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ORIGINAL ARTICLE

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Trabecular bone score: a useful clinical tool for the evaluation of skeletal health in women of short stature

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Abstract

Purpose Areal bone mineral density (aBMD) by DXA is underestimated in those with smaller bones and overestimated in those with larger bones. Trabecular bone score (TBS) predicts fracture risk, and is not influenced by bone size. The aim of this study was to evaluate TBS and BMD in women with short stature.

Methods We retrospectively analyzed DXA scans of all women aged 50–90 years with short stature (<144 cm) obtained in a single center, from 2006 to 2016. The comparison group comprised women >161 cm in height, matched for age and LS BMD, selected from the same database.

Results The study population included 342 women. The two groups were similar in age, and aBMD at the LS and total hip. Femoral neck aBMD was lower in cases than in taller women. In contrast, TBS was higher in women with short stature than in their taller counterparts (1.347 ± 0.102 vs. 1.250 ± 0.110; $p < 0.001$). Bone mineral apparent density (BMAD) and the LS TBS-adjusted BMD T-score were also significantly higher in shorter than in taller women. From the entire cohort, 121 women (67 cases) were osteoporotic by aBMD determinations. Among these subjects, TBS was also greater in cases (1.303 ± 0.103) than in women with standard height (1.190 ± 0.099; $p < 0.001$). Despite being considered osteoporotic, 36% of short women, but none of the taller ones, had a normal TBS.

Conclusions TBS can be a useful adjunct to aBMD for assessing bone quality in short women, in whom aBMD measurement tends to read lower, and, thus could overestimate fracture risk.

Keywords Trabecular bone score · DXA · Short stature · Fracture risk · Osteoporosis

Introduction

Low bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) is a strong predictor of fracture risk, and in addition to serving as a diagnostic criterion, a BMD T-score ≤ −2.5 is a widely accepted threshold for pharmacological intervention in osteoporosis [1, 2]. Despite being widely used for the assessment of fracture risk in clinical medicine, the measurement of BMD by DXA has disadvantages. It cannot assess other skeletal indices, such as the rate of bone turnover, bone microarchitecture, and microdamage, all of which are importantly related to bone strength [3]. Another disadvantage of DXA is that it is a

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2-dimensional imaging technology that measures areal BMD (aBMD; g/cm^2) rather than true volumetric BMD (vBMD; g/cm^3). Therefore, aBMD could underestimate true BMD in those with smaller bones and overestimate true BMD in those with larger bones [4, 5].

Recent data have shown that short women, despite having a greater prevalence of osteoporosis by self-report, had a lower risk of any incident fracture than taller women over a mean follow-up period of 8.4 years [6]. These discordant observations suggest that aBMD overestimates fracture risk in short individuals. With this in mind, additional diagnostic tools that are not influenced by body size might be more accurate and help to justify therapeutic decisions in short individuals.

The Trabecular Bone Score (TBS) assesses skeletal texture from lumbar spine (LS) DXA images [7, 8]. Many clinical studies have demonstrated that TBS predicts osteoporotic fracture risk independent of DXA BMD and clinical risk factors in postmenopausal women and older men [9–15]. Relevant to the subject of this report, previous data have suggested that TBS is not influenced by bone size [16, 17].

To this end, we assessed BMD by DXA and TBS in a group of women >50 years with short stature compared with an age- and BMD-matched control group. The study was predicated on the hypothesis that TBS in short women would demonstrate metrics that are better than those that would be expected, on the basis of the aBMD determination.

Materials and methods

Study population

In this retrospective study, we analyzed DXA scans of all women aged 50–90 years with short stature (<144 cm (<4′9″) in height) obtained in a single reference center, as part of their routine clinical care, between 2006 and 2016. The comparison group comprised women >161 cm (>5′3″) in height (standard-stature group), matched for age and LS BMD with cases, selected from the same database. The height cutoffs were based on the Z-score of height, defined by the World Health Organization (WHO) growth standard curves and anthropometric data of a population survey by the Brazilian Institute of Geography and Statistics [18, 19]. In the WHO female chart of height, the 144 cm corresponds to −3.0 standard deviations (SD) of the mean, at the age of 19, the age at which the final height (adulthood) is reached. The 161-cm cutoff point represents the median height of Brazilian women of 19 years old.

