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ORIGINAL ARTICLE

Factors associated with low trabecular bone scores in patients with end-stage kidney disease

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Abstract

The trabecular bone score (TBS) is a textural index that indirectly assesses bone trabecular microarchitecture using lumbar spine images obtained by dual-energy X-ray absorptiometry (DXA). This study compared the TBS of patients with end-stage kidney disease (ESKD) with that of matched controls to identify risk factors associated with a low TBS. TBS and bone mineral density (BMD) were assessed in ESKD patients ($n=76$) and age- and sex-matched control subjects ($n=76$) using DXA. The TBS of both groups was then compared, and risk factors associated with a low TBS (defined as ≤ 1.31) were evaluated. The mean TBS in the ESKD group was significantly lower than that in the control group (1.34 ± 0.15 vs. 1.43 ± 0.08, respectively; $p<0.001$). More subjects in the ESKD group had a low TBS [34.2% (ESRD) vs. 5.3% (controls); $p<0.001$]. The TBS was negatively correlated with age, alkaline phosphatase and C-reactive protein levels, and dialysis vintage, and positively correlated with BMD at the lumbar spine, femoral neck, and hip. Multivariate analysis identified lower estimated glomerular filtration rate and increased C-reactive protein levels as being significantly associated with a low TBS. In conclusion, ESKD patients had abnormal bone microarchitecture (as assessed by the TBS). The TBS was positively correlated with BMD. Renal function and inflammatory marker levels were independently associated with a low TBS. Thus, TBS may be a useful clinical tool for assessing cancellous bone connectivity in ESKD patients.

Keywords Bone microarchitecture · Bone quality · Chronic kidney disease · End-stage kidney disease · Trabecular bone score

Introduction

Patients with chronic kidney disease (CKD) are at increased risk of fracture as the condition progresses [1]. Bone disease in CKD patients is multi-factorial, and includes CKD-mineral bone disorder (CKD-MBD), a systemic disorder of mineral, bone, and vasculature resulting from CKD [2]. Renal osteodystrophy is the bone component of CKD-MBD and involves alterations in bone turnover, mineralization, collagen structure, and cortical and trabecular microarchitecture [3]. Therefore, renal osteodystrophy affects bone quantity and quality, compromises bone strength, and increases fracture risk.

Bone quantity can be assessed by measuring bone mineral density (BMD), which is determined by peak bone mass and amount of bone loss [4]. Dual-energy X-ray absorptiometry (DXA) is the standard method of measuring bone mass and predicts fracture risk in the general population [3]. The use of DXA to predict fracture is controversial; however, the 2017 KDIGO guidelines recommend BMD testing in all CKD patients, because BMD predicts fracture risk across all stages of CKD [5]. Nevertheless, BMD provides information on bone mass only; CKD patients with normal BMD may develop fracture due to abnormal bone texture [6]. The limited utility of DXA for those with CKD is due to the fact that it provides a 2-dimensional assessment of a 3-dimensional structure and, therefore, cannot discriminate

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effectively between cortical and trabecular bone. Both the quantity and quality of bone need to be assessed to gain accurate information regarding fracture risk in CKD patients [7]. Quantitative computed tomography (QCT) and high-resolution peripheral QCT have been developed to measure bone microarchitecture and assess bone quality, and can predict future fracture. However, they are not routinely available in clinical practice [8]. Therefore, a clinically available and non-invasive technique that can evaluate bone microarchitecture accurately in CKD patients is required.

The trabecular bone score (TBS) is a novel tool for evaluating bone microarchitecture. The TBS is a gray-level textural metric that can be extracted from DXA images of the lumbar spine and provides skeletal information of cancellous bone connectivity that is not captured by the standard BMD measurements [9]. The TBS derived from DXA images correlates with the 3-dimensional microarchitecture parameters measured by QCT [10]. Better trabecular bone structure results in a higher TBS, and a weaker skeletal microstructure correlates with a lower TBS. The TBS is a prognostic tool for assessing fracture risk in the general population [11–15]. Recent reports show that the TBS is significantly lower in patients with end-stage kidney disease (ESKD) on dialysis [16–18]; in addition, a lower TBS is associated with higher fracture risk in non-dialysis CKD patients [19]. To date, no studies have evaluated risk factors in ESKD patients related to a low TBS. Here, we compared the TBS between ESKD patients and matched controls and identified factors associated with a low TBS.

