WHOLE BODY AND REGIONAL BONE MINERAL CONTENT AND DENSITY IN WOMEN AGED 20-75 YEARS

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Abstract

Background. Dual-energy X-ray absorptiometry (DXA) allows measurement of whole body (WB) and regional bone mineral content (BMC) and density (BMD).

Objective. To measure WB and regional bone area, BMC and BMD (arms, legs, ribs and pelvis) in women of different ages.

Subjects and Methods. 140 women participated (age range 20-75 yrs). Three subgroups were built: 20-44 yr (30 premenopausal women), 45-59 (80 women), and 60-75 (30 women). WB DXA was performed on a Hologic QDR 4500 A bone densitometer (Hologic Inc., Bedford MA). WB BMD T-scores were calculated by using the manufacturer-provided and the NHANES 1999-2004 reference databases, while the WB BMC Z-scores - based on the latter. Statistical analysis was performed on an IBM SPSS Statistics 19.0 for Windows platform (Chicago, IL).

Results. WB BMC and BMD Z-scores were consistently lower than the reference databases showing a difference of about 0.4 – 0.5 SD. The arms, legs and ribs lost more BMC after the age of 50-55, while the pelvis – much earlier. The total decreases in BMC were highest in the pelvis (26.36 %), followed by the arms (16.81 %) and whole body (15.91 %), while the bone area decreased mostly in the pelvis (13.23 %).

Conclusion. The age-related declines in regional BMC, bone areas and BMD follow different patterns in appendicular and axial bones.

Key words: Dual-energy X-ray absorptiometry, whole body, regional, bone mineral content, bone mineral density.

established (2). Dual-energy X-ray absorptiometry (DXA) allows measurements of total body and regional bone mineral content (BMC), area and BMD (3). The precision and clinical utility of these measurements have already been well validated (4-6). They could provide useful clinical information regarding changes of the entire skeleton under specific conditions.

Total and regional BMC and BMD were studied in healthy women to describe age- and menopause-related changes (7-11). Regional bone mass measurements revealed significant local bone losses after atraumatic vertebral fractures and during immobilization (12, 13). On the contrary, physical activity was shown to positively alter regional BMC and BMD (14, 15). The differences in the effects of antiresorptive drugs on regional BMD have also been tested (16).

The DXA manufacturers incorporate different reference databases for total BMD and BMC primarily. The NHANES 1999-2004 database is an effort to provide reliable and internationally validated reference values for several body composition indices (17). The 2013 International Society for Clinical Densitometry (ISCD) Position Development Conference on Body Composition recommends using them instead of manufacturer-provided reference databases (18, 19). Until now no data on regional BMC, bone area and BMD in our country are available.

The aim of the present study was to determine age-adjusted means of regional BMC and BMD in women aged 20-75 years.

INTRODUCTION

Bone mineral density (BMD) is one of the key components of bone strength (1). The value of the classical measurement sites (lumbar spine, proximal femur and distal forearm) in the diagnosis of osteoporosis and fracture risk prediction is very well

SUBJECTS AND METHODS

Subjects

This is a post hoc analysis of a cross-sectional observational study performed in a hospital-based outpatient DXA setting. The results of the primary

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analysis had been published elsewhere (20). A total of 159 women (mean age 49.1 ± 10.0 years) participated in the original study but after reviewing only 140 were suitable for proper analysis of regional BMC and BMD. Three subgroups were built according to age: 30 women aged 20-44 years, 80 women aged 45-59 years and 30 women aged 60-75 years. The age groups were not matched as this age distribution reflected the real DXA referral population – most women were in the early postmenopausal years. The participants came from an urban background. 72 of them were referred for bone density testing (65 postmenopausal and 7 premenopausal women), 56 were referred for body composition analysis because of overweight or obesity (22 premenopausal and 34 postmenopausal women) and 12 were healthy volunteers (1 premenopausal and 11 postmenopausal women). None of them was taking calcium or vitamin D supplements or antiresorptive drugs at the time of the study.

