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Bone densitometry by radiofrequency echographic multi-spectrometry (REMS) in acromegaly patients

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Abstract

Introduction: Radiofrequency echographic multi-spectrometry (REMS) is a recently introduced non-ionising technology employed in the evaluation of osteoporosis. The aim of our study was to compare bone mineral density (BMD) in acromegaly patients and healthy controls by performing novel REMS densitometry. The second objective was to analyse the correlation between results of REMS and classical dual-energy X-ray absorptiometry (DXA) in acromegaly patients.

Material and methods: We enrolled 33 patients with acromegaly (AG) and 24 controls (CG). The acromegaly patients were divided into two subgroups: well-controlled acromegaly (WCA) and surgery-cured acromegaly (SCA). REMS was performed in all participants, while DXA was performed only in the acromegaly group. IGF-I and GH levels were measured in acromegaly patients.

Results: Bone mineral density of the lumbar spine (LS) and the femoral neck (FN) obtained from REMS did not reveal significant differences between AG, CG, WCA, and SCA. Similarly, there were no significant differences in BMD measured by DXA at the LS and at the FN between WCA and SCA. Significant positive correlations between IGF-I concentrations and BMD obtained from both REMS and DXA were detected in the AG and WCA. In the AG and WCA, there were positive correlations between T-scores and LS BMD obtained from both methods.

Conclusions: Radiofrequency echographic multi-spectrometry is a potential method in assessment of bone status in acromegaly. Further studies with participation of active disease patients are needed. (**Endokrynol Pol 2020; 71 (6): 524–531)**

Key words: *acromegaly; REMS; DXA; osteoporosis; densitometry*

Introduction

Acromegaly is a rare disease characterised by elevated levels of growth hormone (GH) and insulin-like growth factor I (IGF-I) mainly due to pituitary adenoma [1]. An excess amount of these hormones leads to a lot of systemic complications including secondary osteoporosis and vertebral fractures [2, 3]. Growth hormone and IGF-I are anabolic hormones responsible for enhanced bone formation and achievement of peak bone mass. In acromegaly patients an increased bone turnover as well as an imbalance between bone resorption and formation were described [4–7]. Growth hormone and IGF-I affect the cortical and trabecular bone differently [4, 8]. The impact on cortical bone is complex — the excess of GH and IGF-I promotes development of cortical thickness, but at the same time it contributes to increased cortical porosity [9]. What is more, a negative impact on trabecular tissue was observed [2, 10]. Impaired structure of trabecular bone was reported not only in active disease but also after achieving remission [11, 12]. Reduced trabecular thickness, increased trabecular separation, and cortical porosity could be reasons for increased fracture risk in acromegaly [2, 7, 12, 13]. Fractures with coexisting pain and immobility are among the most important problems deteriorating the quality of life in patients with acromegaly [14].

Nowadays dual-energy X-ray absorptiometry (DXA) remains a gold standard for bone mineral density (BMD) measurement in diagnostics of osteoporosis. In acromegaly, BMD has some limitations. Increased bone size and spine deformities are factors affecting BMD values [15, 16]. Bone mineral density does not have adequate potential to reflect bone microarchitecture; therefore, it is not appropriate for bone quality assessment [7]. Co-existing diseases also influence BMD. Hypogonadism, which often accompanies acromegaly, may contribute to lower BMD [8]. In turn, diabetes is associated with paradoxically high BMD despite increased risk of fractures [2]. Osteoarthritis may also lead to an overestimation of BMD [7]. Moreover, the presence of fractures and calcifications disturb the accuracy of DXA. It has been highlighted that patients with acromegaly are at risk of fractures despite normal or high BMD values [2,7]. On account of limitations of BMD measured by DXA, some alternative methods for

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bone status assessment such as quantitative computed tomography (QCT) [15,17], quantitative ultrasound (QUS) [18–20], and impact microindentation [11] have been investigated. Further search for diagnostic tools, especially to assess status of bone microarchitecture, is needed.