Materials and methods

Study population

The case–control study was conducted between April 2011 and December 2016, and recruited 76 consecutive ESKD patients from Incheon Saint Mary's Hospital. All were aged between 20 and 69 years. Seventy-six age- and sex-matched subjects who attended routine health check-up examinations during the same period were included as age- and sex-matched controls. None of the control subjects took corticosteroids, calcium, or bisphosphonate agents. ESKD patients and control subjects with thyroid disorders, parathyroid malignancies, chronic liver disease or rheumatoid arthritis, those with history of lumbar spine compression fracture, and those who had vascular calcification in plain radiographs of pelvis were excluded. The TBS and BMD were measured in all ESKD patients and matched control subjects at the time of enrollment. Demographic data were collected at the time of TBS measurement, which included sex and body mass index (BMI; kg/m^2). Risk factors associated with osteoporosis included smoking status and excess alcohol (≥ 3 units daily) consumption. Alkaline phosphatase (ALP), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels were measured at the time of TBS assessment. In control subjects, the estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation [20]. Since the dialysis modality varied among ESRD patients, the eGFR for ESRD patients was calculated from the serum urea and creatinine concentrations using the equation proposed by Shafi et al. [21]: eGFR (mL/min/1.73 m^2) $= 2.4 \times$ blood urea nitrogen$^{0.984} \times$ creatinine$^{-1.868}$. Two ESKD patients received hemodialysis less than 2 weeks before they underwent preemptive kidney transplantation. As the BMD and TBS were measured before transplantation, the eGFR in those two patients were calculated from the same equation proposed by Shafi et al. In the hemodialysis patients, blood samples were drawn before the first dialysis session in the week, not in fasting state. In the peritoneal dialysis patients, sampling was taken anytime during daytime, generally in the morning and not in fasting state. Lower eGFR for the ESKD group was defined as < 4.25 mL/min/1.73 m^2 according to the median eGFR value. Dyslipidemia was defined as a triglyceride concentration of ≥ 150 mg/dL or a low-density lipoprotein-cholesterol concentration of ≥ 100 mg/dL and/or taking cholesterol-lowering medication.

Disease-related data and history of concurrent diseases were collected from ESRD patients, including intact parathyroid hormone (PTH), dialysis vintage, dialysis modality (hemodialysis versus peritoneal dialysis), history of parathyroidectomy, and the use of medications such as phosphate binders, vitamin D, paricalcitol, cinacalcet, or corticosteroids. The study was approved by the ethics committee at Incheon Saint Mary's Hospital (OC16TISI0057), and conducted in accordance with the principles of the Declaration of Helsinki.

BMD assessment

Areal BMD was measured at the lumbar spine (L1–L4) and left hip using DXA (Lumbar Prodigy densitometer, Madison, WI, USA). All measurements were taken by experienced operators using the same machine and standardized procedures for participant positioning. BMD was measured at the lumbar spine (L1–L4) and left hip (femoral neck and total proximal femur), and expressed as the number of grams of bone mineral per square centimeter (g/cm^2). The World Health Organization (WHO) T score cut-off values were used to define osteopenia ($-2.5 < T < -1.0$) and osteoporosis ($T \leq -2.5$) [22].

TBS assessment

The TBS was analyzed using DXA images of the lumbar spine (L1–L4). Lumbar spine DXA images were reanalyzed in an operator-independent automated manner using TBS iNight® software version 2.1 (Med-Imaps, Merignac, France). The software uses posterior–anterior images, including the BMD region of interest and edge detection; thus, the TBS is calculated over exactly the same region as the lumbar BMD assessment. Matched control subjects and ESKD patients were divided into three TBS groups according to the risk of fracture published in a recent meta-analysis [14]: high risk of fracture, TBS < 1.23; intermediate risk, TBS 1.23–1.31; low risk, TBS > 1.31. A low TBS was defined as ≤ 1.31 [14].

Statistical analysis

Statistical analyses were performed using SPSS (version 21.0; SPSS Inc., Chicago, IL, USA). Continuous data were expressed as the mean ± SD and categorical data as percentages. Clinical variables were compared using an independent *t* test, and the Chi-squared test was used to compare categorical variables between two groups. Spearman's correlation coefficient was used to analyze the correlation between variables. Multiple logistic regression models were used to assess the association between clinical variables and low TBS in ESKD patients. All variables with a *p* value < 0.10 in univariate logistic regression analysis were incorporated as explanatory variables (the forward method). All tests were two-tailed, and a *p* value < 0.05 was considered statistically significant.

