ОЦІНКА МІКРОАРХІТЕКТУРИ ХРЕБТА ЗА ДОПОМОГОЮ TBS ДОПОМАГАЄ РОЗРІЗНИТИ ПАЦІЄНТІВ З ОСНОВНИМИ ОСТЕОПОРОТИЧНИМИ ПЕРЕЛОМАМИ ТА КОНТРОЛЬНУ ГРУПУ ЗАЛЕЖНО ТА НЕЗАЛЕЖНО ВІД МЩКТ: СХІДНОЄВРОПЕЙСЬКЕ ДОСЛІДЖЕННЯ TBS

EVALUATING SPINE MICRO-ARCHITECTURAL TEXTURE (VIA TBS) DISCRIMINATES MAJOR OSTEOPOROTIC FRACTURES FROM CONTROLS BOTH AS WELL AS AND INDEPENDENT OF SITE MATCHED BMD: THE EASTERN EUROPEAN TBS STUDY

Introduction

Osteoporosis is a common bone disease leading to increased bone fragility and escalated fracture risk. Osteoporosis is characterized by low bone mass, but also by alterations in bone microarchitecture. In routine daily clinical practice, the gold standard for osteoporosis assessment is the evaluation of areal Bone Mineral Density (aBMD), via dual-energy X-ray absorptiometry (DXA). Traditionally, aBMD has been considered the major determinant of bone strength and fracture risk [1]. However, it has been shown that: (1) aBMD is insufficient at determining bone strength [2, 3]; (2) aBMD is insufficient at predicting fractures [4, 5]; and (3) aBMD is inadequate at assessing response to drug therapy [6]. Other parameters play a key role in bone strength, such as bone microstructure [7, 8]. Until recently, assessing bone microstructure was not feasible in routine clinical practice.

Trabecular bone score (TBS) is a grey-level texture parameter which can be applied to DXA imag-
es. TBS quantifies spatial variations of local grey level values into the 2D projected image [9, 10]. TBS is derived from the experimental variogram [9, 10]. It correlates with standard 3D bone microarchitecture parameters such as connectivity density, trabecular number, and negatively with trabecular separation [9, 10]. Recently [12], it has been shown that TBS is also related to bone strength. More precisely, in this study, authors have shown that TBS was correlated with SMI (r = –0.62, p = 0.01) as well as bone stiffness (r = 0.64, p = 0.007), independently of the bone mass. TBS is an indirect evaluation of the trabecular bone structure but also to the bone strength. Previous studies have demonstrated the added clinical value of TBS [13–20]. It has been shown that: (1) TBS is able to discriminate subjects with fractures from subjects without fractures, matched for age, BMD or both, even after adjusting for BMI [13–17]; and (2) TBS can predict major osteoporotic fractures as well as BMD, independent of it [18–20]. Nevertheless, daily clinical implications regarding the use of TBS are not clearly defined.

We conducted the current study to validate the ability of TBS to detect all osteoporotic fracture types in an Eastern European cohort. In this study, we focused on the clinical added values of TBS in combination with the BMD in term of sensitivity, specificity, accuracy but also considering the reclassification induced by the use of TBS and on the number of subject needed to diagnose.

**Materials and methods**

**Study subjects**

We conducted a retrospective, non-random, multicentre case-control study. Recruitment of female subjects was performed using the medical record database at six centres: The Railway Healthcare Institute of Belgrade (Serbia), the Rheumatology Clinic at the Medical University of Sofia (Bulgaria), the Institute for Treatment and Rehabilitation in Niska Banja (Serbia), the Department of Clinical Physiology and Pathology of Locomotor Apparatus, in Kiev (Ukraine) and the «C.I. Parhon» and Elias Hospital clinical facilities, Department of Endocrinology, Carol Davila University of Medicine and Pharmacy in Bucharest (Romania). During the observation period, between the six centres, 1762 women ages 30 and older were recruited.

