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Literature review of Radiofrequency Echographic Multi-Spectrometry (REMS) in the diagnosis of osteoporosis and bone fragility

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ABSTRACT

Background. Osteoporosis is a frequent comorbidity among patients with inflammatory rheumatic diseases, due to the impact of their therapies, the hish systemic inflammation and the large scale use of glucocorticoid treatment.

Use of DXA and REMS. Dual X-ray Absorptiometry (DXA) is the "gold standard" for detecting patients with low bone mineral density (BMD), using Z and T scores to define the thresholds for diagnosis of osteopenia and osteoporosis, but this method has proven many disadvantages in time, especially in patients with inflammatory rheumatic diseases, those diagnosed with a disease in the spectrum of spondyloarthritides. Therefore, in the last years, a new method of evaluating bone mineral density (BMD) was developed and benefited from numerous efficiency studies: REMS (Radiofrequency Echographic Multi-Spectrometry). The basis of the method is its ability to identify and analyze native unfiltered ultrasound waves that reflect from the bone surface of the vertebra and femoral neck, the so-called echographic radiofrequency (RF) waves. The analysis of all RF waves spectra allows both a quantitative as well as a qualitative assessment of the bone, thus effectively obtaining estimates of bone resistance and evaluating fracture risk through indirect analysis of bone architecture.

Conclusions. The studies concluded that REMS is a method at least as good as DXA in detecting patients with osteoporosis by applying the definitions of the World Health Organization (WHO), and also discovered many advantages of the REMS method, probably the biggest advantages being the ability of this ultrasound method of evaluating bone fragility independent of BMD by introducing the Fragility Score (FS) and the possibility of using the ultrasound method in identifying bone demineralization and fragility in pregnant women. Furthermore, numerous studies begin to recognize the usefulness of REMS in diagnosis and evolution of patients with osteoporosis and inflammatory rheumatic diseases.

Discussions. A new concept that should be considered is the fact that REMS could potentially more accurately evaluate BMD and bone fragility through the FS in patients with diseases from the spectrum of spondyloarthritides (especially those with ankylosing spondylitis and psoriatic arthritis).

Keywords: ultrasound densitometry, DXA, REMS, inflammatory rheumatic diseases

INTRODUCTION

Osteoporosis is a frequent comorbidity among patients with inflammatory rheumatic diseases, that has a major impact on the quality of life of these individuals (1). Aside from the high inflammatory activity in cases of systemic lupus erythematosus, rheumatoid arthritis, spondyloarthritides, polymyalgia rheumatic and other connective tissue diseases, of importance is also the impact of therapies used for the afore mentioned pathologies in the onset and evolution of osteoporosis (1). The large scale use of glucocorticoid treatment, mandatory in many cases, is an essential factor in the initiation and augmentation of bone loss processes and inhibition of bone reparatory processes. The role of cortisole and its therapeutic derivates are complex, acting locally by modulating the activity of osteocytes,

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osteoblasts and osteoclasts, as well as systemically by influencing the phospho-calcic metabolism (lower intestinal intake and higher excretion of calcium) and the muscle functionality. Aside from the impact on bone mineralization, systemic inflammation and glucocorticoid treatment also influences bone micro-architecture, additionally raising bone fragility and fracture risk (3).

THE ROLE OF DUAL X-RAY ABSORBTIOMETRY (DXA)

At this moment, Dual X-ray Absorbtiometry (DXA) is the "gold standard" for detecting patients with low bone mineral density (BMD), and Z and T scores are used to define the thresholds for diagnosis of osteopaenia and osteoporosis (4). The major advantages of this method are at times eclipsed by the lack of accuracy detected in patients with inflammatory rheumatic diseases, and also in patients with osteoarthritis. Therefore, the main disadvantages of DXA scans are represented by high maintenance cost, need of a special separate room with leaded walls for the examination, the impact of vertebral deformities and presence of osteophytes and syndesmophytes in determining a correct BMD measurement, falsely elevated BMD in the case of patients with vertebral fragility fractures. Aside from the aforementioned deficits, DXA is also lacks when it comes to fully assessing bone fragility, it is a 2D evaluation, lacking the ability to evaluate volumetric density and geometry of the bone, and can't distinguish between trabecular and cortical types of bone tissue, thus scores used in concordance with DXA all use BMD as an important variable (5). We can clearly observe that many of the modifications that lead to erroneous DXA measurements can be found in patients with inflammatory rheumatic diseases, especially those diagnosed with a disease in the spectrum of spondyloarthritides, where a marker of these types of pathologies is represented by bone formation (osteosclerosis and the presence of syndesmophytes and entesophytes). Furthermore, typical osteoarthritic modifications, which are mostly seen in elderly patients who already have lower bone resistance due to bone fragility related to age and menopause, could present with falsely elevated BMD values, thus delaying the diagnosis of osteoporosis and initiation of specific therapies (6).

THE USEFULNESS OF REMS (RADIOFREQUENCY ECHOGRAPHIC MULTI-SPECTROMETRY)

REMS (Radiofrequency Echographic Multi-Spectrometry) is a novel, innovative and non-ionizing method of evaluating bone mineral density (BMD). This is recently developed technology, that benefited from numerous efficiency studies that evaluated the potential of REMS in detecting and differentiating patients with normal bone mineralization and architecture from those with osteopenia, osteoporosis and fragility due to micro-architectural changes. The basis of the method is its ability to identify and analyze native unfiltered ultrasound waves that reflect from the bone surface of the vertebra and femoral neck, the so-called echographic radiofrequency (RF) waves. Usually, during an imagistic echographic evaluation most softwares use only a small portion of the reflected ultrasound waves are filtered in order to obtain a B-type image on the screen. The analysis of all RF waves spectra allows both a quantitative as well as a qualitative assessment of the bone, thus effectively obtaining estimates of bone resistance and evaluating fracture risk through indirect analysis of bone architecture (7,8).

