



Ocena gęstości mineralnej kości na podstawie badań wybranych populacji szkieletowych pochodzących z mikroregionu Brześcia Kujawskiego

Karolina Bajon^{1, 2}, Alicja Śmiszkiewicz-Skwarska³, Henryk Stolarczyk³, Arkadiusz Zygmunt^{4, 5},
Maciej Rutkowski², Ewa Sewerynek^{1, 4, 5}

¹Zakład Metabolizmu Kostnego, Uniwersytet Medyczny, Łódź

²Katedra Chemii i Biochemii Klinicznej, Uniwersytet Medyczny, Łódź

³Katedra Antropologii Uniwersytetu Łódzkiego

⁴Klinika Endokrynologii i Chorób Metabolicznych, Uniwersytet Medyczny, Łódź

⁵Instytut Centrum Zdrowia Matki Polki, Łódź

Streszczenie

Wstęp: Osteoporoza to systemowa choroba układu kostnego charakteryzująca się obniżeniem wytrzymałości kości, co prowadzi do zwiększonego ryzyka złamań. Wytrzymałość kości jest pochodną gęstości mineralnej kości (BMD, *bone mineral density*) i jakości tkanki kostnej. Osteoporoza stanowi duży problem medyczny ze względu na powikłania w postaci najczęściej występujących złamań kręgosłupa, dalszej części przedramienia, a w późniejszym okresie życia szyjki kości udowej. Obniżenie BMD stanowi niezależny czynnik ryzyka osteoporozy.

Celem pracy była ocena gęstości mineralnej kości ludności pochodzącej z okresu obejmującego czas od XI do początku XIX wieku z mikroregionu Brześcia Kujawskiego.

Materiał i metody: Badaniom poddano ludzkie kości z czterech stanowisk archeologicznych: Kolonia (XI–XIII), SBK-4 (XII–XVI), Fara (XIV–XVII) oraz Święty Duch (XVI–XIX) uzyskane z wykopalisk i pochodzące za zbiorów Katedry Antropologii Uniwersytetu Łódzkiego. Gęstość mineralną kości populacji szkieletowych porównano z grupą kontrolną, którą stanowiła ludność współczesna z regionu województwa łódzkiego. Występowanie osteoporozy oceniano na podstawie badań wykonanych techniką DXA.

Wyniki: Przeprowadzone pomiary densytometryczne pozwoliły stwierdzić różnice w gęstości mineralnej tkanki kostnej. Badane grupy szkieletowe charakteryzowała znamienne wyższa średnia BMD w porównaniu z grupą współczesną. Zmiany gęstości mineralnej wskazujące na osteopenię w większości odnotowano u kobiet.

Wnioski: Na podstawie uzyskanych wyników nie można jednoznacznie stwierdzić, że badane grupy szkieletowe, mimo iż charakteryzują się znamienne wyższą gęstością mineralną kości, były obciążone niższym ryzykiem występowania osteoporozy i jej powikłań. Wymagana jest kontynuacja badań składu mineralnego kości i ich korelacji z gęstością mineralną kości.

(*Endokrynol Pol* 2006; 5 (57): 494–500)

Słowa kluczowe: gęstość mineralna kości, osteoporoza, osteopenia, osteologia, datowanie



Prof. dr hab. med. Ewa Sewerynek
Zakład Metabolizmu Kostnego
Uniwersytet Medyczny w Łodzi
ul. Sterlinga 5, 91-425 Łódź
tel./faks: 042 632 25 94
e-mail: ewa.sewerynek@wp.pl



Evaluation of bone mineral density on the basis of the results of studies of selected skeleton populations from the microregion of Brześć Kujawski

Karolina Bajon^{1, 2}, Alicja Śmiszkiewicz-Skwarska³, Henryk Stolarczyk³, Arkadiusz Zygmunt^{4, 5}, Maciej Rutkowski², Ewa Sewerynek^{1, 4, 5}