To be included in the study, subjects had to be Caucasian, aged between 45 and 85 years, and have a body mass index (BMI) between 17 and 35 kg/cm². To be fully eligible as a case, the woman had to present with at least one low-energy fracture. All types of osteoporotic fracture were considered for this study (All OP). Conversely, controls could not have any evidence of any low-energy fracture at any bone site. Individuals were excluded if they (1) had undergone any spinal surgery; (2) had any evidence of inflammatory changes or arthrosis in the lumbar spine; or (3) had three or more non-observable lumbar vertebra; (4) have treatments affecting bone metabolism.

Areal bone density at lumbar spine levels L1–L4 (aBMD) was evaluated with Hologic Discovery and
GE Prodigy densitometers as per routine clinical practice. TBS was evaluated in the same regions of measurement as those used for aBMD, using the program TBS Insight® (V1.9.2, Med-Imaps, France). aBMD and TBS were calculated as the mean values of the individual measurements for vertebrae L1–L4 after excluding any fractured and/or vertebrae with the presence of severe artrhosis. TBS then was assessed by the University of Lausanne (Switzerland) based on the anonymized DXA scan, blinded to all clinical parameters and outcomes.

Centres were cross-calibrated for TBS using a custom-made phantom (Med-Imaps, France) which exhibits five different TBS values. This calibration phantom is also composed of a soft tissue kit which mimics a mean thickness of 17 cm and fat content of 25%. After TBS calibration, differences between Prodigy and Hologic devices represents an absolute value of 0.028. A standardization on aBMD values (saBMD) has been done using conversions equations for GE-Lunar Prodigy and Hologic Apex systems proposed by Fan et al. [21]. All BMD values have been standardized to GE-Lunar Prodigy systems using the following equation:

\[ \text{saBMD at } L1–L4 = \frac{\text{GE-Lunar Prodigy}}{1.140 \times \text{Hologic} + 0.037}. \]

After standardization, difference in term of saBMD between Prodigy and Hologic devices represents an absolute value of 0.026 g/cm².

This study was conducted in accordance with the current version of the Declaration of Helsinki and under the laws and regulations enforced by the Department of Health. Each subject enrolled into the study was ensured anonymity.

**Statistical analysis**

All statistical analyses were performed using MedCalc software (v12.3.0, http://www.medcalc.be). Inter-group differences were identified by means of the parametric Student’s T test or the non-parametric Wilcoxon’s signed-ranks test, depending on the normality of parameter distribution. Pearson’s correlation analysis was used to assess correlations between the various studied parameters. Univariate and multivariate logistic regression models (with backward variable entry) were used to investigate possible correlations between independent variables (age, weight, height, BMI, aBMD and TBS) and fracture status. The detection value for each parameter was further evaluated both by odds ratios (OR) — expressed for each decrease of one standard deviation — and by determining the receiving operator curve (ROC) and area under the ROC (AUC); for both these estimates, OR and AUC, 95% confidence intervals were calculated. Differences between AUC were detected by means of pair-wise comparisons. Any p value < 0.05 was considered statistically significant. The additional clinical values of aBMD and TBS were analyzed via a classification tree approach. This classification tree was formulated within a two-step process, starting with aBMD T-score classification followed by Discovery and GE Prodigy for the z-value run-time method. TBS oцинювали на тому ж рівні, що й МЩКТ, за допомогою програми TBS Insight (v1.9.2, Med-IMAPS, Франція). Після виключення будь-яких переломів і/або ознак наявності серйозного артрозу хребта розраховувалися середні значення, окрім для показників МЩКТ і TBS на рівні хребців L1–L4. В Університеті Лозанни (Швейцарія) на основі анонімного ДРА-сканування із заспіллюванням усіх клінічних параметрів та даних проводили оцінку TBS. Центри були перехресно відкалибровані щодо отриманих результатів TBS за допомогою спеціально створеного фантому (Med-IMAPS, Франція), що показує п’ять різних значень TBS. Цей калібрувальний зразок складається також із комплекту імітаційних жічих тканин середньою товщиною 17 см із вмістом жиру 25%. Після калібрування відмінність між пристроями Prodigy і Hologic за TBS становила в абсолютному значенні 0,028. Стандартизаційне значення МЩКТ хребта для систем GE-Lunar Prodigy і Hologic Apex було проведено за допомогою рівняння конвертації Fan et al. [21]. Всі значення МЩКТ хребта були стандартизовані для системи GE-Lunar Prodigy з використанням наступного рівняння:

Стандартизовано МЩКТ (L1–L4) = \text{GE-Lunar Prodigy} = \frac{1.140 \times \text{Hologic} + 0.037}{1.140 \times \text{Hologic} + 0.037}. 