Radiofrequency echographic multi-spectrometry (REMS) is a recently introduced non-ionising technology employed in the evaluation of osteoporosis. The method is based on the analysis of radiofrequency (RF) signals acquired after conversion ultrasound spectra obtained during echographic scan of lumbar vertebrae or femoral neck. During the examination the operator visualises the target bones employing a 3.5-MHz convex probe placed at the abdomen or hip. The software automatically detects regions of interest (ROI) by comparing obtained images to matrices of the RF signals. Then ROI RF signals are compared with reference models [age-, sex-, body mass index (BMI)-, and site-matched] from the dedicated database and matched to pathological or normal condition. It is important to note that the system distinguishes spectra of trabecular bone and of cortical bone and cartilage. The analysed spectrum is classified in the Osteoporosis Score and then transformed into a BMD value by linear equations. T- and Z-score are calculated based on National Health and Nutrition Examination Survey (NHANES) database. Before the examination no special preparation is needed, the procedure is short (up to two minutes), and can be performed in any setting because the densitometer is mobile. REMS technology was proposed as a new tool in screening of primary osteoporosis. In a multicentre study involving 1914 women, the new technique was described as precise, and the results were comparable with those obtained from DXA [21]. So far, no research assessing the usefulness of the method was performed in evaluating endocrine related osteoporosis.

The aim of our study was to compare BMD and T-scores evaluated by novel REMS densitometry of the lumbar spine and femoral neck in a group of acromegaly patients and healthy controls. Second objective was to analyse the correlation between results of REMS and DXA densitometries in acromegaly patients. To our knowledge, this is the first study comparing these techniques in acromegaly.

Material and methods

Patient population

We enrolled 33 patients with acromegaly (25 women and 8 men) and 24 healthy subjects as a control group (CG) (17 women and 7 men). All participants were recruited from the Department of Endocrinology, Diabetes and Isotope Therapy, Wroclaw Medical University. Approval for the study was obtained from the ethics committee of Wroclaw Medical University. Informed consent was obtained from all individual participants. In the acromegaly group (AG) we enrolled patients (mean age 59.1 ± 9.8 years) with diagnosis of acromegaly based on clinical features and laboratory results (elevated IGF-I and GH not suppressed during oral glucose tolerance test), with long-term observation of controlled or cured disease (IGF-I < 1.3 upper limit of normal was a criterion of well-controlled or cured disease). Patients were divided into two subgroups: 20 patients with controlled disease during treatment with long-acting somatostatin analogues were assigned to the well-controlled acromegaly subgroup (WCA), and 13 patients were assigned to the surgically cured acromegaly subgroup (SCA). To the control group (CG) we recruited age-matched subjects without clinical features of acromegaly or diagnosis of other secondary osteoporosis-related diseases in their medical history.

Questionnaires concerning coexisting diseases, history of fractures, surgeries, and current pharmacology treatment were taken from all participants of the study. Fractures defined as fragility fractures [22, 23] were observed in five patients from the AG group and in no patients from the CG group. Traumatic fractures were recognised in two acromegaly patients and in six controls. Additionally, some participants of the study had recommendations to take vitamin D and calcium: nine acromegaly patients and three controls took vitamin D (1000–4000 U daily); four patients with acromegaly and two controls took calcium (500–1000 mg daily). Moreover, two patients with acromegaly were treated with bisphosphonates (ibandronic acid). In CG one woman received hormone replacement therapy. Among the acromegaly group 11 patients had pituitary insufficiency at least affecting one axis (seven thyrotropic, five corticotropic, and three gonadotropic). None of the patients with hypogonadism received hormone replacement therapy. In addition, nine acromegaly patients and two controls suffered from diabetes mellitus.

The analyses were performed based on the division into subgroups. The first classification was used to analyse the differences between a group of acromegaly patients (AG) and controls (CG). The second division was done on the basis of the status of the disease (WCA; SCA) and CG.

The study was approved by the local ethical committee. Informed consent was obtained from all participants.

Laboratory assays

Blood samples were obtained from acromegaly patients. Serum GH and IGF-I were measured with a chemiluminescent immunometric method (Immulite 2000, Siemens Healthcare Diagnostics, USA). Analytical sensitivity was 0.01 ng/mL for GH and 20.0 ng/mL for IGF-I.

