

Evaluation of trabecular bone score in patients with a distal radius fracture

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Abstract

Summary We compared bone mineral density (BMD) and trabecular bone score (TBS) in postmenopausal women with a distal radius fracture older than 50 years with controls. Total hip BMD was significantly different, but TBS was not different between two groups, suggesting TBS does not reflect microarchitectural changes of the distal radius.

Introduction The purpose of this study was to determine whether trabecular bone score (TBS) has additive value for discriminating distal radius fracture (DRF) independent of BMD.

Methods We compared BMD and TBS in 258 postmenopausal women with a DRF older than 50 years of age with age- and body mass index (BMI)-matched controls who had no history of osteoporotic fracture. BMD was measured at the lumbar spine and hip using dual energy X-ray absorptiometry scans (GE Lunar Prodigy). TBS was calculated on the same spine image. A multivariate logistic regression analysis was used to analyze the odds ratio (OR) for the occurrence of DRF using age, BMI, lumbar spine BMD, total hip BMD, and TBS.

Results Patients with a DRF had significantly lower BMDs at hip (neck, trochanter and total) than those of controls:

0.752 ± 0.097 , 0.622 ± 0.089 , and 0.801 ± 0.099 in patients and 0.779 ± 0.092 , 0.648 ± 0.089 , 0.826 ± 0.101 in controls. However, lumbar spine BMD and TBS were not significantly different between the groups ($p = 0.400$ and 0.864 , respectively). The multivariate analysis indicated that only total hip BMD was significantly associated with the occurrence of DRF (OR, 10.231; 95 % confidence interval, 1.724–60.702; $p = 0.010$).

Conclusions TBS was not different between women with a DRF and those without a history of osteoporotic fracture, suggesting that TBS measured at the lumbar spine does not reflect early microarchitectural changes of the distal radius. Only total hip BMD is associated with the risk of DRF in Korean women.

Keywords Bone microarchitecture · Bone mineral density · Distal radius fracture · Osteoporosis · Trabecular bone score

Introduction

Osteoporosis and fragility fractures are a major public health issues with considerable social and economic costs [1]. The diagnosis of osteoporosis is based on dual energy X-ray absorptiometry (DXA), currently considered the reference standard for determining bone mineral density (BMD) [2]. However, BMD does not always accurately reflect fracture risk and up to 50 % of those who sustain fragility fractures do not have osteoporosis based on BMD testing [3]. In particular, BMD is not consistently lower than normal controls in patients with a distal radius fracture (DRF) [4–6], suggesting that factors other than BMD, such as bone microarchitecture, bone geometry, micro-damage, mineralization, bone turnover, and propensity to fall, influence bone strength and fracture

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risk [7–9]. However, these structural properties of bone cannot be evaluated by using DXA [10].

The trabecular bone score (TBS) is a textural index that evaluates pixel gray-level variations in a lumbar spine DXA image, providing an indirect index of trabecular microarchitecture and bone quality [11]. TBS is significantly associated with vertebral and non-vertebral fractures in several cross-sectional and prospective studies involving a large number of postmenopausal women [12–15]. However, no studies have evaluated the result of TBS for patients with only a DRF.

An osteoporosis evaluation of patients with a DRF is important. DRF is the most common upper extremity fracture in women aged equal to or more than 50 years [16] as it is a predictor of osteoporosis and subsequent fractures [17] and typically occurs earlier than a hip fracture by an average of 15 years [18]. Therefore, patients with a DRF offer physicians an opportunity to diagnose osteoporosis and start secondary prevention [19]. However, because BMD determined by DXA does not reflect microstructural changes in trabecular bone, some osteoporotic fragile patients can be misdiagnosed as normal or osteopenia according to DXA results [14]. TBS, which evaluates the trabecular bone quality, would have a complementary role for the evaluation of osteoporosis in the patients with a DRF.

In this study, we examined the additive value of TBS for discriminating a DRF independent of BMD. We assessed TBS and BMD in patients with a DRF and compared the values with controls which were selected from a large cohort of women with use of propensity score-matched analysis.