¹Department of Bone Metabolism, Medical University, Lodz

²Chair of Chemistry and Clinical Biochemistry, Medical University, Lodz

³Chair of Anthropology, University of Lodz

⁴Clinic of Endocrinology and Metabolic Diseases, Medical University, Lodz

⁵Polish Mother's Memorial Hospital — Research Institute of Lodz

Abstract

Introduction: Osteoporosis is a systemic disease of the skeletal system characterised by reduced bone strength leading to increased risk of fracture. Bone strength is a combined derivative of bone mineral density (BMD) and of bone tissue quality. Osteoporosis is a serious medical problem because of its complications, most frequently manifesting itself in spine fractures, fractures of distal sections of the forearm and, in later periods of life, hip fractures. Reduced BMD is an independent risk factor of osteoporosis.

The goal of the study was an evaluation of bone mineral density of the population inhabiting the micro-region of Brześć Kujawski from the 11th century until the beginning of the 19th century.

Material and methods: Human bones obtained from archaeological excavations at four archaeological sites: Kolonia (11th–13th centuries), SBK-4 (12th–16th centuries), Fara (14th–17th centuries) and Święty Duch (16th–19th centuries) and from the collections of the Katedra of Anthropology of the University of Łódź were subjected to study. Bone mineral densities of the skeleton populations were compared with those of the control group, namely the present living population of the Łódź Province. The incidence of osteoporosis was evaluated by densitometric assessment, which was performed by dual energy X-ray absorptiometry (DXA) on a DPX device (LUNAR, USA).

Results: The densitometric measurements performed enabled differences to be identified in the mineral density of the osseous tissue. The skeletal groups studied were characterised by a significantly higher mean BMD than the contemporary living population. Changes in BMD indicative of osteopenia prevailed in women.

Conclusions: On the basis of the results obtained it cannot definitively be stated that the skeletal groups studied, despite their significantly higher BMD, were affected by a lower risk of osteoporosis and its complications. A continuation of studies on the mineral content of bones and on the relationship between the mineral content and bone mineral density is required.

(*Pol J Endocrinol* 2006; 5 (57): 494–500)

Key words: bone mineral density, osteoporosis, osteopenia, osteology, dating



Ewa Sewerynek, M.D., Ph.D.
Department of Bone Metabolism
The Medical University of Łódź
Sterlinga 5, 91-425 Łódź
phone/fax: 042 632 25 94
e-mail: ewa.sewerynek@wp.pl

Introduction

Osteoporosis is a systemic disease of the skeletal system, characterised by decreased bone mineral density and changes in the microarchitecture of the osseous tissue, which is associated with a reduction in tissue strength and an increased risk of fractures [1, 2]. At present, among the American population, approximately 10 million cases of overt osteoporosis have been found as well as about 34 million persons affected by low bone

mineral density (BMD) [3]. Osteoporosis is a serious social problem because of the growing costs of medical treatment of spine fractures, fractures of the distal forearm section and, especially, hip fractures [4].

Bone is a metabolically active tissue which undergoes a continuous process of reconstruction controlled by osseous tissue cells, namely osteoblasts (bone formation) and osteoclasts (bone resorption). In adults, in

normal conditions, bone formation and bone resorption are in a state of balance. Homeostasis of the metabolic processes of the osseous tissue is maintained by hormonal interactions and local mediators [5]. In metabolic diseases of the bones the activity of these factors is either excessive or too weak, thus disturbing bone turnover stability [5, 6].

According to the standards accepted by the WHO in Geneva in 1994, the values of bone mineral density are defined as normal when the T-score is between 1 SD and -1 SD, as osteopenia when $-1 \text{ SD} > \text{T-score} > -2.5 \text{ SD}$ and as overt osteoporosis when the T-score $< -2.5 \text{ SD}$ [7]. In the diagnosis of osteoporosis on the basis of densitometric examination of the lumbar spine T-score values calculated for the lumbar vertebrae L₂-L₄ should be taken into account. In assessment of the mineral density of the femoral neck the lowest T-score value from the following three examined areas should be considered: the femoral neck (Neck T-score), the trochanter (Troch T-score) and the mean value (total T-score) [8, 9]. The standards presented above have been accepted for the femoral neck of women of post-menopausal age in the USA population. They are also used for diagnosing osteoporosis in men [10].

