Ultrasound Osteoporosis Score: A Novel Parameter for the Estimation of Spine Mineral Density

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Abstract—**Aim of this work was to evaluate the effectiveness of a recently introduced ultrasound (US) parameter for the estimation of bone mineral density (BMD) of the lumbar spine, when extensively used in a clinical context to investigate adult women of variable body mass index (BMI). A total of 414 female patients (aged 51-60 years) underwent a spinal dual X-ray absorptiometry (DXA) and an abdominal echographic scan of the lumbar spine. US images and corresponding unfiltered radiofrequency signals were analyzed through a new fully automatic algorithm, which performed a series of spectral and statistical analyses to calculate the novel diagnostic parameter, called the Osteoporosis Score (O.S.). Effectiveness of O.S. in BMD estimation and subsequent osteoporosis diagnosis was assessed through a direct comparison with DXA measurements (assumed as the gold standard reference), by quantifying the agreement between the two methods through accuracy calculation and Pearson correlation coefficient (r). A very good and significant correlation was found between O.S.-estimated BMDs and corresponding DXA values over the whole considered study population ($r=0.81$, $p<0.001$). The subsequent diagnostic classifications of patients as osteoporotic, osteopenic or healthy on the basis of O.S.-estimated BMD values resulted in an overall accuracy of 90.1%. Interestingly, both the adopted metrics (r value and accuracy) were not appreciably influenced by patient BMI, demonstrating that US-measured O.S. is significantly correlated with spinal BMD in adult women independently of their BMI. Therefore, the clinical translation of this innovative method for osteoporosis diagnosis can be envisioned.**

Keywords—osteoporosis diagnosis; bone mineral density measurement; lumbar spine; bone densitometry; radiofrequency signal processing.

I. INTRODUCTION

Osteoporosis is characterized by increased bone fragility and augmented fractures risk [1]. Currently, the high and unacceptable rates of under-diagnosis [2,3] are responsible for the high incidence of osteoporotic fractures [4] and the huge associated costs for national healthcare systems [5-7].

Osteoporosis diagnosis is based on the assessment of bone mineral density (BMD), which is typically obtained from dual X-ray absorptiometry (DXA) investigations on the reference anatomical sites (lumbar vertebrae and femoral neck) [8-12].

Unfortunately, DXA cannot be employed for population mass screenings because of important intrinsic limitations, including ionizing radiation exposure, high costs and unavailability in primary care settings. In order to overcome these limitations, several alternative approaches based on ultrasound (US) technologies have been proposed, with the aim of exploiting their numerous potential advantages, mainly related to absence of ionizing radiation, lower costs, portability, wide availability also in primary care settings [8-10,13-15]. Nevertheless, commercially-available US devices for bone characterization and osteoporosis diagnosis can be presently applied only to peripheral sites (e.g. calcaneus), with a limited clinical effectiveness [16]. In this context, the latest research frontier is represented by the development of an US approach to osteoporosis diagnosis that is applicable on femoral neck [17-19] and/or lumbar spine [20,21].

Our research group has recently introduced a novel US methodology for estimating BMD of lumbar spine, providing an initial test of the corresponding diagnostic accuracy on 79 women having a body mass index (BMI) lower than 25 kg/m^2 (i.e., normal- or under-weight subjects) [20]. The aim of the present work was to evaluate the actual diagnostic effectiveness of the proposed approach through a more extended clinical validation, focusing in particular on possible accuracy variations as a function of patient BMI in a wider interval.

II. MATERIALS AND METHODS

A. Patients

The study was conducted at the Operative Unit of Rheumatology of Galateo Hospital (San Cesario di Lecce, Lecce, Italy) and included a total of 414 consecutive female patients, according to the following inclusion criteria: Caucasian ethnicity, aged 51-60 y, medical prescription for a spinal DXA.

All the enrolled patients underwent two different investigations: a lumbar spine DXA and an abdominal US scan of the lumbar vertebrae L1-L4, as detailed in the following paragraphs.

The study protocol was approved by the Hospital Ethics Review Board and all patients gave their informed consent.