Densitometry

Radiofrequency echographic multi-spectrometry examinations were performed in the acromegaly and control groups. Ultrasound scans of lumbar spine and femoral neck were performed employing EchoS (Echolight, Italy). Bone mineral density, T-score, and Z-score values were obtained by system calculation and compared with a dedicated database. Densitometry with dual-energy X-ray absorptiometry (DXA) was performed in the acromegaly group. Bone mineral density was measured at the lumbar spine (L1–L4) and femoral neck using dual-energy X-ray absorptiometry (DXA, Hologic — Discovery QDR Series) equipped with reference values based on NHANES III. According to WHO definitions, osteoporosis was diagnosed if the T-score was ≤ –2.5, and low bone density if > –2.5 and < –1.0.

Statistical analysis

Statistical analysis was performed using R for Windows, version 3.5. Differences between groups were analysed with the Wilcoxon rank sum and Kruskal-Wallis rank sum tests. Associations between variables were tested by Spearman correlation analysis. P values less than 0.05 were considered statistically significant.

Results

The general characteristics of the groups are presented in Table 1. Anthropometric parameters (weight, height, BMI), age, menopause age, and years after menopause did not differ significantly between the analysed groups. There were no significant differences in IGF-I and GH concentrations between WCA and SCA subgroups.

Bone mineral density, T-scores, and Z-scores of the lumbar spine (LS) and the femoral neck (FN) obtained from REMS did not reveal significant differences between acromegaly patients and the controls (Tab. 2 and Tab. 3). Similarly, we did not observe significant differences in T-scores, Z-scores, and BMD measured by REMS and DXA at the LS and at the FN between WCA and SCA subgroups.

The number of patients with diagnosis of osteoporosis and low bone density varied depending on the used

Table 1. *Characteristics of acromegaly patients and the control group*

	AG			CG			WCA			SCA		
	Mdn	q1	q3	Mdn	q1	q3	Mdn	q1	q3	Mdn	q1	q3
No.		33			24			20			13	
Sex: F (M)		25 (8)			17 (7)			13 (7)			12 (1)	
Age (yrs)	60.0	53.0	65.0	55.5	51.0	64.3	61.5	54.5	67.5	58.0	48.0	64.0
Weight [kg]	80.0	70.0	95.0	77.0	62.8	82.8	82.5	75.0	95.5	76.0	69.0	94.0
BMI [kg/m^2]	29.0	26.4	31.4	27.9	25.0	29.8	29.2	27.3	31.3	28.6	25.7	33.3
Menopause age (yrs)	50.0	45.5	52.0	49.0	44.5	55.0	48.5	45.8	52.3	50.0	46.5	51.5
Years after menopause (yrs)	6.0	0.0	14.0	0.0	0.0	8.75	4.5	0.0	14.0	6.0	0.0	14.0
IGF-I [ng/mL]	152.0	124.0	189.0	NA	NA	NA	153.5	117.3	196.8	141.0	133.0	166.0
GH [ng/mL]	1.0	0.4	1.9	NA	NA	NA	1.5	0.6	2.1	0.4	0.2	1.1

AG — acromegaly group; CG — control group; WCA — well-controlled acromegaly; SCA — surgery-cured acromegaly; Mdn — median; q1 — first quartile; q3 — third quartile; BMI — body mass index; IGF-I — insulin-like growth factor I; GH — growth hormone

Table 2. *Comparison of radiofrequency echographic multi-spectrometry (REMS) and dual-energy X-ray absorptiometry (DXA) results of the lumbar spine (median)*

