

Full Length Article

Impact of abdominal adiposity correction on trabecular bone score (TBS) in obese women: A comparative study of software versions 3.0 and 4.0 with a predictive model

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ABSTRACT

Purpose: To evaluate the impact of soft-tissue thickness correction on trabecular bone score (TBS) in obese women across different BMI categories, comparing software versions 3.0 and 4.0, and to examine their associations with bone mineral density (BMD), fracture occurrence, and clinical variables.

Methods: This cross-sectional study included 247 obese women (BMI ≥ 30 kg/m²) who underwent lumbar spine densitometry with TBS assessment using versions 3.0 and 4.0 of the TBS iNsite® software. Demographic, anthropometric, and BMD data were analyzed. Correlations and multivariate linear regression models were used to assess associations between TBS 4.0, BMD, fractures, and clinical parameters.

Results: TBS 4.0 were lower than TBS 3.0 across all BMI categories ($p < 0.001$), with the largest reductions observed in women with BMI ≥ 37 kg/m². Classification of TBS changed in 34% of cases when using version 4.0, with a greater proportion reclassified to degraded categories. TBS 4.0 showed a positive correlation with lumbar spine BMD ($r = 0.51$, $p < 0.001$) and BMI ($r = 0.17$, $p = 0.007$), but showed no significant correlation with abdominal wall thickness ($r = -0.08$, $p = 0.229$). The correlation between TBS and BMI was stronger for version 3.0 than for version 4.0 ($r = 0.32$ vs. $r = 0.17$, respectively). In multivariate analysis, abdominal wall thickness emerged as an independent predictor of TBS 4.0. A multivariate regression model including TBS 3.0, age, L1–L4 BMD, and abdominal wall thickness explained 86% of the variability in TBS 4.0, enabling estimation of TBS 4.0 from clinical variables and the earlier software version. Women with fractures showed lower TBS values, though not significant.

Conclusions: The TBS 4.0, by incorporating automatic correction for soft-tissue thickness, provides lower values that possibly better characterize trabecular microarchitecture in individuals with obesity, especially in those with higher BMIs, and mitigates the bias attributable to differences in body composition observed with previous versions of the TBS software.

1. Introduction

Osteoporosis is a systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration, leading to increased skeletal fragility and a higher risk of low-impact fractures, which are associated with substantial morbidity, mortality, and healthcare costs worldwide [1,2]. It is estimated that one in three women and one in five

men over the age of 50 will experience an osteoporotic fracture during their lifetime, underscoring the clinical and epidemiological relevance of this condition [2].

The global prevalence of obesity has reached epidemic proportions. Although excess body weight was traditionally regarded as protective for the skeleton due to greater mechanical loading, emerging evidence indicates that obesity can adversely affect bone microarchitecture

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through inflammatory, hormonal, and metabolic mechanisms [3,4]. In postmenopausal women with obesity, the prevalence of fragility fractures reaches approximately 27%, frequently occurring at atypical sites for osteoporosis, such as the ankle, lower limbs, and proximal humerus [5,6].

Diagnosing osteoporosis in obese individuals remains challenging. Bone mineral density (BMD)—the current gold-standard diagnostic parameter—may be normal or even elevated in these patients, leading to underestimation of fracture risk. This limitation seems partly from the attenuation of the X-ray beam by soft tissue, but also from the complex interplay between excess adiposity and intrinsic bone quality. Consequently, reliance on BMD alone may mask skeletal fragility and hinder accurate identification of individuals at risk, highlighting the need for complementary diagnostic tools [7–10].

Bone strength and fracture risk depend not only on bone mass but also on other components such as bone microarchitecture and remodeling dynamics, which are not captured by BMD assessment [10,11].

The Trabecular Bone Score (TBS; TBS iNsight®, Medimaps Group, Geneva, Switzerland) has emerged as a promising, non-invasive index that provides an indirect evaluation of trabecular microarchitecture from lumbar spine dual-energy X-ray absorptiometry (DXA) images. TBS quantifies the variation in pixel gray-level texture across the DXA image: greater numbers of low-amplitude gray-level variations correspond to denser, better-connected trabeculae (higher TBS values), whereas fewer, high-amplitude variations indicate more porous and fragile bone (lower TBS value). Accordingly, low TBS values reflect deterioration of trabecular microarchitecture [12,13]. TBS provides an index of bone quality that predicts osteoporotic fracture risk independently of BMD and clinical risk factors [14]. However, earlier versions of the TBS iNsight® software (e.g., version 3.0) had methodological limitations, including susceptibility to image noise and particularly to the impact of abdominal soft-tissue thickness. This effect could artifactually reduce TBS values, especially in individuals with high body mass index (BMI > 37 kg/m²), compromising diagnostic accuracy and risk stratification in this population [10]. Version 3.0 partially addressed this issue by applying a global BMI-based adjustment; however, BMI is an imperfect surrogate for regional adiposity and does not account for local variations in soft-tissue distribution, limiting its corrective precision in certain patients [12].

To overcome these limitations and enhance accuracy in individuals with obesity, the Medimaps Group introduced a new version of the software (TBS iNsight® 4.0), incorporating an automatic correction algorithm for X-ray attenuation caused by regional soft-tissue thickness measured directly from the DXA image [12,15].

Validating and understanding the clinical implications of this updated version is crucial, particularly given the consistent observation that TBS 4.0 yields lower values than TBS 3.0 among individuals with obesity. Furthermore, establishing the relationship between measurements obtained from both versions can facilitate study comparability and enable retrospective application of clinical data.

The present study aimed to evaluate the impact of soft-tissue thickness correction on TBS values in women with obesity across different BMI categories, comparing the results obtained with versions 3.0 and 4.0 of the software, and to analyze their associations with BMD, fracture occurrence, and clinical variables.