We excluded patients with a body mass index (BMI) outside of the range 15–37 kg/m^2, those with artifacts at the LS that precluded image analyses and women with a BMD Z-score ≤ −2.0 at any skeletal site. The study was approved by the Institutional Review Board of Mater Dei Hospital, Belo Horizonte, Brazil.

Measurements of BMD and TBS

Areal BMD of three skeletal sites (LS, femoral neck, and total hip) was measured by DXA (GE Lunar Prodigy, GE Healthcare, Boston, USA; software Encore v. 9.3). The lowest aBMD T-score among the three sites measured was used to diagnose osteoporosis or osteopenia, according to the WHO criteria. As previously described [4], bone mineral apparent density (BMAD) of the LS, an estimate of volumetric bone density (g/cm^3), was calculated using the formula BMAD = BMD/square root of BA (where BA = bone area). Site-matched TBS data were retrospectively extracted from LS DXA images (GE-Lunar Prodigy Advance) using the TBS iNsight software (TBS iNsight, MedImaps, Switzerland v. 2.1). TBS was calculated based on pixel gray-level variations of the LS DXA images as the slope at the origin of the log–log transform of the experimental variogram [7]. TBS was classified as normal (≥1.350), partially degraded (1.200–1.350) or fully degraded (<1.200), as previously proposed [8]. In addition, TBS was used to calculate the TBS-adjusted aBMD T-score, an offset adjustment to the aBMD T-score, recently proposed as a single metric that takes into account both the density and the quality of bone [20]. In short, TBS (mean-centered and age-normalized), a multiplicative interaction term with age (mean-centered), and BMD T-score at the LS, total hip, or femoral neck were used to estimate the TBS-adjusted BMD T-score at each skeletal site [20].

Statistical analysis

Descriptive data are expressed as mean ± SD, median (25th–75th percentile), or *n* (%). The normality of the distribution of each variable was assessed by the Kolmogorov–Smirnov test. Between-group differences in means for normally distributed continuous variables were analyzed using the *t*-test. For skewed variables, differences of medians between short and standard-stature groups were analyzed using the Mann–Whitney test. Categorical variables were compared by the chi-squared test. The correlation between BA and TBS was assessed by the Pearson correlation test. Statistical tests were performed at the two-sided 0.05 level of significance. All statistical analyses were performed using the Statistic Package for the Social Sciences (Version 20, SPSS Inc., Chicago, IL, USA).

Results

This report consists of 171 women with short stature (cases) and 171 women with standard height. Baseline

Table 1 Anthropometric and densitometric characteristics (mean + SD)

Characteristics	Short stature ($n = 171$)	Standard stature ($n = 171$)
Age (years)	69.8 ± 8.6	69.7 ± 8.5
Weight (kg)	54.7 ± 8.4**	71.3 ± 11.8
Height (cm)[a]	142.0 (140.5; 143.0)**	164.0 (162.5; 166.0)
BMI (kg/m^2)	27.4 ± 4.2*	26.3 ± 4.2
LS TBS (unitless)	1.347 ± 0.102**	1.250 ± 0.110
LS aBMD (g/cm^2)[a]	0.973 (0.880; 1.090)	0.974 (0.880; 1.090)
T-score[a]	−1.7 (−2.5; −0.7)	−1.7 (−2.5; −0.8)
Z-score[a]	−0.1 (−0.9; 0.8)	−0.1 (−1.0; 0.8)
LS TBS-adjusted T-score	−1.2 ± 1.6*	−1.8 ± 1.7
LS BMC (g)	38.82 ± 10.52**	48.50 ± 13.92
LS area (cm^2)	39.15 ± 7.46**	48.52 ± 9.39
LS BMAD (g/cm^3)	0.160 ± 0.028**	0.144 ± 0.024
TH aBMD (g/cm^2)	0.850 ± 0.127	0.856 ± 0.124
T-score	−1.3 ± 1.0	−1.2 ± 1.0
Z-score	0.2 ± 0.9	0.2 ± 0.9
TH TBS-adjusted T-score	−1.1 ± 1.1	−1.3 ± 1.1
TH BMC (g)	25.86 ± 3.99*	24.33 ± 4.45
TH area (cm^2)	28.72 ± 2.73**	30.32 ± 2.72
TH BMAD (g/cm^3)	0.159 ± 0.025	0.155 ± 0.023
FN aBMD (g/cm^2)	0.789 ± 0.115*	0.829 ± 0.117
T-score	−1.8 ± 0.8*	−1.5 ± 0.9
Z-score	−0.1 ± 0.8*	0.1 ± 0.8
FN TBS-adjusted T-score	−1.6 ± 0.9	−1.6 ± 1.0
FN BMC (g)	3.83 ± 0.64*	3.63 ± 0.65
FN area (cm^2)	4.56 ± 0.61*	4.76 ± 0.49
FN BMAD (g/cm^3)	0.371 ± 0.061	0.381 ± 0.058

