Integrate Trabecular Bone Score (TBS) directly into patients’ FRAX score and enhance osteoporosis management outcomes

Introduction

In the last several years more than 70 peer reviewed publications have assessed the value of using TBS as an independent predictor of fracture and as an adjunct to bone mineral density (BMD) and clinical risk factors. This large volume of published research and clinical interest has led the Sheffield University FRAX™ Group to explore TBS interaction with FRAX in order to provide a new model for the use of TBS in a clinical environment.

Based on the analysis of the published data and on a large population-based meta-analysis study, the FRAX Group concluded that TBS significantly and consistently predicts vertebral and non-vertebral fracture, in both men and women, independent of BMD, clinical risk factors as well as FRAX. They also concluded that TBS can be used in conjunction with FRAX to adjust risk assessment and help improve the prediction of risk of fracture and risk of death.

Based on a retrospective analysis of 33,352 patients, the FRAX Group developed a model that uses the TBS score to modify the FRAX 10-year fracture probability of hip fracture and major osteoporotic fracture. This new FRAX adjustment model now makes it very easy to use and integrate TBS in a clinical environment. The clinicians’ workflow remains unchanged as the TBS score is obtained with very limited additional input into the FRAX score sheet.

FRAX adjusted for TBS now assists healthcare professionals as the predictability of fracture increases and individual patient management can be significantly fine-tuned.

As reviewed in this paper, FRAX adjusted for TBS allows a physician to:

- Integrate TBS easily into daily clinical practice
- Enhance fracture predictability using FRAX
- Refine individual fracture risk assessment
- Tighten selection of patients in need of therapeutic treatment.

Calculating the FRAX adjusted for TBS

As of the 15th of April 2015, FRAX Adjusted for TBS can be calculated on the Sheffield FRAX calculation tool website (https://www.shef.ac.uk/FRAX/tool.jsp). Within several months this capability should be available directly on the TBS iNsight™ software using the FRAX score obtained on the compatible DXA operating system software.

Once the FRAX questionnaire is filled in with the bone mineral density (BMD) results – the FRAX risk is calculated. At this point, an icon/button underneath the FRAX results box is available and allows the user to enter the patient’s spine TBS value (requires TBS values obtained from TBS iNsight Version 2.1 or above). The resulting output is the 10 year FRAX predictability adjusted for TBS.
Development of the FRAX adjusted for TBS model

The integration of TBS as an adjustment parameter into FRAX risk assessment was based on a model that took the following into account:

- Hip BMD-FRAX, TBS and age;
- Retrospective analysis of the prospective cohort of Manitoba, Canada, analyzing 33,352 women and men aged 40 to 99, with a mean follow-up of 4.7 years.
- Cross-validation in an individual level population-based meta-analysis – gathering 17,809 women and men from 14 international prospective cohorts, with a mean follow-up of 6.7 years.

The meta-analysis included the following cohorts:

- CaMoS: Canadian Multicentre Osteoporosis Study
- FORMEN: Fujiwara-Kyo Osteoporosis risk in men
- GOS: Geelong Osteoporosis Study
- JPOS: Japanese Population-based Osteoporosis
- MrOS HK: Mr OS Hong-Kong
- MsOS HK: Ms OS Hong-Kong
- MrOS SW: Mr OS Sweden
- OFELY: Os des Femmes de Lyon
- OPUS: Osteoporosis and Ultrasound Study
- RSI & RSIi: Rotterdam study I & II
- SEMOF: Swiss Evaluation of the Methods of Measurement of Osteoporotic Fracture Risk
- SOS: Salt Osteoporosis Study
- STRAMBO: Structure of Aging Men’s Bones

FRAX Adjusted for TBS: Clinical Application

In both their conception and cross-validation studies, the FRAX Group evaluated the gradients of risk of incident osteoporotic fractures for each fracture risk parameter alone, as well as in the FRAX Adjusted for TBS model. These studies aimed at finding the best approach to integrate TBS as an independent fracture risk parameter into physician daily practice. The outcome of FRAX Group study is therefore to use TBS as an adjustment parameter of FRAX scores.