	REMS L1–L4						DXA L1–L4					
	BMD	p	T-score	p	Z-score	p	BMD	p	T-score	p	Z-score	p
AG	0.977	0.69 [a]	–0.6	0.66 [a]	0.7	0.25 [a]	1.042	–	0.0	–	0.9	–
CG	0.977	0.69 [a]	–0.7	0.66 [a]	0.7	0.25 [a]	–	–	–	–	–	–
WCA	1.037	0.70 [b]	–0.3	0.65 [b]	1.1	0.07 [b]	1.069	0.51 [c]	0.0	0.30 [c]	0.9	0.08 [c]
SCA	0.971	0.70 [b]	–0.7	0.65 [b]	0.4	0.07 [b]	0.971	0.51 [c]	–0.7	0.30 [c]	0.9	0.08 [c]

BMD — bone mineral density; AG — acromegaly group; CG — control group; WCA — well-controlled acromegaly; SCA — surgery-cured acromegaly; [a] — comparison between AG and CG; [b] — comparison between WCA, SCA and CG; [c] — comparison between WCA and SCA

Table 3. *Comparison of radiofrequency echographic multi-spectrometry (REMS) and dual-energy X-ray absorptiometry (DXA) results of the femoral neck (median)*

	REMS femoral neck						DXA femoral neck					
	BMD	p	T-score	p	Z-score	p	BMD	p	T-score	p	Z-score	p
AG	0.841	0.23 [a]	–0.2	0.24 [a]	0.8	0.11 [a]	0.879	–	–0.1	–	1.2	–
CG	0.777	0.23 [a]	–0.7	0.24 [a]	0.6	0.11 [a]	–	–	–	–	–	–
WCA	0.848	0.49 [b]	–0.1	0.49 [b]	1.0	0.22 [b]	0.871	0.51 [c]	–0.2	0.30 [c]	1.0	0.08 [c]
SCA	0.748	0.49 [b]	–0.9	0.49 [b]	0.6	0.22 [b]	0.879	0.51 [c]	0.3	0.30 [c]	1.4	0.08 [c]

AG — acromegaly group; CG — control group; WCA — well-controlled acromegaly; SCA — surgery-cured acromegaly; [a] — comparison between AG and CG; [b] — comparison between WCA, SCA and CG; [c] — comparison between WCA and SCA

Table 4. *Comparison of bone mineral density (BMD) (median), diagnosis of osteoporosis and low bone density (% of the group) obtained by radiofrequency echographic multi-spectrometry (REMS) and dual-energy X-ray absorptiometry (DXA)*

	BMD				Osteoporosis				Low bone density			
	Lumbar spine		Femoral neck		Lumbar spine		Femoral neck		Lumbar spine		Femoral neck	
	REMS	DXA	REMS	DXA	REMS	DXA	REMS	DXA	REMS	DXA	REMS	DXA
AG	0.977	1.042	0.841	0.879	3.7	12.1	3.3	0.0	29.6	24.2	26.7	27.3
CG	0.977	–	0.777	–	0.0	–	0.0	–	37.5	–	30.0	–
WCA	1.037	1.069	0.848	0.871	6.3	10.0	5.3	0.0	31.3	35.0	26.3	35.0
SCA	0.971	0.971	0.748	0.879	0.0	15.4	0.0	0.0	27.3	7.7	27.3	15.4

AG — acromegaly group; CG — control group; WCA — well-controlled acromegaly; SCA — surgery-cured acromegaly

densitometry technique. These results are presented in Table 4. The results of REMS revealed osteoporosis at LS and FN in 3.7 and 3.3%, respectively, of AG and in none of the participants of CG. However low bone density was observed more often in CG than in AG: 37.5 *vs.* 29.6 % at LS and 30.0 *vs.* 26.7% at FN.

In the AG group, and also in the WCA and SCA subgroups, we analysed correlations between IGF-I and GH concentrations and BMD measured by REMS and DXA densitometries (Tab. 5). The study revealed significant positive correlations between IGF-I concentrations and LS BMD and FN BMD obtained from both REMS and DXA methods in the AG and WCA groups. There was no correlation between GH concentration and BMD for REMS or for DXA method.

We also checked correlations between BMD and anthropometric parameters. LS BMD (REMS technique) correlated positively with height and weight in the AG, CG, and WCA groups. Similarly, positive correlations were found for LS BMD by DXA in the AG and WCA groups. At femoral neck, for the REMS method, we also observed positive correlations with height and weight in the AG, CG, and WCA groups. FN BMD (DXA technique) correlated positively with weight in the AG and WCA groups, and with height, but only in the AG group.