BMI body mass index, *aBMD* areal bone mineral density, *BMC* bone mineral content, *BMAD* bone mineral apparent density, *TBS* trabecular bone score *LS* lumbar spine, *TH* total hip, *FN* femoral neck

*$p < 0.05$; **$p < 0.001$ vs. subjects with standard stature

[a]Data are expressed as median (25th and 75th percentiles) and the difference between groups assessed by the Mann–Whitney test

characteristics are shown in Table 1. The two groups were well matched by age, LS BMD, and LS BMD T-score. As expected, compared with standard-stature women, cases were shorter, weighed less, and tended to have a slightly greater BMI. BMD data of total hip and femoral neck were not available in 5 (3%) subjects in the case group and in 12 (7%) in the standard-stature group.

TBS and aBMD by DXA

Mean LS TBS, and aBMD, aBMD T-scores, BA, bone mineral content (BMC), and BMAD of the LS, total hip, and femoral neck are shown in Table 1. Despite similar or lower aBMD values in cases, TBS measurements were greater in women with short stature than in their taller counterparts. Accordingly, women with short stature had a significantly lower proportion of fully degraded and partially degraded TBS than taller women (Fig. 1). TBS was low (<1.200) in only 12 (7%) cases, whereas a fully degraded TBS was seen in 53 (31%) women with standard stature. A normal TBS (TBS > 1.350) was observed in 89 (52%) cases, but in only 36 (21%) subjects in the standard-stature group (Fig. 1). The two groups were well matched by LS aBMD, and the prevalence of osteoporosis and osteopenia, as determined by DXA, was similar between the groups. However, aBMD and T-score at the femoral neck were lower in short stature than in taller women. Similar to the TBS results, and despite the comparable values of LS aBMD between the groups, LS BMAD was significantly higher in the group of women with short stature than in the standard-stature group (Table 1). BMAD at the hip sites was similar between the groups. There was no correlation between BA at the spine and TBS ($r = -0.061$; $p = 0.262$).

TBS-adjusted BMD T-scores

TBS-adjusted BMD T-scores of the LS, total hip, and femoral neck are shown in Table 1. LS TBS-adjusted T-score was significantly higher in short women than in their taller counterparts. Femoral neck T-score was lower in cases than in women with standard height, but this difference was no longer observed after the adjustment of the femoral neck T-score by TBS. Following the adjustment of T-score by TBS, in the group of cases, the prevalence of osteoporosis fell from 39 to 34%, whereas in the group of standard stature, the frequency of osteoporosis increased from 32 to 45%.

TBS and aBMD by DXA in osteoporotic patients

As shown in Table 2, when evaluating only subjects with osteoporosis, defined by an aBMD T-score ≤ −2.5 at any skeletal site, the two groups were similar in age, T-score at the LS, and aBMD and T-score at the total hip. The aBMD at the LS was slightly greater in cases, whereas femoral neck aBMD and T-score were higher in the standard-stature group. In this group of osteoporotic subjects, TBS was much greater in cases than in women with standard height, as was the LS BMAD. In agreement, despite being considered osteoporotic by aBMD, 35% ($n = 24$) of women with short stature had a normal TBS, while none of the taller individuals displayed a normal TBS value (Fig. 2).