The following are risk factors of the development of osteoporosis: an age of over 60, hormonal disorders, post-menopausal periods, low body mass index (BMI), habitual tobacco smoking, alcohol abuse, insufficient calcium supplementation in the diet, lack of physical activity and a sedentary life style [1, 3, 4, 11, 12]. Most of these factors contribute to the development of the so-called "diseases of civilisation", one of which is osteoporosis.

The goals of the present study were as follows:

- to evaluate of BMD in skeletal populations dated to the period between the 11th and the 19th centuries in comparison with the values measured in the contemporary population;
- to determine as far as possible whether low bone mineral density, at least according to present criteria for osteopenia and osteoporosis, did in fact occur in the selected skeletal groups.

Material and methods

The study comprised 75 skeletons made available by the Katedra of Anthropology of the University of Łódź. The bones were obtained from excavations performed during the 1960s and 1970s in the microregion of Brześć Kujawski and were dated from the 11th to the 13th centuries (the Kolonia Site), from the 14th to the 17th centuries (the Fara Site), from the 12th to the 16th centuries (the SBK-4 Site) and from the 16th to the 19th centuries (Święty Duch Site).

The control group was identified in the course of screening studies performed by the Outpatient Clinic of the Regional Centre of Menopause and Osteoporosis in Łódź.

Evaluation of BMD changes was performed by a DPX-Lunar densitometer using dual energy X-ray absorptiometry (DXA). This is now the most frequently used method in the evaluation of bone mineral density. It enables bone tissue mass to be evaluated in the femoral neck area, in the lumbar spine and in the proximal part of the forearm [11]. It is a sensitive technique, safe to the patient, and thus applicable for constant monitoring of BMD changes [12].

The DXA technique employs two X-ray beams, each beam of a different energy level, so that one beam is absorbed by the soft tissue and the other by the osseous tissue. In the case of the bones from archaeological excavations, the bone surrounding tissue was replaced by bags filled with rice [2].

The statistical analysis of data was performed using the Statistica 6.0 program. The normality of distribution was checked by the Shapiro-Wilk test. In order to confirm statistical significance the analysis of variance for five independent trials (Anova test) was performed. In order to perform a broader analysis of the statistical significance of data, relationships between two groups were compared by means of the post-hoc Tukey test.

Results

The sex and age structures of the studied groups are presented in Table I. The studies have demonstrated that no cases of osteoporosis were noted in any of the skeletal groups except SBK-4 and that of the subjects

Table I
Breakdown by age and sex of the groups studied

Tabela I
Struktura wieku i płci badanych grup

Groups	N	Mean age (± SD)	Women [%]	Men [%]
Kolonia (11 th -13 th centuries)	15	40.34 ± 11.25	53	47
Fara (14 th -17 th centuries)	17	40.45 ± 13.58	60	40
SBK-4 (12 th -16 th centuries)	23	39.03 ± 15.85	55	45
Święty Duch (16 th -19 th centuries)	20	48.08 ± 11.55	60	40
Contemporary Group (20 th century)	17	42.02 ± 20.09	53	47

Table II

Incidence of osteopenia and osteoporosis in the groups studied.
Sex: F — women, M — men

Tabela II

Częstość występowania osteopenii i osteoporozy w badanych grupach. Płeć: F — kobiety, M — mężczyźni

Groups	Disorder		Healthy subjects
	Osteopenia	Osteoporosis	
	% of subjects		
Kolonia (11 th –13 th centuries)	26.6% (3 F/1 M)	0%	73.4% (5 F/6 M)
Fara (14 th –17 th centuries)	29.4% (3 F/2 M)	0%	70.6% (7 F/5 M)
SBK-4 (12 th –16 th centuries)	30.4% (4 F/3 M)	4.4% (1 F)	65.2% (8 F/7 M)
Święty Duch (16 th –19 th centuries)	30% (3 F/3 M)	0%	70% (9 F/5 M)
Contemporary Group (20 th century)	53% (6 F/3 M)	9% (1 M)	38% (2 F/4 M)

with osteopenia, women prevailed in all the studied groups (Tab. II, III).