All women had given their informed consent prior to any procedure. The study had been approved by the responsible authorities at the University Hospital. The only inclusion criterion was the patient's informed consent and technically valid DXA regional data. Subjects with any medical conditions or medications known to cause excessive obesity, dehydration, and water retention or electrolyte disturbance affecting whole body measurements have been excluded from this study. The exclusion criteria included also the presence of deformed or fractured lumbar vertebrae, severe scoliosis ($>15^\circ$) and other conditions which would interfere with the proper analysis of BMD scans. Age (yrs), height (in cm, measured on a Harpenden stadiometer), weight (in kg, measured on a standard weight balance) and age at menopause (if menopausal), were recorded prior to the whole body DXA scans. Body mass index (BMI) was calculated from weight and height in kg / m^2 .

Body composition analysis

The whole body DXA was performed in the early morning after an overnight fasting for at least 12 hours. The subjects were required to adhere to standard body composition testing guidelines, wearing light clothes (21). They were positioned lying supine with the entire body, including all soft tissue, within the table margins. The arms were positioned palm down with a space straight at the patient's sides; the legs were kept together with the feet relaxed. Fan-beam dual-energy X-ray (DXA) body composition analysis was performed on a Hologic QDR 4500 A bone densitometer (Hologic

Inc., Bedford, MA 02154, USA). All DXA scans were read by the same technologist in a semi-automatic way including manual modifications of the regions of interest. The software (version 8.26:3) assumed that brain fat represented 17 % of body fat (a manufacturer-provided algorithm). BMC was calculated in grams (g), the bone area in centimetres squared (cm^2), and the BMD in g/cm^2 (BMC divided by the area). Data were presented as whole body values and separately for the different body sub-regions (arms, legs, ribs and pelvis). Thoracic and lumbar spine were excluded from the analyses as the age-related bone changes in the lumbar spine are well known from studies using the standard posterior-anterior projection. Whole body BMD T- and Z-scores were calculated by using the manufacturer-provided reference database (PS reference database issued 25 Oct 1991). BMC and BMD Z-scores were additionally calculated based on NHANES 1999-2004 (according to the 2013 ISCD guideline) (3,19).

Precision study

The manufacturer-provided Hologic tissue bar was scanned once weekly. The *in vivo* coefficient of variation (CV %) of the whole body DXA was calculated from duplicate measurements of 30 female subjects according to Glüer *et al.* ($\text{CV}\% = \text{root-mean-squares}/\text{mean} \times 100$) (22). They were randomly selected from the study participants. All retests were performed on the same day within a very short time limit. The *in vivo* CV % of DXA was 0.79 % for % body fat, 760 grams for fat mass (corresponding to 2.05%), 710 grams for fat-free mass (1.46 %), and 40 grams for BMC (2.01%), which is in the limits advocated by the ISCD 2013 conference (21).

Statistical analysis

An IBM SPSS 19.0 for WINDOWS package (Chicago, IL, USA) was used for processing the numerical data. The Kolmogorov-Smirnov test for normal distribution was first performed, followed by tests for homogeneity of variance, and t-tests. Statistical significance was set as $p \leq 0.05$.

RESULTS

The anthropometric and whole body data of the participants are presented in Table 1. Total body BMD T-scores decreased with age, while BMD and BMC Z-scores remained stable showing a parallelism of our data with the reference databases although at lower absolute levels. The BMD Z-scores were lower when

Table 1. Anthropometric and whole body bone mineral T- and Z-scores of the study population are shown as means (standard deviations). T- and Z-scores are expressed in numbers of standard deviations by which the actual values are above/below the peak/age-adjusted reference values

