

Longitudinal changes in mandibular bone mineral density compared with hip bone mineral density and quantitative ultrasound at calcaneus and hand phalanges

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Abstract. The aim of this prospective study was to evaluate changes in bone mineral density (BMD) of the mandible (m-BMD) compared with hip BMD and ultrasound parameters of the calcaneus and hand phalanges over 28 months. The study group consisted of 18 post-menopausal edentulous women with no reasons known to affect bone metabolism, such as disease or medication. Each woman had undergone natural menopause. No previous fractures were noted. Measurements were performed at baseline and repeated after 28 months. Bone status was assessed by measuring BMD using dual energy X-ray absorptiometry (DXA) at the mandible and hip and by measuring speed of sound (SOS), broadband ultrasound attenuation (BUA), stiffness index (SI) and amplitude-dependent SOS (Ad-SOS) using quantitative ultrasound at the calcaneus and phalanges of the hand. The coefficient of variation for mandibular measurements was 2.06%. BMD of the mandible, femoral neck and Ward's triangle decreased significantly (-7.54% , -1.2% , -1.97% per year, respectively, $p < 0.05$), whilst BUA, SI and Ad-SOS decreased, but not significantly (-1.1% , -0.47% , -0.08% per year, respectively). Both SOS and BMD of the trochanter had almost the same value without significant differences. The least significant change (LSC), denoting the minimum difference between two successive results in an individual that can be considered to reflect a real change, was calculated. With the exception of changes in m-BMD, no significant changes were observed at any of the sites for the majority of the women (39–89%). 67% of women had a decrease in m-BMD greater than the LSC and 22% had an increase in m-BMD greater than the LSC. Apart from the mandible, other sites showing a large percentage of women with a decrease in BMD greater than the LSC were the Ward's triangle (39%) and the femoral neck (28%). In conclusion, a 28-month longitudinal study of post-menopausal women revealed mandibular bone loss assessed by DXA to be much higher than in other skeletal sites.

Problems associated with age-related skeletal osteopenia have received widespread attention. The human skeleton undergoes a continuous physiological decrease in bone mass with advancing age. This bone loss starts at approximately 35 years of age and continues at different speeds throughout life. Women lose more mineralized bone than men, especially post menopause when bone loss accelerates and can result in fractures. Fractures are often the first symptoms of osteoporosis. Bone mass at specific sites, which are also sites where osteoporotic fractures occur, can be measured using dual energy X-ray absorptiometry (DXA), quantitative ultrasound or quantitative CT.

The earliest suggestion of an association between osteoporosis and oral bone loss was made in 1960

[1]. The mandible seems to undergo a decrease in mineralized bone throughout life, as with other bones. This decrease is caused by systemic diseases or medical treatment known to affect bone metabolism, and also by local bone diseases that can result in total loss of teeth [2]. A number of investigators have stated that the progressive loss of alveolar bone may be a manifestation of osteoporosis [3–7]. Hildebolt [8], in a recent review of the literature on the possible association between osteoporosis and oral bone loss, stated that although not all studies found associations between osteoporosis and oral bone loss, this association exists.

The aim of this study was to evaluate the changes in bone mineral density (BMD) of the mandible and hip, and in ultrasound values of the calcaneus and hand phalanges over a period of 28 months. To our knowledge, this is the first

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prospective study evaluating mandibular BMD (m-BMD) compared with DXA and quantitative ultrasound measurements at other skeletal sites.

Subjects and methods

Study population

The present study group was derived from our previously described population, comprising 36 edentulous women and 6 men without any medical reasons known to affect bone metabolism, such as disease or medication [9]. Some individuals were patients referred to the Prosthodontic Department for complete denture construction while the rest were volunteers recruited through advertisements in the local press. Selection of edentulous patients was connected with the fact that the presence of teeth could introduce error in m-BMD measurements. Prior to and during follow-up, none of the subjects was on hormone replacement therapy or taking calcitonin, bisphosphonates or fluorides, whilst some subjects were taking low doses of calcium or vitamin D (up to 400 IU daily). Each woman had undergone natural menopause. No previous fractures were noted in the group studied. The study group was submitted to baseline examinations in 1999. After 28 months, the same 36 women were invited to take part in corresponding examinations. 18 women participated on both occasions. 18 women did not answer our invitation and the 6 men were not invited for follow-up. At baseline and after 28 months: mean age was 61.3 ± 6.3 years and 63.6 ± 6.2 years, respectively; mean years since menopause (YSM) was 12.8 ± 7.4 years and 14.5 ± 7.3 years, respectively; mean weight was 67.5 ± 12.8 kg and 68.5 ± 11.5 kg, respectively; mean height was 158.3 ± 6.1 cm and 157.4 ± 5.5 cm, respectively; and mean body mass index (BMI) was 27.0 ± 4.5 kg m⁻² and 27.9 ± 5.1 kg m⁻², respectively. Body size did not change significantly during follow-up. The study was approved by a local ethics committee and informed consent was obtained from all subjects studied.

