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The importance of bone mineral density and structure in fracture risk assessment of patients with rheumatoid arthritis and ankylosing spondylitis — perspectives

ABSTRACT

Osteoporosis is a metabolic bone disease that is associated with an increased risk of fractures. The increased risk of fractures in osteoporosis occurs both due to a decrease in bone mineral density (BMD) and bone microarchitecture impairment. Dual-energy X-ray absorptiometry (DXA) is the current gold standard in osteoporosis diagnosis. In a DXA scan, fracture risk is only assessed based on a BMD measurement. This is sufficient to estimate true fracture risk in the general population. Unfortunately, in rheumatic diseases, such as rheumatoid arthritis (RA) or ankylosing spondylitis (AS), BMD often increases. However, the incidence of fractures in RA/AS patients is higher than in the general population. Put together, it becomes obvious that a BMD measurement alone is not sufficient to estimate the risk of fractures in rheumatic diseases. The increase in fracture incidence is strongly associated with bone microarchitecture impairment, which is not evaluated in a standard DXA scan. Therefore, it is necessary to introduce other diagnostic methods. One such assessment is the trabecular bone score (TBS). TBS is a numerical method that can be used during a DXA scan. It allows for a fracture risk assessment in patients with rheumatic diseases, much more accurately than just a BMD measurement.

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INTRODUCTION

Osteoporosis is a relatively common metabolic bone disease that increases the risk of fractures. It is estimated that approximately 9 million osteoporotic fractures occur annually worldwide, which means that an osteoporotic fracture occurs approximately every three seconds [1]. In Europe alone, it is estimated that about 32 million people over the age of 50 suffer from osteoporosis, which is about 5.6% of the population at that age — in total it is about 25.5 million women (22.1% of the population) and 6.5 million men (6.6% of the population) [2].

Osteoporosis is a serious problem from both a social and a clinical point of view. Osteoporotic fractures and their sequelae have a significant impact on patients' lives. They are associated with limited physical activity, pain, and, consequently, a decrease in the quality of life.

The development of the disease is usually asymptomatic — early diagnosis is therefore extremely important, especially in patients with an increased risk of osteoporosis.

The current gold standard in osteoporosis diagnosis is a bone mineral density (BMD) measurement based on dual-energy X-ray absorptiometry (DXA). Unfortunately, de-

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spite DXA being the gold standard, this method of fracture risk assessment has some limitations.

It is important to remember that an increase in fracture risk is not only associated with a decrease in BMD. Bone microarchitecture impairment also has a real impact on the increased risk of bone fractures. The DXA scan assesses fracture risk based only on a decrease in BMD, which is sufficient in most cases. However, clinical practice shows that there are cases in which BMD values are high, e.g. type 2 diabetes or ankylosing spondylitis (AS), but bone microarchitecture is impaired, which in turn leads to an increased risk of fractures [3]. Degenerative changes in the lumbar spine may also result in a falsely increased BMD and thus an underestimated fracture risk [4]. Therefore, it is recommended to perform scans of both the lumbar spine and the femoral neck in people over 60 years of age in the general population.

In the case of rheumatic diseases, especially AS or rheumatoid arthritis (RA), the measurement of BMD is also often insufficient. In addition, diagnostics in RA/AS patients may be made more complicated by their relatively young age — the decrease in femoral neck BMD occurs later than in the lumbar spine due to differences in bone turnover rates [4].

Therefore, fracture risk assessment based on BMD is not always reliable in patients with RA and AS. This is a great challenge from a clinical perspective, as fractures occur more frequently in both diseases than in the general population [5, 6]. Osteoporotic fractures and the progression of each disease significantly increase the degree of physical disability in patients, which leads to both therapeutic problems and a decrease in the quality of life.

For this reason, other methods of fracture risk assessment are sought in the diagnosis of osteoporosis. Quantitative computed tomography (QCT) is one such method. QCT allows for a quick and very accurate assessment of bone density that excludes the cortical bone, where degenerative changes most often occur and which have the greatest impact on BMD measurements in a DXA scan. In case of degenerative changes, QCT may be a more sensitive method than DXA in the diagnosis of osteoporosis [7, 8]. However, QCT is currently not routinely used in osteoporosis diagnosis, which may be partly related to the very large role of computed tomography (CT) in routine clinical practice. Performing QCT scans would be an additional burden for radiology departments for this method to be widely used.

Therefore, another widely available method is needed to assess bone structure. The assessment of bone microarchitecture with the use of DXA may be such a method.

TRABECULAR BONE SCORE

The trabecular bone score (TBS) was initially used in CT scans, and only later was it adopted for DXA [9]. The TBS algorithm has been implemented into DXA in such a way as to not affect how the scan is performed and, most importantly, TBS can be measured retrospectively. From a clinical standpoint, this is very important as it does not extend the duration or modify the protocol of the scan. Thanks to this, it does not constitute an additional burden for densitometric laboratories, which is one of the disadvantages of QCT in the case of radiology departments.

In a DXA scan, the assessment of bone density is based on the Beer-Lambert law [10]. As a result, a three-dimensional (3D) object that is the bone, gets turned into a two-dimensional (2D) object during the BMD calculation. Therefore, the measurement is reported as areal bone density in g/cm^2.