	Total study group (n=140)	20-44 yrs (n = 30)	45-59 yrs (n = 80)	60-75 yrs (n = 30)
Age (y)	51.9 (10.0)	35.6 (7.4)	52.2 (3.3)	66.1 (4.9)
Age at menopause (y)	45.8 (7.2)	NA	46.5 (5.3)	44.0 (11.9)
Height (cm)	161.4 (6.0)	161.5 (6.4)	161.9 (6.0)	160.1 (5.6) _a
Measured weight (kg)	87.22 (18.62)	93.92 (19.60)	87.86 (19.18) _a	78.36 (11.43) _a
Weight from DXA (kg)	87.65 (19.47)	94.33 (21.32)	88.36 (19.95) _a	78.62 (11.84) _a
BMI (kg/m ²)	33.5 (7.2)	36.0 (8.3)	33.5 (7.6) _a	30.6 (6.3) _a
Total BMD T-score _b	-1.34 (1.15)	-0.79 (1.12)	-1.30 (1.11)	-2.00 (1.04) _a
Total BMD Z-score	-0.34 (1.10)			
Hologic PS _b	-0.79 (1.07)	-0.44 (1.14)	-0.32 (1.10)	-0.31 (1.11)
NHANES 1999-2004 _c		-0.62 (1.17)	-0.82 (1.07)	-0.85 (1.01)
Total BMC Z-score _c	-0.29 (1.10)	-0.06 (1.29)	-0.33 (1.04)	-0.38 (1.14)

_a P<0.05 when compared to the previous age group

_b according to the manufacturer-provided PS reference database issued 25 Oct 1991

_c according to NHANES 1999-2004 reference data

Table 2. Percentage of age-dependent decline in the measured area and BMC of the different body regions

Region of Interest	Whole body		Arms		Legs		Ribs		Pelvis	
	Area. cm ²	BMC. g	Area. cm ²	BMC. g	Area. cm ²	BMC. g	Area. cm ²	BMC. g	Area. cm ²	BMC. g
% decline 45-59 vs. 20-44 yr	-1.84%	-6.50%	-3.39%	-6.22%	0.29%	-6.34%	0.67%	-6.44%	-10.21%	-17.30%
% decline 60-75 vs. 45-59 yr	-4.02%	-10.06%	-5.58%	-11.29%	-3.10%	-6.52%	-3.27%	-8.99%	-3.36%	-10.95%
% decline 75-60 vs. 20-44 yr	-5.78%	-15.91%	-8.79%	-16.81%	-2.82%	-12.45%	-2.63%	-14.85%	-13.23%	-26.36%

using the NHANES 1999-2004 database. All Z-scores were negative meaning that the studied Bulgarian women had lower BMC and BMD values based on both reference databases.

The mean values of the regional area and BMC in the different age groups are shown in Figure 1 A-E. The arms, legs and ribs lost more BMC after the age of 50-55, while the pelvis showed the greatest decrease between 20-44 and 45-59 years of age. The projected areas of the legs and ribs remained stable with aging, while those of the arms and pelvis decreased slightly. The combined changes of BMC and to a lesser extent of the projected area resulted in BMD decreases which were almost linear (see Fig. 2).

The age-dependent decline in the regional area and BMC is shown in percentages in Table 2. The BMC decreases were almost twice as high as those of the projected area resulting in a steady decline of BMD. The highest BMC losses were seen in the pelvis, followed by the arms, ribs and legs. The highest decreases in the projection area were seen in the pelvis and arms with ribs and legs remaining practically stable. This resulted in greater decreases of calculated BMD in the ribs and legs, than in the arms and pelvis.

Table 2 shows that in the arms, legs and ribs

the greatest decreases in area and BMC were seen when comparing 60-75 *versus* 45-59 years of age, while in the pelvis they were seen at younger ages - between 20-44 and 45-59 years.

DISCUSSION

This is the first Bulgarian study reporting DXA-derived estimates of whole body and regional bone mineral analyses. Total BMC and BMD of the studied women were consistently lower than reference databases issued by the manufacturer (Hologic Inc.) and the NHANES 1999-2004 databases resulting in a difference of about 0.4 – 0.5 standard deviations between calculated total body BMD Z-scores. The age-related decreases in BMC were greatest in the pelvis (26.36 %), followed by the arms (16.81 %) and whole body (15.91 %), while the bone area decreased mostly in the pelvis (13.23 %) followed by the arms (8.79 %).