B. DXA Measurements

DXA scans were performed on the lumbar spine (L1-L4) using a Hologic Discovery W scanner (Hologic, Waltham, MA, USA). Measurement results were expressed both as BMD and as T-score values, where T-score is defined as the number of standard deviations (SDs) from the peak BMD of young women found in the standard Hologic reference database for Caucasian women.

According to the commonly used definition of osteoporosis given by the World Health Organization (WHO), patients were classified as "osteoporotic" if T-score ≤ -2.5, "osteopenic" if -2.5 < T-score < -1.0, or "healthy" if T-score ≥ -1.0.

C. US Acquisitions

Abdominal US scans of lumbar spine were carried out employing an innovative device developed in Lecce (Italy) within the ECHOLIGHT Project through a collaboration between CNR-IFC (National Research Council, Institute of Clinical Physiology) and Echolight srl. This US device was equipped with a 3.5-MHz broadband convex transducer and configured to provide both echographic images and unprocessed "raw" radiofrequency (RF) signals.

Each patient underwent a sagittal scan of lumbar spine moving the US probe back and forth from the xiphoid process. The scan lasted 80 seconds and generated 100 frames of RF data, which were acquired and stored in a PC hard-disk for subsequent offline analyses.

Transducer focus and scan depth were specifically adjusted for each acquisition in order to have vertebral interfaces located in the US focal region and in the central part of the image. The other acquisition parameters were kept constant to the following values: mechanical index (MI) = 0.4, gain = 0 dB, linear time gain compensation (TGC).

D. US Data Analysis

Acquired US data were analyzed through a novel fully automatic algorithm that performed a series of combined spectral and statistical analyses involving both the echographic images and the underlying RF signals. The final output was a new US parameter, called the Osteoporosis Score (O.S.), which has been recently demonstrated to have a strong correlation with BMD in a small cohort of normal- and under-weight adult women [20].

The implemented algorithm performed diagnostic calculations on RF signal segments corresponding to specific regions of interest internal to the vertebrae, automatically identified by the algorithm itself (200-point Hamming-windowed signal portions starting after the vertebral surface echo, when the amplitude of the RF signal envelope reached 15% of the peak value shown in correspondence of the vertebral surface). Aim of these calculations was to measure the percentage of vertebral segments whose signal spectral features correlated better with those of an osteoporotic bone model rather than with those of a healthy one. This was accomplished by comparing RF spectra calculated from the considered patient dataset with reference models of healthy and osteoporotic vertebrae obtained from previous US acquisitions on DXA-classified patients.

The algorithm implementation has been described in detail in a very recent paper [20] and is briefly recalled herein. The main data analysis steps performed on each patient dataset were:

1. automatic identification of vertebral interfaces in the acquired images;

2. for each vertebra image, automatic identification of a specific RF signal portion for each scan line crossing the bone surface;

3. classification of each RF signal portion as "osteoporotic" or "healthy" on the basis of the correlation between its frequency spectrum and each of the two age- and BMI-matched spectral models stored in a previously obtained reference database;

4. for each vertebra, calculation of the O.S. value, defined as the percentage of the analyzed vertebra segments that were classified as "osteoporotic" in the previous step;

5. calculation of the O.S. value for the considered patient as the average of single vertebra values;

6. calculation of an US-estimated BMD value as a function of the O.S., using a mathematical equation contained in the reference model database, whose analytical expression depends on both patient age interval and BMI range.

Patients enrolled for the present study were subdivided into two different age intervals (51-55 y, 56-60 y), and within each interval they were further subdivided into three BMI ranges: BMI < 25 kg/m^2 (corresponding to normal- or under-weight women), BMI in the range 25-30 kg/m^2 (corresponding to over-weight subjects), BMI > 30 kg/m^2 (corresponding to obese patients). For each of the 6 possible combinations of considered age intervals and BMI ranges, a couple of reference spectral models (an "osteoporotic" one and a "healthy" one) was available in the previously built database. In particular, every couple of models had been obtained following the same procedure detailed in [20] for the case normal- and under-weight women.

E. Statistical Analysis

A linear regression was used to estimate spinal BMD from O.S. values and Pearson correlation coefficient (r) was employed to evaluate these estimations with respect to DXA results as a function of both patient age and BMI.