Results

Patient characteristics

Table 1 lists the demographic, clinical, and laboratory characteristics of the age- and sex-matched control and ESKD subjects. The mean age of both groups was 48 ± 11 years, and 40% were male. There were no significant differences between the groups in terms of BMI, alcohol consumption, previous fracture rate, and presence of diabetes mellitus. The proportion of current smokers was higher in the matched control group, whereas the proportions of subjects with hypertension and dyslipidemia were higher in the ESKD group. Systolic and diastolic blood pressure levels, and urea nitrogen, ALP, phosphorus, ESR, and CRP levels, were higher, while the eGFR, calcium, and hemoglobin levels, and platelet counts, were lower, in the ESKD group than in the matched controls.

The mean dialysis vintage was 1.7 years, and 76% of ESRD subjects were on hemodialysis, 21% were on peritoneal dialysis, and 3% received preemptive renal transplantation. One patient had undergone parathyroidectomy and 78% of patients used calcium-based phosphorus binders.

Assessment of the TBS and fracture risk according to the TBS

The mean TBS was lower in ESKD patients than in matched controls (1.34 ± 0.15 vs. 1.43 ± 0.08, respectively; $p < 0.001$). In the ESKD group, 26 patients (34.2%) had a low TBS, while four in the control group (5.3%) had a low TBS ($p < 0.001$).

Subjects were classified as low, intermediate, and high fracture risk according to the TBS [14]. Fracture risk according to the TBS was significantly higher in the ESKD group than in the matched control group ($p < 0.001$). In the matched control group, 72 (94.7%), one (1.3%), and four subjects (3.9%) had low, intermediate, and high TBS fracture risk, respectively. In the ESRD group, 50 (65.8%), 14 (18.4%), and 12 subjects (15.8%) had low, intermediate, and high TBS fracture risk, respectively.

Assessment of BMD and BMD classification according to WHO criteria

BMDs at the lumbar spine, femoral neck, and total hip were lower in ESKD patients than in matched controls (1.12 ± 0.18 vs. 1.19 ± 0.15, $p = 0.026$; 0.84 ± 0.12 vs. 0.95 ± 0.14, $p < 0.001$; and 0.89 ± 0.13 vs. 1.00 ± 0.16, $p < 0.001$, respectively).

According to the WHO criteria, subjects were classified as follows: normal BMD, osteopenia, and osteoporosis. More subjects in the ESKD group than in the matched control group had osteopenia and osteoporosis ($p = 0.001$). In the matched control group, 25 (32.9%) subjects had osteopenia and none had osteoporosis. In the ESKD group, 33 (43.4%) and 10 (13.2%) subjects had osteopenia and osteoporosis, respectively.

Correlation between clinical data, inflammatory markers, BMD, and TBS

In both groups, the TBS showed a significant negative correlation with age and ALP levels, and a positive correlation with BMD at the lumbar spine, femoral neck, and total hip (Table 2). The TBS was positively correlated with BMI in the matched control group, but negatively correlated with CRP and dialysis vintage in the ESKD group.

Table 1 Charsubjects and patients with ESKD

Variables [*N* (%) or mean ± SD]	Control (*N* = 76)	ESKD (*N* = 76)	*p* value
Age, years	48 ± 11	48 ± 11	0.961
Male	30 (40)	30 (40)	1.000
BMI (kg/m^2)	23.7 ± 3.1	23.2 ± 4.2	0.408
Current smoking	22 (29)	8 (11)	0.007
Alcohol ≥ 3 units/day	0 (0)	1 (1)	1.000
Previous fracture	2 (3)	5 (7)	0.442
Diabetes mellitus	15 (20)	25 (33)	0.097
Hypertension	13 (17)	69 (91)	< 0.001
Dyslipidemia	12 (16)	36 (49)	< 0.001
Systolic BP	115 ± 13	132 ± 19	< 0.001
Diastolic BP	74 ± 10	80 ± 13	< 0.001
eGFR (mL/min/1.73 m^2)	99.9 ± 12.6	3.0 ± 2.0	< 0.001
Laboratory findings			
Urea nitrogen (mg/dL)	13 ± 4	62 ± 23	< 0.001
ALP (U/L)	69 ± 22	113 ± 117	0.002
Calcium (mg/dL)	9.2 ± 0.4	8.5 ± 1.1	< 0.001
Phosphorus (mg/dL)	3.6 ± 0.6	5.2 ± 1.7	< 0.001
ESR (mm/h)	15 ± 12	36 ± 28	< 0.001
CRP (mg/L)	0.9 ± 1.0	7.6 ± 18.9	0.003
Hemoglobin (g/dL)	14.0 ± 1.6	10.1 ± 1.5	< 0.001
Platelet (10^3/μL)	250 ± 58	207 ± 76	< 0.001
Intact PTH (pg/mL)	–	301 ± 213	
Disease-related data			
Dialysis vintage (years)		1.7 ± 2.7	
Type of dialysis			
Hemodialysis		58 (76)	
Peritoneal dialysis		16 (21)	
Preemptive renal transplantation		2 (3)	
Parathyroidectomy		1 (1)	
Calcium-based phosphorus binder		59 (78)	
Non-calcium-based phosphorus binder		20 (26)	
Vitamin D		27 (36)	
Paricalcitol		3 (4)	
Cinacalcet		2 (3)	
History of corticosteroid treatment		8 (11)	