2. Materials and methods

2.1. Study design

This was a single-center, cross-sectional study conducted through a retrospective analysis of a database of patients with obesity from the Endocrinology and Metabolism Division of the Hospital de Clínicas, Federal University of Paraná (SEMPR). Female patients diagnosed with obesity who were followed at SEMPR and had participated in a previous obesity study approved by the Institutional Ethics Committee (CAAE:

51231215.5.0000.0096; approval no. 2.042.484) were included.

Eligible participants were women aged 18 years or older, with a diagnosis of obesity (BMI ≥ 30 kg/m²), body weight within the operational limit of the densitometer (up to 120 kg), who were under regular endocrinology follow-up and had undergone BMD assessment and TBS evaluation using both software versions (3.0 and 4.0).

Exclusion criteria included missing medical records, absence of DXA examination, or the presence of diabetes or other chronic conditions such as malabsorptive, rheumatologic, or autoimmune diseases, chronic inflammatory disorders, history of uncontrolled hyperthyroidism, neoplasia, chronic use of anticonvulsants, hypogonadism, chronic kidney disease (eGFR <60 mL/min/1.73 m²) or chronic glucocorticoid use. In addition, women using any anti-fracture therapy—such as oral or intravenous bisphosphonates, denosumab, anabolic agents, selective estrogen receptor modulators—were excluded to avoid potential effects of treatment on bone microarchitecture or TBS values.

2.2. Study assessments

Demographic and anthropometric data — including age, race, weight, height, and BMI — were extracted from medical records. Bone densitometry results were obtained either from the records or directly from the DXA system (Lunar Prodigy Advance, GE Medical Systems Lunar, Madison, WI, USA; weight limit 120 kg). Lumbar spine (L1–L4), total hip, and femoral neck BMD data were collected. All tests were performed by the same DXA technician and evaluated by the same densitometrist. The least significant variance at the 95% confidence level, obtained for lumbar spine and total hip was 0.036 g/cm² and 0.022 g/cm², respectively. The TBS was not done in our center and we do not have the TBS - LSC.

BMD values were interpreted according to the diagnostic criteria established by the World Health Organization (WHO) and the International Society for Clinical Densitometry (ISCD). According to these reference ranges, BMD, in postmenopausal women, was classified as follows: normal (T-score ≥ -1.0), osteopenia (-2.5 < T-score < -1.0), and osteoporosis (T-score ≤ -2.5). For premenopausal women Z-scores were used, with values ≤ -2.0 defined as *below the expected range for age* (BERA), as recommended by the ISCD Official Positions [16,17].

The NHANES III, Caucasian female reference population was used for T-scores and the GE Lunar reference database for women was used for Z-scores, in accordance with ISCD recommendations [17].

TBS evaluation (versions 3.0 and V4.0 beta v18.4.2-2.5) was performed by the Medimaps Group (TBS iNsight®, Medimaps Group, Geneva, Switzerland). For TBS v3.0, microarchitecture was classified according to the Latin American reference as degraded (TBS ≤ 1.267), partially degraded (1.267 < TBS < 1.347), and normal (TBS ≥ 1.347). For TBS version 3.0, the Latin American reference database was applied. For this population, the manufacturer proposed normative TBS reference values for women (published as an abstract) [17,18].

As no validated cut-off points are currently available in the literature for TBS v4.0, thresholds for this version were derived from the tertile distribution of the total sample, and therefore, apply specifically to the current study population: First tertile - Normal microarchitecture: TBS > 1.345; second tertile - Partially degraded: 1.219 < TBS ≤ 1.345; third tertile - Degraded: TBS ≤ 1.219. Homogeneity of marginal proportions between TBS versions 3.0 and 4.0 was evaluated using the Stuart–Maxwell symmetry test.

Patients were analyzed individually and subsequently stratified into two groups according to BMI: <37 kg/m² and ≥ 37 kg/m². This cutoff was chosen due to the known limitation of interpreting TBS v3.0 values in individuals with BMI ≥ 37 kg/m².

Information on prior fractures was obtained exclusively through patient self-report during routine endocrinology outpatient visits. No radiographic confirmation or medical documentation of these events was systematically available. Vertebral morphometric assessment was not performed.

2.3. Statistical analysis

Data analysis was performed using IBM SPSS Statistics, version 29.0.2 (IBM Corp., Armonk, NY, USA). Quantitative variables were described as mean, standard deviation, minimum, and maximum values, while categorical variables were expressed as absolute and relative frequencies.

Normality of quantitative variables was assessed using the Kolmogorov–Smirnov test, and homogeneity of variances was evaluated with Levene's test. Comparisons of quantitative variables between two groups defined by categorical variables were performed using the independent-samples *t*-test. For comparisons involving more than two groups, one-way analysis of variance (ANOVA) with Bonferroni post hoc test was applied, or, when appropriate, the nonparametric Kruskal–Wallis test followed by Dunn's post hoc test.

Associations between categorical variables were evaluated using Fisher's exact test or the chi-square (χ^2) test. Comparison between TBS versions 3.0 and 4.0 in terms of classification categories (normal, partially degraded, degraded) was conducted using the Stuart–Maxwell symmetry test. Linear correlation between TBS v4.0 and v3.0 values was estimated using Pearson's correlation coefficient. Agreement between versions was examined using Bland–Altman analysis, with evaluation of mean bias and limits of agreement.

The prediction model for TBS v4.0 based on TBS v3.0 was developed using a linear regression approach, with TBS v4.0 as the dependent variable and TBS v3.0 as the explanatory variable, along with selected clinical covariates. Initially, correlations among predictor variables were evaluated to identify potential multicollinearity risks.

To assess predictive performance, the total sample was randomly divided into two subsets: 70% of cases for model training and 30% for validation (testing sample). In the testing sample, descriptive statistics of predicted and observed values, as well as their differences, were computed to assess bias and predictive accuracy. After model fitting, residuals were analyzed, and the coefficient of determination (R^2) was reported. The variance inflation factor (VIF) was calculated to assess multicollinearity among independent variables.

