TBS ADDED-VALUE IN CLINICAL CARE PATHWAYS

MM-PS-136-MIG-EN-01

SUMMARY OF THE DISEASES

WOMEN'S HEALTH		MEN'S' HEALTH		METABOLIC/CARDIOLOGY
Primary Osteoporosis	✓	Primary Osteoporosis	✓	
Secondary Osteoporosis	✓	Secondary Osteoporosis	✓	✓ (DIABETES)
Gynecology	✓			
Osteoarthritis	✓	Osteoarthritis	✓	
Sports	✓	Sports	✓	
Orthopedics	✓	Orthopedics	✓	

1- PRIMARY OSTEOPOROSIS

Osteoporosis is a common bone disease characterized by low bone mass and altered bone microarchitecture, resulting in decreased bone strength with an increased risk of fractures. The diagnosis of osteoporosis, currently based on bone mineral density (BMD) which considers only the density of the bone, doesn't provide a measure of bone microarchitecture. It is well known that over 50% of fractures occur in patients with BMD values that do not fall within the osteoporotic range, which can be explained by microarchitecture defects that were not detected by the BMD alone.

Trabecular bone score (TBS) is a texture parameter related to bone microarchitecture that provides skeletal information that is not captured from the standard BMD measurement. TBS is lower in men and postmenopausal women with prevalent vertebral, hip or major osteoporotic fractures compared to controls. The use of TBS in conjunction with BMD and Clinical risk factors (CRFs) improves the fracture risk assessment and prediction. TBS can be used as an adjustment parameter of the FRAX tool to better predict osteoporotic fractures in conjunction with other clinical risk factors. Added to the FRAX, the TBS's greatest utility lies in individuals whose BMD levels are close to an intervention threshold (up to 25% of the patients will then be impacted).

Since the different treatments have differential effect on both BMD and TBS, the combination of bone density and bone microarchitecture may help to select the most appropriate treatment for a given risk profile.

TBS has been endorsed by many local, national and international medical societies and guidelines[1–6].

2- SECONDARY OSTEOPOROSIS

Secondary osteoporosis is caused by certain medical conditions or treatments that cause alterations of bone strength, involving bone mass and mostly bone microarchitecture deterioration and resulting in bone fragility and fracture. Since BMD only measures bone mass, providing no information on bone microarchitecture, which is also adversely affected in Secondary Osteoporosis, it cannot be a stand-alone risk factor for making management decisions on these patients. TBS is an important aid in the diagnosis of secondary osteoporosis, and ultimately in the assessment of fracture risk. In some situations, like glucocorticoid-induced osteoporosis and in diabetes mellitus, the TBS appears to out-perform BMD[7]. Diseases of interest are the following:

2.1 DIABETES

Diabetic patients with poor glycemic control present an elevated risk of fracture but paradoxically their BMD is higher than in healthy patients.

Poor glycemic control has been associated with degraded microarchitecture (and therefore low TBS) and high fracture risk, while diabetes patients with good glycemic control show preserved microarchitecture and low risk of fracture. TBS is an excellent predictor of fracture risk, better than the BMD[8] in diabetic patients.

The added value of TBS in patients with Diabetes is to better estimate the fracture risk, hence improving the osteoporosis management (and, since it is related to glycemic control, also the diabetes management). As such TBS has been included the guidelines for the management the Osteoporosis and the Diabetes[1,9].

2.2 HYPERPARATHYROIDISM

Primary hyperparathyroidism (PHPT) is a common endocrinopathy often accompanied by bone fragility and elevated risk of fracture which is not fully captured by the BMD. In PHPT patients, TBS shows a partially degraded microarchitecture- including those that are predominantly asymptomatic with mild disease. TBS helps to identify the PHPT patients that are under a risk of fracture to improve the osteoporosis management as such it has been included in the guidelines for the management of Osteoporosis and PHPT[1,10].

2.3 GLUCOCORTICOIDS

Glucocorticoids (GCs) are therapeutically used to suppress various allergic, inflammatory and autoimmune disorders and it is one of the most common secondary causes of osteoporosis. GCs treatment increases fracture risk, which is not entirely captured by the BMD. GCs-treated individuals have been found to have a significant deterioration of bone microarchitectural texture as assessed by TBS which is more marked in those with osteoporotic fractures. The added value of TBS in these patients is to predict fractures.