Discussion

This is the first study examining trabecular architecture by TBS in postmenopausal women with short stature. Despite having similar LS BMD by DXA, women with reduced height have greater TBS than their taller counterparts. The prevalence of osteoporosis was higher by aBMD in shorter women than in the taller women. In contrast, the TBS analysis shows greater rates of normal or only partially

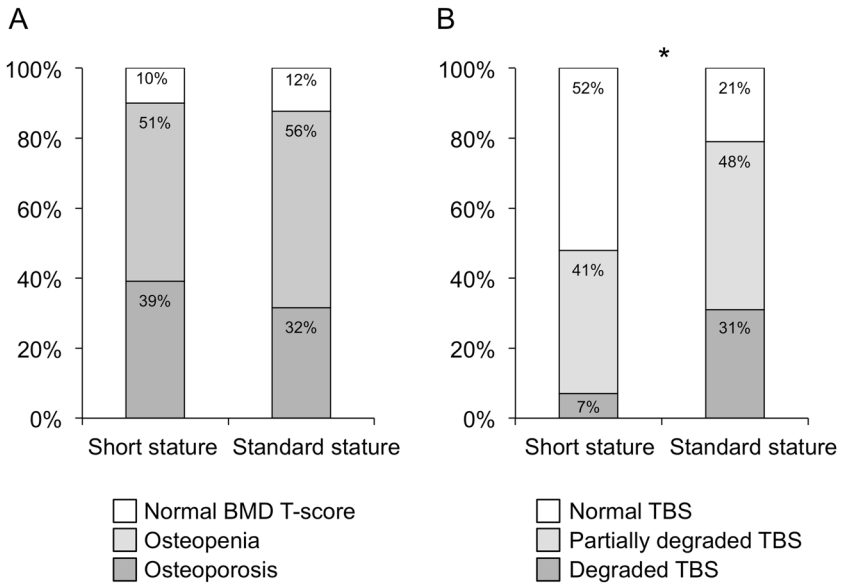

Fig. 1 Prevalence of **a** normal aBMD, osteopenia, and osteoporosis; and **b** normal, partially degraded, and fully degraded TBS in cases and standard-stature women in the entire study population. Asterisk represents significant differences of the frequency of normal, partially degraded and fully degraded TBS between the short-stature and the standard-stature groups ($p < 0.001$)

Table 2 Anthropometric and densitometric characteristics in osteoporotic subjects (mean + SD)

Characteristics	Short stature ($n = 67$)	Standard stature ($n = 54$)
Age (years)	72.7 ± 8.0	71.6 ± 8.0
Weight (kg)	52.4 ± 7.7**	66.6 ± 11.3
Height (cm)[a]	142.0 (140.0; 142.0)**	164.0 (163.0; 166.0)
BMI (kg/m^2)	26.3 ± 3.9*	24.6 ± 4.2
LS TBS (unitless)	1.303 ± 0.103**	1.190 ± 0.099
LS aBMD (g/cm^2)[a]	0.859 (0.810; 0.940)*	0.832 (0.790; 0.870)
T-score[a]	−2.7 (−3.2; −2.0)	−2.9 (−3.3; −2.6)
Z-score[a]	−1.0 (−1.6; −0.6)*	−1.3 (−1.6; −0.9)
LS BMC (g)	33.44 ± 7.76*	37.81 ± 7.93
LS BMAD (g/cm^3)	0.145 ± 0.026**	0.126 ± 0.018
TH aBMD (g/cm^2)	0.764 ± 0.109	0.762 ± 0.097
T-score	−1.9 ± 0.9	−2.0 ± 0.8
Z-score	−0.3 ± 0.9	−0.4 ± 0.7
FN aBMD (g/cm^2)	0.705 ± 0.091*	0.754 ± 0.101
T-score	−2.4 ± 0.7*	−2.0 ± 0.7
Z-score	−0.5 ± 0.7	−0.3 ± 0.7

BMI body mass index, *aBMD* areal bone mineral density, *BMC*: bone mineral content, *BMAD* bone mineral apparent density, *TBS* trabecular bone score, *LS* lumbar spine, *TH* total hip, *FN* femoral neck/

*$p < 0.05$; **$p < 0.001$ vs. subjects with standard stature

[a]Data are expressed as median (25th and 75th percentiles) and the difference between groups assessed by the Mann–Whitney test