The derivation of the prediction formula followed three sequential steps:

1. Univariate model: A simple linear regression model was fitted using TBS v4.0 as the dependent variable and TBS v3.0 as the sole explanatory variable.
2. Global multivariate model: To improve predictive power, clinical and demographic variables significantly correlated with TBS v4.0 (age, L1–L4 BMD, and abdominal wall thickness) were included. The final regression equation was derived from the training sample, with each coefficient representing the specific and independent contribution of its variable to the prediction of TBS v4.0.
3. Model validation: The adequacy of the final multivariate model was tested in the validation subset.

For all analyses, $p < 0.05$ was considered statistically significant. For multiple post hoc comparisons, p -values were adjusted using the Bonferroni correction method.

3. Results

3.1. General characteristics of the study population

From a total sample of 283 patients, 36 were excluded (21 due to comorbidities; 6 due to incomplete data; 7 were male; and 2 presented extreme TBS values). The final sample included 247 women, mean age of 59.2 ± 15 years, predominantly White, and with a mean body mass index (BMI) of 35.0 ± 3.7 kg/m², all with a diagnosis of obesity.

The BMD at the lumbar spine (L1–L4) was 1.110 ± 0.195 g/cm², the mean abdominal wall thickness was 26.0 ± 2.3 mm, and the mean total body fat percentage was $41.4 \pm 6.9\%$. BMD was normal in 40.1% of the

patients, 38.1% had osteopenia, 19.4% had osteoporosis, and 2.4% were below the expected range for age.

Sample stratification according to BMI showed 183 (74.1%) patients with BMI < 37 kg/m² and 64 (25.9%) BMI ≥ 37 kg/m². Participants with BMI ≥ 37 kg/m² showed significantly greater abdominal wall thickness (28.1 ± 1.8 mm) and higher total body fat percentage ($44.3 \pm 5.6\%$) compared with those with BMI < 37 kg/m² (25.2 ± 1.9 mm and $40.3 \pm 7.1\%$, respectively; $p < 0.001$ for both).

Patients clinical and densitometric characteristics are summarized in Table 1.

3.2. Comparison of TBS between versions 3.0 and 4.0

Mean TBS values were significantly higher in version 3.0 compared with version 4.0 (1.308 ± 0.166 vs. 1.284 ± 0.125 ; $p = 0.001$), showing a strong positive correlation ($r = 0.75$; 95% confidence interval [CI]: 0.68–0.80; $p < 0.001$) and a mean absolute difference of 0.024 ± 0.111 (95% CI: 0.010–0.037) Fig. 1. On average, TBS v4.0 corresponded to 98.9% \pm 9.3% of the value obtained with version 3.0, representing a mean reduction of approximately 1.1%. The intraclass correlation coefficient (ICC) was 0.83 (95% CI: 0.78–0.87), indicating good agreement between the versions.

3.3. Impact of BMI on agreement between TBS versions

When stratified by BMI, a distinct pattern was observed between

Table 1

Demographic and densitometric characteristics of the total sample and according to body mass index (BMI) categories.

Variable Mean \pm SD (min-max.)	Total sample (n = 247)	BMI < 37 (n = 183)	BMI \geq 37 (n = 64)	p
Age (years)	59.2 \pm 15 (18–86)	61.7 \pm 14.3 (18–86)	52.1 \pm 14.7 (20–83)	<0.001
Race n(%)				
White	232 (93.9%)	174 (95.1%)	58 (90.6%)	0.183
Black	14 (5.7%)	9 (4.9%)	5 (7.8%)	
Asian	1 (0.4%)	0 (0%)	1 (1.6%)	
Weight (kg)	83.9 \pm 12.3 (47.7–128)	79.4 \pm 8.3 (46.7–100)	96.9 \pm 12.7 (60–128)	<0.001
Height (m)	1.55 \pm 0.07 (1.20–1.74)	1.54 \pm 0.07 (1.24–1.74)	1.55 \pm 0.09 (1.20–1.71)	0.691
BMI (kg/m²)	35.0 \pm 3.7 (30–51.1)	33.2 \pm 1.7 (30–36.9)	40.3 \pm 2.7 (37.1–51.1)	<0.001
BMD (g/cm²)				–
L1–L4	1.11 \pm 0.19 (0.63–1.85)	1.15 \pm 0.18 (0.63–1.85)	1.14 \pm 0.18 (0.76–1.67)	0.101
Femoral neck	0.92 \pm 0.16 (0.51–1.44)	0.91 \pm 0.15 (0.62–1.44)	0.96 \pm 0.18 (0.58–1.34)	0.034
Total Hip	1.00 \pm 0.16 (0.53–1.50)	0.98 \pm 0.15 (0.60–1.50)	1.05 \pm 0.18 (0.53–1.38)	0.009
Abdominal wall thickness (mm)	26.0 \pm 2.3 (20.5–32.6)	25.2 \pm 1.9 (20.5–32.6)	28.1 \pm 1.8 (23.8–32.5)	<0.001
Total body fat percentage (%)	41.4 \pm 6.9 (19.9–60.1)	40.3 \pm 7.1 (19.9–60.1)	44.3 \pm 5.6 (31.9–57.9)	<0.001
BMD, n (%)				
Normal	69 (37.7%)	3 (1.6%)	30 (46.9%)	0.110
BERA	99 (40.1%)	70 (38.3%)	3 (4.7%)	
Osteopenia	6 (2.4%)	41 (22.4%)	24 (37.5%)	
Osteoporosis	94 (38.1%)	69 (37.7%)	7 (10.9%)	
BMD classification, n (%)				
Normal	99 (40.1%)	69 (37.7%)	30 (46.9%)	0.302
Low	149 (60.3%)	114 (62.3%)	35 (54.7%)	
Fractures, n(%)	86 (35%)	69 (37%)	17 (27%)	0.110

Student's *t*-test for independent samples (quantitative variables); Fisher's exact test or chi-square test (categorical variables); $p < 0.05$. BERA = below the expected range for age; BMI = Body mass index; BMD = Bone mineral density; Min = Minimum; Max = Maximum; SD = Standard deviation.