A negative correlation between LS BMD measured by REMS and age was noted in the AG and WCA groups, but not in the CG group. For the DXA method, this association was observed for LS BMD in the AG and SCA groups. At the FN area a negative correlation between BMD (REMS method) and age was revealed only in the WCA group. Moreover, there were negative correlations between FN BMD (DXA method) and age in the AG and WCA groups. Additionally, we noted significant negative correlations between BMD and years after menopause in the AG and WCA groups, independently of the method used. What is more, a similar correlation, but only for LS area, was found in the CG (REMS method) and in the SCA (DXA method) groups.

In the AG and in the WCA groups, we found statistically significant positive correlations between T-scores obtained from REMS and from DXA at LS and FN areas (Fig. 1). They were observed between LS T-scores ($r = 0.482$, $p = 0.011$) and FN ($r = 0.431$; $p = 0.018$) in the AG group. In WCA positive correlations were revealed between LS T-scores ($r = 0.537$, $p = 0.032$) and FN ($r = 0.528$, $p = 0.020$).

Likewise, for LS BMD positive correlations between methods were revealed in the AG and WCA groups ($r = 0.546$, $p = 0.003$ and $r = 0.544$, $p = 0.032$, respectively). There was no correlation for FN BMD assessed by REMS and by DXA techniques.

Discussion

Patients with acromegaly have an increased risk of fracture, which might be correlated with poor quality of bone. Prevalence of vertebral fractures is three- to eight-fold higher than in the general population [3]. In our study 15% of acromegaly patients experienced osteoporotic fracture, while this was not observed in the control group. Although screening for osteoporosis is recommended in acromegaly [3, 24] and DXA remains a gold standard, vertebral fractures may be present in patients with normal or slightly decreased BMD, which makes BMD obtained from DXA an inadequate fracture predictor [8, 20, 25]. Using of FRAX has not been validated in patients with acromegaly [26]. Nevertheless, we do not have other useful tools to detect bone damage and estimate real risk for fractures. As we showed in a previous study, usage of FRAX could be functional in combination with other tools such as TBS [27]. The early diagnosis of acromegaly and investigations for new markers as well as for new diagnostic methods for assessing the risk of osteoporotic fractures are very important to improve care of acromegaly patients. REMS technology is one of the promising new methods proposed in the screening of osteoporosis [21, 28]. In our study we analysed results of densitometry performed with novel REMS method and traditional DXA in acro-

Table 5. *Correlations of patients' characteristics and densitometry results*

			IGF-I		GH		Age		Height		Weight		Years after menopause	
			r	p	*r*	p	*r*	p	*r*	p	*r*	p	*r*	p
DXA – BMD	SCA	Neck	0.355	0.234	0.412	0.163	–0.474	0.102	0.473	0.103	0.105	0.734	–0.473	0.103
		Lumbar	0.305	0.310	0.451	0.125	–0.686	0.010	0.396	0.181	0.022	0.943	–0.597	0.031
	WCA	Neck	0.564	0.011	–0.027	0.911	–0.625	0.003	0.438	0.054	0.656	0.002	–0.483	0.031
		Lumbar	0.623	0.004	–0.021	0.932	–0.398	0.082	0.487	0.029	0.577	0.008	–0.481	0.032
	AG	Neck	0.424	0.014	0.062	0.733	–0.553	< 0.001	0.439	0.011	0.409	0.018	–0.481	0.005
		Lumbar	0.540	0.001	0.108	0.550	–0.530	0.002	0.486	0.004	0.360	0.039	–0.567	< 0.001
REMS – BMD	CG	Neck	NA	NA	NA	NA	–0.070	0.847	0.804	0.005	0.909	< 0.001	–0.374	0.288
		Lumbar	NA	NA	NA	NA	–0.336	0.108	0.819	0.000	0.911	0.000	–0.611	0.002
	SCA	Neck	0.556	0.076	0.200	0.558	0.036	0.915	0.258	0.445	0.888	< 0.001	0.196	0.563
		Lumbar	0.160	0.640	0.336	0.313	–0.461	0.153	0.511	0.108	0.400	0.225	–0.225	0.507
	WCA	Neck	0.592	0.008	–0.029	0.906	–0.487	0.035	0.873	0.000	0.910	0.000	–0.809	0.000
		Lumbar	0.594	0.017	0.088	0.746	–0.598	0.015	0.842	0.000	0.877	0.000	–0.842	0.000
	AG	Neck	0.573	< 0.001	0.044	0.816	–0.319	0.086	0.749	0.000	0.909	0.000	–0.530	0.003
		Lumbar	0.441	0.021	0.153	0.447	–0.428	0.026	0.724	0.000	0.771	0.000	–0.664	< 0.001