Afterwards, taking into account the specific BMD diagnostic thresholds corresponding to T-score = -1.0 and T-score = -2.5, all the patients were again classified as "osteoporotic", "osteopenic" or "healthy" on the basis of O.S.-derived BMD values. The level of agreement between DXA

and US-based diagnoses was assessed through the calculation of accuracy (i.e., correct diagnoses/analyzed patients).

III. RESULTS AND DISCUSSION

The distribution of the enrolled patients as a function of age interval, BMI range, and DXA diagnosis (osteoporotic, osteopenic, healthy) is reported in Tab. I. As expected, the percentage of osteoporotic subjects was higher for the older patients and for the thinner ones, while the percentage of healthy subjects had an opposite trend.

TABLE I.   DISTRIBUTION OF ENROLLED PATIENTS AS A FUNCTION OF AGE INTERVAL, BMI RANGE AND DXA DIAGNOSIS

Age Interval (y)	BMI Range (kg/m^2)	Number of Patients (n)	DXA Diagnosis
51-55	< 25	113	18.9% Osteoporotic 53.7% Osteopenic 27.4% Healthy
	25-30	53	18.9% Osteoporotic 49.0% Osteopenic 32.1% Healthy
	> 30	36	16.7% Osteoporotic 38.9% Osteopenic 44.4% Healthy
56-60	< 25	104	42.3% Osteoporotic 46.2% Osteopenic 11.5% Healthy
	25-30	77	27.3% Osteoporotic 51.9% Osteopenic 20.8% Healthy
	> 30	31	25.8% Osteoporotic 35.5% Osteopenic 38.7% Healthy

In order to evaluate the robustness of O.S.-derived BMD estimates with respect to BMI variations, patients were grouped on the basis of their BMI only and the correlation between DXA-measured and US-estimated BMD values was
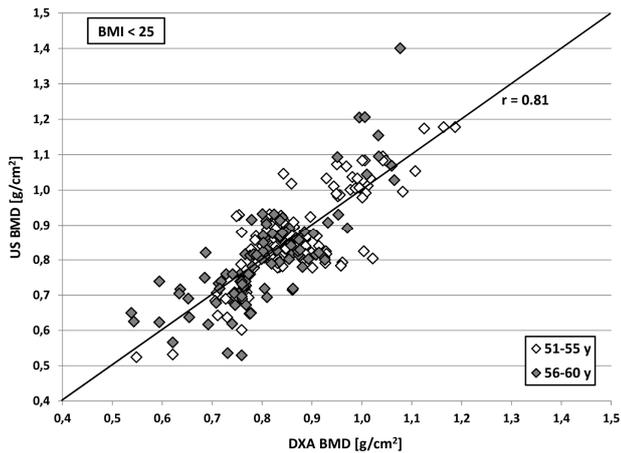

Fig. 1. Scatterplot of DXA-measured and US-estimated BMD values for patients having BMI < 25 kg/m^2. The line of equality and the global Pearson correlation coefficient are also illustrated ($p < 0.001$).
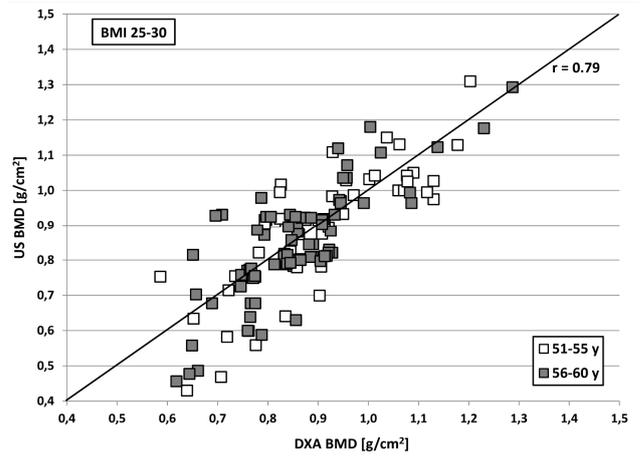