Materials and methods

Study population

We obtained approval for this study from the Institutional Review Board of our institute. We enrolled women (age, 50–79 years) who suffered a DRF between May 2010 and December 2014 and who met the following inclusion criteria: (1) acute DRF caused by minor trauma, such as a fall from standing height, (2) underwent a DXA scan (Lunar Prodigy; GE Lunar, WI, USA) within 2 weeks after the fracture. We excluded patients with other conditions, such as renal insufficiency, adrenal insufficiency, rheumatoid arthritis, thyroid disease, parathyroid disease, Parkinson's disease, chronic obstructive pulmonary disease, malignancy, history of osteoporotic fracture, or those who received medication known to affect bone quality, such as steroids, menopausal hormone therapy, or medications for osteoporosis. Patients who had undergone spine surgery, or had severe scoliosis, spondylitis, or vertebral infection were also excluded.

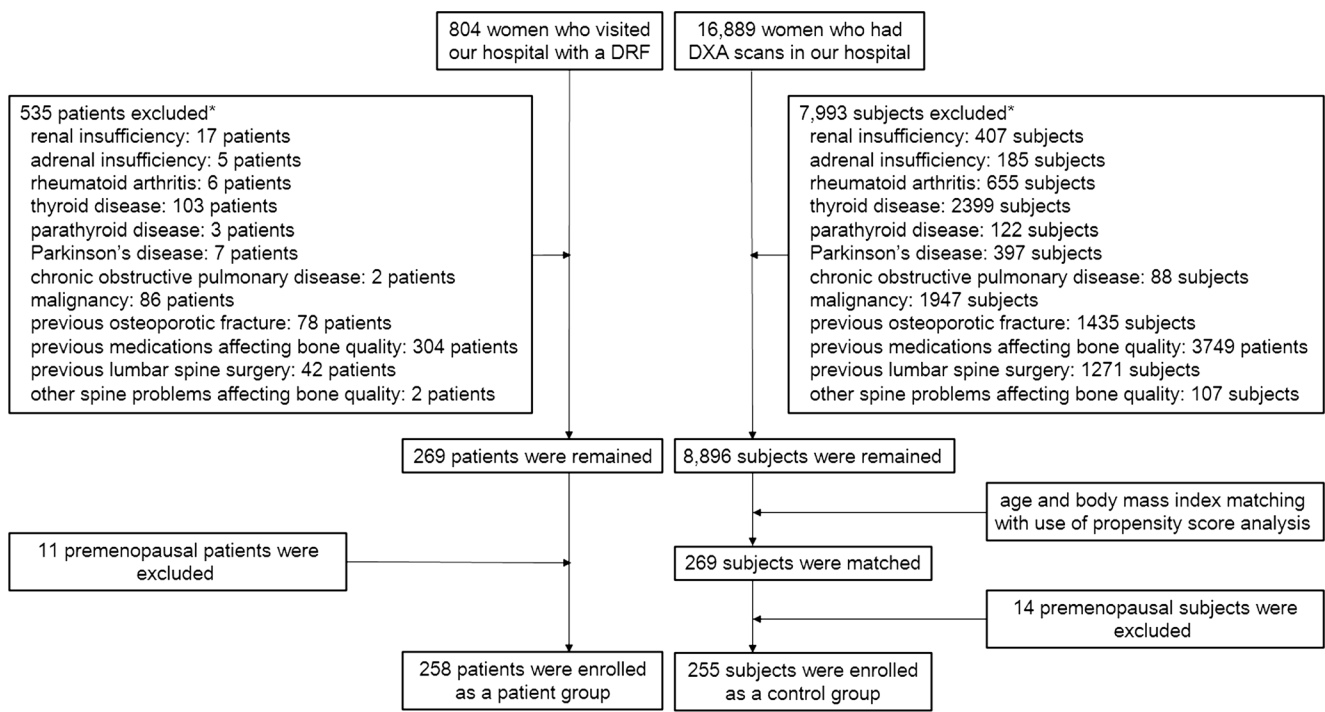
Figure 1 illustrates the patient and control group enrollment process. Most of the patients who had a previous osteoporotic fracture, previous medication affecting bone surgery, previous lumbar spine surgery, and other spine problems affecting bone quality, had BMD examinations before sustaining DRF. These patients were excluded by the exclusion criteria. Among the 804 consecutive women who visited our hospital with a DRF, 269 who met the inclusion criteria were enrolled as the patient group. During the same period, 16,889 women (age, 50–79 years) had DXA scans in our hospital; 7993 subjects were excluded from the cohort using the patient exclusion criteria and 8896 remained as controls. To reduce bias between patients and controls, we used a propensity score analysis to select the 269 case-matched controls. The propensity score is the conditional probability of being selected given the covariates; thus, it can be used to balance confounding factors between two groups [20]. The propensity score was calculated for each group based on a logistic regression analysis, using subject age and body mass index (BMI) for matching. From each group, subjects who were in premenopausal status were excluded from cohort to avoid the bias. Eleven patients (4.1 % of 269 patients) were excluded from patient group and 14 subjects (5.2 % of 269 controls) were excluded from control group. The proportion of premenopausal women was not significantly different between two groups ($p = 0.533$). Finally, 258 DRF patients and 255 controls were enrolled in the cohorts.