The values of total BMD and total T-score for the femoral neck were higher for the samples studied than those in the control group and statistical significance in relation to the contemporary group was observed only in samples excavated at the Święty Duch site (Fig. 1, 2).

No significant differences were found between the groups compared with regard to Troch T-score and Neck T-score (Fig. 2).

In the present study statistically significantly higher values of BMD and of the T-score in lumbar vertebrae

L₂–L₄ were found in all groups, when compared to the respective values of the control group (Fig. 1, 2).

Discussion

Osteoporosis, especially in developed countries, is a serious social and economic problem, mostly because of the increased risk of fractures [1, 13, 14]. In prophylactic activity for prevention of this disease attention is drawn to maximising the peak bone mass between the 20th and the 30th years of life and to preventing its rapid reduction after the 40th and especially after the 50th year of life [13].

Densitometry is regarded to be the most useful method of assessing BMD changes because it is the only one which directly and quantitatively determines bone mass reduction [14]. It is, however, important to consider whether the BMD standards for osteopenia and osteoporosis accepted by the WHO in 1994 [7, 15], which were defined for contemporary women of post-menopausal age, may automatically be applied to populations of previous ages. They are, however, used for diagnosing osteoporosis in young women and men [1].

In the present study bone mineral density was measured by dual energy X-ray absorptiometry (DXA) on a DPX device in adult subjects of the available skeletal groups. T-score values for lumbar vertebrae were significantly higher in all the study groups in comparison with the respective values in the control group. When BMD and T-score values in the femoral neck region were analysed, no statistically significant differences were noted except in the sample from the Święty Duch site. The distinct statistical significance observed in the study of the lumbar spine results from the fact that the vertebral bodies, because of their trabecular structure, are characterised by higher dynamics of change to the

Table III

Mean BMD values and Total (g/cm²) T-score for the femoral neck and the lumbar spine in individuals with osteopenia and osteoporosis; mean ± SD

Tabela III

Średnie wartości BMD Total (g/cm²) T-score dla szyjki kości udowej i kręgosłupa lędźwiowego osobników z osteopenią i osteoporozą; średnia ± SD

Groups	Sex	Mean age ± SD	FEMORAL BONE			SPINE		
			Mean T-score			BMD mean [g/cm ²]	T-score (L ₂ –L ₄) mean	BMD mean [g/cm ²]
			Total	Troch	Neck			
Kolonia	3 F/1 M	44.09 ± 8.12	-0.475 ± 0.23	-0.225 ± 0.46	-1.6 ± 0.56	0.9617 ± 0.04	0.85 ± 0.09	1.276 ± 0.78
Fara	2 F/1 M	41.25 ± 20.20	-1.0 ± 0.81	-1.1 ± 0.9	-1.6 ± 1.0	0.902 ± 0.06	-1.05 ± 0.11	3.112 ± 1.3
SBK-4	5 F/3 M	47.32 ± 14.37	-0.92 ± 0.66	-0.81 ± 0.81	-1.67 ± 0.71	0.91 ± 0.71	-0.2 ± 0.11	0.99 ± 0.01
Święty Duch	3 F/1 M	61.06 ± 11.81	-0.5 ± 0.75	-0.6 ± 0.69	-1.6 ± 0.4	0.912 ± 0.06	-1.2 ± 0.00	1.1 ± 0.00
Control	6 F/4 M	43.20 ± 18.48	-0.981 ± 1.15	0.707 ± 1.46	-1.27 ± 0.94	1.398 ± 0.16	-1.576 ± 1.1	0.767 ± 0.12