Therefore, the specificity of REMS in distinguishing between normal, osteopenic and osteoporotic bone was evaluated at 91.7% for the lumbar column, compared to DXA specificity that is around 92%, and 91.5% for femoral REMS evaluation compared to 91.8% DXA evaluation respectively. The grade of correlation between the two methods was initially determined at 94% for lumbar spine and 93% for the femur. A recently published study made in Poland strengthens the concept of the good concordance between REMS and DXA results, determining a correlation of 82.8% for the lumbar spine and 84.8% for the femoral neck. (9) Validation of REMS came from numerous studies performed initially in Italy, that involved 7 healthcare centers that enrolled 1914 postmenopausal women, and demonstrating the good accuracy of REMS, and also it's precision for diagnosis of osteoporosis as compared to DXA scans. This study underlines a very important aspect of this method, which is represented by the need of a good training for the operator of the ultrasound machine in order to limit the number of acquisitioning errors. Probably the high variation when it comes to the specificity rates of REMS compared to DXA described in many different studies are due to the higher rate of acquisition errors for the ultrasound method (280 errors for REMS compared to only 78 for DXA) (10). Larger studies, with highly trained operators confirmed however the good specificity and sensibility rates of REMS when it comes to osteoporosis diagnosis. Therefore, a study that involved 4307 caucasian females, aged between 30 and 90 years old demonstrated a specificity of 95.5% at the level of the lumbar spine and 95.1% at the femoral neck, and a sensibility of 90.4% in the lumbar spine and 90.9% in the femur respectively (11). Amorim et al also demonstrated in a study on 343 women with osteoporosis, where he compared DXA with REMS, that the ultrasound method has similar accuracy as the "gold standard" method of detecting osteoporosis (12).

We saw until now that REMS is a method at least as good as DXA in detecting patients with osteoporosis by applying the definitions of the World Health Organization (WHO), but there's still and important aspect of bone pathology represented by bone fragility. FRAX score, which is used nowadays on large scale in evaluating fracture risk is a score dependent on BMD, although we know that this variable is insufficient for fully assessing bone quality. Probably the biggest advantage of REMS compared to DXA stems from the ability of this ultrasound method of evaluating bone fragility independent of BMD by introducing the Fragility Score (FS). FS is a parameter obtained by comparing results of spectral analysis derived from radiofrequency (RF) waves evaluated in patients and compared to representative models from individuals with and without osteoporosis. Thus an adimensional parameter is obtained, with values ranging from 0 to 100, which correlates with fracture risk, independent from BMD. A study that included 533 women, follow-up for approximately 5 years showed that mean values of the T-score obtained both with REMS and DXA show a lower risk of fracture compared to FS which predicts a statistically significant higher fracture risk (12). In this context, being faced with a method that has recently been developed and approved for use in diagnosis and evaluation of osteoporosis and bone fragility, more time needs to pass in order to fully characterize the usefulness of the FS specific to REMS evaluation.

Another major advantage of REMS compared to DXA is the possibility of using the ultrasound method in identifying bone demineralization and fragility in pregnant women. We already know that during pregnancy females tend to have lower levels of calcium in the blood and that they constantly lose bone mass in this period, in order to assure adequate levels of nutrients and phospho-calcic elements for fetal development. During pregnancy, compared to the status prior to it's onset, females present a reduction of about 8.1% of BMD. In this context, REMS offers the possibility of evaluating the rate of bone mass loss without any obstetrical risks (14).

REMS AND INFLAMMATORY RHEUMATIC DISEASES

When it comes to the usefulness of REMS in evaluating bone fragility in patients with inflammatory rheumatic diseases, medical literature is still at the beginning. However, an important study that included patients with rheumatoid arthritis (RA) demonstrated the higher risk of osteoporosis onset and the higher fracture risk in patients with a longer evolution of the rheumatic disease. BMD values where significantly lower in RA patients compared to the control group, without any inflammatory rheumatic disease (15). These results obtained with REMS are comparable with previous studies that evaluated RA patients using DXA scans and quantitative computed tomography (QCT) (16). Furthermore, numerous studies begin to recognize the usefulness of REMS in diagnosis and evolution of patients with osteoporosis. A study done on patients with acromegaly demonstrated a good correlation between DXA and REMS scan results and underlines the usefulness of the ultrasound method in closely evaluating evolution of osteoporosis in these types of patients (17).

REMS IN THE FUTURE

This novel diagnostic method for osteoporosis and bone fragility is still young. More studies are needed in the area of rheumatology are needed in order to prove the usefulness of REMS as an initial evaluation method and also as a screening procedure in patients at high risk of osteoporosis onset and with increased bone fragility. A new concept that should be considered is the fact that REMS could potentially more accurately evaluate BMD and bone fragility through the FS in patients with diseases from the spectrum of spondyloarthritides (especially those with ankylosing spondylitis and psoriatic arthritis). These pathologies are characterized, along other specific markers, by excessive bone formation with the apparition of osteosclerotic lesions and the presence of different types of excessive calcifications (syndesmophytes, entesophytes) (18,19).

CONCLUSIONS

REMS is a novel diagnostic method for osteoporosis and has a significant advantage compared to DXA in correctly assessing bone fragility. The method has been recently approved for use in Europe for the diagnosis and evaluation of patients with osteoporosis. Further research is required in order to fully characterize the usefulness of this method in patients with inflammatory rheumatic diseases, and determine the place of REMS in the schedule of evaluation for patients with such pathologies (7,8,18,19,20).

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