

# Skeletal Status Assessed by Quantitative Ultrasound in Elderly Women Compared with Early Postmenopausal Women

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**Abstract:** *Background:* The aim of the retrospective study was to reveal the pattern of bone loss in elderly women compared with early postmenopausal women.

*Material:* The group of 254 women was studied, among them were 40 elderly women (mean age 74.7±/−4.0 y.) and 214 early postmenopausal women (mean age 53.4±/−3.7 y.). Skeletal status was evaluated using quantitative ultrasound (QUS) at the calcaneus (Achilles, Lunar, USA). Parameters measured were: Speed of Sound (SOS [m/s]), Broadband Ultrasound Attenuation (BUA [dB/MHz]) and Stiffness Index (SI [%]).

*Results:* In elderly women age, years since menopause (YSM) and body size did not influence significantly ultrasound values, only positive influence of weight and body mass index on BUA was observed ( $p < 0.05$ ). In early postmenopausal women YSM negatively affected SOS ( $p < 0.05$ ), BUA ( $p = 0.05$ ) and SI ( $p < 0.05$ ), body size had generally a positive impact on all QUS parameters, and the percentage of life with menstruation positively affected SOS ( $p < 0.05$ ). In multiple stepwise regression analyses in elderly women only weight had a positive effect on BUA, and in early postmenopausal women, weight was a protective factor for all parameters, age negatively influenced BUA and SI, and YSM negatively influenced SOS. Multiple stepwise regression analysis in the whole group showed that weight was a protective factor and age was a negative factor for all QUS parameters.

*Conclusion:* The pattern of bone loss in the elderly differs in comparison to younger postmenopausal women, and the weight among factors assessed was the only protective one in postmenopausal women. Maintenance of body weight seems to be the most important in osteoporosis prevention.

**Keywords:** Quantitative ultrasound, elderly women, early postmenopausal women.

## INTRODUCTION

Skeletal status and bone loss depends on several factors including mainly age, body size, function of endocrinological system, diet, physical activity, medications, smoking. However, in different age decades bone loss is under control of different factors. For example, in early postmenopausal women the main factor is diminished amount of estrogens and later in life the role of menopause decreases. Nordin *et al.* estimated that the majority of bone loss between 55 and 75 years was due to aging (62%) rather than to menopause [1].

Bone loss leads to skeletal fragility and susceptibility for fractures. The most important are spine and hip fractures. The number of fractures increases with advancing age. Senile osteoporosis is one of the most important diseases in the elderly because its' health and economic impact. The knowledge which factors mainly affect skeletal status are essential for management of patients with osteoporosis. These informations are especially important in elderly subjects because

of multifactorial pathogenesis of the disease including also the risk of falls.

Currently, densitometric methods are the most commonly used in order to assess skeletal status in subjects with osteoporosis [2]. Last years were a period of the development of Dual Energy X-ray Absorptiometry (DXA) called a *gold standard* of densitometry. DXA widely used in a clinical practice does not provide any data on bone qualitative features. Obviously, both bone mineral density (BMD) and qualitative features of bone like elasticity or microarchitecture play a significant role in biologic competence of the skeleton. The role of bone quality is currently widely accepted and there is a need to develop new methods able to assess not only bone quantity.

Among techniques potentially expressing bone quality is quantitative ultrasound (QUS). QUS measurements were performed at several skeletal sites including calcaneus, radius, tibia and hand phalanges. QUS may give additional data on bone tissue qualitative features [3, 4] and in comparison with DXA has got some important advantages like the lack of ionizing radiation, relatively low costs and small sizes of equipment. QUS has also disadvantages involving difficulty in precise determination of measured bone tissue

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features, measurements of skeletal sites limited only to peripheral skeleton and relatively poor precision.

The assessment of fracture risk is the most important issue in osteoporotic patients. QUS measurements at calcaneus were performed in several case-control [4-16] and longitudinal studies [17-21]. In all of cited studies QUS measurements at the calcaneus were able to predict future osteoporotic fracture. Recently, in several studies the authors showed the utility of combining of clinical risk factors and heel bone ultrasound for fracture assessment [22-25].

In several studies were studied changes of calcaneal QUS parameters in respect to several factors like age, age at menopause or body size [26-38]. These data show the nature of bone changes over time and are important in patients' management.

The aim of the retrospective study was to reveal the pattern of bone loss in elderly women compared with early postmenopausal women.