REMS — radiofrequency echographic multi-spectrometry; DXA — dual-energy X-ray absorptiometry; BMD — bone mineral density; AG — acromegaly group; CG — control group; WCA — well-controlled acromegaly; SCA — surgery-cured acromegaly; IGF-I — insulin-like growth factor I; GH — growth hormone

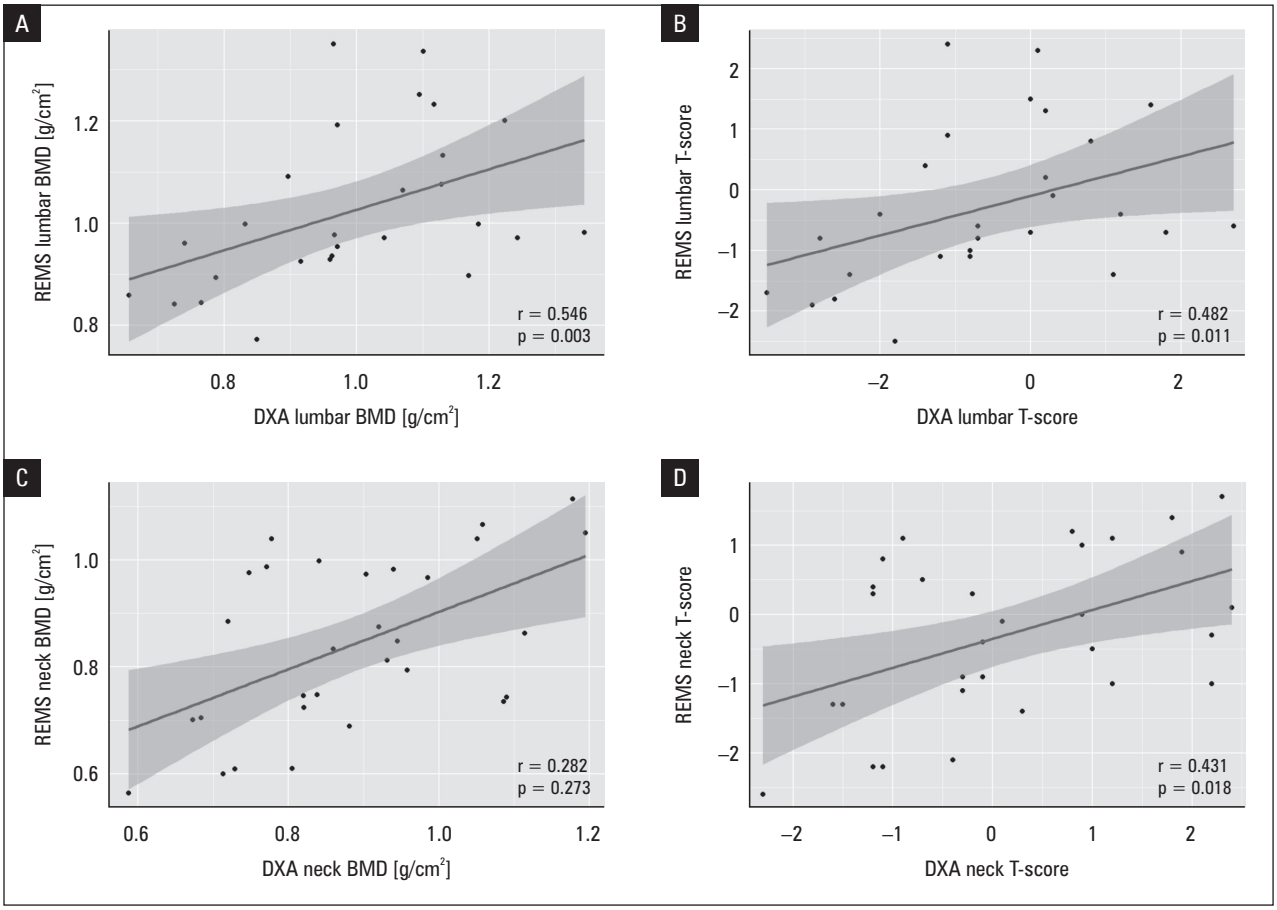

Figure 1. *Correlations between radiofrequency echographic multi-spectrometry (REMS) and dual-energy X-ray absorptiometry (DXA) in the acromegaly patients (AG).* **A.** *Correlation between REMS and DXA lumbar spine bone mineral density (BMD);* **B.** *Correlation between REMS and DXA lumbar spine T-scores;* **C.** *Correlation between REMS and DXA femoral neck BMD;* **D.** *Correlation between REMS and DXA femoral neck T-scores*

megaly patients. To our knowledge, this is the first study comparing these techniques in acromegaly.

Bone mineral density is a parameter measured in both DXA and REMS techniques. In our study we found no statistically significant differences in BMD among the groups in each method. This observation is consistent with some previous reports. Tuzcu et al. found no differences for T-score and BMD values obtained from DXA between the active acromegaly and control groups [29]. Among patients with active, controlled, and cured disease Madeira et al. also did not observe differences for BMD value [30]. Also comparison between the active acromegaly, GH deficiency, and control groups did not reveal BMD distinctions [10]. In our study, there were no differences for BMD by DXA between the WCA and SCA subgroups. What is more, the study did not prove differences for BMD obtained from REMS between the AG and CG. We did not evaluate bone microarchitecture, but we imply that BMD in acromegaly may be overestimated due to higher cortical bone thickness [9]. In acromegaly a high prevalence of osteoarthritis might be a factor which disrupts DXA accuracy. Bone degenerations, presence of osteophytes and calcifications contribute to higher results of BMD, especially in the