Bone mineral density and trabecular bone score

In our institute, BMD (g/cm^2) was measured at the lumbar spine, femoral neck, trochanter, Ward's triangle, and the total hip with DXA scans and analyzed with Encore Software ver. 11.0. The BMD precision error (percentage of the coefficient of variation) was 1.7 % for lumbar spine, 1.8 % for femoral neck, and 1.7 % for total hip, which were measured by assessing 30 individuals with two scans at our institution. Calculated from the formula $2.77 \times$ precision error, the least significant change of BMD was $0.044 \text{ g}/\text{cm}^2$ for lumbar spine, $0.038 \text{ g}/\text{cm}^2$ for femoral neck, and $0.038 \text{ g}/\text{cm}^2$ for total hip in a 95 % confidence level. For lumbar spine BMD, the L1–4 value was used for analysis. All TBS measurements were performed retrospectively using TBS iNsite Software, ver. 2.0.0.1 (Med-Imaps, Needham, MA, USA) using spine DXA files from the database to ensure blinding of the investigators to all clinical parameters. The software uses the raw DXA images of the anteroposterior spine for the same region of interest as the lumbar spine BMD measurement.

Statistical analysis

All statistical analyses, except the propensity score analysis, were performed using IBM-SPSS ver. 22.0 software (IBM Corp., Armonk, NY, USA) and a p value <0.05 was



*If a patient or subject had more than two situations simultaneously, those were recorded separately.

Fig. 1 Flow chart describing process of patient and control group enrollment

considered significant. The propensity score analysis was performed with R statistical software (Foundation for Statistical Computing, Vienna, Austria, ver. 3.1.0; <http://cran.r-project.org/>). Descriptive statistics, including means and 95 % confidence intervals, were estimated for both groups. The chi-square test was used to compare the proportion of premenopausal women and incidence of osteoporosis between the groups. Differences in subject characteristics, BMDs, and TBS between the groups were assessed with the Student's *t* test or the Mann–Whitney *U* test after assess normality of the distribution for the tested parameter. Correlations between all parameters were evaluated with Pearson correlation test. Linear regression was used to study the relationships between TBS and age, BMI, and BMDs in each group. A multivariate logistic regression analysis was used to analyze the odds ratio (OR) for the occurrence of DRF using age, BMI, lumbar spine BMD, total hip BMD, and TBS (binary logistic regression, forward conditional method). Femoral neck BMD and trochanter BMD were excluded from the multivariate analysis because these variables are correlated with total hip BMD.

Result

Bone mineral density

A total of 128 of the 258 DRF patients (49.6 %) had BMD in the osteoporotic range (lowest T-score among measured sites

was ≤ -2.5), whereas 39.2 % of controls (100 of 255 subjects) were in the osteoporotic range ($p = 0.018$). The DRF patient group had significantly lower BMD values at femoral neck, femoral trochanter, and total hip than those of the control group: 0.752 ± 0.097 , 0.622 ± 0.089 , and 0.801 ± 0.099 in patient group and 0.779 ± 0.092 , 0.648 ± 0.089 , 0.826 ± 0.101 in control group. However, lumbar spine BMD was not significantly different between the groups ($p = 0.400$) (Table 1).

