

## Original Article

# Ultrasound Measurements of Proximal Phalanges in Polish Early Postmenopausal Women

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**Abstract.** The aim of this cross-sectional study was to evaluate skeletal status in Polish early postmenopausal women using ultrasound measurement at the proximal phalanges of the hand. We assessed the ability of the method to discriminate between healthy and osteoporotic individuals, the influence of age and menopause on ultrasound values, the impact of hormone replacement therapy and the relationships between ultrasound measurement and type of fracture. Five hundred and three early postmenopausal women were divided into three groups: (1) healthy ( $n=398$ , mean age 53.4 years), (2) fractured ( $n=43$ , mean age 53.9 years), (3) treated with estrogens ( $n=62$ , mean age 53.5 years). Groups were matched for age and years since menopause (YSM). Group 2 was subdivided into those with and without wrist fracture. No drugs except estrogens were used by the subjects studied and no diseases known to affect bone metabolism were observed. Bone status was assessed by a DBM Sonic 1200 (Igea, Italy), a device that measures amplitude-dependent speed of sound (AD-SoS) at the proximal phalanges II–V of the hand. AD-SoS had the highest value in estrogen-treated women ( $1996.5 \pm 66.5$  m/s), the lowest in fractured persons ( $1883.6 \pm 77.1$  m/s) and a medium value in healthy women ( $1949.2 \pm 78.0$  m/s). All values were significantly different from each other ( $p<0.0001$ ). AD-SoS values for the subgroups of group 2 were  $1873.0 \pm 80.6$  m/s for those with wrist fracture and  $1914.0 \pm 73.0$  m/s for those without; they were not statistically different. The hypothesis that AD-SoS at the proximal phalanges might be more sensitive to wrist fracture was not

confirmed by Fisher's exact test for frequencies. Linear regression showed age-related changes, with  $r$  values  $-0.4$  ( $p<0.00001$ ),  $-0.47$  ( $p<0.005$ ),  $-0.37$  ( $p<0.005$ ), and YSM-related changes, with  $r$  values of  $-0.44$  ( $p<0.00001$ ),  $-0.32$  ( $p<0.005$ ), and  $-0.18$  (NS) in groups 1, 2 and 3, respectively. It is concluded that: (1) ultrasound measurements of the proximal phalanges were able to discriminate between healthy and osteoporotic individuals; (2) the method is useful in detecting age and postmenopause-related changes within the skeleton; and (3) hormone replacement therapy significantly reduced the impact of the menopause on bone loss as detected by ultrasound.

**Keywords:** Aging; Fracture risk; Hormone replacement therapy; Menopause; Osteoporosis; Quantitative ultrasound

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## Introduction

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture [1]. Bone mass measurements are of major importance in the detection and follow-up of subjects with osteoporosis. Several techniques for assessment of bone status, including single-photon absorptiometry (SPA), dual-photon absorptiometry (DPA), dual X-ray absorptiometry (DXA) and quantitative computed tomography (QCT) have been developed in the past 17 years. The disadvantages of these techniques are their high cost and the exposure of the subject to ionizing radiation, although the radiation dose is extremely low for DXA. Furthermore, none of

them provides insight into qualitative factors of bone tissue, such as trabecular bone structure or connectivity, which alone may account for up to 30% of the capability of bone to resist force [2].

Ultrasound assessment of bone has been proposed as a cost-effective and radiation-free technique [3,4]. Furthermore, it has been suggested that ultrasound investigations may provide insight into the qualitative aspects that contribute to bone strength [5,6]. One of the most important questions concerning the use in a clinical setting of quantitative ultrasound (QUS) is whether this technology is capable of detecting subjects at risk of fracture. Cross-sectional studies have demonstrated that subjects with osteoporotic fractures have lower values of ultrasound velocity and of broadband ultrasound attenuation (BUA) than subjects without fractures [7,8]. In the majority of studies the calcaneus was used as the measurement site [9–12]. Several recent investigations have focused on ultrasound measurement at the phalanges [13–21]. In these studies changes in ultrasound velocity due to aging and years since menopause (YSM) were evaluated [17–21]. Furthermore, significant correlation between ultrasound parameters measured at the phalanges and densitometric values were reported [18,20,21]. In the above-mentioned studies, researchers did not evaluate the influence of hormone replacement therapy (HRT) or a history of osteoporotic fractures on phalangeal ultrasound velocity. This information is necessary for the validation of the method in clinical practice.