lumbar area [8]. Preliminary research has reported that the REMS method should be able to automatically remove signals that arise from artifacts like calcifications and osteophytes [31], which makes REMS a potentially beneficial method in bone assessment in acromegaly. Further investigations and evaluation of BMD by REMS among patients with active acromegaly and osteoarthritis are necessary.

We obtained a positive correlation between IGF-I and BMD in both methods in the AG and WCA groups. This association may reflect the anabolic effect of IGF-I on bones. Nevertheless, such a correlation was not observed for GH concentration, which may indicate a complex effect of the GH-IGF-I axis on bone status. Consistent results were reported in Tuzcu's study [29]. Moreover acromegaly treatment was reported to increase BMD, but decrease trabecular bone score (TBS), which is a promising marker of bone quality [2, 5]. Positive correlation between IGF-I and BMD support the thesis that BMD reflects mainly the condition of cortical

tissue. The influence of IGF-I on BMD in acromegaly patients masks impairment of bone quality in this group. Bone mineral density correlated positively with height and weight in both methods in all groups except for SCA (in this subgroup, the only correlation was between FN BMD measured by REMS and weight). Low BMI is a known factor contributing to higher risk of osteoporosis [32]. In both acromegaly and control groups the median BMI was diagnostic of overweight. Bone mineral density within normal limits in the acromegaly group might be related to high BMI values. Lack of typical correlations for height and weight in the SCA subgroup are quite surprising observations. We speculate that this discrepancy might be due to heterogeneity of the group. Factors that might contribute to these results are divergence in length of active disease, length of period from operation, age of disease appearance, and gonadal status. Also, the small number of participants in the group may influence these results.