Methods

Dual energy X-ray absorptiometry examinations of the mandible and hip

DXA examinations of the mandible and hip were performed using a DPX-L densitometer (Lunar, Madison, WI).

No DXA software specifically designed for the mandible is available. Therefore m-BMD measurements were performed in the body of the mandible according to the methodology proposed by Horner et al [10]. For mandibular scanning, patients were positioned semiprone, right side raised, with the neck slightly extended and the

head in a true lateral position. The aim was to superimpose the contralateral sides of the mandible while avoiding superimposition of the cervical spine. Scanning was performed in a rectilinear manner, beginning from the mandibular angle and continuing through the whole of the mandible. To derive data for m-BMD, manual analysis was performed using rectangular customized region of interest (ROI) placed over the mandibular body. The shape and size of ROI was altered to conform to the shape of the bone images of each patient. During the baseline and second measurements all DXA scans were performed by the same operator. There were no significant changes in bone area detected. The coefficient of variation (CV%) for mandibular measurements was calculated on the basis of 15 measurements in 5 persons (3 measurements each); $CV\% = (\text{standard deviation}/\text{mean}) \times 100$. These individuals were randomly selected from women evaluated in this study. Each measurement taken for calculation of precision was performed with repositioning and standing up between scans.

DXA of the right hip included BMD measurements at the femoral neck (neck-BMD), Ward's triangle (Ward's-BMD) and trochanter (troch-BMD). CV% for hip measurements was calculated on the basis of 50 measurements in 10 persons (5 measurements each).

Quantitative ultrasound examinations of the calcaneus and hand phalanges

Ultrasound measurements of the calcaneus using an Achilles ultrasound system (Lunar, USA) were performed at the right (dominant) heel. Speed of sound (SOS) and broadband ultrasound attenuation (BUA) were measured. The Achilles system also calculates a stiffness index (SI), which does not represent a biological stiffness of bone tissue. All measurements were taken by the same operator. Short-term *in vivo* precision was established on the basis of 100 measurements in 20 healthy women (5 measurements each).

Phalangeal ultrasound measurements were obtained using a DBM Sonic 1200 device (IGEA, Carpi, Italy), consisting of two probes mounted on an electronic caliper. The emitter probe, positioned on the medial surface of the measured phalanx, generates a single period at 1.25 MHz every 128 μ s. The receiver probe is positioned on the lateral side of the phalanx and detects ultrasound that has crossed the phalanx. The time interval between emission and reception of the ultrasound signal was measured. SOS in the distal metaphyses of the proximal phalanges of the second through fifth digits of the right hand were determined. SOS in bone was calculated using the first signal with an amplitude of more than 36 pixels on-screen. Thus, the measured SOS

was dependent on signal amplitude; amplitude-dependent SOS (Ad-SoS). Acoustic coupling was achieved using a standard ultrasound gel. All measurements were taken by the same person. *In vivo* short-term precision was assessed based on 75 measurements taken in each of 15 healthy persons (5 measurements each) by the same operator.

Statistics

Calculations of means and standard deviations (SDs), as well as linear correlations using Pearson's coefficient of correlation, were performed using the Statistica program (Statistica, Tulsa, OK) on an IBM PC. Differences between baseline and second values of the variables studied were assessed using the Wilcoxon test in the whole group and using the least significant change (LSC) for each individual. The LSC, or critical difference, denotes the minimum difference between two successive results in an individual that can be considered to reflect a real change. The LSC was calculated for each skeletal variable studied by the formula $CV\% \times 2 \times 1.41$, which would represent a significant statistical difference at the 95% confidence level [11]. The correlations of changes in m-BMD between baseline and second measurements, as well as for age, YSM and years edentulous,

were calculated using Pearson's coefficient of correlation. The statistically significant level was achieved with $p < 0.05$.

Results

Table 1 presents BMD and ultrasound values in the study group at baseline and after 28 months. m-BMD, neck-BMD and Ward's-BMD decreased significantly (-7.54% , -1.2% and -1.97% per year, respectively; $p < 0.05$), whilst BUA, SI and Ad-SoS decreased, but not significantly (-1.1% , -0.47% and -0.08% per year, respectively). Both SOS of the trochanter and troch-BMD had almost the same values during baseline and second measurements, without significant differences.