SD standard deviation, *ESKD* end-stage kidney disease, *BMI* body mass index, *BP* blood pressure, *eGFR* estimated glomerular filtration rate, *ALP* alkaline phosphatase, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *PTH* parathyroid hormone

Comparison of clinical characteristics, disease-related variables, and BMD between TBS subgroups of ESKD patients

Table 3 compares demographic and disease-related variables between two TBS subgroups of ESKD subjects. Current smokers were more common in the normal TBS group than in the low TBS group. The eGFR was lower, the CRP level was higher, and the dialysis vintage was longer in the low TBS group. In the low TBS group, BMD at the femoral neck was significantly lower than that in the normal TBS group.

Factors associated with low TBS in ESKD patients

Table 4 shows the univariate and multivariate logistic regression analyses of low TBS in ESKD patients. Univariate analysis identified diabetes mellitus, lower eGFR, *T* score of lumbar spine (L1–L4), and increased CRP as being associated with low TBS ($p < 0.10$). Multivariate analysis identified lower eGFR and increased CRP as significant factors associated with a low TBS ($p < 0.05$).

Table 2 Correlation between clinical data, inflammatory markers, BMD, and TBS in patients with ESKD and matched controls

Group	Age, years	BMI, kg/m^2	ESR, mm/h	CRP, mg/L	ALP, U/L	Calcium, mg/dL	Phosphorus, mg/dL	Intact PTH, pg/mL	EGFR, mL/min/1.73 m^2	Dialysis vintage, years	BMD, g/cm^2		
											Lumbar spine	Femoral neck	Total hip
Control													
TBS, L1–4	−0.384 (0.001)	0.252 (0.028)	−0.143 (0.235)	−0.115 (0.235)	−0.230 (0.045)	0.026 (0.827)	−0.191 (0.104)	–	0.149 (0.200)	–	0.373 (0.001)	0.439 (<0.001)	0.450 (<0.001)
ESKD													
TBS, L1–4	−0.243 (0.034)	−0.125 (0.280)	−0.030 (0.800)	−0.305 (0.007)	−0.304 (0.008)	0.164 (0.157)	0.033 (0.780)	0.001 (0.996)	0.148 (0.202)	−0.232 (0.044)	0.337 (0.003)	0.259 (0.025)	0.353 (0.002)

Data are expressed as *r* coefficients (*p* value)

ESKD end-stage kidney disease, *TBS* trabecular bone score, *BMD* bone mineral density, *BMI* body mass index, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *ALP* alkaline phosphatase, *PTH* parathyroid hormone, *eGFR* estimated glomerular filtration rate

Discussion

Here, we used the TBS to assess bone microarchitecture (cancellous bone connectivity), and investigated the relationship between TBS and clinical parameters and BMD in ESKD patients. ESKD patients had a lower TBS than age- and sex-matched controls. In addition, more subjects in the ESKD group than in the matched control group had a low TBS. The TBS was positively correlated with BMDs at all skeletal sites measured. Lower eGFR and increased CRP were independently associated with a low TBS. These results suggest that ESKD patients have poor cancellous bone connectivity, and that renal function and inflammation are associated with the low TBS.