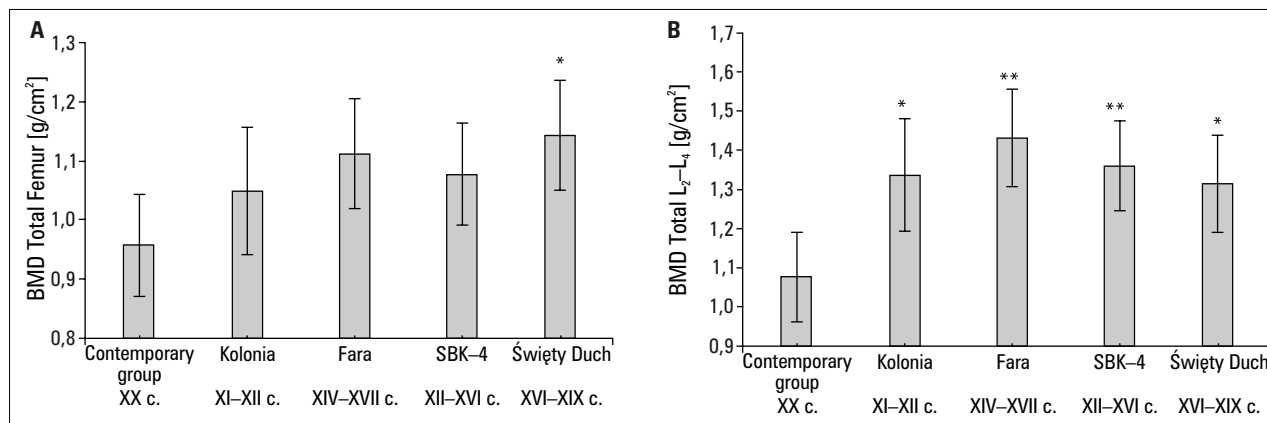


Figure 1A. Bone mineral density (BMD Total — g/cm²) of the femoral neck; **B.** Bone mineral density (BMD Total — g/cm²) of lumbar vertebrae L₂-L₄. Mean ± SD. Level of significance: p* < 0.05; p** < 0.01

Rycina 1A. Gęstość mineralna kości (BMD Total — g/cm²) szyjki kości udowej; **B.** Gęstość mineralna kości (BMD Total — g/cm²) kręgow łędźwiowych L₂-L₄. Średnia ± SD. Poziom istotności: p* < 0,05; p** < 0,01