Після стандартизації відмінності показників стандартизованої МЩКТ хребта між пристроями Prodigy і HOLOGIC становили абсолютною величину 0,026 г/см². Це дослідження було проведено відповідно до чинної версії Гельсінської декларації та відповідно до законодавства і норм Департаменту охорони здоров'я. Кожному суб’єкту, включеному в дослідження, було забезпечено анонімність.

**Статистичний аналіз**

Усі статистичні аналізи проводилися з використанням програмного забезпечення MedCalc (v12.3.0, http://www.medcalc.be). Міжгрупові відмінності визначалися за допомогою параметричного Т-критерію Стьюдента або непараметричного критерію Вілкоксон на залежно від закономірності розподілу показників. Для оцінки кореляції між різними показниками, що вивчалися, використовували кореляційний аналіз Пірсона. Для виявлення можливих кореляцій між незалежними показниками (вік, маса тіла, зріст, ІМТ, МЩКТ і TBS) та статусом перелому використовувався однонаправлений критерій Вілкоксон. Для оцінки значень кожного параметра оцінювали за показником відношення шансів (OR, odds ratio), що відображає кількість зниження на одне стандартне відхилення, обчислювали ROC-криву й площу під нею (AUC); для обох цих показників, OR і AUC, були розраховані 95% довірчі інтервали. Відмінності між AUC виявляли за допомогою парних порівнянь. Будь-яке значення ρ < 0.05 вважалося статистично значущим. За допомогою методу дерев класифікації аналізувалися додаткові клінічні значення МЩКТ і TBS. Дерева класифікації були сформовані дворівнево-
TBS tertile classification. The added clinical value of the tree classification approach was evaluated considering an aBMD T-score of \(-2.5\) and first TBS tertile (lowest TBS values) thresholds, in terms of the sensitivity, specificity and accuracy of fracture detection. The added clinical value performance of the combined model was compared against the clinical performance of using an aBMD T-score of \(-2.5\) and the lowest TBS tertile, each alone. Classification improvement of the combined model was assessed by calculating the Net Reclassification Index (NRI) [22]. Finally, the number of subjects needed to diagnose was evaluated as the inverse value of the Youden’s index [23].

**Results**

**Description of the study group**

Out of the 1762 potentially-eligible Caucasian women recruited, 271 women were deemed eligible as cases, exhibiting at least one osteoporosis-related fracture; meanwhile, 760 women without fractures were deemed eligible as controls. Sites of osteoporotic fracture were the hip (7.7%), spine (41.3%), humerus (13.3%) and forearm (42.1%). Subjects with and without fractures were no different in mean weight (p > 0.3) and BMI (p > 0.1); but women with fractures were older (p < 0.001) and shorter (p < 0.001) as presented Table 1. In addition, both saBMD and TBS were significantly lower in subjects with a fracture (p < 0.001).

Significant weak to moderate correlations were observed between TBS and subject height (r = 0.08, p < 0.005), age (r = \(-0.34\), p < 0.001) and saBMD (r = 0.47, p < 0.001), whereas no correlations were evident between TBS and weight (r = 0.05, p = 0.13) or BMI (r = \(-0.09\), p < 0.005).

**Association between sBMD, TBS, anthropometric data and the presence of the fracture**

Age, height, saBMD and TBS were associated with the presence of an osteoporotic fracture (Table 2). After adjusting for age, saBMD and TBS remained significant (p < 0.001), with an OR per SD of 1.74 [1.48–2.04] and 1.52 [1.29–1.78], respectively.