## MATERIAL AND METHODOLOGY

### Material

The group of 254 patients recruited from Outpatient Osteoporotic Clinic was studied. The main inclusion criteria were female sex and postmenopausal status. Exclusion criteria included: surgical menopause, prior osteoporotic fracture, prior fractures of any origin within lower extremity in order to avoid their impact on the result of calcaneus measurements, the presence of medical reasons known to affect bone metabolism (either chronic diseases or prolonged medications), current or prior therapy for osteoporosis (hormonal replacement therapy, calcitonin, bisphosphonates, strontium ranelate, teriparatide, raloxifen), with the exception of preventive doses of vitamin D (200-400 IU daily) and calcium supplementation. We have used described exclusion criteria in order to follow nature of bone loss after menopause and in elderly subjects. We excluded 106 women; 67 due to therapy for osteoporosis, 20 because of secondary osteoporosis and 15 because of former osteoporotic fracture and four because of traumatic lower limb fracture. Clinical characteristics of women studied is given in Table 1.

### Methodology

#### Quantitative Ultrasound

Skeletal status was evaluated using quantitative ultrasound (QUS) of calcaneus. QUS measurements at the dominant calcaneus were performed. The Speed of Sound - SOS [m/s] and Broadband Ultrasound Attenuation - BUA [dB/MHz] were measured with the Achilles system (Lunar, Madison, WI, USA). The Achilles software calculates a Stiffness Index (SI [%] =  $[0.67 \times \text{BUA} + 0.28 \times \text{SOS}] - 420$ ) which does not express biomechanical stiffness but rather is an attempt by the manufacturer to derive a clinically useful index combining BUA and SOS. T-score and Z-score were derived from the value of SI and expressed as a number of standard deviations (SDs) from the peak value and the mean value for age-matched population, respectively.

The device was calibrated daily in accordance with the manufacturer's recommendations. All measurements were

made by the same operator. Precision was expressed using coefficient of variation (CV). They were calculated using following formulas:  $\text{CV}\% = (\text{SD}/\text{mean}) \times 100$ . The CV% values were: 3.8% for BUA, 0.45% for SOS, and 2.5% for SI.

**Table 1. Clinical Characteristics of Women Studied (Mean +/- SD)**

	Early Postmenopausal Women (n=214)	Elderly Women (n=40)	p-Value
Age [Years]	53.4+/-3.7	74.7+/-4.0	<0.000001
Weight [kg]	68.4+/-12.6	72.4+/-13.4	ns
Height [cm]	159.2+/-5.3	156.9+/-5.11	<0.05
BMI [kg/m <sup>2</sup> ]	27.0+/-4.5	29.4+/-5.4	<0.01
Age at Menarche [Years]	13.8+/-1.6	14.1+/-1.74	ns
Age at Menopause [Years]	49.8+/-3.0	49.95+/-4.7	ns
Reproductive Period [Menstrual Years]	35.9+/-3.3	35.85+/-4.2	ns
YSM	3.7+/-2.6	24.5+/-1.56	<0.000001

BMI: body mass index. ns - not significant.

YSM: years since menopause.

### Statistics

Statistical analysis was performed using Statistica for Windows. Descriptive statistics were presented as mean values and standard deviations (SDs). Statistics included:

- differences established using Student t-test,
- Pearson's correlation of ultrasound parameters with age, YSM, age at menopause and menarche, menstrual years, weight, height and BMI (body mass index [kg/m<sup>2</sup>]) in elderly women and in early postmenopausal women,
- multiple stepwise regression analyses of SOS, BUA and SI vs age, age at menopause, YSM, menstrual years, weight and height in elderly women, in early postmenopausal women and for the whole group.

Significance was achieved with p value lower than 0.05.

## RESULTS

The whole group of women studied was divided into:

- elderly women (n=40) - older than 60 years and about 25 years after menopause,
- early postmenopausal women (n=214) - mean age about 53 years and up to ten years after menopause.

There were no differences between subgroups studied in age at menarche, age at menopause and in menstrual years (reproductive period). Clinical characteristics of women studied is given in Table 1.

Values of QUS parameters are shown in Table 2. As expected all QUS values were lower in elderly women.

**Table 2. Results of QUS Measurements (Mean +/- SD)**

Parameter	Early Postmenopausal Women (n=214)	Elderly Women (n=40)	p-Value
<b>SOS [m/s]</b>	1520.2+/-27.0	1504.5+/-53	<0.001
<b>Z-Score</b>	0.01+/-0.97	0.21+/-1.08	Ns
<b>BUA [dB/MHz]</b>	108.9+/-10.5	101.9+/-0.89	<0.001
<b>Z-Score</b>	-0.06+/-1.05	0.21+/-1.02	Ns
<b>SI [%]</b>	78.3+/-13.3	69.2+/-13.5	<0.0001
<b>T-Score</b>	-1.97+/-1.21	-2.77+/-1.22	<0.001
<b>Z-Score</b>	-0.32+/-1.2	-0.08+/-1.23	Ns

SOS: Speed of Sound. Ns: not significant.  
 BUA: Broadband Ultrasound Attenuation.  
 SI: Stiffness Index.  
 T-score: number of SD from peak value.  
 Z-score: number of SD from age-matched value.