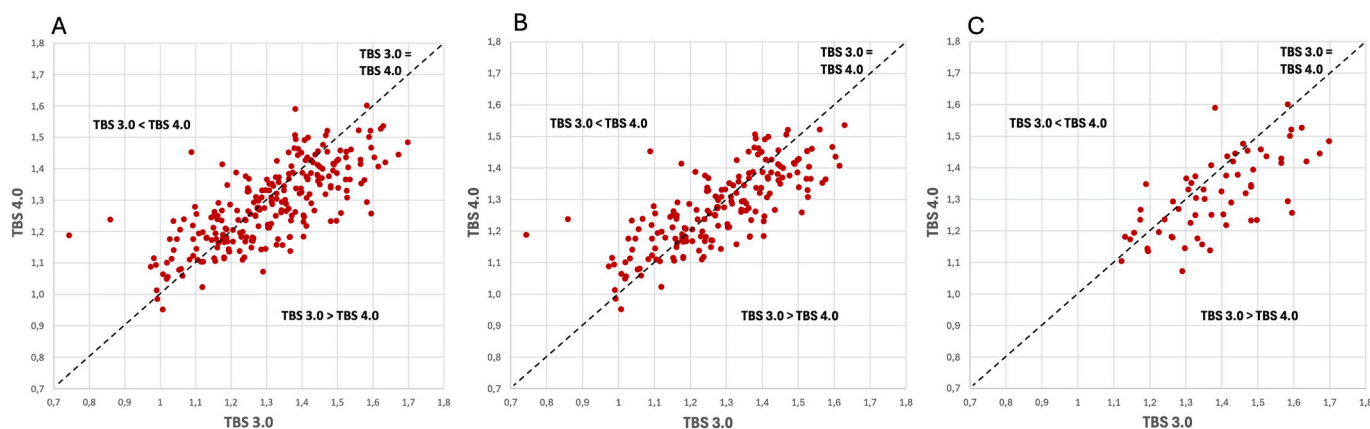


Fig. 1. Correlation between software versions 3.0 and 4.0 of Trabecular Bone Score (TBS). (A) Total sample ($n = 247$); (B) Subgroup with BMI $< 37 \text{ kg/m}^2$ ($n = 183$); (C) Subgroup with BMI $\geq 37 \text{ kg/m}^2$ ($n = 64$). TBS = trabecular bone score.

groups. Among patients with BMI $< 37 \text{ kg/m}^2$ ($n = 183$), there was a strong positive correlation between versions ($r = 0.76$; 95% CI: 0.69–0.81; $p < 0.001$), and TBS values were virtually identical (1.280 ± 0.165 vs. 1.274 ± 0.124 ; $p = 0.402$), with a mean absolute difference of only 0.007.

± 0.107 (95% CI: -0.009 to 0.022) and an ICC of 0.84 (95% CI: 0.79–0.88).

In contrast, among patients with BMI $\geq 37 \text{ kg/m}^2$ ($n = 64$), a positive correlation between versions was also observed ($r = 0.69$; 95% CI: 0.54–0.80; $p < 0.001$), but TBS values were significantly higher in version 3.0 than in version 4.0 (1.386 ± 0.146 vs. 1.314 ± 0.125 , respectively; $p < 0.001$). The mean absolute difference was 0.072 \pm 0.108 (95% CI: 0.045–0.099), with TBS v4.0 corresponding, on average, to 95.2% \pm 7.5% of the value obtained with version 3.0 (95% CI: 93.3%–97.1%). The ICC remained high (0.81; 95% CI: 0.69–0.89), reflecting a strong correlation between the versions, although with a tendency toward overestimation of TBS values by version 3.0 in individuals with higher BMI.

3.4. Microarchitectural classification agreement between versions

The classification of TBS (normal, partially degraded, and degraded) differed significantly between versions 3.0 and 4.0 ($p < 0.001$). Although the overall agreement between the versions was 66%, a discrepancy was observed in 34% of cases, with 19% of patients classified by version 3.0 in a better microarchitectural category than that assigned by version 4.0. The Kappa coefficient was 0.49 (95% CI: 0.41–0.57), indicating moderate agreement between versions.

When stratified by BMI, distinct patterns were observed between subgroups. Among patients with BMI $< 37 \text{ kg/m}^2$, the agreement rate was slightly higher (69.4%), with a Kappa coefficient of 0.54 (95% CI: 0.44–0.63), still reflecting moderate agreement. In this BMI category, the distribution of classifications was similar between the two versions ($p < 0.001$).

In contrast, in the group with BMI $\geq 37 \text{ kg/m}^2$, the version 4.0 classified a greater proportion of cases as partially degraded (18.8% vs. 35.9%). Agreement between classifications was observed in only 36 cases (56.3%), with a Kappa coefficient of 0.32 (95% CI: 0.15–0.50), consistent with fair agreement. Overall, 16 patients (25%) who were not identified as having degraded TBS in version 3.0 were reclassified as degraded in version 4.0, suggesting that the older version may have underestimated microarchitectural impairment in patients with higher degrees of obesity.

3.5. Correlation between demographic and clinical variables and both TBS versions

The correlation between demographic and clinical variables with TBS values was initially analyzed in the total sample and subsequently stratified by BMI (< 37 and $\geq 37 \text{ kg/m}^2$), as shown in Table 2. A positive correlation with BMI and a negative correlation with age were observed for both TBS versions and across all BMI categories.

Abdominal wall thickness showed a negative correlation with TBS values in version 3.0; however, in version 4.0, this association was significant only among patients with BMI $< 37 \text{ kg/m}^2$. Total body fat percentage did not show any relevant association with TBS in any of the analyses. Lumbar spine (L1–L4) BMD demonstrated a positive correlation with TBS values in all subgroups and for both software versions.