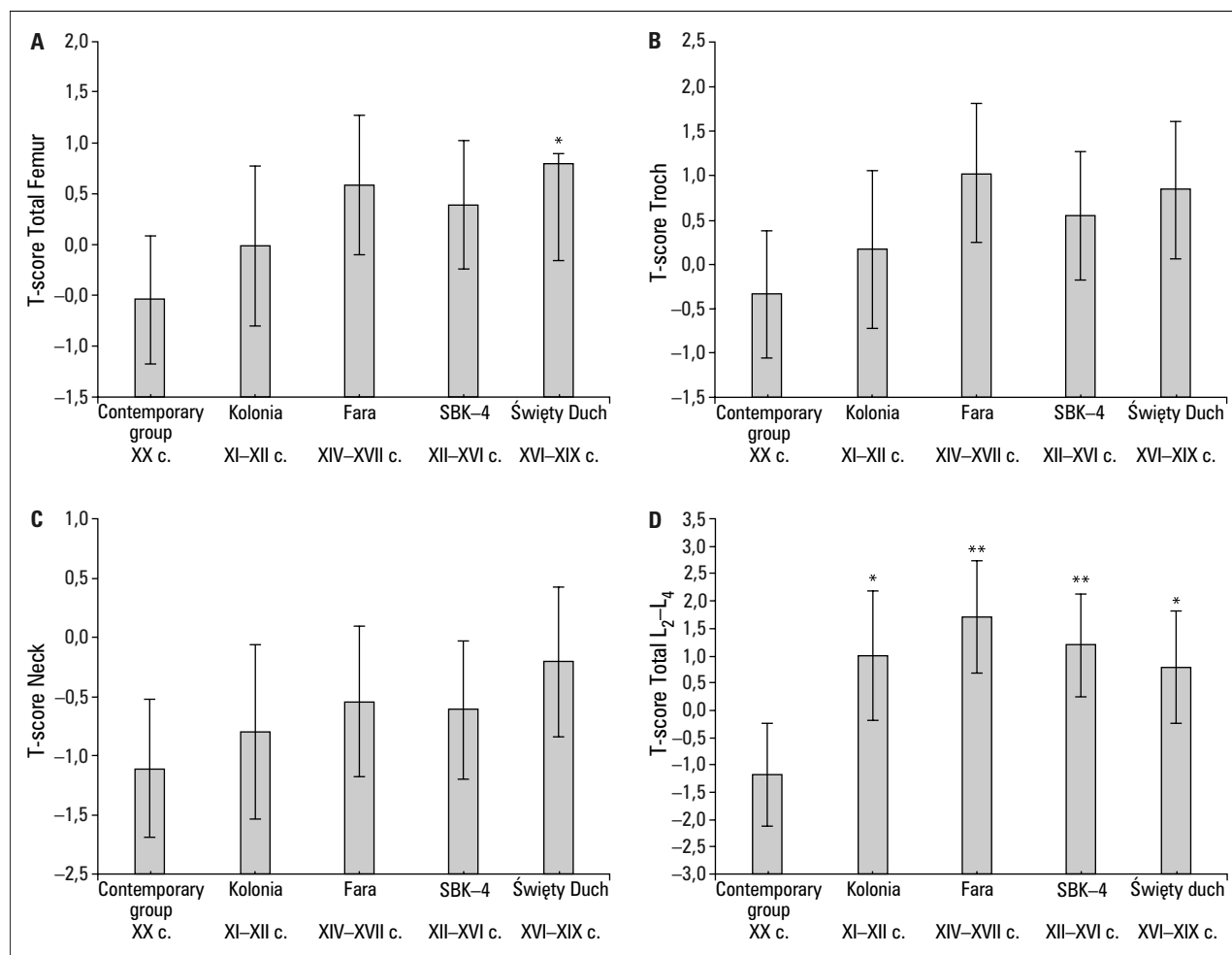


Figure 2A. T-score values of the femoral bone (Total); **B.** T-score values of the femoral trochanter (Troch); **C.** T-score values of the femoral neck (Neck); **D.** Total T-score values of lumbar vertebrae L₂-L₄. Mean ± SD. Level of significance: p* < 0.05; p** < 0.01

Rycina 2A. Wartości T-score kości udowej (Total); **B.** Wartości T-score krętarza kości udowej (Troch); **C.** Wartości T-score szyjki kości udowej (Neck); **D.** Wartości T-score Total kręgow łędźwiowych L₂-L₄. Średnia ± SD. Poziom istotności: p* < 0,05; p** < 0,01

bone tissue microarchitecture than the upper region of the femoral bone [15].

The higher bone mineral density found in the skeletal populations may, causatively, have been related to the much higher levels of physical activity of those people than of their contemporary counterparts. It has been shown in many studies that all kinds of physical exercise contribute to an increase in spinal BMD both before and after the menopause [16–22]. Gibson et al. [20] demonstrate that training with a muscular load stimulates BMD increase much more effectively than does endurance effort. As a result of the lack of active axial load on the skeleton, particularly low BMD values are noted among individuals with low levels of physical activity [15, 16, 18] and in the disabled [23].

Improved muscular strength and better motor coordination decrease the risk of osteoporotic fractures by reducing the number of falls. Physical activity eliminates the pain associated with osteoporosis development and increased thoracic kyphosis, which enforces a certain body position and leads to a deterioration in respiratory capacity [14, 21].

