Suchowierska E.: Guidelines of Polish Foundation of Osteoporosis and Polish Osteoarthrology Society on Osteoporosis. Ortop. Traumatol. Rehabi. 2007; 9 (suppl. 2): 67–86.
24. Kanis J.: Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO Study Group. Osteoporos. Int. 1994; 4: 368–381.
25. Siris E.S., Chen Y.T., Abbott T.A. et al.: Bone mineral density thresholds for pharmacological intervention to prevent fractures. Arch. Intern. Med. 2004; 164: 1108–1112.
26. Burger H., de Laet C.E., van Daele P.L. et al.: Risk factors for increased bone loss in an elderly population: the Rotterdam Study. Am. J. Epidemiol. 1998; 147: 871–879.
27. Holecki M., Zahorska-Markiewicz B., Nieszporek T. et al.: Selected parameters of bone turnover in obese perimenopausal women. Ann Acad. Med. Siles. 2006; 60: 186–191.
28. Holecki M., Zahorska-Markiewicz B., Janowska J. et al.: Osteoprotegerin — does it play a protective role in the pathogenesis of bone loss in obese perimenopausal women. Endokrynol. Pol. 2007; 58: 7–10.
29. Khosla S., Atkinson E.J., Riggs B.L. et al.: Relationship between body composition and bone mass in women. J. Bone Miner. Res. 1996; 11: 857–863.
30. Douchi T., Yamamoto S., Oki T. et al.: Relationship between body fat distribution and bone mineral density in premenopausal Japanese women. Obstet. Gynecol. 2000; 95: 722–725.
31. Lau E.M., Chan Y.H., Chan M. et al.: Vertebral deformity in Chinese men: prevalence, risk factors, bone mineral density, and body composition measurements. Calcif. Tissue Int. 2000; 66: 47–52.
32. Janicka A., Wren T.A., Sanchez M.M. et al.: Fat mass is not beneficial to bone in adolescents and young adults. J. Clin. Endocrinol. Metab. 2007; 92: 143–147.
33. Yi-Hsiang Hsu, Venners S.A., Herwedow H.A. et al.: Relation of body composition, fat mass, and serum lipids to osteoporotic fractures and bone mineral density in Chinese men and women. Am. J. Clin. Nutr. 2006; 83: 146–154.
34. Castro J.P., Joseph L.A., Shin J.J. et al.: Differential effect of obesity on bone mineral density in White, Hispanic and African American women: a cross sectional study. Nutr. Metab. 2005; 2: 1–7.
35. Wearing S.C., Hennig E.M., Byrne N.M. et al.: Musculoskeletal disorders associated with obesity: a biomechanical perspective. Obes. Rev. 2006; 7: 239–250.