Renal osteodystrophy is the histological feature of skeletal component of CKD-MBD, and is characterized by a spectrum of bone diseases, including osteitis fibrosa, adynamic bone disease, osteomalacia, and mixed bone disease [23]. Renal osteodystrophy has a marked effect on all aspects of bone quality, including bone turnover, microarchitecture, mineralization, micro-damage, and collagen properties [3]. In addition, ESKD patients have abnormal cancellous bone volume, trabecular thickness, and material and nano-mechanical abnormalities [24]. Osteoporosis is a skeletal disorder resulting in compromised bone strength, which predisposes an individual to an increased risk of fracture [4]. Measuring BMD at the hip and spine using DXA is the most common method of diagnosing osteoporosis and of monitoring patients [25]. BMD determines bone mass [4]. Here, we found that ESKD patients had lower BMD at all skeletal sites measured, and more ESKD had osteopenia and osteoporosis patients than matched controls. The ESKD group also had higher levels of serum ALP and phosphorus, and lower calcium levels. Although intact PTH levels in the matched controls were not included in the analysis, intact PTH levels in ESKD patients were high. These laboratory findings are consistent with the laboratory features of mineral component of CKD-MBD. Thus, subjects in the ESKD group had both features of reduced bone mass and mineral derangements of CKD-MBD.

The 2017 KDIGO guidelines now recommend BMD testing for CKD patients [5]. Nevertheless, BMD provides information only about bone mass, and CKD patients with normal BMD may develop fracture due to bone texture abnormalities [6]. CKD-related mineral abnormalities such as hyperparathyroidism have different effects on bone compartments. Increased PTH has catabolic effects on cortical bone, leading to increased cortical porosity, while at the same time having an anabolic effect on trabecular bone, resulting in increased turnover and thickened irregular bone [26–28]. DXA does not effectively discriminate between cortical and trabecular

Table 3 ESKD patients' characteristics stratified according to the TBS

Variables, *N* (%) or mean ± SD	Normal TBS (> 1.31, *N* = 50)	Low TBS (≤ 1.31, *N* = 26)	*P* value
Age, years	46 ± 12	51 ± 10	0.069
Male	22 (44)	8 (31)	0.327
BMI, kg/m^2	22.6 ± 3.8	24.4 ± 4.6	0.096
Current smoking	8 (16)	0 (0)	0.045
Previous fracture	2 (4)	3 (12)	0.331
Diabetes mellitus	13 (26)	12 (46)	0.121
Hypertension	47 (94)	22 (85)	0.222
Dyslipidemia	22 (45)	14 (56)	0.463
eGFR, mL/min/1.73 m^2	3.3 ± 2.2	2.3 ± 1.3	0.009
Laboratory findings			
Urea nitrogen, mg/dL	65 ± 26	57 ± 16	0.129
ALP, U/L	106 ± 112	126 ± 126	0.155
Calcium, mg/dL	8.6 ± 0.9	8.2 ± 1.4	0.224
Phosphorus, mg/dL	5.0 ± 1.4	5.6 ± 2.2	0.396
Intact PTH, pg/mL	282 ± 168	337 ± 285	0.707
ESR, mm/h	35 ± 29	37 ± 26	0.597
CRP, mg/L	6.7 ± 20.7	9.2 ± 14.8	0.006
Hemoglobin, g/dL	10.3 ± 1.6	9.8 ± 14.8	0.189
Platelet, 10^3/μL	206 ± 66	209 ± 93	0.844
Disease-related data			
Dialysis vintage (years)	1.3 ± 2.4	2.3 ± 3.0	0.047
Type of dialysis			0.215
Hemodialysis	40 (80)	18 (69)	
Peritoneal dialysis	8 (16)	8 (31)	
Preemptive renal transplantation	2 (4)	0 (0)	
Calcium-based phosphorus binder	38 (76)	21 (81)	0.775
Non-calcium-based phosphorus binder	11 (22)	9 (35)	0.278
Vitamin D	19 (38)	8 (31)	0.618
Paricalcitol	2 (4)	1 (4)	1.000
Cinacalcet	1 (2)	1 (4)	1.000
History of corticosteroid treatment	6 (12)	2 (8)	0.708
TBS, L1–L4	1.414 ± 0.074	1.189 ± 0.136	< 0.001
BMD (g/cm^2)			
Lumbar spine	1.153 ± 0.144	1.068 ± 0.224	0.088
Femoral neck	0.860 ± 0.114	0.786 ± 0.122	0.025
Total hip	0.904 ± 0.112	1.847 ± 0.159	0.082