CV% values were: 2.06% for mandibular DXA; 2.5% for hip measurements; 0.22% for SOS; 1.8% for BUA; 1.1% for SI; and 0.64% for Ad-SoS. On the basis of CV% values the following changes in parameters studied were considered as LSCs: 5.81% (0.069 g cm^{-2}) for m-BMD; 7.05% for hip measurements (0.06 g cm^{-2} for neck-BMD, 0.051 g cm^{-2} for Ward's-BMD, and 0.054 g cm^{-2} for troch-BMD); 0.62% (9.3 m s^{-1}) for SOS; 5.08% (5.3 dB MHz^{-1}) for BUA; 3.1% (2.2%) for SI; and 1.8% (35 m s^{-1}) for Ad-SoS.

Table 1. Bone mineral densities (BMDs) and ultrasound values of the study group ($n=18$)

	At baseline	After 28 months	Bone changes (% per year)	p-value
m-BMD (g cm^{-2})	1.19 ± 0.30	0.98 ± 0.26	-7.54%	<0.05
neck-BMD (g cm^{-2})	0.85 ± 0.14	0.83 ± 0.15	-1.2%	<0.05
Ward's-BMD (g cm^{-2})	0.72 ± 0.16	0.69 ± 0.16	-1.97%	<0.05
troch-BMD (g cm^{-2})	0.77 ± 0.16	0.77 ± 0.15	$+0.04\%$	ns
SOS (m s^{-1})	1506.1 ± 27.5	1508.3 ± 25.4	$+0.04\%$	ns
BUA (dB MHz^{-1})	103.6 ± 7.6	100.9 ± 8.2	-1.1%	ns
SI (%)	71 ± 12	70 ± 12	-0.47%	ns
Ad-SOS (m s^{-1})	1938 ± 47	1933 ± 47	-0.08%	ns

m-BMD, BMD of the mandible; neck-BMD, BMD of the femoral neck; Ward's-BMD, BMD of the Ward's triangle; troch-BMD, BMD of the trochanter; SOS, speed of sound; BUA, broadband ultrasound attenuation; SI, stiffness index; Ad-SOS, amplitude-dependent speed of sound; ns, not significant.

Table 2. Number of women with the least significant change (LSC) in skeletal parameters

	No. of women with negative LSC	No. of women with positive LSC	No. of women without LSC	Total
m-BMD (g cm^{-2})	12 (67%)	4 (22%)	2 (11%)	18 (100%)
neck-BMD (g cm^{-2})	5 (28%)	0	13 (72%)	18
Ward's-BMD (g cm^{-2})	7 (39%)	0	11 (61%)	18
troch-BMD (g cm^{-2})	3 (17%)	3 (17%)	12 (66%)	18
SOS (m s^{-1})	1 (6%)	5 (28%)	12 (66%)	18
BUA (dB MHz^{-1})	3 (17%)	1 (6%)	14 (77%)	18
SI (%)	4 (22%)	7 (39%)	7 (39%)	18
Ad-SOS (m s^{-1})	0	2 (11%)	16 (89%)	18

m-BMD, bone mineral density of the mandible; neck-BMD, bone mineral density of the femoral neck; Ward's-BMD, bone mineral density of the Ward's triangle; troch-BMD, bone mineral density of the trochanter; SOS, speed of sound; BUA, broadband ultrasound attenuation; SI, stiffness index; Ad-SOS, amplitude-dependent speed of sound.

Table 2 shows the number of women with LSCs in measured skeletal parameters. Generally no bone changes that could be considered as LSCs were observed in the majority of women (39–89%) over 28 months, with the exception of bone changes in m-BMD. In the latter, 67% of women showed a decrease greater than the LSC and 22% of women showed an increase greater than the LSC. The sites with most cases of a decrease greater than the LSC other than m-BMD were Ward's-BMD and neck-BMD (39% and 28%, respectively). No woman revealed an increase greater than the LSC in these sites. Cases with an increase greater than the LSC occurred in 6–39% of women. Analysis of whether changes in m-BMD were related to age, YSM or years edentulous revealed no significant correlations between these variables.