3.6. Association between TBS, clinical fractures and BMD

Among the 247 women evaluated, 86 (34.8%) had a history of clinical fracture, most of them with only one event (72.1%). The mean TBS values were significantly lower in patients with fractures compared to those without, both in version 3.0 (1.258 ± 0.164 vs. 1.334 ± 0.162 ; $p < 0.001$) and in version 4.0 (1.251 ± 0.129 vs. 1.302 ± 0.119 ; $p = 0.003$).

Receiver operating characteristic (ROC) curve analysis demonstrated moderate accuracy for both versions in predicting fractures, with areas under the curve (AUC) of 0.624 (95% CI: 0.551–0.696) for TBS v3.0 and 0.621 (95% CI: 0.547–0.695) for TBS v4.0, with no significant difference

Table 2

Correlations between trabecular bone score (TBS) versions 3.0 and 4.0 and quantitative variables.

Variable	Sample	r (TBS 3.0)	r (TBS 4.0)
BMI	Total	0.32*	0.17*
	Total	-0.51*	-0.58*
Age	BMI $< 37 \text{ kg/m}^2$	-0.50*	-0.61*
	BMI $\geq 37 \text{ kg/m}^2$	-0.38**	-0.43*
	Total	-0.27*	-0.08
Abdominal wall thickness	Total	-0.27*	-0.08
	BMI $< 37 \text{ kg/m}^2$	-0.51*	-0.21**
	BMI $\geq 37 \text{ kg/m}^2$	-0.57*	-0.12
Total body fat percentage	Total	-0.04	0.05
	BMI $< 37 \text{ kg/m}^2$	-0.11	0.01
	BMI $\geq 37 \text{ kg/m}^2$	-0.12	0.01
L1–L4 BMD	Total	0.35*	0.51*
	BMI $< 37 \text{ kg/m}^2$	0.33*	0.51*
	BMI $\geq 37 \text{ kg/m}^2$	0.36**	0.49*
	Total	0.32*	0.17*

BMI = Body mass index; BMD = Bone mineral density; TBS = Trabecular Bone Score; r = Pearson's correlation coefficient. $p < 0.05$ indicates statistically significant correlation. * $p < 0.01$; ** $p < 0.05$.

between them ($p = 0.927$), as shown in Fig. 2.

When stratified by BMI, diagnostic performance remained similar in both groups. Among patients with BMI $< 37 \text{ kg/m}^2$, the AUCs were 0.618 (95% CI: 0.535–0.702) for TBS v3.0 and 0.620 (95% CI: 0.537–0.703) for TBS v4.0 ($p = 0.961$). In the group with BMI $\geq 37 \text{ kg/m}^2$, the AUCs were 0.590 (95% CI: 0.434–0.747) and 0.595 (95% CI: 0.408–0.782), respectively ($p = 0.945$).

Patients with low densitometry results showed significantly lower mean TBS values in both software versions. For TBS v3.0, mean values were 1.253 ± 0.160 versus 1.391 ± 0.140 ($p < 0.001$), and for TBS v4.0, 1.229 ± 0.111 versus 1.368 ± 0.095 ($p < 0.001$). ROC curve analysis indicated good discriminative ability of TBS for identifying low DXA results, with areas under the curve (AUC) of 0.743 (95% CI: 0.681–0.805) for TBS v3.0 and 0.831 (95% CI: 0.780–0.881) for TBS v4.0, showing a significant advantage for version 4.0 ($p < 0.001$) (Fig. 2).

When stratified by BMI, this superiority of version 4.0 was maintained among patients with BMI $< 37 \text{ kg/m}^2$ (AUC = 0.768 vs. 0.875; $p < 0.001$). In the group with BMI $\geq 37 \text{ kg/m}^2$, the AUC values were lower (0.651 vs. 0.694), with no significant difference between versions ($p = 0.457$).

Among patients with normal bone densitometry, the distribution of TBS v4.0 categories was similar between those with and without fractures ($p = 0.956$). A normal TBS v4.0 was observed in 58.5% of patients without a fracture and 62.5% of those with a fracture; partially degraded scores were found in 34.1% and 31.3%, and degraded scores in 7.3% and 6.3%, respectively.

In patients with low densitometry results, TBS v4.0 showed a higher frequency of degraded or partially degraded classifications ($p = 0.369$). The degraded category was identified in 45.6% of patients without fracture and 57.1% of those with fracture; the partially degraded category in 36.7% and 28.6%; and the normal category in 17.7% and 14.3%, respectively.

In multivariate analysis, abnormal bone densitometry was significantly associated with the presence of fracture (odds ratio [OR] = 3.93; 95% confidence interval [CI]: 1.92–7.99; $p < 0.001$), whereas TBS v4.0 categories were not independently associated: partially degraded (OR = 0.90; 95% CI: 0.42–1.90; $p = 0.776$) and degraded (OR = 1.40; 95% CI: 0.64–3.04;

$p = 0.396$).

3.7. Estimation of TBS v4.0 based on TBS v3.0, demographic and clinical variables

Significant correlations were observed between TBS v4.0 and TBS v3.0, age, BMI, abdominal wall thickness, and lumbar spine BMD (L1–L4), which justified the development of linear regression models to estimate TBS v4.0. Multicollinearity analysis indicated the absence of relevant collinearity among predictors (VIF < 5).

The univariate model, using only TBS v3.0 as the independent variable, explained 57.4% of the variance in TBS v4.0 (adjusted $R^2 = 0.574$; $p < 0.001$). The inclusion of clinical and demographic variables associated with TBS v4.0 (age, L1–L4 BMD, and abdominal wall thickness) significantly increased the explanatory power of the model, raising the adjusted R^2 to 68.7% ($p < 0.001$), as shown in Supplementary Table 1.

Based on this multivariate model, a predictive equation for TBS v4.0 was derived, presented in Fig. 3, with coefficients reflecting the independent contribution of each variable. In the validation sample, the model demonstrated excellent performance, with a low mean prediction error (0.012 ± 0.071) and good calibration between observed and predicted values, confirming its robustness for estimating TBS v4.0 from clinical parameters and TBS v3.0.