Fig. 2. Scatterplot of DXA-measured and US-estimated BMD values for patients having BMI in the range 25-30 kg/m^2. The line of equality and the global Pearson correlation coefficient are also illustrated ($p < 0.001$).
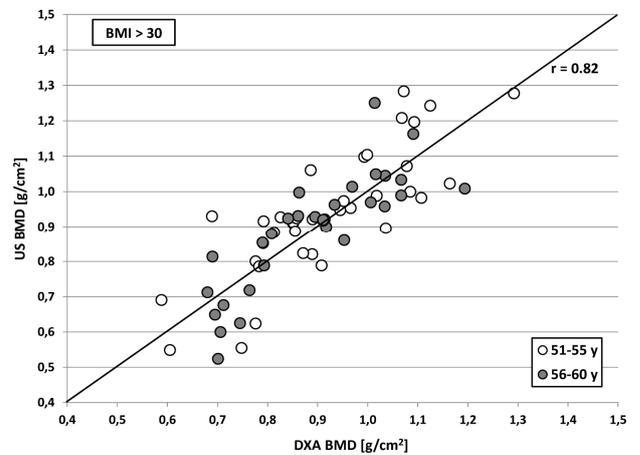

Fig. 3. Scatterplot of DXA-measured and US-estimated BMD values for patients having BMI > 30 kg/m^2. The line of equality and the global Pearson correlation coefficient are also illustrated ($p < 0.001$).

calculated. The corresponding scatterplots are reported in Figures 1-3, showing that all the calculated r values were in a very narrow range ($r = 0.81$ for normal- or under-weight patients, $r = 0.79$ for over-weight patients, $r = 0.82$ for the obese ones; $r = 0.81$ for the whole population; $p < 0.001$ for all) and documenting the unaltered effectiveness of O.S. in BMD estimation for patients with different BMI.

Tab. II reports the obtained values of the Pearson correlation coefficient r between the paired BMD values for each single combination of patient age interval and BMI range, together with the corresponding accuracy levels obtained from the new diagnostic classification of the patients based on O.S.-derived BMD values. The obtained correlations resulted always strong and statistically significant, without appreciable variations between different patient groups. The diagnostic accuracy with respect to DXA classifications, in turn, showed an almost constant level, since all the values

were in the range 88.7-90.9% (Tab. II). Overall, 373 out of the 414 studied patients received the same diagnostic classification from DXA and US investigations (total accuracy = 90.1%), and this rate of correct diagnoses was substantially confirmed in the single considered BMI ranges: 196/217 (90.3%) for BMI < 25 kg/m^2, 117/130 (90.0%) for BMI in the range 25-30 kg/m^2, 60/67 (89.6%) for BMI > 30 kg/m^2.

TABLE II. EFFECTIVENESS OF US-BASED BMD ESTIMATIONS AND SUBSEQUENT DIAGNOSTIC CLASSIFICATIONS AS A FUNCTION OF AGE INTERVAL AND BMI RANGE

Age Interval (y)	BMI Range (kg/m^2)	Number of Patients (n)	US vs DXA	
			Correlation between paired BMD values (r)	Diagnostic Accuracy
51-55	< 25	113	0.81*	90.3%
	25-30	53	0.79*	88.7%
	> 30	36	0.81*	88.9%
56-60	< 25	104	0.79*	90.4%
	25-30	77	0.79*	90.9%
	> 30	31	0.84*	90.3%

*p<0.0001.

The illustrated results documented the clinical effectiveness of the proposed US approach in the diagnosis of osteoporosis in adult women independently of their BMI, since the diagnostic performance of O.S., as reported in a very recent study conducted on a small cohort of normal- or under-weight adult women [20], was essentially confirmed by the present work on a larger population including significant portions of over-weight and obese subjects.

IV. CONCLUSION

The clinical effectiveness of the US-measured O.S. in lumbar spine BMD estimation and subsequent osteoporosis diagnosis was demonstrated in a population of adult female patients of variable BMI, going from under-weight subjects to obese ones.

The reported agreement with DXA outcome and the fully automated processing of echographic images and RF signals provide the adopted approach with a strong potential for an effective clinical translation.

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