2.4 CHRONIC KIDNEY DISEASE (CKD)

Patients under advanced stages of CKD have an increased risk of fragility fractures due to the alterations of bone strength, involving bone mass and bone microarchitecture deterioration. As BMD only measures bone mass, providing no information on bone microarchitecture, which is also adversely affected in CKD, it cannot be a stand-alone risk factor for making management decisions on these patients. TBS has found to be lower in these patients and it was shown to be a good and independent predictor of fragility fractures in patients with CKD or who underwent kidney transplantation. The added value of TBS in CKD clinical practice is to be an assessor of bone microarchitecture and a fracture risk predictor.

2.5 HIV

With increased survival of HIV-infected patients, osteoporotic fractures have developed as a major cause of morbidity in these patients, which is not captured by the BMD. It has been shown that these patients had lower TBS which is associated with vertebral fractures. The added value of TBS in HIV patients is to predict fracture risk more accurately.

3- GYNECOLOGY

3.1 MENOPAUSAL HORMONE THERAPY

Menopausal hormone therapy (MHT) is the first-line therapy in the prevention of postmenopausal osteoporosis for the prevention of bone loss in at- risk women before age of 60 years. MHT has been shown to be associated with bone microarchitecture preservation, as assessed by TBS. The added value of TBS in these patients is to improve the management of the Osteoporosis as it allows measuring the effect on bone microarchitecture.

3.2 BREAST CANCER

Breast cancer patients treated with aromatase inhibitors are known to have an increased risk of fracture. These patients present a decrease in TBS independently of BMD. The combination of FRAX®, TBS, and BMD maximizes the identification of patients with risk fracture. The added value of TBS in breast cancer patients is to enhance the detection of patients under risk of fracture.

4- OSTEOARTHRITIS

Unlike BMD, TBS results has been demonstrated to be minimally affected by the presence of osteophytes – a common artifact in late postmenopausal patients and those presenting with osteoarthritis. As such BMD would be falsely elevated leading to miss diagnosis unlike TBS which would provide a more accurate fracture risk assessment.

5- SPORTS

TBS helps to monitor bone health in athletes undergoing different types of sports. A pilot study has demonstrated that TBS could predict stress fractures in elite sports players. Moreover, TBS has been shown to be very low in anorexic patients.

6- ORTHOPEDICS

Patients TBS has been related with different parameters of bone strength and bone quality. Bone microarchitecture is related to the mechanical strength of bone and hence its greater or lesser risk of fracture. Indeed, for the same quantity of bone, different mechanically resistant bone structures may exist. The added value of TBS in Orthopedics is to assess bone quality. There are several ongoing studies which show promising results TBS on X-ray technology.

SELECTED REFERENCES

There are 500 peer reviewed publications on TBS. We have selected few but would be happy to share more upon request.

1. Silva, B. C. *et al.* Fracture Risk Prediction by Non-BMD DXA Measures: the 2015 ISCD Official Positions Part 2: Trabecular Bone Score. *J Clin Densitom* **18**, 309–330 (2015).
2. Harvey, N. C. *et al.* Trabecular bone score (TBS) as a new complementary approach for osteoporosis evaluation in clinical practice. *Bone* **78**, 216–224 (2015).
3. Kanis, J. A., Cooper, C., Rizzoli, R., Reginster, J.-Y. & the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF). Executive summary of European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Aging Clin Exp Res* (2019). doi:10.1007/s40520-018-1109-4
4. Briot, K. *et al.* Actualisation 2018 des recommandations françaises du traitement de l'ostéoporose post-ménopausique. *Revue du Rhumatisme* (2018). doi:https://doi.org/doi:10.1016/j.rhum.2018.02.005
5. Pfeilschifter, J. [Diagnosing osteoporosis: what is new in the 2014 DVO guideline?]. *Dtsch. Med. Wochenschr.* **140**, 1667–1671 (2015).
6. Naranjo Hernández, A. *et al.* Recomendaciones de la Sociedad Española de Reumatología sobre osteoporosis. *Reumatología Clínica* (2018). doi:10.1016/j.reuma.2018.09.004
7. Ulivieri, F. M. *et al.* Utility of the trabecular bone score (TBS) in secondary osteoporosis. *Endocrine* **47**, 435–448 (2014).
8. Chen, F.-P., Kuo, S.-F., Lin, Y.-C., Fan, C.-M. & Chen, J.-F. Status of bone strength and factors associated with vertebral fracture in postmenopausal women with type 2 diabetes. *Menopause* **Publish Ahead of Print**, (2018).
9. Ferrari, S. L. *et al.* Diagnosis and management of bone fragility in diabetes: an emerging challenge. *Osteoporos Int* 1–12 (2018). doi:10.1007/s00198-018-4650-2
10. Bilezikian, J. P. *et al.* Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the Fourth International Workshop. *J. Clin. Endocrinol. Metab.* **99**, 3561–3569 (2014).