Table 3 presents correlation analyses of QUS parameters with others. In elderly women age, YSM, menstrual years,

**Table 3. Correlation Analysis in Women Studied**

Parameter	Age	Weight	Height	BMI	Menarche	Menstrual Years	Menopause	YSM
<b>- In Elderly Women (n=40)</b>								
<b>SOS</b>	-0.09	0.14	-0.12	0.18	0.07	-0.21	-0.16	0.11
<b>BUA</b>	-0.21	<b>0.38</b> <b>p&lt;0.05</b>	-0.01	<b>0.38</b> <b>p&lt;0.05</b>	-0.11	-0.09	-0.12	-0.01
<b>SI</b>	-0.16	0.29	-0.07	0.31	-0.01	-0.17	-0.16	0.06
<b>- In Early Postmenopausal Women (n=214)</b>								
<b>SOS</b>	-0.09	<b>0.28</b> <b>p&lt;0.001</b>	<b>0.19</b> <b>p&lt;0.01</b>	<b>0.23</b> <b>p&lt;0.01</b>	-0.07	0.05	0.012	<b>-0.15</b> <b>p&lt;0.05</b>
<b>BUA</b>	-0.08	<b>0.41</b> <b>p&lt;0.001</b>	<b>0.19</b> <b>p&lt;0.01</b>	<b>0.38</b> <b>p&lt;0.001</b>	-0.01	0.01	0.01	<b>-0.13</b> <b>p=0.05</b>
<b>SI</b>	-0.1	<b>0.38</b> <b>p&lt;0.001</b>	<b>0.21</b> <b>p&lt;0.01</b>	<b>0.33</b> <b>p&lt;0.001</b>	-0.05	0.03	-0.001	<b>-0.15</b> <b>p&lt;0.05</b>

**Table 4. Results of Multiple Regression Analysis in Women Studied**

Parameter	Equation	R <sup>2</sup>	p	SEE
<b>- In Elderly Women (n=40)</b>				
BUA	BUA (dB/MHz)=79.9 + 0.37 x weight (kg)	0.14	<0.05	10.2
<b>- In Early Postmenopausal Women (n=214)</b>				
SOS	SOS (m/s) = 1419 + 0.23 x weight (kg) - 0.13 x YSM + 0.09 x height (cm)	0.1	<0.0001	25.7
BUA	BUA (dB/MHz) = 102.2 + 0.42 x weight (kg) - 0.12 x age (years)	0.18	<0.0001	9.5
SI	SI (%) = 76.1 + 0.39 x weight (kg) - 0.14 x age (years)	0.16	<0.0001	12.1
<b>- In Whole Group (n=254)</b>				
SOS	SOS (m/s) = 1526 + 0.25 x weight (kg) - 0.25 x age (years)	0.34	<0.000001	26.3
BUA	BUA (dB/MHz) = 105 + 0.39 x weight (kg) - 0.29 x age (years)	0.47	<0.000001	9.6
SI	SI = 77.8 + 0.35 x weight (kg) - 0.30 x age (years)	0.44	<0.000001	12.4

weight, height and BMI did not correlate significantly with QUS parameters, except for positive influence of weight and BMI on BUA ( $p<0.05$ ). In early postmenopausal women negative influence of YSM on SOS ( $p<0.01$ ), BUA ( $p<0.05$ ) and SI ( $p<0.05$ ) was observed. Body size (weight, height, BMI) had a positive impact on all ultrasound parameters.

Table 4 presents results of multiple regression analyses. In elderly women only weight positively affected BUA ( $p<0.05$ ). In early postmenopausal women, weight was a protective factor for all QUS parameters, age negatively influenced BUA and SI, and YSM affected negatively SOS ( $p<0.0001$ ). Multiple stepwise regression analysis for the whole group of women studied revealed that the weight was a protective factor and age was a negative factor for all ultrasound parameters.

In order to show the influence of age and YSM in the whole group two figures were created. Fig. (1) presents the association of age with SI which decreases with advancing age ( $r = -0.27$ ,  $p<0.001$ ). Fig. (2) shows the association of YSM with SI which is weaker in elderly women ( $r = -0.25$ ,

$p < 0.001$ ). Fig. (3) shows the association of weight with SI ( $r = +0.32$ ,  $p < 0.001$ ).