In the case of TBS, there is also a transition from a 3D object into a 2D model. In TBS, the differences in grayscale between pixels that make up the bone image in DXA are assessed. The greater the grayscale differences between pixels, the lower the TBS value. In turn, this means a greater bone structure impairment and thus higher fracture risk. A detailed theoretical description of TBS was presented by Pothuaud et al. in 2008 [10].

In the case of BMD, a T-score of –2.5 is the cut-off point below which osteoporosis can be diagnosed — a high risk of fractures. The cut-off value is based on empirical research. An estimated 30% of postmenopausal women have a T-score of less than or equal to –2.5, which roughly corresponds to a lifetime fracture risk [11].

In the case of TBS, there is currently no established cut-off point. It is assumed that a TBS ≤ 1.200 means a strongly impaired bone structure, which may result in a higher risk of fractures [12]. It is worth noting here that TBS has no units — it is a dimensionless quantity. This is because the TBS measurement itself is actually a numerical method and not an actual physical measurement as is the case with BMD.

TBS assessment is currently associated with several significant limitations. The first is the body mass index (BMI). Currently, it is assumed that a patient's BMI should be in the range of 15–37 kg/m^2 for an accurate TBS. Outside of this range, TBS is prone to greater

measurement error, which is directly related to the absorption of radiation by soft tissues. In addition, the TBS index is so far recommended only in the case of Caucasian patients, as further research is needed for other ethnic groups [13]. This limitation is related to differences in bone tissue microarchitecture.

In addition, there may be significant differences in the assessment of TBS between DXA devices from different manufacturers [13]. These differences may result from both differences in scanner resolution and methods of measurement. Finally, it is also worth noting that older DXA devices that use the so-called pencil beam cannot be used to measure TBS.

For the reasons mentioned above, there are no official guidelines for the use of TBS in fracture risk assessment. One of the largest societies dealing with osteoporosis diagnosis — the International Society of Clinical Densitometry (ISCD) — indicated in its latest guidelines from 2019 that a TBS measurement alone cannot be the basis for osteoporosis treatment [14]. However, it stated that TBS is associated with fracture risk in postmenopausal women, men over 50, and women with type 2 diabetes [14].

Results from the Manitoba Registry study show how important TBS may be in the future of fracture risk assessments [15]. The study retrospectively analyzed DXA scans of 47736 women and 4348 men aged at least 40, taken in 1999–2011. The analysis showed that in the case of diseases such as RA, AS, type 2 diabetes or patients treated with glucocorticosteroids (GCs), the incidence of osteoporotic fractures is higher than in the general population, despite high BMD values [15]. However, despite the high BMD measurements, TBS values were low, which reflected fracture risk much better.

IMPORTANCE OF TBS IN RHEUMATIC DISEASES

Patients with rheumatic diseases have a higher risk of osteoporotic fractures than people from the general population [5, 6]. This stems from several factors, primarily the use of GC treatments, reduced physical fitness as a result of underlying disease progression, which directly affects the risk of falls and thus increases fracture risk, or bone remodeling caused by the underlying condition.

As mentioned earlier, osteoporotic fractures in rheumatic patients are a serious problem. They worsen a patient's disability and complicate therapy.

The disease itself and the treatments used may increase BMD, therefore it is necessary to use other methods of fracture risk assessment.

Most studies examining the usefulness of TBS in rheumatic diseases indicate that in this group of patients, TBS reflects the actual risk of fractures much better than BMD alone [16].

An example of possible differences between BMD and TBS is presented in Figures 1 and 2. They present the case of an AS patient who had already suffered an osteoporotic fracture.

In the case of AS, the importance of TBS in the diagnosis of osteoporosis is demonstrated by studies carried out by two independent research groups of Richards et al. and Żuchowski et al. [5, 17]. The studies included 188 and 67 AS patients, respectively. Both studies came to identical conclusions — TBS reflects the risk of osteoporotic fractures much better than the BMD score.

In addition, Żuchowski et al. also assessed the relative risk of fractures in the study group [5]. The presence of syndesmophytes and TBS values ≤ 1.310 were associated with a more than two-fold increase in the relative risk of fractures. It is worth noting that for the general population, it is assumed that only TBS values ≤ 1.200 are associated with a significant increase in fracture risk [12].

In turn, Choi et al. conducted a study on a large population of patients with RA [18]. 279 RA patients over 50 years of age were included in the study. In the study group, 34 (13%) patients had vertebral body fractures. No significant differences were observed in BMD scores between groups of patients with and without fractures. However, as was the case with AS studies mentioned earlier, significant differences in TBS results were found. They were lower in the group of patients with fractures.

The authors of the study also drew attention to the fact that RA patients constitute one of the largest groups of patients for whom GCs are a standard treatment [18]. Glucocorticoid treatment changes the structure of the cortical bone and the trabecular bone, where significant bone structure impairment occurs [18]. This is why TBS may be a much more sensitive method for assessing fracture risk than BMD. Especially given the fact that the biggest degenerative changes occur in the cortical bone, which further increases the BMD score and thus masks the real fracture risk.

SUMMARY

TBS is an extremely useful tool in assessing the risk of fractures in patients with rheumatic diseases. This is related to an increase in BMD due to the rheumatic disease itself and the treatment used.

At the moment, the greatest limitation in the use of TBS is the lack of strict recommendations regarding diagnosis and treatment, but it can be expected that this situation will change in the coming years.

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AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST

None.

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