3.7.1. BMI-stratified predictive models

Given the clinical relevance of BMI, separate predictive models were also developed for patient BMI subgroups.

Patients with BMI $< 37 \text{ kg/m}^2$ ($n = 183$): A multivariate model including TBS v3.0, L1–L4 BMD, abdominal wall thickness, and age achieved an adjusted R^2 of 70.4% ($p < 0.001$), representing a 13.1% improvement over the univariate model. The predictive equation derived for this group is shown in Fig. 3. Model adequacy assessment revealed a mean difference of 0.000 between predicted and observed values, with a standard error of 0.067, indicating consistent predictive performance and the absence of systematic bias.

Patients with BMI $\geq 37 \text{ kg/m}^2$ ($n = 64$): In this subgroup, the inclusion of L1–L4 BMD, abdominal wall thickness, and age in the model containing only TBS v3.0 significantly improved the predictive ability for TBS v4.0. The adjusted R^2 of the multivariate model reached 60.1% ($p < 0.001$), representing a 12.9% increase compared to the univariate model. A specific predictive equation for patients with BMI $\geq 37 \text{ kg/m}^2$ was derived by fitting a multivariate linear regression model using the estimated coefficients (presented in Supplementary Table 2) for the predictor variables, allowing more accurate estimation of TBS v4.0 in this high-risk population. The predictive equation for this subgroup is displayed in Fig. 3.

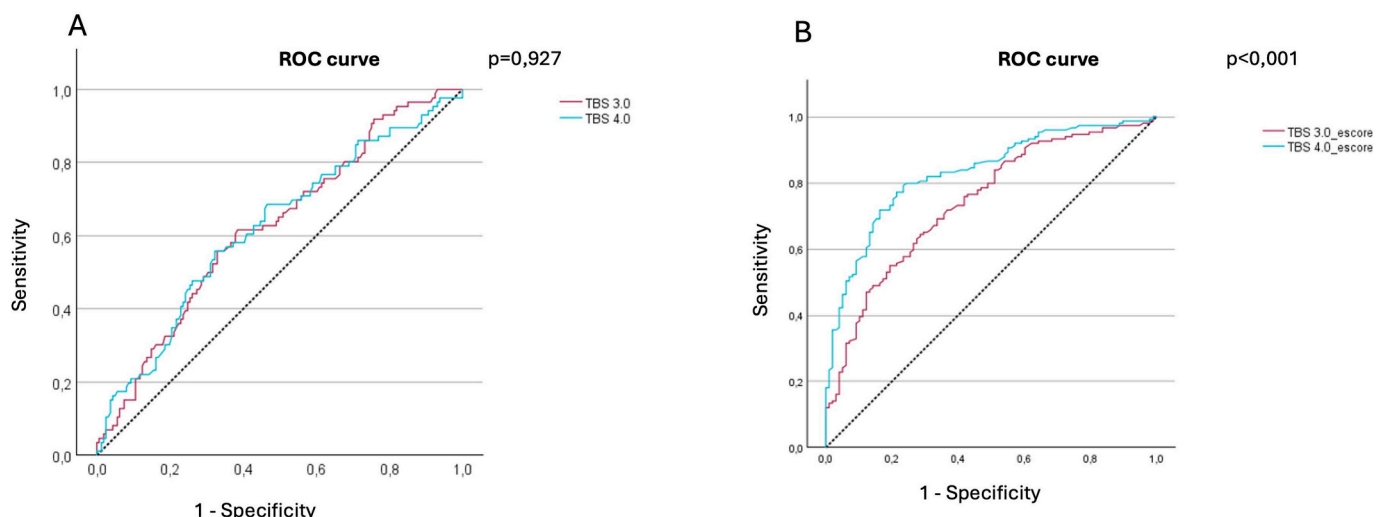


Fig. 2. Accuracy of the trabecular bone score (TBS) for predicting (A) clinical fracture and (B) low bone mineral density. TBS = trabecular bone score.

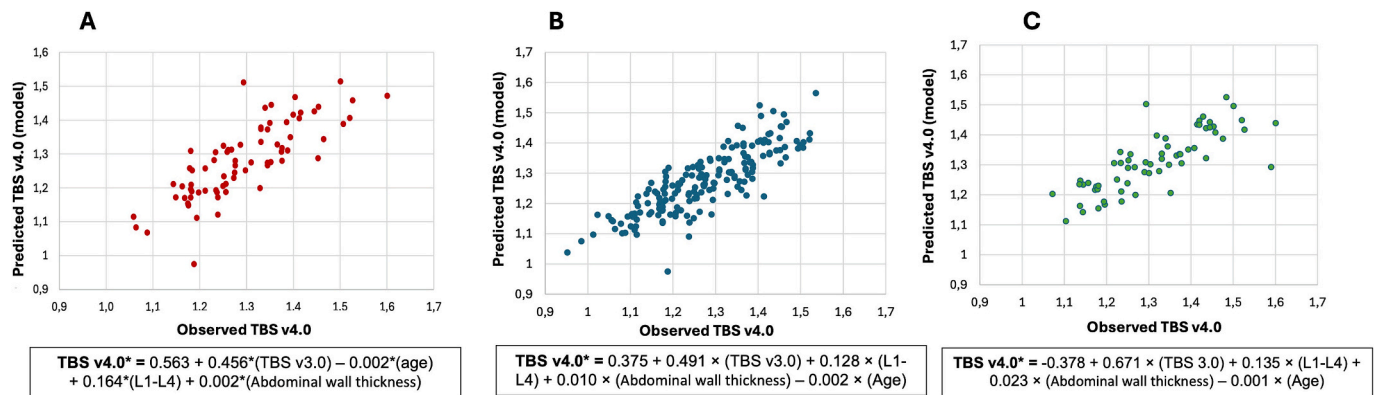


Fig. 3. Predictive equations and performance of the linear regression model for estimating TBS v4.0 from TBS v3.0 in the total sample and in BMI-stratified subgroups. (A) Total sample ($n = 247$); (B) Subgroup with BMI $< 37 \text{ kg/m}^2$ ($n = 183$); (C) Subgroup with BMI $\geq 37 \text{ kg/m}^2$ ($n = 64$). TBS = trabecular bone score. *Predictive equation for estimating TBS v4.0 values.