Combined saBMD and TBS model (Model 1, see Table 2) improved fracture detection by 35–43% compared to the individual models. The added clinical value of the TBS classification was evaluated considering an aBMD T-score of \(-2.5\) and first TBS tertile (lowest TBS values) thresholds, in terms of the sensitivity, specificity and accuracy of fracture detection. The added clinical value performance of the combined model was compared against the clinical performance of using an aBMD T-score of \(-2.5\) and the lowest TBS tertile, each alone. Classification improvement of the combined model was assessed by calculating the Net Reclassification Index (NRI) [22]. Finally, the number of subjects needed to diagnose was evaluated as the inverse value of the Youden’s index [23].
pared to saBMD or TBS alone as demonstrated by ORs (1.93 [1.67–2.23] vs. 1.50 [1.27–1.77] and 1.58 [1.32–1.78] respectively). The AUC of Model 1 was significantly higher than the AUC for saBMD (p < 0.01), whereas no significant difference was apparent for TBS (p > 0.05).

Using multivariate analysis, age, saBMD and TBS cofactors remained significant (p < 0.01) for osteoporotic fracture detection (Model 2). The combined Model 2 significantly improved osteoporotic fracture detection (OR = 2.20 [1.89–2.55]) relative to each parameter used alone or relative to the Model 1, as shown by significant differences (p < 0.001) between their AUCs (Table 2; Fig. 1).

Clinical added value of TBS combined with saBMD: sensitivity, specificity, accuracy, NRI and NDD

In terms of clinical usability (two-step classification tree), the TBS tertile thresholds obtained in this study were 1.155 and 1.252 for the lowest and highest tertiles, respectively. An saBMD T-score of −2.5 and first (lowest) TBS tertile thresholds were similar in terms of

<table>
<thead>
<tr>
<th>Модель / Model</th>
<th>OR [95% ДI] / OR [95% CI]</th>
<th>AUC [95% ДI] / AUC [95% CI]</th>
<th>AUC (p) / AUC (p)</th>
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<tr>
<td>Однофакторна / Univariate</td>
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<tr>
<td>Вік / Age</td>
<td>1.88 [1.62–2.18]***</td>
<td>0.674 [0.645–0.703]***</td>
<td>ns, b</td>
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<tr>
<td>Маса тіла / Weight</td>
<td>1.07 [1.05–1.09] ns</td>
<td>0.506 [0.475–0.537] ns</td>
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</tr>
<tr>
<td>Зріст / Height</td>
<td>1.26 [1.1–1.45]***</td>
<td>0.568 [0.538–0.599]***</td>
<td>a, b</td>
</tr>
<tr>
<td>IMT / BMI</td>
<td>1.14 [0.99–1.31] ns</td>
<td>0.533 [0.502–0.564] ns</td>
<td>a, b</td>
</tr>
<tr>
<td>Стандартизована МЩКТ / saBMD</td>
<td>1.87 [1.59–2.2]***</td>
<td>0.646 [0.616–0.675]***</td>
<td>a, b</td>
</tr>
<tr>
<td>TBS / TBS</td>
<td>1.79 [1.54–2.08]***</td>
<td>0.663 [0.633–0.692]***</td>
<td>ns, b</td>
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<td>Багатофакторна з поправкою на вік / Multivariate age adjustment</td>
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<tr>
<td>Зріст / Height</td>
<td>1.02 [0.87–1.19] ns</td>
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<tr>
<td>Стандартизована МЩКТ / saBMD</td>
<td>1.74 [1.48–2.04]***</td>
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<tr>
<td>Багатофакторна зі стандартизованою МЩКТ та TBS / Multivariate with saBMD and TBS</td>
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<tr>
<td>Модель 1 / Model 1</td>
<td>1.93 [1.67–2.23]***</td>
<td>0.681 [0.652–0.710]***</td>
<td>b</td>
</tr>
<tr>
<td>Стандартизована МЩКТ / saBMD</td>
<td>1.50 [1.27–1.77]***</td>
<td></td>
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<tr>
<td>TBS / TBS</td>
<td>1.58 [1.32–1.87]***</td>
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<td>Багатофакторна з віком, стандартизованою МЩКТ та TBS / Multivariate with age saBMD and TBS</td>
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<tr>
<td>Модель 2 / Model 2</td>
<td>2.20 [1.89–2.55]***</td>
<td>0.722 [0.693–0.749]***</td>
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<td>Вік / Age</td>
<td>1.68 [1.43–1.97]***</td>
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<tr>
<td>Стандартизована МЩКТ / saBMD</td>
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Примітки: відмінності між AUC багатофакторної моделі 1 та досліджуваними параметрами: a — p < 0.01, ns — p > 0.05; відмінності між AUC багатофакторної моделі 2 та досліджуваними параметрами: b — p < 0.001; *** — p < 0.0001, ** — p < 0.01, * — p < 0.05, ns — p > 0.05.