**DISCUSSION**

In the study were shown distinct differences in skeletal changes in elderly vs early postmenopausal women. In elderly,

the risk of osteoporotic fracture is modified by two main factors: skeletal status and number of falls. In current study we attempt to reveal which factors are responsible for bone loss and the analysis gave also an opportunity to show protective factors. The pattern of bone loss differs in regard to early postmenopausal women; age had only weak, non-significant negative influence and YSM did not affected

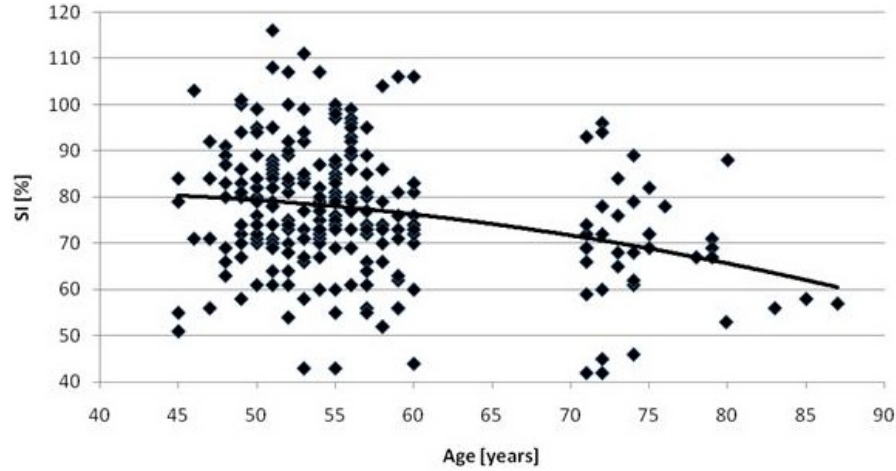


Fig. (1). The correlation of age with SI in the whole group.

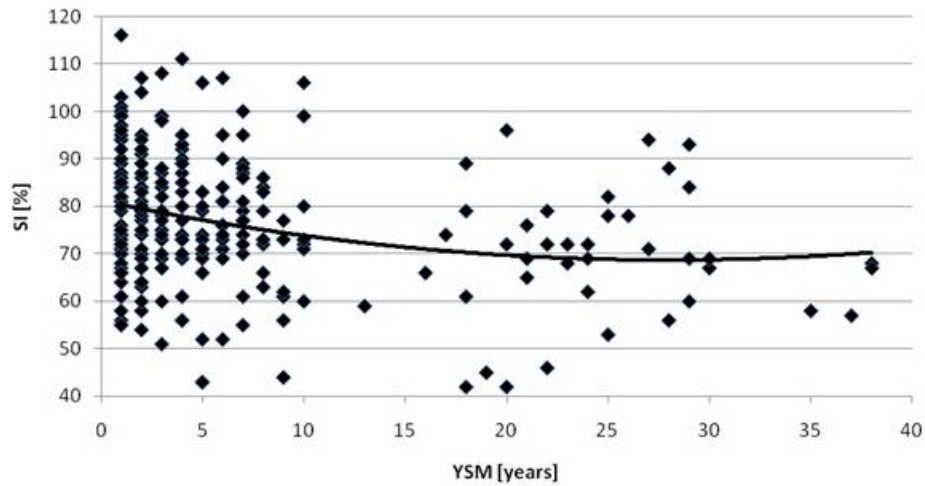


Fig. (2). The correlation of YSM with SI in the whole group.

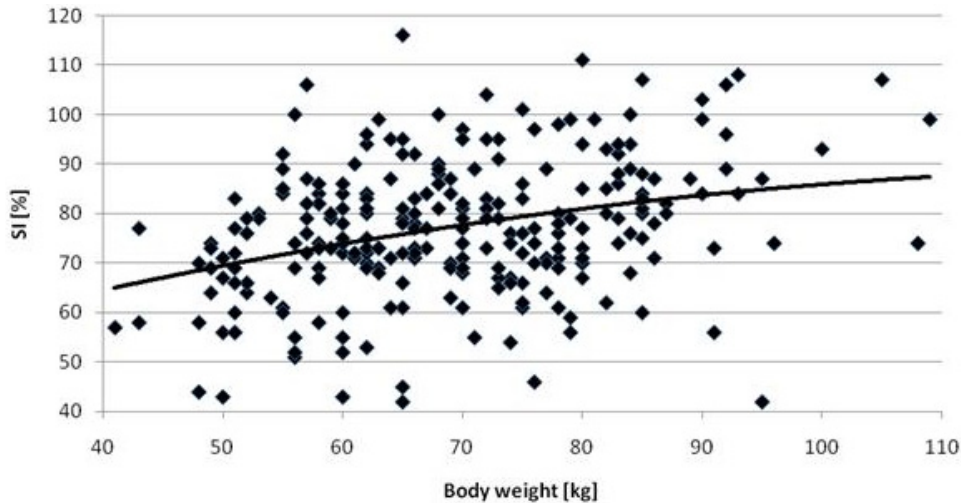


Fig. (3). The correlation of body weight with SI in the whole group.