Model validation demonstrated a mean difference of 0.000 between predicted and observed values (standard deviation = 0.076), confirming the adequacy of the fit and the absence of systematic bias. The performance of the predictive models is summarized in Fig. 3, showing strong agreement between observed and predicted TBS v4.0 values, both in the total sample and in BMI-stratified subgroups.

4. Discussion

The present study compared TBS versions 3.0 and 4.0 in 247 obese women, assessing abdominal wall thickness as a soft-tissue proxy, correlations with BMD, age, BMI, and fracture history, and their discriminatory ability for clinical fractures and low BMD (T-score ≤ -2.5). We also developed a multivariate model to predict TBS 4.0 from TBS 3.0. The versions showed good agreement (ICC > 0.90), but TBS 4.0 yielded lower values (mean difference: -0.024 ; $p < 0.001$), with greater reductions (up to 4.8%) in higher BMI subgroups, reclassifying 34% into degraded microarchitecture categories. This indicates that TBS 4.0's soft-tissue correction addresses version 3.0's overestimation bias from adipose attenuation, providing a more sensitive bone microarchitecture assessment in adiposity, and better identifying fragility risk. TBS 4.0 retained associations with age, L1–L4 BMD, BMI, and abdominal thickness (independent predictor). It matched TBS 3.0's fracture detection accuracy (AUC ≈ 0.62) but improved low BMD discrimination (AUC 0.831 vs. 0.743; $p < 0.001$), particularly in lower BMI. The model performed robustly (adjusted $R^2 = 68.7\%$), enabling reliable TBS 4.0 estimation using TBS 3.0, age, L1–L4 BMD, and abdominal thickness for cross-version harmonization.

In our cohort, the mean reduction between TBS 3.0 and TBS 4.0 values was small among women with BMI $< 37 \text{ kg/m}^2$ (approximately 1.1%), a difference that is unlikely to meaningfully alter clinical interpretation and suggests that soft-tissue interference is relatively modest in this subgroup. In contrast, women with BMI $\geq 37 \text{ kg/m}^2$ exhibited a substantially larger reduction of approximately 4.8%, a shift that may be clinically relevant for individuals near diagnostic thresholds, as it can lead to reclassification into worse microarchitectural categories. These findings demonstrate the differential impact of the soft-tissue correction across BMI strata and reinforce that attenuation bias in TBS 3.0 becomes increasingly pronounced with greater abdominal adiposity. The updated TBS 4.0 algorithm therefore provides a more accurate representation of trabecular microarchitecture in women with severe obesity, consistent with previous evidence indicating that increased soft tissue thickness leads to an artificial reduction in TBS values. As described by Silva et al., excess soft tissue acts similarly to image noise, resulting in lower TBS measurements and potential underestimation of trabecular bone quality when using earlier TBS versions [19]. Although this correction appears particularly critical for individuals with BMI $\geq 37 \text{ kg/m}^2$, universal use

of TBS 4.0 remains advantageous because it ensures consistency across populations and prevents misclassification in patients whose fat distribution may not be fully captured by BMI alone. Furthermore, TBS 4.0 may be especially relevant in clinical scenarios marked by discordance between BMD and fracture risk, such as type 2 diabetes, where individuals often present with higher body weight and preserved or elevated BMD despite increased skeletal fragility [20–22]. In such contexts, enhanced adjustment for soft-tissue attenuation may improve the ability of TBS to detect microarchitectural impairment that is not reflected in BMD measurements.

The enhancement achieved with TBS v4.0 has been supported by several studies. The OsteoLaus cohort demonstrated that TBS v4.0 eliminates the previously observed negative correlation between TBS and BMI, resulting in greater accuracy in fracture-risk stratification [23]. Similarly, analyses from the FREEDOM trial confirmed that the updated TBS retains its independent predictive value for osteoporotic fractures even after adjustment for BMD and other clinical risk factors [12]. More recently, McClung et al. showed that TBS v4.0 not only improves diagnostic precision, particularly in individuals with obesity, but also enhances fracture-risk reclassification when combined with BMD [24].

Despite the significant mean differences in TBS values between patients with and without fractures, the discriminative accuracy of TBS for predicting clinical fractures was only moderate in our cohort, with no significant difference between versions 3.0 and 4.0 or between BMI subgroups as detailed in the results. This finding, while seemingly modest for a bone quality marker, requires careful interpretation in light of several study characteristics. This finding likely reflects the limited number of fracture events, the predominance of non-classical osteoporotic fracture sites in obesity, and the specific characteristics of this population. Importantly, similar results were reported in the updated OsteoLaus cohort, in which Gatineau et al. (2025) also observed no significant difference in fracture prediction performance between TBS versions 3.0 and 4.0 [23]. In line with current recommendations, our results reinforce the role of TBS as a complementary marker—intended to be interpreted alongside BMD and/or FRAX (adjusted for TBS)—in the integrated assessment of fracture risk [12,15,23].

Despite the significant mean differences between patients with and without fractures, the area under the curve (AUC ≈ 0.62), indicated limited discriminative ability for TBS—similar to that reported in other cross-sectional studies with a restricted number of events and predominantly non-vertebral fractures [13,14]. Nonetheless, the consistent pattern of lower TBS values among patients with fractures supports its value as an indicator of trabecular quality, particularly when analyzed in conjunction with BMD and clinical risk factors, as in the FRAX algorithm, which provides greater predictive robustness [15,25].