The present observations indicate that decreased BMD, referred to as osteopenia and osteoporosis, affects mostly the female population. The examinations performed demonstrated a higher incidence of osteopenia in women both in the selected skeletal groups and in the control group. The accelerated bone turnover observed in women may result from lower peak bone mass and from oestrogen deficiency of varying aetiology [11, 24–26]. The advantageous effect of oestrogens on the bone system has been underlined in a number of reports [24–26] and has been confirmed during hormonal replacement therapy.

The higher incidence of osteopenia observed among contemporary women may be associated with a disturbed function of the hypothalamus-pituitary-ovary axis, resulting in oestrogen deficiency and, in consequence, menstruation disorders and secondary amenorrhoea [24]. Not only may a deficit of sex hormones occur in women of post-menopausal age but it is also increasingly observed in young people with fatty tissue deficiency and in individuals involved in professional sports [17, 18, 20].

Periods of pregnancy and lactation affect the metabolism of bone tissue by changes in hormonal metabolism. An increased use of intrasystemic calcium reserves and of alkaline phosphatase is observed at these times, associated with building the foetal skeleton and with milk production. Additionally, calcium absorption from the gastric tract increases, together with plasmatic concentration of bone formation markers. In the course of gestation a BMD increase is noted. The reduction in the average number of pregnancies currently expe-

rienced by women and the frequency of menstruation disorders lead to oestrogen deficiency and, in consequence, to lower peak bone mass and to bone turnover acceleration [23].

The examinations performed indicate the complexity of the problems associated with disorders of bone mineral density. On the basis of the results obtained no unequivocal statement is possible regarding the incidence of osteoporosis during the chronological periods studied. However, the present observations may be confirmed, namely that those predisposed to the occurrence of osteoporosis include women and that physical exercise with loading of the axial skeleton stimulates bone formation.

In order to be able to determine more accurately the tendency of changes in bone mineral density through particular ages it is necessary to study larger groups of skeletons. An analysis of elements contained in the bone tissue, while providing some information on the nutritional habits of the populations studied, may also provide valuable information regarding the aetiology of changes in BMD.

Conclusions

The following conclusions may be drawn: 1. A significantly higher mineral density of the bone tissue in lumbar vertebrae L₂–L₄ was observed in all the skeletal groups studied than in the control group; 2. A significantly higher percentage of patients with osteopenia is found among the contemporary population, predisposing this population to the occurrence of osteoporosis; 3. Of those with osteopenia, from all the periods studied, disorders of bone mineral density affected mainly women.

Acknowledgements

We are extremely grateful to Prof. Andrzej Lewiński, Rector Magnificus of the Medical University of Łódź, for giving permission for the densitometric studies of the bone material at the Regional Centre of Menopause and Osteoporosis in Łódź.

We greatly appreciate the assistance given by Prof. Józef Kędziora, Head of the Katedra of Chemistry and Clinical Biochemistry of the Medical University of Łódź, in the selection of study subject and in co-ordinating the design of the paper.

References

1. Francisco A, Conde RN, William J et al. Risk factors for male osteoporosis. *Urol Oncol Semin Origin Invest* 2003; 21: 380–383.