The present study was designed to collect ultrasound measurements from a large sample of postmenopausal women. We assessed: age and YSM-related changes in the skeletal status of early postmenopausal women, ability of ultrasound measurements of the proximal phalanges to discriminate between healthy and osteoporotic subjects, the impact of HRT on ultrasound velocity and the relationships between ultrasound measurement and type of fracture.

## Materials and Methods

### Materials

A total of 503 early postmenopausal women aged 45–60 years were evaluated. All were volunteers participating

in a bone measurement screening program developed by the Polish Osteoporosis Foundation in 1995. The women were from six towns in the south of Poland. Each woman filled in a special questionnaire concerning history of fractures, diseases known to influence bone metabolism, medications, lifestyle factors, family history, diet, etc., and gave her informed consent for the study. In the group studied no additional medical pathologies known to affect bone metabolism were reported. Women with surgical menopause were excluded from the trial.

The subjects were divided into three groups: (1) healthy women ( $n = 398$ ), (2) women with a history of osteoporotic fractures ( $n = 43$ ) and (3) healthy women treated with estrogens ( $n = 62$ ). Group 2 was subdivided according to the type of osteoporotic fracture: group 2a ( $n = 27$ ), women with wrist fracture; and group 2b ( $n = 16$ ), women with fractures other than wrist. In group 2, a total of 63 fractures were reported, including: wrist 39, foot 8, ankle 6, vertebral crush fracture 2, hip 2, humerus 2, ribs 2, clavícula 2. Of these the following were in subgroup 2a: wrist 39, foot 3, vertebral crush fracture 1; and the following in subgroup 2b: foot 5, ankle 6, vertebral crush fracture 1, hip 2, humerus 2, ribs 2, clavícula 2. Because of the limited number of subjects considered, group 2a includes a few subjects with fractures at both the wrist and other sites. Time since the occurrence of fracture ranged from 6 months to 8 years (mean  $3.2 \pm 1.8$  years). Most of the subjects were hospital staff.

Analysis of the questionnaires did not reveal any significant differences between the groups regarding physical activity (an average of 30–60 min of physical exercises per week), dietary calcium (0.5–0.8 g of elemental calcium daily), social position, etc. Fractured women were interviewed additionally to obtain detailed information on the fracture dynamic. Osteoporotic fracture was defined as a result of minimal trauma such as a fall during normal, daily activity. None of the women was on the therapy for osteoporosis, except for preventive use of estrogens in group 3.

Table 1 reports the clinical characteristics of the groups studied. Clinical features of subgroups are shown in Table 2. Women were matched for age and YSM. There were significant differences in weight and body mass index (BMI) and no differences in height between the groups. Mean duration of hormone therapy was  $2.3 \pm$

**Table 1.** Clinical characteristics of the groups studied

	Age (years)	YSM (years)	Weight (kg)	Height (cm)	BMI (kg/m <sup>2</sup> )
Group 1 ( $n = 398$ )	$53.4 \pm 4.0^0$	$4.7 \pm 4.0^0$	$68.0 \pm 10.9^*$	$160.9 \pm 5.5^0$	$26.3 \pm 3.9^{00}$
Group 2 ( $n = 43$ )	$53.9 \pm 3.7^0$	$5.4 \pm 3.7^0$	$71.4 \pm 12.0^{**}$	$161.7 \pm 5.4^0$	$27.3 \pm 4.7^{**}$
Group 3 ( $n = 62$ )	$53.5 \pm 3.8^0$	$4.6 \pm 2.7^0$	$65.2 \pm 9.6^{***}$	$161.1 \pm 5.6^0$	$25.1 \pm 3.4^{***}$

Values are the mean  $\pm$  SD.