Trabecular bone score

TBS was not significantly different between the patient and control groups ($p = 0.864$). When the subjects were divided into two age categories: 50 to 64 and 65 to 79, TBS was not different between the groups in either category ($p = 0.867$ and 0.988 , respectively). The patient group had 128 subjects (46.1 %) in the osteopenic range and the control group had 145 subjects (54.9 %) in the osteopenic range. No difference in TBS was detected between the osteoporosis and osteopenia groups ($p = 0.449$ and 0.307 , respectively) (Table 2).

Correlation between TBS and BMDs

TBS was positively correlated with all BMD values, but the correlation coefficients were lower than the *r*-value between femur BMDs and lumbar spine BMD. A moderate correlation was observed between TBS and lumbar spine BMD ($r = 0.445$, $p < 0.001$). A negative correlation was observed

Table 1 Characteristics and BMD of the patient group and control group

	Patient group (<i>n</i> = 258)	Control group (<i>n</i> = 255)	<i>p</i> value
Age (years)	62.7 ± 7.3	62.0 ± 7.4	0.588
BMI (kg/m ²)	23.8 ± 2.9	23.9 ± 2.9	0.346
Lumbar BMD (g/cm ²)	0.937 ± 0.121	0.947 ± 0.100	0.400
Femur neck BMD (g/cm ²)	0.752 ± 0.097	0.779 ± 0.092	0.002*
Trochanter BMD (g/cm ²)	0.622 ± 0.089	0.648 ± 0.089	0.002*
Total hip BMD (g/cm ²)	0.801 ± 0.099	0.826 ± 0.101	0.009*

p < 0.05 is considered significant

**p* < 0.05

between age and the BMD values or TBS (Table 3). TBS decreased linearly as age increased and increased linearly as total hip and lumbar BMD increased in each group (all *p* < 0.001) (Fig. 2).

Relationship with the occurrence of DRF

The multivariate analysis indicated that only total hip BMD was significantly associated with the occurrence of DRF (OR, 10.231; 95 % confidence interval, 1.724–60.702; *p* = 0.010), meaning that a decrease of 1.000 g/cm² in total hip BMD increases the risk of DRF by 10.231 times.

Discussion

Bone microarchitectural deterioration is a major contributing factor for fracture risk, and TBS has been studied as a convenient tool for evaluating the bone microarchitectural structure [21]. Although previous studies revealed that TBS has additive value for predicting vertebral and non-vertebral fractures in postmenopausal women [12–15, 22], our results demonstrate that TBS is not reliable to evaluate bone frailty in patients with a DRF.

This result contrasts with previous studies that reported microarchitectural deterioration of trabecular bone structure in the distal radius in pre- and postmenopausal women with a DRF, as assessed by high resolution peripheral quantitative computed tomography (HR-pQCT) [23, 24]. In addition, a few studies have shown a significant correlation between TBS and skeletal microarchitecture of the distal radius in human cadavers and postmenopausal women with primary

hyperparathyroidism [21, 25]. However, these two studies were not comparative studies between patient and control groups.

The lack of relationship between TBS and the occurrence of a DRF could be explained in a few ways. First, frailty of the distal radius may be mainly associated with the cortical compartment, which cannot be assessed by the lumbar spine TBS. It has been reported that patients with a displaced DRF have lower cortical bone density than that of patients with a non-displaced DRF [26]. In addition, bicortical thickness of the distal radius on a radiograph and cortical thickness of the distal radius on HR-pQCT are studied as indicators of bone quality [24, 27]. Furthermore, metacarpal cortical bone density, which is assessed by digital X-ray radiogrammetry, is significantly associated with a DRF in elderly women [28, 29]. The occurrence of DRF is significantly related to hip BMD but not lumbar spine BMD [5, 27], and severity of a DRF and cortical thickness of the distal radius are not related to BMD of the lumbar spine, which is mainly trabecular [27, 30]. Second, even if trabecular microstructure affects frailty of the distal radius, it may not be accurately evaluated by the lumbar spine TBS due to anatomic site differences. Several studies have pointed out that the trabecular microstructure of the distal radius is weakly or not correlated with that of vertebra and iliac bone [21, 31]. Different loading properties, distribution of weight bearing forces, and aging patterns between the axial and appendicular skeleton could contribute to this discrepancy [27, 32].