Similar age-dependent changes in regional BMD were described in two Japanese studies (8, 23). In one of those studies BMD values at the ribs, pelvis and legs decreased mostly between 40 and 50 years of age, while bone loss in the arms occurred later (between 50

Figure 1. The mean values of the measured area (in square centimeters) and BMC (in grams) of the body regions in the different age groups are shown. A/ Whole body; B/ Arms (left + right); C/ Legs (left + right); D/ Ribs (left + right); E/ Pelvis.

Figure 2. The mean BMD values of the body regions in the different age groups are shown.

and 60 years of age) (8). The second study found a peak of total and all regional BMD values in the 20's to 40's and most prominent decreases with age in the spine and

pelvis (23). In a similar Chinese study the overall bone decrease from 35-39 to 70-80 years old was highest in the spine (29 %), arms and pelvis (approx. 23 % for both), followed by the ribs and legs (24).

These differences can be explained by at least three factors: 1/ the different weight-bearing roles of long bones (limbs) and flat bones (pelvis, ribs); 2/ the different proportions of cortical and trabecular bone with the limbs being predominantly cortical sites 3/ the perimenopausal and postmenopausal transition, as almost all studied women under 45 were premenopausal, while the elder were predominantly postmenopausal. Those differences had been defined in the classical hypothesis about the changes in bone mineral density of the appendicular and axial skeleton with aging as formulated by Riggs *et al.* (25). They had been confirmed in earlier studies based on bone

densitometry and are responsible for the heterogeneity of bone mineral density across skeletal sites (26,27), and the T-score discordance between the hip and spine sites (28). On the other hand, the regional BMC and BMD at various sites might be differently affected by the chronological age and the menopause as is the case with regional fat and lean mass (11). The menopausal status can modulate the effects of body composition on regional bone mineral density (29). The declines in regional lean and bone mass with advancing age might also show discordance (30). One must keep in mind that chronological age is not equal to biological age in terms of BMD (31). Physical activity also affects regional BMC and BMD. A meta-analytic review of randomized trials proved that both aerobic and anaerobic training enhanced regional BMD and slowed the rate of perimenopausal bone loss, but data were insufficient for strong conclusions (14). The physical activity level of post-menopausal women proved tightly related to their actual BMD (15). All these studies underline the need for whole-body DXA studies in different clinical situations.

Another important problem with whole body DXA scans and subregional analyses is the lack of reference data. A few studies have published figures on regional BMD, but they are not representative for other patient populations (32). We tried to compare our data with the NHANES 1999-2004 reference population as published by the ISCD 2013 (19). Almost all bone mineral indices were lower in the studied Bulgarian women, showing the presence of a systematic difference which might be explained by genetic or ethnic factors and more probably by the small studied population. The impact of race-ethnicity can easily be seen in the publications based on the 1999-2004 NHANES data (17). The NHANES data provide data for different age groups (20-39, 40-59, 60-79 etc.) but the publication does not specifically cite figures for BMC (18). Our data therefore underline the need for local data on regional BMC and BMD which might improve our understanding of longitudinal bone changes in health and disease.

Our study has a number of limitations. First, the number of participants is rather modest which prevented us from separate analyses based on BMI and fat distribution which are expected to affect BMD (33, 34). Second, we were unable to study separately the contribution of the menopause to the BMC and BMD changes as the younger age group consisted of premenopausal women, while the middle-aged and elderly group – of postmenopausal ones only. Third,

this is a post hoc analysis based on a sample referred for DXA for a variety of indications. Due to the small sample size our results cannot be generalized. And fourth, the study design is cross-sectional, thus allowing rough estimates of real age-related changes in BMC and BMD. To our knowledge there are no studies reporting longitudinal changes of regional BMC and BMD for longer periods of time (e.g. > 10 yrs).

In conclusion, this study is the first one in our country looking for whole body and regional BMC and BMD assessed by DXA. It showed differing patterns of age-related decline in regional BMC, bone areas and BMD. It displayed some directions for future research in the assessment of bone mass and osteoporosis in different female populations.

Conflict of interest

No financial support or competing financial interests in relation to this work.

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