YSM, years since menopause; BMI, body mass index.

<sup>0</sup>Nonsignificant differences of mean values.

<sup>00</sup>Nonsignificant difference between group 1 versus group 2.

\*Mean value significantly different in group 1 versus group 2 ( $p < 0.05$ ).

\*\*Mean value significantly different in group 2 versus group 3 ( $p < 0.05$ ).

\*\*\*Mean value significantly different in group 1 versus group 3 ( $p < 0.05$ ).

**Table 2.** Clinical characteristics of subgroups

	Age (years)	YSM (years)	Weight (kg)	Height (cm)	BMI (kg/m <sup>2</sup> )
Subgroup 2a ( <i>n</i> = 27) (with fracture of wrist and others)	53.9 ± 3.6	4.63 ± 3.0	71.4 ± 12.2	162.8 ± 5.3	26.8 ± 3.8
Subgroup 2b ( <i>n</i> = 16) (with fractures other than wrist)	52.8 ± 4.8	5.5 ± 4.3	71.2 ± 11.1	161.2 ± 7.1	27.4 ± 4.1

Values are the mean ± SD.

All differences between mean values of the subgroups were nonsignificant.

1.3 years, with daily estrogen dose equivalent to 0.6 mg of conjugated estrogens. Local ethics committee approval was obtained for the study.

### Methods

Skeletal status was assessed by ultrasound measurements of the proximal phalanges using a DBM Sonic 1200 (Igea, Carpi, Italy). This unit consists of two probes mounted on an electronic caliper: an emitter and a receiver. The latter records the ultrasound energy after it has crossed the phalanx. We determined the amplitude-dependent speed of sound (AD-SoS) in the distal metaphyses of the proximal phalanges of the second through fifth fingers of the nondominant hand. Speed of sound in bone tissue was calculated considering the first signal with an amplitude of 2 mV at the receiving probe; thus, the measured speed of sound is amplitude-dependent. Acoustic coupling was achieved using a standard ultrasound gel. All measurements were done by the same operator. In the case of past fractures at the upper extremity, measurements were done on the opposite side. In vivo short-term precision was assessed based on mean coefficients of variation for 75 measurements made in each of 15 healthy persons (8 males, 7 females) by the same operator. CV % was 0.64%.

### Statistics

Calculation of means and standard deviations, and linear regression analyses, were performed using a Statistica program run on an IBM computer. Differences between mean values were established using Student's *t*-test. Relationships between AD-SoS values and type of fracture were established by Fisher's exact test of frequencies. Fisher's test was used for comparing correlation coefficients.

### Results

Ultrasound values in groups 1, 2 and 3 are presented in Table 3. Mean values were significantly different between groups studied ( $p < 0.0001$ ). In subgroup 2a, the mean AD-SoS value was  $1873 \pm 80.6$  m/s and in

**Table 3.** Ultrasound measurements in the women studied

	AD-SoS [m/s]
Group 1 ( <i>n</i> = 398)	1949.2 ± 78.0*
Group 2 ( <i>n</i> = 43)	1883.6 ± 79.1*
Group 3 ( <i>n</i> = 62)	1996.5 ± 66.5*

Values are the mean ± SD.

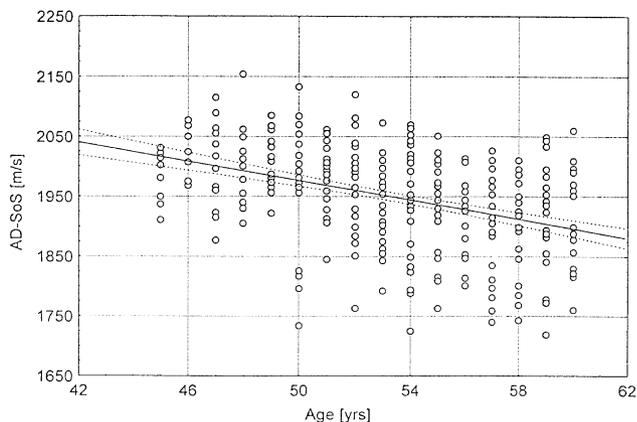
AD-SoS, amplitude-dependent speed of sound.