Del Rio et al. reported a significant association between TBS and femoral fracture, although they are cortical [22]. However, mean patient age in their study was much higher than that of the current study. The relatively similar pattern of

Table 2 Lumbar spine TBS of the patient group and control group

	Patient group	Control group	<i>p</i> value
TBS	1.317 ± 0.078 (<i>n</i> = 258)	1.316 ± 0.085 (<i>n</i> = 255)	0.864
TBS in 50 to 64 years of age	1.336 ± 0.073 (<i>n</i> = 173)	1.334 ± 0.086 (<i>n</i> = 170)	0.867
TBS in 65 to 79 years of age	1.279 ± 0.077 (<i>n</i> = 85)	1.278 ± 0.070 (<i>n</i> = 85)	0.988
TBS in osteoporosis subjects	1.283 ± 0.074 (<i>n</i> = 128)	1.278 ± 0.069 (<i>n</i> = 100)	0.449
TBS in osteopenia subjects	1.345 ± 0.068 (<i>n</i> = 119)	1.335 ± 0.085 (<i>n</i> = 140)	0.307

Table 3 Correlation coefficient (*r*) between parameters in study population

	Age (years)	BMI (kg/m ²)	Lumbar BMD (g/cm ²)	Femur neck BMD (g/cm ²)	Trochanter BMD (g/cm ²)	Total hip BMD (g/cm ²)
BMI (kg/m ²)	0.115**					
Lumbar BMD (g/cm ²)	-0.351**	0.141**				
Femur neck BMD (g/cm ²)	-0.474**	0.057 NS	0.548**			
Trochanter BMD (g/cm ²)	-0.374**	0.223**	0.519**	0.742**		
Total hip BMD (g/cm ²)	-0.432**	0.152**	0.535**	0.852**	0.875**	
Lumbar TBS	-0.384**	-0.057 NS	0.445**	0.383**	0.332**	0.389**

p < 0.05 is considered significant

NS not significant

***p* < 0.001

bone loss between the femur and lumbar spine during aging, which may be accelerated after peri-menopause, could contribute to the association between femoral fracture and lumbar TBS [33–35].

In this study, TBS was positively correlated with BMD at all sites and inversely correlated with age. The correlation (*r* = 0.45) between TBS derived from the GE Lunar device and lumbar BMD was similar with that of a Spanish case-