Difference between AUC of the multivariate model 1 and the tested parameters: a p < 0.01, ns p > 0.05
Difference between AUC of the multivariate model 2 and the tested parameters: b p < 0.001

*** p < 0.0001, ** p < 0.01, * p < 0.05, ns p > 0.05
of sensitivity (35 vs. 39%), specificity (78 vs. 80%) and accuracy (64 vs. 66%), as presented in Fig. 2. When combined (Fig. 2), a major improvements in sensitivity (+28 and +24%, respectively) and accuracy (+17 and +15%, respectively) were evident with somewhat less marked improvement noted for specificity (+9 and +7%) relative to isolated performance of the −2.5 aBMD T-score threshold and first TBS tertile threshold, respectively.

NRI of the combined model were +38 and +31% compared with saBMD and TBS alone respectively. NRI results indicate that, using the combined model, 38% of the overall subjects were reclassified correctly in addition to those already classified using the −2.5 T-score threshold. Among those subjects, additional subjects with fracture were detected and represent 21% of the overall subjects with fracture (57/271). Finally, the combined model decrease significantly the number of subjects needed to diagnose to reach 2 patients in comparison to 7.4 and 5.3 for saBMD and TBS, respectively.

Discussion

In this study, we investigated the capacity of the TBS to detect osteoporotic fractures within the context of a multicentre Eastern European cohort. As expected, TBS detected osteoporotic fractures as well as areal Bone Mineral Density of the lumbar spine, even after adjusting for age and/or TBS and saBMD (OR TBS = 1.27 [1.07–1.51] vs. OR saBMD = 1.59 of sensitivity (35 vs. 39%), specificity (78 vs. 80%) and accuracy (64 vs. 66%), as presented in Fig. 2. When combined (Fig. 2), a major improvements in sensitivity (+28 and +24%, respectively) and accuracy (+17 and +15%, respectively) were evident with somewhat less marked improvement noted for specificity (+9 and +7%) relative to isolated performance of the −2.5 aBMD T-score threshold and first TBS tertile threshold, respectively.

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![Figure 1. AUC comparison between the best model which includes age, aBMD and TBS and aBMD or TBS alone](image)

![Figure 2. Sensitivity, specificity, accuracy and NRI of the clinical added value of saBMD, TBS or saBMD and TBS combination (Combined Model) using saBMD –2.5 T-score threshold and TBS 1st tertile threshold for patient discrimination. As presented, the combined model improved significantly the sensitivity and the accuracy in comparison with saBMD (gains are express as an absolute value) or TBS alone. Whereas, a slight increase was observed on specificity](image)

![Figure 2. Sensitivity, specificity, accuracy and NRI of the clinical added value of saBMD, TBS or saBMD and TBS combination (Combined Model) using saBMD –2.5 T-score threshold and TBS 1st tertile threshold for patient discrimination. As presented, the combined model improved significantly the sensitivity and the accuracy in comparison with saBMD (gains are express as an absolute value) or TBS alone. Whereas, a slight increase was observed on specificity](image)
The observed added detection value of TBS over saBMD and/or age, in terms of fracture detection. Furthermore, the combination of age, saBMD and TBS significantly improved osteoporotic fracture detection, as demonstrated by significant differences between the AUC of the combined model and those for each of the three parameters used alone (p < 0.01).