\*Mean value significantly different with  $p < 0.00001$ .

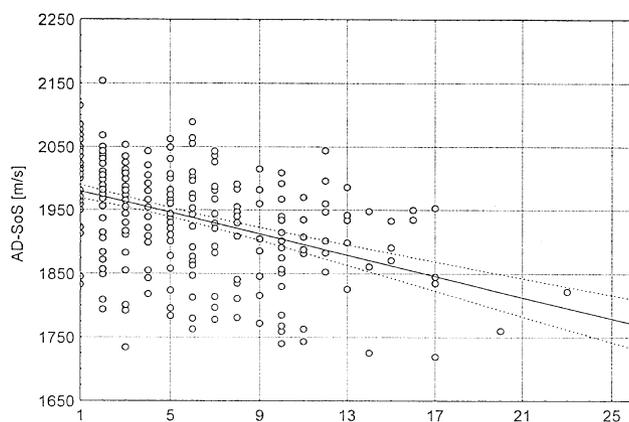
**Table 4.** The correlations and regressions between AD-SoS and age, and YSM

Linear regression equation	<i>r</i>	<i>p</i> value
<i>Age (years)</i>		
Group 1		
SOS = $-8.0 \times \text{age} + 2376.6$	-0.40	<0.00001
Group 2		
SOS = $-10.23 \times \text{age} + 2439.1$	-0.47	<0.005
Group 3		
SOS = $-6.47 \times \text{age} + 2336.3$	-0.37	<0.005
<i>YSM (years)</i>		
Group 1		
SOS = $-8.65 \times \text{YSM} + 1989.8$	-0.44	<0.00001
Group 2		
SOS = $-6.84 \times \text{YSM} + 1920.9$	-0.32	<0.05
Group 3		
SOS = $-4.31 \times \text{YSM} + 2016.2$	-0.18	NS

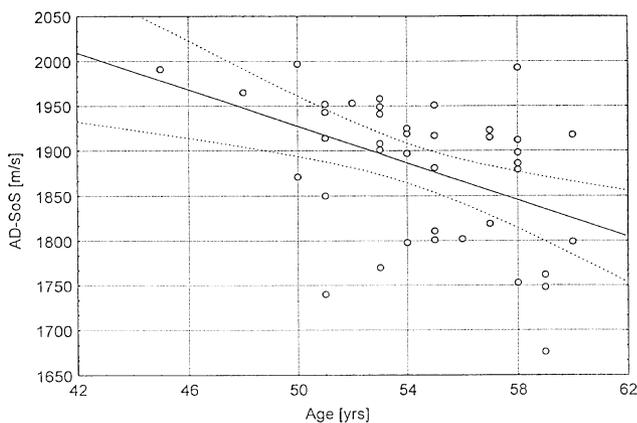
subgroup 2b  $1914 \pm 73$  m/s. These values did not differ significantly. Using linear regression analysis the AD-SoS values in groups 1, 2 and 3 were significantly correlated with age ( $r = -0.4$ ,  $-0.47$  and  $-0.37$ , respectively). Using linear regression analysis the AD-SoS values in groups 1 and 2 were significantly correlated with YSM ( $r = -0.44$  and  $-0.32$ , respectively), and in group 3 was not significantly correlated. Linear regression equations are presented in Table 4. Figures 1–6 show these relationships graphically. To establish relationships between AD-SoS values and type of fracture (fracture of wrist and others in subgroup 2a, or fractures other than wrist in subgroup 2b) the fractured women were divided into two subgroups: those with an AD-SoS value higher than 1950 m/s and those with an AD-SoS value lower than 1950 m/s. The cutoff value of AD-SoS 1950 m/s was established as being close to the