Discussion

To our knowledge, this is the first prospective study evaluating bone density changes of the mandible using DXA. Payne et al. [7] investigated alveolar bone loss longitudinally. Their prospective study identified a relationship between systemic BMD status and progressive alveolar bone height and density loss in a 2-year longitudinal investigation. 21 osteoporotic and osteopenic post-menopausal women exhibited a higher frequency of alveolar bone height loss ($p < 0.05$), and also crestal and subcrestal density loss (23.4% and 15.3%, respectively) relative to that of 17 women with normal BMD of the lumbar spine (14.3% and 9.2%, respectively). However, to assess changes in bone density at the crestal and subcrestal regions the authors used a different bone densitometric method. Radiographs were examined using computer assisted densitometric image analysis. Owing to this, direct comparison with our results is not possible.

Although bone loss occurs at all skeletal sites, the amount of loss is not uniform [12]. The rate of bone loss in healthy men is low, probably in the order of 3–5% per decade, whereas in women the process is more complicated [13]. Bone loss before the menopause is small and rather similar to that of men. During the early post-menopausal years the amount of bone lost from the peripheral skeleton (largely cortical bone) differs from that lost from the axial skeleton (mainly cancellous bone) and, for example, the rate of bone loss is more rapid at the spine than at the forearm. The rate of bone loss in the first 10 post-menopausal years also varies widely. It ranges from less than 1% to more than 5% per year for cancellous bone and from 0.5% to 2% for cortical bone. Thereafter post-menopausal bone loss declines in rate [13].

Over 28 months, bone loss in the women

studied occurred in all sites measured, with the exception of SOS at the heel and troch-BMD (Table 1). These values remained almost stable. The rest of the parameters, both densitometric (neck-BMD and Ward's-BMD) and ultrasound (BUA, SI and Ad-SoS), decreased by 0.08–1.97% per year. Contrary to BMD parameters (except troch-BMD), ultrasound parameters did not reveal significant changes in values. A much greater, and significant, decrease of 7.54% per year was observed in the mandible. There are no precise data regarding oral bone loss but the mandible seems to undergo a decrease in mineralized bone throughout life, as do other skeletal bones. The mandible consists primarily of cortical bone, while the trabecular bone mass is small. Its cortical bone mass constitutes more than 80% of the total bone mass at the level of mandibular body that was measured in this study [2]. One could expect that mandibular bone loss is similar to other sites consisting mainly of cortical bone, and is not more than 2% per year. On the basis of our data we are not able to suggest why the rate of mandibular bone loss was so high. We can only suspect that this part of the skeleton shows fast bone loss owing to additional, uncertain local factors. The possible clinical implications of our findings will require further longitudinal assessment.

To assess whether the difference between measurements at baseline and after 28 months in an individual can be considered to reflect a real change, the LSC or critical difference was calculated (Table 2). CV% of the method used affects the detection of the LSC. The better the CV% of the method, the smaller the difference between two successive results in an individual required to reflect a real change. Despite our good precision for DXA and ultrasound measurements, generally no bone changes that can be considered as the LSCs were observed in most women (39–89%) during 28 months, with the exception of bone changes in m-BMD. In the jaw, 67% of women experienced a decrease greater than LSC and 22% an increase greater than LSC. Bone changes within the mandible did not appear to be connected with age, YSM or years edentulous. Apart from the mandible, the sites with most cases of a decrease in BMD greater than the LSC were the Ward's triangle and the femoral neck (39% and 28%, respectively). No woman revealed an increase greater than LSC in these sites. Overall, an increase greater than LSC occurred in 6–39% of women. Rates of bone loss decline several years post menopause, so a longer interval between measurements is required to evaluate a given change [13]. Further observations may provide a decrease of parameters measured in all subjects.

Progressive mandibular bone loss in postmenopausal women as noted by us, and longitudinal alveolar bone loss as noted by Payne et al [7], may have significant stomatological implications. Mandibular bone loss could affect dental implant success and is sufficient to preclude primary dental implant stability, which can compromise osseous support in totally edentulous women, leading to difficulty in wearing dentures [7].

The limitation of this study is the small size of the study group and the practical difficulties associated with scanning patients at the mandibular site. The mandible is a difficult site at which to perform conventional methods of bone densitometry. Owing to this, the operator must possess considerable positioning and scanning skills. Experience and careful operator training are required to ensure consistency of results in longitudinal studies. Also, some patients may find positioning uncomfortable and difficult to maintain during the scan time.

Conclusion

A 28-month longitudinal study of postmenopausal women revealed mandibular bone loss assessed by DXA to be much higher than in other skeletal sites. The relationship between skeletal status and the local process within the mandible ought to be studied longitudinally, and inexpensive methods must be developed for sensitive and specific measurements of oral bone loss.

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