Previously published cross-sectional studies [13–17] have shown that TBS is significantly lower in those with a fracture, even after adjusting for age and/or BMD and/or BMI [13–17]. In particular, in [15], the investigators evaluated TBS detection capability within the OsteoLaus cohort, a population-based survey involving 631 women between 50 and 80 years old. In this study, the age-and BMI-adjusted ORs for all osteoporotic fracture detection were 1.3 [1.1–1.6] and 1.4 [1.1–1.7] for spine BMD and spine TBS, respectively. More recently, Leib et al. [17] evaluated TBS discrimination-ability in a large US population of non-Hispanic Caucasian women. This study, which dealt with all types of osteoporotic fracture, involved 305 subjects (mean age 59.7±8.3 years) with fractures and 1877 (mean age 57.4±7.3 years) controls. The ORs were 1.24 [1.10–1.41] and 1.36 [1.21–1.53] for TBS and BMD, respectively. After adjusting for spine BMD and several clinical risk factors, the value of TBS remained significant, with an OR of 1.18 [1.02–1.35]. Finally, two prospective studies have shown that TBS predicts osteoporotic fractures as well as BMD, and independently from it, with an OR of 1.17 [1.09–1.25] after adjusting for spine BMD and major clinical risk factors [18], and an OR of 1.34 [1.04–1.73] after adjusting for age and prevalent fracture [19]. Results obtained in our study corroborate those previously obtained results. Similar and homogeneous ORs per standard deviation decrease were obtained for TBS in our study after adjusting for age and spine BMD and/or other clinical risk factors [13–20]. This consistency in OR suggests that TBS discrimination performance is partially independent of the study protocol, other common parameters taken into account for osteoporosis diagnosis, and the type of DXA device used.

Combining TBS and saBMD in a model (Model 1) improved fracture detection, since the OR of Model 1 was 1.93 [1.67–2.23]. When an additional age adjustment was performed (Model 2), the OR for Model 2, which incorporated age (p < 0.0001), aBMD (p < 0.001) and TBS (p < 0.01), ultimately reached 2.20 [1.89–2.55]. In both Model 1 and 2, the improvement in fracture detection was significant, when compared against saBMD alone, as demonstrated by significant differences between their AUCs (p < 0.001). The observed added detection value of TBS over spine BMD was in agreement with results obtained in [1.33–1.89]. The correlation between saBMD and TBS was moderate (r = 0.44), explaining 19.4% of its variance. This correlation level is similar (r = 0.44 vs. 0.2 < r < 0.6) to levels observed in studies performed using the Hologic and GE device series. Even though the correlation between saBMD and TBS was moderate in strength, TBS exhibited a significant added value over saBMD and/or age, in terms of fracture detection.
In this earlier prospective study, which involved 29407 Canadian women, fracture prediction improved when spine BMD and TBS were combined, relative to fracture prediction with BMD or TBS used alone (p < 0.0001). Furthermore, for Model 2, the significant improvement was also apparent versus the AUC of TBS and age used alone (p < 0.001 and p < 0.001, respectively). From a clinical point of view, combining saBMD and TBS makes sense, since aBMD evaluates bone quantity whereas TBS assesses bone microarchitectural texture status [9–11], both of which contribute to bone strength [3, 4, 7, 12]. Previous studies have yielded two major conclusions about TBS: (1) any correlation between spine BMD and TBS is weak to moderate (from 0.1 to 0.6, depending on the study [13–20]); and (2) TBS performs as well as spine BMD at detecting osteoporotic fractures [1420]. Consequently, we can argue that using TBS permits us to detect different individuals at risk for fracture than BMD. To illustrate this last statement, we used a two-step classification tree (WHO stratification coupled with TBS tertile stratification) and evaluated this combination, in terms of fracture detection. In this study, sensitivity, specificity and accuracy of aBMD (with a –2.5 T-score threshold) and TBS (with a first/lowest tertile threshold) were comparable (38 vs. 43%, 76 vs. 78%, and 62 vs. 66% for sensitivity, specificity and accuracy, respectively).

