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Ultrasound Fragility Score: An innovative approach for the assessment of bone fragility

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ABSTRACT

Aim of this paper was to assess the clinical effectiveness of a novel ultrasound (US) approach for the estimation of bone fragility. A total of 85 female patients (40–80 years) were recruited and underwent conventional DXA investigations of both lumbar spine and proximal femur, an abdominal US scan of the lumbar spine and the FRAX® questionnaire for the calculation of osteoporotic fracture probabilities. Acquired US data were analyzed through an automatic algorithm that calculated the Fragility Score (F.S.), a parameter that estimates skeletal fragility from dedicated spectral and statistical analyses. F.S. showed a good correlation with the most reliable fracture risk predictions obtained by FRAX® ($r = 0.71$, $p < 0.001$). Since this correlation level with FRAX® outcomes was much better than lumbar BMD one ($|r| = 0.43$) and very similar to that obtained for femoral neck BMD ($|r| = 0.72$), F.S. has the potential to become a simple and non-ionizing method for bone fragility assessment.

1. Introduction

Osteoporosis is a very common skeletal disease, characterized by bone tissue deterioration and increased bone fragility, which leads to enhanced fracture risk and huge costs for the healthcare systems [1].

According to the operational definition of osteoporosis provided by the World Health Organization (WHO) [2], osteoporosis diagnosis is based on bone mineral density (BMD) measurements, which are typically performed through dual-energy X-ray absorptiometry (DXA). However, because of a series of issues related to ionizing radiation employment (the need for dedicated structures with certified operators, high costs, possible long-term health risks for patients and operators) [3], DXA employment is prevented from population screening purposes and osteoporosis results in a highly underdiagnosed disease [4,5], with rates of unidentified cases exceeding 90% [6]. Furthermore, a reliable prediction of osteoporotic fracture probability is difficult to achieve, since it has been demonstrated that BMD is only one of the factors determining the actual fracture risk, whose accurate estimation requires also the combined evaluation of the relevant clinical risk factors (CRFs) [7–9].

Presently, one of the most effective approaches to the pooled evaluation of BMD and CRFs for osteoporotic fracture risk prediction is undoubtedly represented by FRAX®, the Fracture Risk Assessment tool developed by the WHO Collaborating Centre for Metabolic Bone Diseases at Sheffield (UK) [10,11]. This algorithm takes into account a variety of patient data (age, sex, ethnicity, nationality, etc.),

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including a series of CRFs (e.g., smoking habits, alcohol intake, history of previous fragility fractures), and combines them with the DXA-measured BMD value of the femoral neck in order to calculate the 10-year probability of an osteoporotic fracture at the hip and the 10-year probability of a generic major osteoporotic fracture (occurring at hip, spine, humerus or forearm) [12,13]. However, the effective employment of FRAX® requires a good knowledge of lifestyle and general clinical situation of the patient [14–20] and, above all, it also requires the outcome of a femoral DXA investigation.

In a recent conference paper [21], we introduced a new ultrasound (US) parameter, called the Fragility Score (F.S.), which provides an estimate of skeletal fragility based on a trans-abdominal echographic scan of lumbar vertebrae. The main hypothesis underlying F.S. calculation is that the bones of a subject prone to fragility fractures have specific structural characteristics, which reflect in the spectra of unfiltered radiofrequency (RF) signals backscattered by lumbar vertebrae. Actually, F.S. value represents the percentage of analyzed vertebral segments whose signal spectral features are more similar to those of a "frail" vertebral model rather than to those of a "non-frail" one. The considered spectral models were derived from previous US acquisitions on patients that had recently suffered an osteoporotic fracture and patients that had never had a fracture.

The proposed approach also goes in the direction that is being indicated by the most recent literature-reported studies in the field of both osteoporosis diagnosis and biomedical measurements in general: in fact, on the one hand, the latest trends in the development of more effective techniques for osteoporosis diagnosis are increasingly focused on the employment of non-ionizing methods to perform integrated assessments of bone structure quality (and not just BMD measurements) in order to determine the actual bone strength [22] and, on the other hand, several biomedical applications of US systems have been introduced in the last years because of their intrinsic advantages over competing technologies [23–36].

The effectiveness of this new methodology for bone fragility assessment was preliminarily investigated in a group of postmenopausal women aged in 50–80 years, by quantifying the correlation between FRAX® fracture probabilities and F.S. values [21]. In the present work we performed an extended clinical validation of the adopted approach on a larger study population, which also included younger women between the ages of 40 and 50. In fact, since recent literature clearly documented that lifestyle can play a very important role in osteoporosis prevention [37], the assessment of bone fragility in young subjects is of particular interest. On the other hand, this study could not include subjects younger than 40 years because FRAX® calculations cannot be performed in that age range.

Full implementation details of the novel proposed algorithm were also reported and the general clinical usefulness of the new technique has been critically discussed taking into account the most recent literature-available papers.

2. Materials and methods

2.1. Study population

The study was conducted at the Operative Unit of Rheumatology of "A. Galateo" Hospital (San Cesario di Lecce, Lecce, Italy), where a total of 85 women of Caucasian ethnicity were enrolled in this study according to the following criteria: aged between 40 and 80, body mass index (BMI) < 30 kg/m^2, absence of previous vertebral fractures, absence of significant deambulation impairments, medical prescription for a DXA-based BMD measurement in order to assess the osteoporosis condition.

Enrollment criteria were established taking into account a series of factors. First, in order to compare F.S. values with FRAX® predictions, we could not recruit patients younger than 40 years, because FRAX® cannot be applied on subjects younger than 40 year. Second, since low BMI is a recognized risk factor for osteoporosis and fragility fractures [38,39], we excluded obese patients and focused our attention on under-, normal- and overweight people. Furthermore, taking into account that prior osteoporotic vertebral fractures are by themselves a particularly strong predictor of further future fragility fractures [40], we decided to concentrate on the assessment of those patients whose fracture risk is less obvious. Finally, we included only women because there are very few men who are referred for BMD assessments.

All the enrolled patients underwent conventional DXA investigations of both lumbar spine and proximal femur, an abdominal US scan of the lumbar spine and the FRAX® questionnaire for the calculation of osteoporotic fracture probabilities through the assessment of CRFs.

The study protocol was approved by the hospital ethics review board, and each participant gave her informed consent.

2.2. DXA measurements

DXA scans were performed by an Hologic Discovery W scanner (Hologic, Waltham, MA, USA), providing for each patient the BMD values of lumbar spine and femoral neck, expressed as grams per squared centimeters (g/cm^2). Furthermore, the corresponding T-score values, which describe the difference between the BMD of the patient being examined and the mean BMD of a standard young adult population [41], were also recorded for both the considered anatomical sites.

Femoral investigations were conducted just on femoral neck because this site has been the most extensively validated and has been recently indicated as the standard measurement site [42,43].

2.3. US acquisitions

Abdominal US scans of lumbar vertebrae were performed using an innovative device developed in Lecce (Italy) within the ECHOLIGHT Project. The device was equipped with a 3.5-MHz broadband convex US transducer and configured to provide both echographic images and

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