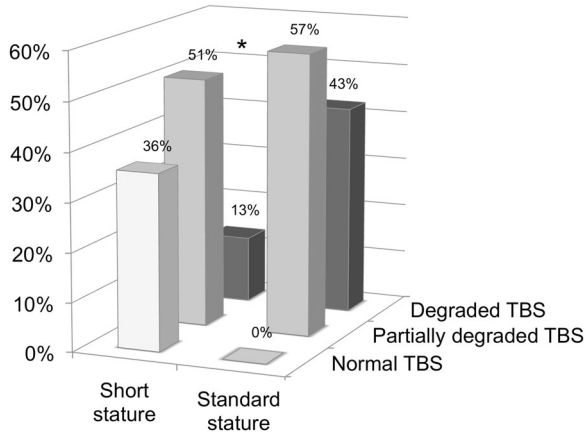

Fig. 2 Prevalence of degraded, partially degraded, and normal TBS in osteoporotic subjects. Asterisk represents significant differences of the frequency of normal, partially degraded, and fully degraded TBS between the short-stature and the standard-stature groups ($p < 0.001$)

degraded microarchitecture in patients with short stature, while a fully degraded microarchitecture was more prevalent in the taller women. Accordingly, the volumetric BMD estimated by BMAD and TBS-adjusted BMD T-scores were greater in women with short stature than in standard-stature women.

In agreement with these findings, it is known that patients with small bone sizes have a lower aBMD, but not necessarily inferior bone quality or greater fracture risk. In fact, while aBMD by DXA is underestimated in individuals with short stature, these subjects have, in fact, lower fracture risk than taller subjects. A recent study of ~800,000 postmenopausal women showed that, compared with taller women, a greater proportion of shorter women reported previous diagnosis of osteoporosis. In contrast, over 8.4 years of follow-up, the risk of any fracture increased by 21% for each 10-cm increase in height [6]. Femoral neck fractures were particularly increased in taller individuals, with a 48% greater risk for each 10-cm increase in height (RR 1.48; 99% CI 1.39–1.57). Increasing height was also associated with increased fracture risk of the forearm, humerus, patella, and ankle. Additional studies have

reported increased fracture risk in taller subjects [21–24]. Several mechanisms may explain this finding, including differences in cortical porosity, true vBMD, and impact forces after a fall [6, 21–24].

Similarly, Chinese Americans are shorter and exhibit lower aBMD by DXA than Caucasian women [25]. In contrast, they have a lower incidence of hip and forearm fractures than Caucasians [26, 27]. This paradox was resolved by studies using high-resolution peripheral quantitative computed tomography (HRpQCT) that demonstrated greater volumetric BMDs and better microarchitecture in Chinese women than in Caucasian subjects [28, 29]. In addition, despite having lower aBMD by DXA, Chinese women have similar TBS values than white controls [17]. Similarly, a recent study of patients with Down syndrome, who are known to have short stature, showed that despite having a lower BMD by DXA than normal controls, these patients with Down Syndrome have normal volumetric densities, as assessed by BMAD, and preserved bone architecture estimated by TBS [16]. These observations are in agreement with our findings that TBS is not influenced by bone size.

The evaluation of vBMD or bone microarchitecture by quantitative computed tomography (QCT) or HRpQCT may be helpful in individuals with very short stature, in whom aBMD overestimates the fracture risk. However, these techniques are not clinically available. Alternatively, DXA-derived analyses, such as BMAD or TBS, are readily available and can reduce the confounding effect of bone size in the measurement of aBMD. BMAD estimates the true (volumetric) BMD, and appears to better correlate with direct measurements of bone volume and fracture risk than aBMD in subjects with short stature or in children [5, 30]. Confirming this point in this present study, BMAD was significantly higher in women with short stature than in the standard-stature group. In addition to the BMAD, TBS can be calculated from DXA images using dedicated software. Our data showed that TBS was not correlated to BA at the spine and it was greater in women with short stature than in those with normal height. Although both methods, BMAD and TBS, could correct for the size artifact inherent in aBMD, TBS has a greater applicability in clinical practice, since it can be used to adjust the FRAX probability of fracture.

The International Society for Clinical Densitometry does not support the use of TBS as a single measurement to determine treatment recommendations in clinical practice. Alternatively, TBS can be used in association with FRAX and BMD to adjust FRAX probability of fracture, guiding treatment decisions [15, 31]. In this work, we could not calculate TBS-adjusted FRAX probabilities of fracture, because clinical data were not available. Instead, we calculated TBS-adjusted BMD T-scores, as recently proposed by Leslie et al. [20], whose results showed that the TBS-adjusted BMD T-score outperformed the unadjusted BMD T-score for prediction of hip and major osteoporotic fractures. We found a significantly greater TBS-adjusted T-score at the LS in short women than in the taller group.