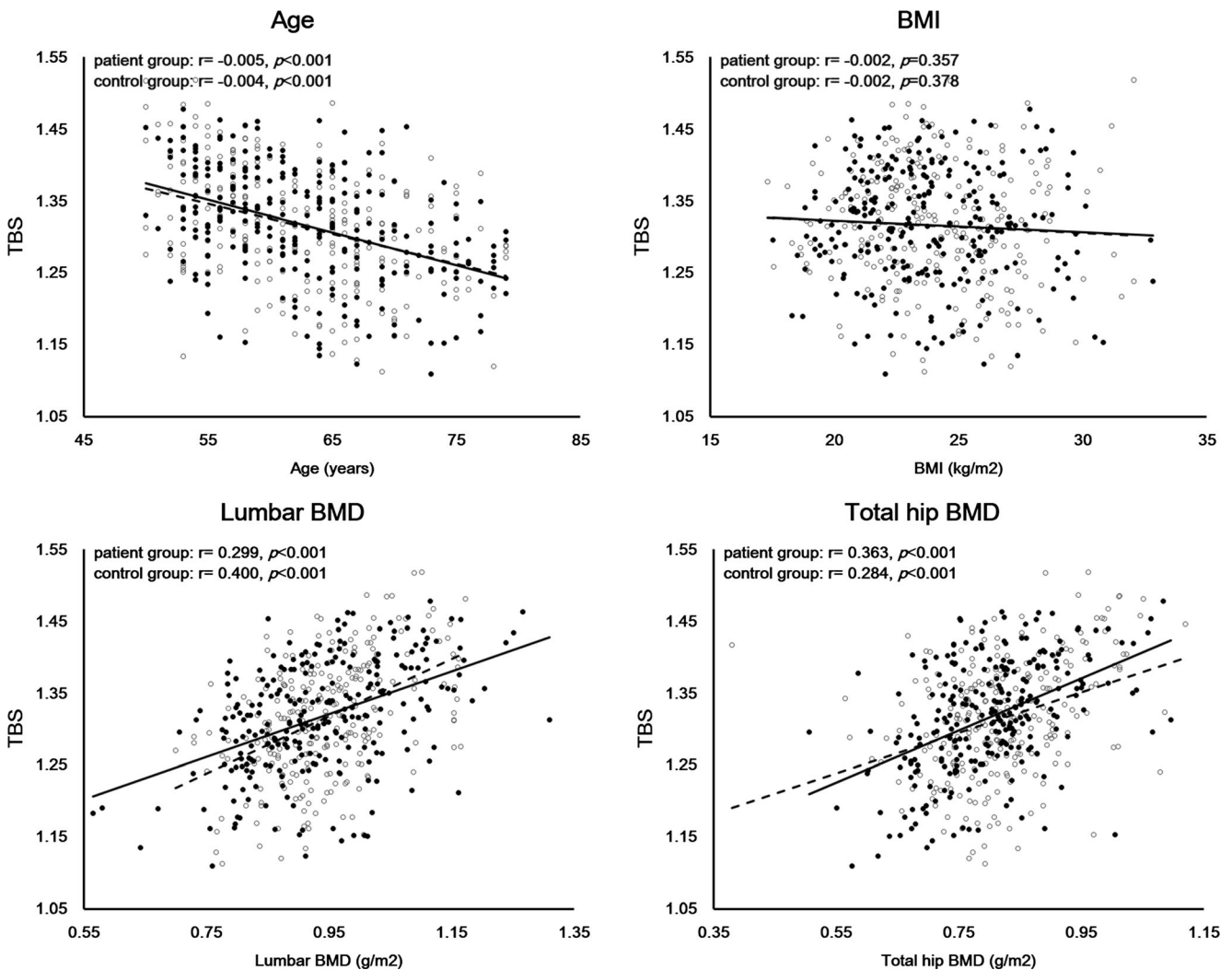


Fig 2 TBS versus age, BMI, lumbar BMD, and total hip BMD in women with DRF (patient group: black dots, solid line) and without fracture (control group: white open circles, dotted line)

control study ($r = 0.52$) [22]. Boutroy et al. also found a significant correlation ($r = 0.58$) between TBS derived from a Hologic scanner and lumbar BMD in the OFELY cohort [12]. However, a weak correlation ($r = 0.33$) was observed between TBS derived from a GE Lunar device and lumbar BMD in the Manitoba Study [36]. Further studies are needed to determine whether TBS differs according to scanner type.

Several limitations in this study should be mentioned. First, we compared our patients with our own hospital-based controls, who were not part of the community-based general population. Second, our institution is a tertiary referral hospital; thus, the included subjects may have more diseases and injuries, which may have affected both the patient and control groups. Third, the study subjects were ethnic Koreans; therefore, our results may not be representative of all women with a DRF. Fourth, although the patients were all postmenopausal and age-matched, we did not evaluate the years since menopause, which could have an impact on the study results. Finally, although we excluded subjects with diseases or who were taking medications affecting bone quality, we could not evaluate other parameters, such as bone turnover markers, due to incomplete control data.

In conclusion, TBS was not different between women with a DRF and those without a history of osteoporotic fracture, suggesting that TBS measured at the lumbar spine, which is mainly trabecular, may not reflect early microarchitectural changes of the distal radius. We found that only total hip BMD is associated with the risk of DRF in Korean women.

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Compliance with ethical standards

Conflicts of interest None.

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