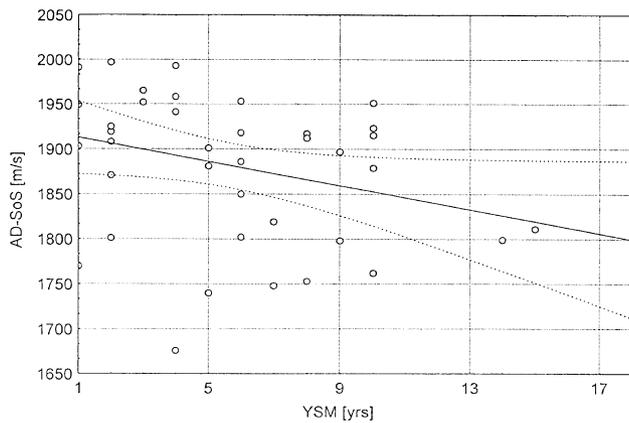
**Fig. 1.** Simple linear regression between age and amplitude-dependent speed of sound (AD-SoS) in group 1.



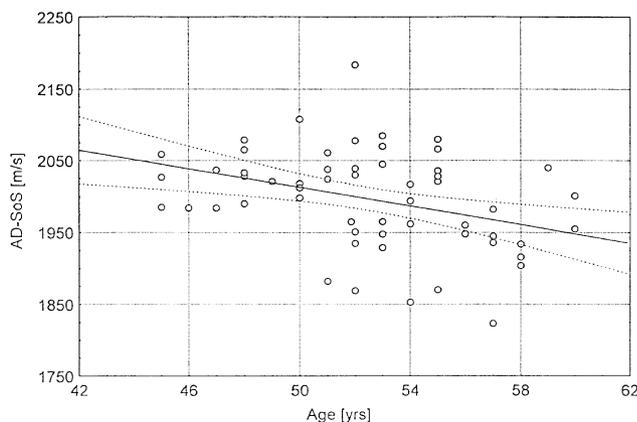
**Fig. 4.** Simple linear regression between years since menopause (YSM) and AD-SoS in group 1.



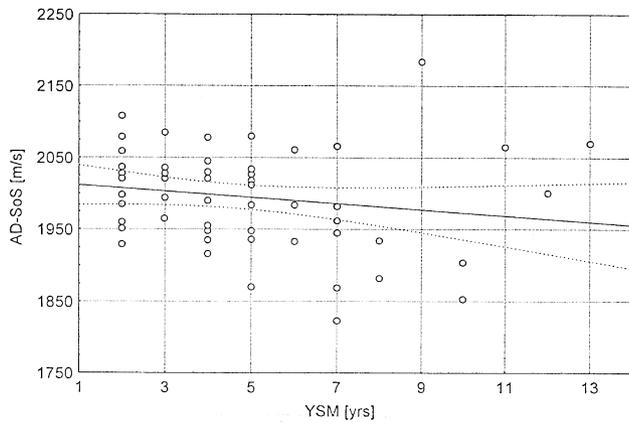
**Fig. 2.** Simple linear regression between age and AD-SoS in group 2.



**Fig. 5.** Simple linear regression between YSM and AD-SoS in group 2.



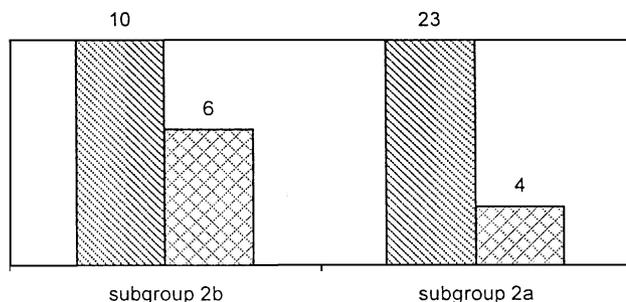
**Fig. 3.** Simple linear regression between age and AD-SoS in group 3.