Our work has limitations. As a convenience sample, the study design did not allow us to obtain subjects' clinical data, such as the etiology of short stature, previous fractures, known metabolic bone diseases, or use of medications that could have affected bone mass and/or microarchitecture. However, the comparison group was drawn from the same population, and was matched with cases by age and BMD, generating balanced groups, and minimizing the potential for selection bias. In addition, in order to avoid the inclusion of patients with severe bone diseases and/or secondary forms of osteoporosis, we excluded individuals with a BMD *Z*-score lower than −2.0. Vertebral fracture assessment (VFA) by DXA is rarely ordered in clinical practice in our country, so that the information regarding morphometric vertebral fracture as assessed by VFA was not available. Since clinical data and vertebral imaging were not available, we could not correlate TBS and BMD with fracture risk. Finally, HRpQCT is also not available in our study center.

This study, however, has important strengths. This is the first study to assess aBMD, BMAD, and TBS in a large number of patients with reduced height. TBS has proven to be a good predictor of fracture risk in various prospective studies [9–15]. Since this measurement is widely available in clinical practice, the results of this work may be useful to assist clinicians in treatment decisions in subjects with short stature.

Our results can be summarized succinctly. Despite having similar or lower BMD by DXA, TBS is greater in women with short stature than in their taller counterparts. BMAD, an estimate of volumetric BMD, and TBS-adjusted BMD T-score, were also greater in patients with reduced height. These findings suggest that TBS may be a useful adjunct to aBMD for assessing bone quality in short women. As previously proposed [31], TBS can be used to adjust the FRAX probability of fracture, or alternatively, it may be used to adjust the BMD T-score in countries where FRAX is unavailable. This approach could help in making therapeutic decisions among women of short stature, whose aBMD measurement tends to read lower, and thus, could overestimate fracture risk.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Statement This work was partially supported by the *Foundation for Research Support of the State of Minas Gerais*—FAPEMIG (to PPMA and MMSS). This study consisted of review of medical records, and involved no more than minimal risks to subjects. The Institutional Review Board approved the protocol. All procedures performed in this study were in accordance with the ethical standards