2. Neville CE, Murray LJ, Boreham CA et al. Relationship between physical activity and bone mineral status in young adults: The Northern Ireland Young Hearts Project. *Bone* 2002; 30: 792–798.
3. Tussing L, Chapman-Novakofski K. Osteoporosis prevention education: behavior theories and calcium intake. *J Am Diet Assoc* 2005; 105: 92–97.
4. Masoni A, Morosano M, Pezzotto SM et al. Construction of two instruments for the presumptive detection of post-menopausal women with low spinal bone mass by means of clinical risk factors. *Maturitas* 2005; 51: 314–24.
5. Lorenc RS. Diagnostyka osteoporozy. In: Lorenc RS, M. Pawlina eds, *Patogeneza i obraz kliniczny osteoporozy*. PWN Warszawa 1998: 9.
6. Seibel MJ. Biochemical markers of bone remodelling. *Endocrinol Met Clin North Am* 2003; 32: 83–113.
7. Assessment of fracture and its application to screening for postmenopausal osteoporosis. WHO Techn Rep Ser 843 Geneva 1994.
8. Kanis JA, Seeman E, Johnell O et al. The perspective of the International Osteoporosis Foundation of the official positions of the International Society for Clinical Densitometry. *J Clin Densitom* 2005; 8: 145–147.
9. Lewiecki EM, Kendler DL, Schmeer P et al. Special report on the official positions of the International Society for Clinical Densitometry. *Osteopor Int* 2004; 15: 779–784.
10. Olszyński WP, Shaw Davisom K et al. Osteoporosis in men: epidemiology, diagnosis, prevention and treatment. *Clin Ther* 2004; 26: 15–28.
11. Bakhireva LN, Barrett-Connor E, Kritz-Silverstein D et al. Modifiable predictors of bone loss in older men: a prospective study. *Am J Prev Med* 2004; 26: 436–442.
12. Thomas T, Burguera B, Melton JL et al. Role of serum leptin, insulin and estrogen levels as potential mediators of the relationship between fat mass and bone mineral density in men versus women. *Bone* 2001; 29: 114–120.
13. Puntilla E, Kroger H, Lakka T et al. Physical activity in adolescence and bone density in peri- and postmenopausal women: a population-based study. *Bone* 1997; 21: 363–367.
14. Malinowska A, Dudkiewicz Z, Kilian Z et al. Społeczne skutki osteoporozy w obrębie narządu ruchu w regionie łódzkim. *Kwart Ortop* 2002; 4: 239–247.
15. Gluer CC. The use of bone densitometry in clinical practice. *Baillieres Clin Endocrinol Metab* 2000; 14: 195–211.
16. Warren MP. The female athlete. *Bailliere's Clin Endocrinol Metab* 2000; 14: 37–53.
17. Nevill AM, Holder RH, Stewart AD. Modelling elite male athletes' peripheral bone mass, assessed using regional dual x-ray absorptiometry. *Bone* 2003; 32: 62–68.
18. Fehling PC, Alekel L, Clasey J et al. A comparison of bone mineral densities among female athletes in impact loading and active loading sports. *Bone* 1995; 17: 200–210.
19. Smeltzer SC, Zimmerman V, Capriotti T. Osteoporosis risk and low bone mineral density in women with physical disabilities. *Arch Phys Med Rehabil* 2005; 86: 582–586.
20. Gibson JH, Harries M, Godfrey R et al. Determinants of bone density and prevalence of osteopenia among female runners in their second to seventh decades of age. *Bone* 2000; 26: 591–598.
21. Sinaki M, Wahner HW, Bergstralh EJ et al. Three-year controlled, randomized trial of the effect of dose-specified loading and strengthening exercises on bone mineral density of spine and femur in non-athletic, physically active women. *Bone* 1996; 19: 233–244.
22. Heinonen A, Oja P, Kannus P. Bone mineral density in female athletes representing sports with different loading characteristics of the skeleton. *Bone* 1995; 17: 197–203.
23. Sengupta S, Arshad M, Sharma S et al. Attainment of peak bone mass and bone turnover rate in relation to estrous cycle, pregnancy and lactation in colony-bred Sprague-Dawley rats: Suitability for studies on pathophysiology of bone and therapeutic measures for its management. *J Steroid Biochem Mol Biol* 2005; 95: 421–429.
24. Kaur M, Pearson D, Godber I. Longitudinal changes in bone mineral density during normal pregnancy. *Bone* 2003; 32: 449–459.
25. Kuller LH, Matthews KA, Meilahn EN. Estrogens and women's health: interrelation of coronary heart disease, breast cancer and osteoporosis. *J Steroid Biochem Mol Biol* 2000; 74: 297–309.
26. Tobias J, Compston JE. Does estrogen stimulate osteoblast function in postmenopausal women? *Bone* 1999; 24: 121–124.