However, when the –2.5 aBMD T-score and first TBS tertile were used together, sensitivity largely improved by 28% relative to the –2.5 aBMD T-score threshold to reach 65%. Accuracy and specificity also improved, by 18 and 10%, respectively. These results corroborate earlier findings [20]. In a previously-published, population-based Swiss study, sensitivities of 33.3 and 42.9% and specificities of 74.1 and 74.6% were observed for aBMD and TBS, respectively. When aBMD and TBS were combined, sensitivity rose to 59.5%, which is roughly the sensitivity we observed in the current study (65%). As for ORs, consistency in fracture detection was noted, in terms of both sensitivity and specificity, in these two studies, indicating the stability of TBS detection rates from one study to the next. Combination of TBS and aBMD induces and NRI of 38% in comparison with aBMD alone.

In addition, in this study we have evaluated the overall reclassification induced by the use of TBS in complement to the saBMD. 36% of the overall subjects were correctly reclassified as evaluated using the NRI. Among these subjects, a major part were subjects with fracture. We have also evaluated this gain in terms of number of subjects needed to diagnose (NND). The use of TBS decrease the NDD to 2. This is an important result since it has several implications in terms of patient screening as well as for the health care cost. This first results has been confirmed in other cohort and cost-effectiveness of the use of TBS have to be evaluated.

The current study is not without limitations. The most relevant is that it was a retrospective case-control study since it has several implications in terms of patient numbers needed to diagnose (NND). The use of TBS decrease the NDD to 2. This is an important result since it has several implications in terms of patient screening as well as for the health care cost. This first results has been confirmed in other cohort and cost-effectiveness of the use of TBS have to be evaluated.

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study. Hence, we cannot directly imply any causative association between low TBS values and osteoporotic fractures. However, in [18–20], TBS was demonstrated to predict osteoporotic fractures both as well as, and independent of BMD, validating the causative link between TBS and osteoporotic fracture incidence. The second major limitation directly concerns subject recruitment, as treatments and other diseases potentially impacting bone metabolism were not taken into account. Consequently, confounding effects upon TBS were not considered. Nevertheless, it has been shown that, although secondary causes of osteoporosis like hyperparathyroidism and rheumatoid arthritis negatively affect TBS (TBS values in these subjects are lower than in controls), subjects with fractures still exhibit lower TBS than subjects without fractures [24, 25]. Similar results have been obtained in glucocorticoid-treated subjects [26, 27].

In conclusion, the current study confirms previous data published on TBS concerning its discriminatory power for osteoporosis fracture detection. In a multicentre Eastern European cohort, we again have shown that combining TBS and BMD dramatically increases the sensitivity and overall accuracy of osteoporotic fracture detection, even after adjusting for age. The clinical added value of TBS permitted to decrease the number of subject needed to diagnose to 2 in this study. This result is very promising for both patient management and in term of cost for the health care system if confirmed.

Conflict of interest. R. Winzenrieth is a senior scientist at Med-Imaps, Didier Hans is co-owner of the TBS patent and has corresponding ownership share in Medimaps group. All the others did not have any conflicts of interest.

Дане дослідження не обійшлося без обмежень. Найбільш актуальним є те, що це було ретроспективне досягнення «випадок – контроль». Отже, ми не можемо передбачати прямий причинний зв’язок між низькими значеннями TBS і переломами, обумовленими остеопорозом. Однак у [18–20] було показано, що TBS передбачає переломи, обумовлені остеопорозом, самостійно й незалежно від МЩКТ, що підвищує причинно-наслідковий зв’язок між TBS і схильністю до остеопоротичних переломів. Друге важливе об’єднення безпосередньо стосується відбору пацієнтів, тому що в даному дослідженні не були взяти до уваги лікувальні процедури та інші захворювання, що потенційно впливають на кістковий метаболізм. Отже, ефект їх впливу на TBS не розглядався. Хоча вторинні причини остеопорозу, такі як гіперпаратиреоз і ревматоїдний артрит, негативно впливають на TBS (показники TBS у них осіб нижче ніж у контролю), було показано, що пацієнти з переломами мають значно низькі показники TBS, ніж особи без переломів [24, 25]. Аналогічні результати були отримані в пацієнтів, які приймають глукокортикоїди [26, 27]. І на завершення відзначимо, що дане дослідження підтверджує попередньо опубліковані результати щодо прогностичних можливостей TBS у визначення остеопоротичних переломів. У багатоцентральному досліді східноєвропейської когорти ми знову показали, що поєднання TBS і МЩКТ різко підвищує чутливість і загальну точність виявлення остеопоротичних переломів, навіть після поправки на вік. У цьому дослідженні додаткове використання TBS дозволило знизити кількість осіб, які потребують додаткової діagnostики, до 2. Цей результат є дуже перспективним як для лікування пацієнтів, так і у разі підтвердження, для зменшення витрат системи охорони здоров’я.