FRAX Adjusted for TBS allows a physician to better refine individual fracture risk assessment, reclassify patients’ risk for future fracture near the intervention threshold and improve the identification of patients that need to start therapeutic treatment for the first time.

FRAX Adjusted for TBS has the following clinical consequences:

- Contributes to the potential shift from one side to the other of the cut-off value for treatment indication (from non-therapy to therapy group and vice-versa – see next section for further details);
- Has a stronger contributing effect in patients whose initial FRAX probabilities are around borders of intervention thresholds;
- Also has a stronger contributing effect in the assessment of major osteoporotic fracture than the contribution to hip Fracture;
- A strong contributing effect in younger adults than the contribution to older adults.

Requirements to obtain FRAX Adjusted for TBS:

- FRAX Calculation with Hip-BMD
- TBS Value calculated with TBS iNsight version 2.1 minimum
- Patient with a BMI within 15 to 37 kg/m²
**TBS Contributing Effects**

Since 2008, WHO FRAX is widely used to assess patient risk for fracture at 10 years\(^5\). It provides, for each patient, a risk for major osteoporotic fractures (MOF) and hip fractures. Based on FRAX evaluated risks, numerous countries have worked on the elaboration of appropriate intervention thresholds (IT) and edited their own local clinical guidelines to define protocols for treatment / non-treatment. Different guidelines strategies have been adopted, for example:

- Fixed thresholds as proposed in USA by the NOF (ex: 10-year probability MOF FRAX score ≥20 %)\(^6\);
- Multiple risk categories as proposed in Canada (Low: 10-year probability MOF FRAX score <10 %, Moderate: 10-year probability MOF FRAX score within 10-20 % or High: 10-year probability MOF FRAX score >20 %)\(^7\);
- Age-dependent thresholds as proposed in the United Kingdom by the NOGG\(^8\).

FRAX adjusted for TBS has two main contributing clinical effects: one in the “Maximum Impact Area” - near the IT and the other in the area outside of the IT. Indeed, adding TBS in the FRAX equation delineates an area within which the highest clinical contribution of TBS can be observed. This area - referred to as the TBS “Maximal Impact Area” is shown in figures 1 and 2.

Essentially, a patient with a FRAX score higher than the IT could be treated depending on specific country guidelines.

When a patient’s FRAX score is close to the IT, either just above (ex: 10-year probability MOF FRAX score of 22 % at 70 of age) or just below (ex: a 10-year probability MOF FRAX score of 19 % at 70 of age), the physician would be able to refine the risk profile of the patient using TBS.

FRAX Adjusted for TBS could be used by the physician to either confirm the established treatment category or determine if a patient should be switched from the “no treatment zone” to the “treatment zone” and vice versa;

- At 70 years, 10-year probability MOF FRAX score = 19 % \(\rightarrow\) MOF FRAX Adjusted for TBS = 21 % with a low TBS of 1.170; switch from “no treatment zone” to “treatment zone”
- At 70 years, 10-year probability MOF FRAX score = 22 % \(\rightarrow\) MOF FRAX Adjusted for TBS = 19.3 % with a high TBS of 1.361; switch from “treatment zone” to “no treatment zone”
- At 70 years, 10-year probability MOF FRAX score = 21 % \(\rightarrow\) MOF FRAX Adjusted for TBS = 22.8 % with a low TBS of 1.181; confirmation of established treatment category.

For patients that are distanced from the IT area, TBS helps to refine both the original 10-year probability MOF and HIP FRAX scores:

- 10-year probability MOF FRAX score = 3.6 % \(\rightarrow\) MOF FRAX Adjusted for TBS = 2.4 %; confirmation of established treatment category.

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**Figure 1:** This illustration of FRAX Adjusted for TBS is based on age-dependant intervention threshold, specifically from the National Osteoporosis Guideline Group (NOGG). Visit the NOGG page on Sheffield website for further information: [http://www.shef.ac.uk/NOGG/index.html](http://www.shef.ac.uk/NOGG/index.html)
The TBS clinical contribution can also be observed using fixed thresholds, such as the ones established by the NOF in the United States of America. The TBS “Maximal Impact Area” is highlighted in color on Figure 2 (red and green areas).