**Fig. 6.** Simple linear regression between YSM and AD-SoS in group 3.

median and mean for all 503 women studied. Figure 7 shows the distribution of cases with high and low AD-SoS values in subgroups 2a and 2b. In persons with a wrist fracture 23 (85.2%) had a low and 4 (14.8%) a high AD-SoS value, while in persons without a wrist fracture

10 (62.5%) had a low and 7 (37.5%) had a high AD-SoS value. Despite this clear difference, the hypothesis that the AD-SoS measured at the proximal phalanges might be more sensitive to wrist fracture is not confirmed with an  $\alpha$  level below 0.05 ( $p = 0.093$  in Fisher's exact test of



**Fig. 7.** Distribution of cases for Fisher's test. Numbers over the bars are the number of cases. *Hatched columns*, women with low AD-SoS (>1950 m/s); *cross-hatched columns*, women with high AD-SoS (<1950 m/s).

frequencies). No significant differences between correlation coefficients were noted, except in a comparison of  $r$  values between AD-SoS and YSM in group 3 versus groups 1 and 2.

## Discussion

Several cross-sectional and prospective studies have demonstrated that subjects with fractures have lower speed of sound values and BUA than subjects without fractures [5–8,22]. The age-adjusted odds ratio for low-trauma fracture for each 1 SD decrease in either speed of sound or BUA in peripheral measurement sites ranges from 1.24 at the patella [23] to 3.7 at the calcaneus [24]. This odds ratio is similar to that reported for each 1 SD decrease in bone mineral density measurements [25].

To our knowledge no data have been published concerning fracture risk assessed by ultrasound measurements of proximal phalanges. We were able to discriminate between healthy individuals (group 1) and subjects with past fractures (group 2). No statistical differences were noted between these two groups regarding age and YSM – two of the main factors influencing bone status. We were not able to confirm hypothesis that the Ad-SoS value measured at the proximal phalanges might be more sensitive to wrist fracture (Fig. 7), although the difference between the two fracture subgroups suggests that in a larger fracture population this hypothesis may be confirmed.

The role of estrogen deficiency in the pathogenesis of osteoporosis is well established [26,27] and estrogen replacement therapy after the menopause has been shown to prevent bone loss and reduce fracture risk at the wrist, spine and hip [28–31]. Most of the studies included younger postmenopausal women. Early postmenopausal women were also considered in this study. Investigations have shown that the menopause is followed by an immediate fall in bone mass and density within 1 year at both peripheral and central sites of the skeleton [32,33]. The increased rate of bone loss reaches equilibrium about 10 years after the menopause [34]. Thus, this period of life is the best time to prevent postmenopausal bone loss [35]. Our results show

significantly higher values of AD-SoS at the proximal phalanges in the HRT group. The duration of the therapy was relatively short, but important for bone status. Similar results were obtained by Benitez and Schneider [13], who also performed ultrasound measurements of the phalanges. The study of the influence of HRT on YSM-related bone changes seems to be especially important. Age-dependent bone loss was slightly less evident in the group treated with estrogens ( $r$  value  $-0.37$  versus  $-0.40$  for healthy persons and  $-0.47$  for women with fractures). The influence of HRT was clearer when considering YSM-related bone changes: the  $r$  value of  $-0.18$  in the HRT group ( $p=0.17$ ) was significantly different from the values in the fracture group ( $-0.32$ ) and in healthy persons ( $-0.44$ ). Thus, YSM does not influence bone loss, i.e., ultrasound velocity, in women treated with estrogens. These results suggest that QUS of proximal phalanges is influenced by early HRT. This observation is supported both by the significantly higher AD-SoS value and by the weaker influence of age and YSM on ultrasound velocity in the HRT group.

## Conclusions

Ultrasound measurements at the proximal phalanges were able to discriminate between healthy and osteoporotic individuals and to detect age and postmenopause-related changes within the skeleton. Furthermore, this study demonstrates a significantly reduced influence of menopause on the AD-SoS value in women on HRT. Limitations of the study were its cross-sectional design, some differences in weight and BMI between the group studied and the relatively small fractured population. Despite these limitations the results are very promising, especially in view of longitudinal studies that are presently in progress.

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*Received for publication 28 February 1997*

*Accepted in revised form 4 March 1998*