Список літератури / References

ОЦЕНКА МИКРОАРХИТЕКТУРЫ ХРЕБТА ЗА ДОПОМОГОЮ TBS ДОПОМАГАЕТ РОЗРИЗНИТИ ПАЦІЄНТІВ З ОСНОВНИМИ ОСТЕОПОРОТИЧНИМІ ХРЕБЕТНИМИ ТА КОНТРОЛЬНУ ГРУПУ ЗАЛЕЖНО ТА НЕЗАЛЕЖНО ВІД МЩКТ: СКІДЮЄВРОПЕЙСЬКІ ДОСЛІДЖЕННЯ TBS

Резюме. Метою дослідження була оцінка клінічної ефективності моделі, що поєднує показники мінеральної щільності кістечки (МЩКТ) і мікроархітектури (TBS) кісткової тканини хребта, що виявляється остеопоротичних переломах. Скіднюєвропейські багатоцентрові дослідження (OFELY, MINOS) в 2010-2011 роках у 26-27 штучних системах охорони здоров'я, необхідно провести додаткові економічні дослідження.

Оцінка мікроархітектури хребта за допомогою TBS допомагає розрізняти пацієнтів з основними остеопоротичними переломами та контрольну групу залежно та незалежно від МЩКТ: Скіднюєвропейські дослідження TBS
Evaluating spine micro-architectural texture (via TBS) discriminates major osteoporotic fractures from controls both as well as and independent of site matched BMD: the Eastern European TBS study

Summary. The aim of the study was to assess the clinical performance of the model combining areal bone mineral density (aBMD) at spine and microarchitectural texture (TBS) for the detection of the osteoporotic fracture. The Eastern European Study is a multicenter study (Serbia, Bulgaria, Romania and Ukraine) evaluating the role of TBS in routine clinical practice as a complement to aBMD. All scans were acquired on Hologic Discovery and GE Prodigy densitometers in a routine clinical manner. The additional clinical values of aBMD and TBS were analyzed using a two steps classification tree approach (aBMD followed by TBS tertiles) for all type of osteoporotic fracture (All-OP Fx). Sensitivity, specificity and accuracy of fracture detection as well as the Net Reclassification Index (NRI) were calculated. This study involves 1031 women subjects aged 45 and older recruited in east European countries. Clinical centers were cross-calibrated in terms of BMD and TBS. As expected, areal BMD (aBMD) at spine and TBS were only moderately correlated ($r^2 = 0.19$). Prevalence rate for All-OP Fx was 26%. Subjects with fracture have significant lower TBS and aBMD than subjects without fracture ($p < 0.01$). TBS remains associated with the fracture even after adjustment for age and aBMD with an OR of 1.27 [1.07–1.51]. When using aBMD T-score of $-2.5$ and the lowest TBS tertile thresholds, both BMD and TBS were similar in terms of sensitivity (35 vs. 39%), specificity (78 vs. 80%) and accuracy (64 vs. 66%). aBMD and TBS combination, induced a significant improvement in sensitivity (+28%) and accuracy (+17%) compared to aBMD alone whereas a moderate improvement was observed in terms of specificity (+9%). The overall combination gain was 36% as expressed using the NRI. aBMD and TBS combination decrease significantly the number of subjects needed to diagnose from 7 for aBMD alone to 2. In a multicentre Eastern European cohort, we have shown that the use of TBS in addition to the aBMD permit to reclassified correctly more than one-third of the overall subjects. Furthermore, the number of subjects needed to diagnose fell to 2 subjects. Economical studies have to be performed to evaluate the gain induced by the use of TBS for the healthcare system.

Key words: Osteoporotic fracture, Bone mineral density, Trabecular bone score (TBS), Bone microarchitecture.