QUS parameters. In early postmenopausal women age had also only negative, non-significant influence, and the main factor were YSM. These relationships are clearly shown in Figs. (1, 2).

Some differences are also shown by correlation analysis; in younger group weight, height and BMI were protective for all QUS parameters, while in elderly weight and BMI had a positive influence only for BUA. An interesting view provides multiple regression analysis; in elderly only weight had a positive influence (for BUA), and in early postmenopausal women relatively strong protective factor was weight and negative factors were age (for BUA and SI) and YSM (for SOS). However, in the same multiple regression analysis performed in the whole group the only bone protector was weight and factor causing bone loss was age.

We consider that the most important clinical finding of the study is observation that weight is an important factor in elderly women in protecting from bone loss.

In some yet published studies [26, 29, 32, 33, 35, 37], calcaneus was assessed by QUS measurements, and the authors evaluated factors affecting skeletal status. In French study [26] both age and YSM affected QUS parameters, but after the age of 60 further bone loss was not observed. Also in the Rotterdam Study [29], age affected SOS and BUA in women, and BMI was a strong protector for both parameters. Age at menopause did not affect QUS parameters and the influence of other parameters like YSM, years of menstruation or age of menarche were not presented. In a group of 712 Polish women aged 52-74 years the main negative factor was age and weight was a protector [32]. In a study conducted in 1333 German women were presented exact values of QUS variables but correlation analysis was not shown [33]. In other study age and BMI [35] affected QUS parameters in postmenopausal women over 50, and further author showed that more than 5 YSM negatively affected QUS parameters [37].

In studies cited above several factors were assessed but the comparison of early postmenopausal women with elderly were not done. In current study we have proven that the pattern of bone loss expressed by QUS measurements differs in elderly women in comparison to early postmenopausal women. Therefore, further direct comparisons are not possible.

In several studies the influence of different factors on bone densitometry measurements were performed [27, 28, 30, 31, 34, 36, 38]. In the study of 555 women aged 60 to 89 years age at menopause and number of reproductive years had positive associations with bone mineral density of radius, hip and spine, and total number of reproductive years explained more of variance in BMD than did either age at menarche or age at menopause [27]. In our study we did not note an influence of menstrual years on QUS parameters, but in early postmenopausal women menstrual years in regard to lifetime significantly improved value of SOS. In elderly women even a negative, non-significant associations of reproductive years was observed. In a great group studied (n=2230) by Fox *et al.* [28] aged 65 years or more, radial BMD increases with lower age of menarche, and each decade of menstruation caused an increase in BMD of 2%. In a group of 1521 Finnish women protective factors against low

BMD was weight, and in multiple regression analysis YSM, age, age at menarche negatively and weight positively affected BMD [30]. Japanese postmenopausal women who had a late menopause and more reproductive years were at decreased risk for low BMD [31]. In a group of early postmenopausal women aged 45-61 years low age at menarche improved spine BMD, years of menstruation were positively associated with BMD of spine, hip, radius and total body, and YSM was constant negative factor [34]. In the same study in multiple regression analysis years of menstruation, hysterectomy status and duration of hormone replacement therapy use were found to have strong associations with BMD at all sites. YSM were not a significant factor. However, in regression analysis body size and age were not taken into consideration.

Interesting data provides a study by Gerdhem and Obrant [36]. A large group of 1044 women aged 75 years was studied. Age at menarche or menopause as well as length of fertile period did not affect spine or femoral neck BMD. These results are in consistency with our results. In a recent study [38] performed in a group of 2769 postmenopausal women the main factor were YSM followed by age at menopause.

Our study has some limitations: a group studied, especially elderly women was small and we did not use bone densitometry. In current retrospective study we were not able to assess some other factors potentially influencing bone status like physical activity, diet, bone turnover.

## CONCLUDING REMARKS

The pattern of bone loss in elderly differs in comparison to younger women, and weight among factors assessed was the only protective factor. Maintenance of body weight seems to be the most important in osteoporosis prevention.

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