of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

References

1. P.M. Camacho, S.M. Petak, N. Binkley, B.L. Clarke, S.T. Harris, D.L. Hurley, M. Kleerekoper, E.M. Lewiecki, P.D. Miller, H.S. Narula, R. Pessah-Pollack, V. Tangpricha, S.J. Wimalawansa, N. B. Watts, American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2016. Endocr. Pract. **22**(Suppl 4), 1–42 (2016). https://doi.org/10.4158/EP161435.GL
2. O. Johnell, J.A. Kanis, An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos. Int. **17**(12), 1726–1733 (2006). https://doi.org/10.1007/s00198-006-0172-4
3. M.L. Bouxsein, Bone quality: where do we go from here? Osteoporos. Int. **14**(Suppl 5), S118–S127 (2003). https://doi.org/10.1007/s00198-003-1489-x
4. D.R. Carter, M.L. Bouxsein, R. Marcus, New approaches for interpreting projected bone densitometry data. J. Bone Miner. Res. **7**(2), 137–145 (1992). https://doi.org/10.1002/jbmr.5650070204
5. L.K. Bachrach, R. Marcus, S.M. Ott, A.L. Rosenbloom, O. Vasconez, V. Martinez, A.L. Martinez, R.G. Rosenfeld, J. Guevara-Aguirre, Bone mineral, histomorphometry, and body composition in adults with growth hormone receptor deficiency. J. Bone Miner. Res. **13**(3), 415–421 (1998). https://doi.org/10.1359/jbmr.1998.13.3.415
6. M.E. Armstrong, O. Kirichek, B.J. Cairns, J. Green, G.K. Reeves; Valerie Beral for the Million Women Study, C., Relationship of height to site-specific fracture risk in postmenopausal women. J. Bone Miner. Res. **31**(4), 725–731 (2016). https://doi.org/10.1002/jbmr.2742
7. D. Hans, N. Barthe, S. Boutroy, L. Pothuaud, R. Winzenrieth, M. A. Krieg, Correlations between trabecular bone score, measured using anteroposterior dual-energy X-ray absorptiometry acquisition, and 3-dimensional parameters of bone microarchitecture: an experimental study on human cadaver vertebrae. J. Clin. Densitom. **14**(3), 302–312 (2011). https://doi.org/10.1016/j.jocd.2011.05.005
8. B.C. Silva, W.D. Leslie, H. Resch, O. Lamy, O. Lesnyak, N. Binkley, E.V. McCloskey, J.A. Kanis, J.P. Bilezikian, Trabecular bone score: a noninvasive analytical method based upon the DXA image. J. Bone Miner. Res. **29**(3), 518–530 (2014)
9. S. Boutroy, D. Hans, E. Sornay-Rendu, N. Vilayphiou, R. Winzenrieth, R. Chapurlat, Trabecular bone score improves fracture risk prediction in non-osteoporotic women: the OFELY study. Osteoporos. Int. **24**(1), 77–85 (2013). https://doi.org/10.1007/s00198-012-2188-2
10. D. Hans, A.L. Goertzen, M.A. Krieg, W.D. Leslie, Bone microarchitecture assessed by TBS predicts osteoporotic fractures independent of bone density: the Manitoba study. J. Bone Miner. Res. **26**(11), 2762–2769 (2011). https://doi.org/10.1002/jbmr.499
11. M. Iki, Y. Fujita, J. Tamaki, K. Kouda, A. Yura, Y. Sato, J.S. Moon, R. Winzenrieth, N. Okamoto, N. Kurumatani, Trabecular bone score may improve FRAX(R) prediction accuracy for major osteoporotic fractures in elderly Japanese men: the Fujiwara-kyo Osteoporosis Risk in Men (FORMEN) Cohort Study. Osteoporos. Int. **26**(6), 1841–1848 (2015). https://doi.org/10.1007/s00198-015-3092-3
12. M. Iki, J. Tamaki, E. Kadowaki, Y. Sato, N. Dongmei, R. Winzenrieth, S. Kagamimori, Y. Kagawa, H. Yoneshima, Trabecular bone score (TBS) predicts vertebral fractures in Japanese women over 10 years independently of bone density and prevalent vertebral deformity: the Japanese Population-Based Osteoporosis (JPOS) cohort study. J. Bone Miner. Res. **29**(2), 399–407 (2014). https://doi.org/10.1002/jbmr.2048
13. W.D. Leslie, B. Aubry-Rozier, L.M. Lix, S.N. Morin, S.R. Majumdar, D. Hans, Spine bone texture assessed by trabecular bone score (TBS) predicts osteoporotic fractures in men: the Manitoba Bone Density Program. Bone **67**, 10–14 (2014). https://doi.org/10.1016/j.bone.2014.06.034
14. J.T. Schousboe, T. Vo, B.C. Taylor, P.M. Cawthon, A.V. Schwartz, D.C. Bauer, E.S. Orwoll, N.E. Lane, E. Barrett-Connor, K.E. Ensrud; Osteoporotic Fractures in Men Mr, O.S.S.R.G., Prediction of incident major osteoporotic and hip fractures by trabecular bone score (TBS) and prevalent radiographic vertebral fracture in older men. J. Bone Miner. Res. **31**(3), 690–697 (2016). https://doi.org/10.1002/jbmr.2713
15. E.V. McCloskey, A. Odén, N.C. Harvey, W.D. Leslie, D. Hans, H. Johansson, R. Barkmann, S. Boutroy, J. Brown, R. Chapurlat, A meta-analysis of trabecular bone score in fracture risk prediction and its relationship to FRAX. J. Bone Miner. Res. **31**(5), 940–948 (2016)
16. M. Garcia-Hoyos, M.T. Garcia-Unzueta, D. de Luis, C. Valero, J. A. Riancho, Diverging results of areal and volumetric bone mineral density in Down syndrome. Osteoporos. Int. **28**(3), 965–972 (2017). https://doi.org/10.1007/s00198-016-3814-1
17. B.C. Silva, M.D. Walker, A. Abraham, S. Boutroy, C. Zhang, D.J. McMahon, G. Liu, D. Hans, J.P. Bilezikian, Trabecular bone score is associated with volumetric bone density and microarchitecture as assessed by central QCT and HRpQCT in Chinese American and white women. J. Clin. Densitom. **16**(4), 554–561 (2013)
18. IBGE: Instituto Brasileiro de Geografia e Estatística, Ministério da Saúde, Brasil. 2008–2009. https://sidra.ibge.gov.br/tabela/2645#resultado. Accessed 6 June 2019.
19. WHO: WHO Growth reference data for children and adolescents. https://www.who.int/growthref/hfa_girls_5_19years_z.pdf. Accessed 6 June 2019.
20. W. Leslie, E. Shevroja, H. Johansson, E. McCloskey, N. Harvey, J. Kanis, D. Hans, Risk-equivalent T-score adjustment for using lumbar spine trabecular bone score (TBS): the Manitoba BMD registry. Osteoporos. Int. **29**(3), 751–758 (2018)
21. S.R. Cummings, M.C. Nevitt, W.S. Browner, K. Stone, K.M. Fox, K.E. Ensrud, J. Cauley, D. Black, T.M. Vogt, Risk factors for hip fracture in white women. Study of Osteoporotic Fractures Research Group. New Engl. J. Med. **332**(12), 767–773 (1995). https://doi.org/10.1056/NEJM199503233321202
22. M. Gunnes, E.H. Lehmann, D. Mellstrom, O. Johnell, The relationship between anthropometric measurements and fractures in women. Bone **19**(4), 407–413 (1996)
23. D. Hemenway, D. Feskanich, G.A. Colditz, Body height and hip fracture: a cohort study of 90,000 women. Int. J. Epidemiol. **24**(4), 783–786 (1995)
24. A. Bjornerem, Q.M. Bui, A. Ghasem-Zadeh, J.L. Hopper, R. Zebaze, E. Seeman, Fracture risk and height: an association partly accounted for by cortical porosity of relatively thinner cortices. J. Bone Miner. Res. **28**(9), 2017–2026 (2013). https://doi.org/10.1002/jbmr.1934
25. D. Xiaoge, L. Eryuan, W. Xianping, Z. Zhiguang, H. Gan, J. Zaijing, P. Xiaoli, T. Hongzhuan, W. Hanwen, Bone mineral density differences at the femoral neck and Ward's triangle: a