**Figure 2**: This illustration of FRAX Adjusted for TBS is based on the fixed intervention threshold (NOF FRAX Score = 20%), specifically from the National Osteoporosis Foundation (NOF). Visit the NOF page for further information: [https://my.nof.org/](https://my.nof.org/)

**Figure 1 & 2 Observations:**

In the TBS “Maximal Impact Area” one would observe the most significant individual clinical benefit in terms of risk re-categorization as patients would potentially shift from one side of the IT to the other as a function of TBS value. Indeed, based on FRAX Adjusted for TBS and on the corresponding risk evaluation, the patient eligibility for treatment will be reclassified.

- **Figure 1:**
  - Patients initially situated in the “green zone” would either shift from non-therapy to the therapy group, based on a low TBS value or conversely be assigned a decreased fracture risk based on a high TBS value.
  - Patients initially situated in the “red zone” would either shift from therapy to the non-therapy group, based on their high TBS score or conversely be assigned an increased risk of fracture based on a low TBS value.

- **Figure 2:**
  - Patients initially situated in the “green zone” would shift from the therapy group to the non-therapy group.
  - Patients initially situated in the “red zone” would shift from the non-therapy group to the therapy group.

On the overall population, FRAX Adjusted for TBS will increase fracture predictability, accuracy and help fine tune individual risk assessment.
Clinical Case

The following two clinical case studies review the TBS clinical contribution when added into the FRAX risk assessment model.

Clinical Case - "Patient A":

Medical Decision:

Based on the NOGG intervention threshold by age-group, the initial FRAX risk for Patient A was situated under the intervention threshold. Considering the FRAX Adjusted for TBS, a treatment might now be required.

TBS highlights an increased risk of fracture for Patient A and a shift from non-therapy to therapy group.
Clinical Case - "Patient B".

**Medical Decision**: Based on the NOGG intervention threshold by age-group, the initial FRAX risk for Patient B was situated above the intervention threshold. Considering the FRAX Adjusted for TBS, a treatment might no longer be required.

TBS highlights a decreased risk of fracture for Patient B and a shift from therapy to non-therapy group.
**Conclusion:**

As a bone texture analysis index, TBS brings a new dimension to overall fracture risk assessment and is increasingly being used for patient management in daily practice. The extensive and increasing amount of published data highlights the contribution that TBS makes in identifying patients at high risk of fracture that are not identified by standard bone assessment techniques. In addition TBS has been demonstrated to be independent of BMD, clinical risk factors, and FRAX.

TBS as an adjustment parameter of FRAX enables physicians to benefit from a more accurate evaluation of fracture risk with no change in the existing workflow.

Using FRAX Adjusted for TBS allows physicians to
- Integrate TBS easily in daily clinical practice
- Enhance fracture predictability using FRAX
- Refine individual fracture risk assessment
- Tighten selection of patients in need of therapeutic treatment.

To learn more about TBS iNsight:
- **How TBS iNsight works:**
  - Please review the white paper entitled: “Advanced DXA Using TBS iNsight™: A New Bone Structure Assessment Technique Enhances Identification of Fracture Risk”;
- **TBS contribution in patient fracture risk evaluation:**
  - Please review the white paper entitled: “TBS iNsight™: A Useful Tool to Potentially Reconsider Patient Fracture Risk”.

**References:**

1. Trabecular bone score: a noninvasive analytical method based upon the DXA image, B.C. Silva et al., J Bone Miner Res., 2014
2. Trabecular bone score (TBS) as a new complementary approach for osteoporosis evaluation in clinical practice, N.C. Harvey et al., Bone, 2015
3. A meta-analysis of trabecular bone score in fracture risk prediction and its interaction with FRAX, J. A. Kanis, Oral presentation, WCO-IOF-ESCEO 2015, Milan
4. Adjust fracture probability by Trabecular Bone Score, E.V. McCloskey et al., CTI, 2015
5. Assessment of osteoporosis at the primary health care level. WHO Collaborating Centre for Metabolic Bone Diseases, University of Sheffield, 2007
7. Fracture risk Assessment, Clinical Guidelines Sidset, Osteoporosis Canada, 2010
8. Guideline for the diagnosis and management of osteoporosis, NOGG, 2014