A particularly critical aspect highlighted by our findings is the

clinical impact of underestimating fracture risk in patients with obesity. Although excess body weight has historically been considered protective for the skeleton due to increased mechanical loading, growing evidence indicates that adipose tissue accumulation exerts direct deleterious effects on bone microarchitecture [3,4,26]. In this context, the use of less precise algorithms, such as TBS v3.0 in individuals with high BMI, may contribute to the underdiagnosis of trabecular fragility and, consequently, to missed opportunities for timely therapeutic intervention—culminating in an increased risk of fragility fractures in this population.

The higher sensitivity of TBS v4.0, especially in the group with BMI ≥ 37 kg/m², helps close this diagnostic gap by allowing a more accurate risk stratification and more appropriate clinical management. In the OsteoLaus study, Gatineau et al. demonstrated that the individual differences between TBS v3.0 and v4.0 were strongly associated with body fat distribution, particularly abdominal adiposity [27]. Patients with greater soft-tissue thickness in the lumbar region exhibited artificially higher TBS v3.0 values, which were corrected by version 4.0, confirming the direct influence of overlying adipose tissue on measurement accuracy. The automated correction for tissue thickness incorporated into the new algorithm effectively neutralizes X-ray attenuation effects, resulting in more precise and physiologically coherent estimates of bone quality—particularly in individuals with central obesity, where BMI alone does not adequately reflect abdominal wall thickness.

In this study, fracture assessment was based on self-reported clinical history without radiographic confirmation, which may have contributed to under- or overestimation of events. Therefore, the absence of a significant association between TBS and fracture should be interpreted with caution. Previous studies have shown that TBS is a strong independent predictor of vertebral, hip, and major osteoporotic fractures even after adjustment for BMD and clinical risk factors [13,28]. Additionally, fracture site distribution tends to differ in individuals with obesity, being more frequent in the ankle, humerus, and other peripheral regions, with a lower incidence of vertebral and hip fractures [3]. This variation reflects not only biomechanical and fall-pattern differences but also region-specific alterations in bone microarchitecture related to adiposity [4]. Thus, the lack of correlation between TBS and fractures in our sample may result both from the self-reported nature of fracture data and from the distinct anatomical distribution of fractures in obese individuals. Given the lack of anatomical detail in our dataset, fracture-risk reclassification combining BMD and TBS—as recommended in prior literature—could not be reliably performed, and predictive models incorporating both measures were not feasible.

An additional and innovative contribution of our study lies in demonstrating that TBS v4.0 can be accurately estimated from TBS v3.0 values when combined with demographic and clinical variables such as age, abdominal wall thickness, and lumbar BMD. The multivariate linear regression model we developed achieved an adjusted R² of 68.7% for the total sample, significantly higher than that of the univariate model. This approach not only validates the applicability of historical data but also enables harmonization and comparability of results across studies using different software versions—overcoming an important methodological challenge in the field. Furthermore, this predictive model may serve as a practical tool in settings where version 4.0 is not yet widely available, offering an estimated correction for TBS values. The reduced concordance between versions observed in patients with higher BMI underscores that the automated correction of version 4.0 is particularly advantageous for this subgroup, in which underdiagnosis has greater clinical implications.

Most studies evaluating TBS have excluded individuals with BMI ≥ 37 kg/m² due to technical limitations related to soft-tissue thickness. However, this population warrants special attention, as obesity is increasingly recognized as a factor potentially detrimental to bone quality. In this context, the present study is clinically relevant because it includes patients with higher degrees of obesity, thereby expanding current knowledge of TBS performance in a group that is often excluded

from analyses and potentially underdiagnosed for fracture risk. As demonstrated by Shevroja et al. TBS v4.0 is the recommended version for use in patients with severe obesity, as it incorporates automatic correction for soft-tissue thickness, reducing attenuation bias and improving the accuracy of trabecular microarchitecture assessment in this population [13].

Despite these important contributions, some limitations of this study must be acknowledged. First, its cross-sectional design precludes causal inference and assessment of longitudinal changes in bone microarchitecture. Second, the sample consisted exclusively of women with obesity from a single center, which may limit external validity to other populations (e.g., men, different ethnicities, or lower BMI ranges) and clinical contexts. The retrospective nature of data collection, although mitigated by the standardized acquisition of BMD and TBS measurements, inherently depends on the completeness and quality of medical records. Additionally, TBS 4.0 currently lacks validated reference ranges and standardized cut-off points, meaning that the categories used in this study are sample-derived, using a tertile approach, and not directly comparable to those established for TBS 3.0 or other populations. Finally, TBS analyses for both versions (3.0 and 4.0) were conducted by the software's proprietary company, which, despite adhering to a standardized protocol, relies on non-transparent proprietary algorithms.

Future research should aim to establish specific and validated cut-off points for TBS v4.0. It is important to note that the thresholds used in this study were derived from the current sample and are therefore specific to this population. External validation of the predictive model in independent and more heterogeneous cohorts is essential to confirm reproducibility and to consolidate the applicability of TBS v4.0 as a standardized tool for assessing bone quality in individuals with obesity.

In conclusion the correction for soft-tissue thickness implemented in TBS iNsite® version 4.0 significantly influenced TBS values in women with obesity, particularly among those with higher BMI. The updated algorithm yielded systematically lower scores compared to version 3.0, reflecting improved adjustment for X-ray attenuation by adipose tissue. TBS 4.0 maintained significant associations with BMD and clinical variables but not with fracture occurrence, reinforcing its complementary role in assessing bone quality. Overall, the new correction enhances the accuracy of TBS interpretation in populations with increased soft-tissue thickness.

CRediT authorship contribution statement

Fernanda Perin Maia Starck: Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Barbara C. Silva:** Writing – review & editing, Supervision. **Victória Zeghbi Cochenski Borba:** Writing – review & editing, Validation, Supervision, Methodology.

Informed consent

All participants provided written informed consent.

Ethical approval

The study was approved by the Research Ethics Committee of the Hospital de Clínicas, Federal University of Paraná, under protocol number 2.042.484.

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Declaration of competing interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bone.2026.117804>.

Data availability

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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