Old age and early menopause are negative predictors for BMD. Age is one of the dominant determinants affecting bone loss in the general population as well as in acromegaly patients [5]. We found a negative correlation between BMD and age in both methods, but it was better expressed in the DXA method. Bone loss increases after menopause due to lower levels of oestrogens [33]. Negative correlation between years after menopause and BMD was more pronounced in the REMS method than in DXA. However, in the SCA group we did not observe any correlation between results obtained from REMS and years after menopause, but there was negative correlation between LS BMD measured by DXA. Insufficiency of gonadotropic axis may be a coexisting factor implicating low bone density in acromegaly [34]. In our study three patients had gonadal axis insufficiency. Among them, only one patient had low bone density of lumbar area diagnosed by DXA method.

REMS accuracy

In the recent multicentre study REMS and DXA examinations were performed in 1914 postmenopausal women [21]. Sensitivity, specificity, and accuracy of REMS compared to DXA were analysed. The study revealed high positive correlation between T-scores measured in REMS and DXA both in lumbar and femoral neck areas. Diagnostic concordance between the two methods was 88.8% for lumbar spine and 88.2% for femoral neck. A high positive correlation between the two techniques was observed for lumbar area ($r = 0.94$; $p < 0.001$) and for femoral neck ($r = 0.93$; $p < 0.001$). In the research of 358 females with normal BMI, Casciaro et al. compared DXA and REMS densitometry in lumbar area [35]. They received 83% corresponding diagnosis. Moreover, previous single-centre studies also proved good accuracy between REMS and DXA results [36, 37]. In our study positive correlations between DXA and REMS lumbar and femoral T-scores were observed in AG and also in WCA but not in the SCA group. The correlations that we obtained are weaker than reported in previous studies, but many factors could contribute to these results. First of all, in previous research the study groups contained postmenopausal women, while in our study we investigated the group of patients at risk of secondary osteoporosis related to acromegaly. DXA, as already mentioned, is not an ideal method in the evaluation of bone quality in the acromegaly population, so a flimsier association between results obtained by REMS and DXA may indicate better accuracy of REMS in screening of osteoporosis in this group. Further investigation to bear out this hypothesis is needed. We observed a positive correlation between LS BMD but not between FN BMD values. Hypothetically, this discrepancy might be due to different composition of spine and hip. Vertebrae contain high amounts of trabecular tissue, which is a target in REMS analysis. Also, joint degeneration may contribute to these results because, as mentioned earlier, the REMS method should eliminate artefacts related to degenerations. Conversaro et al. also proved that results of measured BMD are repeatable and reproducible between interoperates, and the accuracy of the method does not depend on the experience of the operator [36]. From our experience, obtaining good quality echo scans of the hip area is more difficult and takes more time, even for an experienced operator.

Limitations

There are some limitations to this study. First, the sample size of the group of acromegaly patients was small, and the results of this study should be analysed in a larger group. Secondly, we did not enrol patients with active disease. Moreover, we did not perform DXA in the control group, so we could not compare results of REMS and DXA densitometries in controls and results of DXA between acromegaly patients and the control group. Also, we did not perform objective methods to evaluate fractures. The number of declared fractures was too small to perform statistical analysis, and there is a possibility of underestimation due to the probability of asymptomatic fractures. Finally, various duration of the disease, different dosage, and time span of therapy with somatostatin analogues, as well as lack of consideration of vitamin D and calcium taking in the statistical analysis may influence the results of this study.

Conclusions

In conclusion, our study for the first time compared REMS densitometry with traditional DXA in acromegaly. The obtained outcomes did not clearly establish

whether REMS is a better technique for the evaluation of bone status in acromegaly; nevertheless, further studies are needed to evaluate the usefulness of REMS and its potential advantages compared to other methods in acromegaly patients. An investigation comparing REMS parameters with objective markers of resorption is required to determine whether this new technique could be a practical tool in bone turnover evaluation. Methods that can accurately and noninvasively assess bone quality are needed, especially in endocrine diseases related to secondary osteoporosis.

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