comparison study on the reference data between Chinese and Caucasian women. Calcif. Tissue Int. **67**(3), 195–198 (2000)
26. D.S. Lauderdale, S.J. Jacobsen, S.E. Furner, P.S. Levy, J.A. Brody, J. Goldberg, Hip fracture incidence among elderly Asian-American populations. Am. J. Epidemiol. **146**(6), 502–509 (1997)
27. X. Ling, L. Aimin, Z. Xihe, C. Xiaoshu, S.R. Cummings, Very low rates of hip fracture in Beijing, People's Republic of China: the Beijing Osteoporosis Project. Am. J. Epidemiol. **144**(9), 901–907 (1996)
28. M.D. Walker, D.J. McMahon, J. Udesky, G. Liu, J.P. Bilezikian, Application of high-resolution skeletal imaging to measurements of volumetric BMD and skeletal microarchitecture in Chinese-American and white women: explanation of a paradox. J. Bone Miner. Res. **24**(12), 1953–1959 (2009)
29. M.D. Walker, X.S. Liu, E. Stein, B. Zhou, E. Bezati, D.J. McMahon, J. Udesky, G. Liu, E. Shane, X.E. Guo, Differences in bone microarchitecture between postmenopausal Chinese-American and white women. J. Bone Miner. Res. **26**(7), 1392–1398 (2011)
30. N. Crabtree, W. Högler, M. Cooper, N. Shaw, Diagnostic evaluation of bone densitometric size adjustment techniques in children with and without low trauma fractures. Osteoporos. Int. **24**(7), 2015–2024 (2013)
31. B.C. Silva, S.B. Broy, S. Boutroy, J.T. Schousboe, J.A. Shepherd, W.D. Leslie, Fracture Risk Prediction by Non-BMD DXA Measures: the 2015 ISCD Official Positions Part 2: Trabecular Bone Score. J. Clin. Densitom. **18**(3), 309–330 (2015). https://doi.org/10.1016/j.jocd.2015.06.008