ESKD end-stage kidney disease, *TBS* trabecular bone score, *SD* standard deviation, *BMI* body mass index, *eGFR* estimated glomerular filtration rate, *ALP* alkaline phosphatase, *PTH* parathyroid hormone, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *BMD* bone mineral density

bone [7]. QCT and high-resolution peripheral QCT measure bone microarchitecture and predict fracture risk; however, they are not routinely available in clinical practice [8]. The TBS is a measure of gray-scale homogeneity from DXA images of the lumbar spine, which correlates with trabecular microarchitecture [29, 30]. Its clinical significance as a prognostic tool for fracture risk has been demonstrated in the general population [11–15]. In addition, the TBS improves the performance of the WHO Fracture Risk Assessment Tool (FRAX) algorithm, or enables prediction of fracture independently of FRAX [14, 31, 32]. There are limited data about TBS in CKD patients. ESKD patients have a lower TBS than controls [16–18], and a lower TBS predicts higher fracture risk in non-dialysis CKD patients independently of BMD [19]. The results presented herein are consistent with these earlier findings. The TBS in the ESKD group was significantly lower than that in the matched control group, and showed a positive correlation with areal BMDs. This suggests that ESKD patients have altered trabecular bone microarchitecture as well as reduced bone mass.

Table 4 Univariate and multivariate analyses of factors associated with low TBS in patients with ESKD

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Older age (≥ 50 years)	1.88	0.72–4.92	0.196			
BMI			0.130			
< 18.5	1.73	0.25–12.0	0.577			
18.5–22.9	1.00 (Reference)					
23.0–24.9	0.26	0.03–2.30	0.226			
25.0–29.9	3.25	1.00–10.6	0.051			
≥ 30.0	2.60	0.45–15.1	0.287			
Sex	1.77	0.65–4.8	0.265			
Previous fracture	3.13	0.49–20.0	0.228			
Dialysis vintage, per year	1.14	1.00–1.37	0.145			
Type of dialysis	2.22	0.72–6.86	0.165			
Diabetes mellitus	2.71	0.99–7.44	0.052			
Calcium-based phosphorus binder	1.33	0.41–4.28	0.637			
Non-calcium-based phosphorus binder	1.88	0.66–5.36	0.239			
Vitamin D	0.73	0.26–1.99	0.533			
History of corticosteroid treatment	0.96	0.08–11.11	0.974			
Increased intact PTH (≥ 300 pg/mL)	1.04	0.39–2.77	0.940			
Increased ALP (> 110 U/L)	1.47	0.49–4.47	0.493			
Lower eGFR (< 4.25 mL/min/1.73 m^2)	3.38	1.23–9.24	0.018	3.27	1.16–9.25	0.026
Lumbar spine *T* score	0.72	0.51–1.03	0.069			
Phosphorus (mg/dL)			0.370			
< 3.5	1.00 (Reference)					
3.5–5.5	0.72	0.17–2.98	0.651			
≥ 5.5	1.53	0.38–6.21	0.552			
Calcium (mg/dL)			0.385			
< 8.5	1.00 (Reference)					
8.5–9.5	0.58	0.21–1.65	0.308			
≥ 9.5	0.41	0.09–1.76	0.229			
Increased CRP (≥ 5 mg/L)	3.88	1.2–12.57	0.024	3.72	1.10–12.66	0.035
Increased ESR (≥ 20 mm/h)	1.20	0.44–3.22	0.723			

ESKD end-stage kidney disease, *TBS* trabecular bone score, *OR* odds ratio, *CI* confidential interval, *BMI* body mass index, *PTH* parathyroid hormone, *ALP* alkaline phosphatase, *eGFR* estimated glomerular filtration rate, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate

Age, CRP, ALP, and dialysis vintage showed a negative correlation with the TBS, and ESKD patients with low TBS had lower eGFR, higher CRP, and longer dialysis vintage than those with a normal TBS. Age is an important factor in the TBS, and a significant decrease in the TBS occurs with age in both males and females [9, 33]. Serum ALP levels are a marker of renal osteodystrophy [34], and elevated ALP levels in dialysis patients are independently associated with mortality [35]. Inflammation in ESKD patients is closely related to an altered bone-vascular axis [36]. In addition, inflammation induces osteoclast differentiation in CKD patients [37]. These findings suggest that the TBS in ESKD patients may reflect altered cancellous bone connectivity caused by ageing, inflammation, and reduced renal function. The multivariate logistic regression analysis identified lower eGFR and increased CRP as independently associated with a low TBS in ESKD patients. Unexpectedly, older age was not associated with a low TBS in logistic regression analysis. We assume that the effect of age on TBS is modest compared with renal function or inflammation in the ESKD population.

This study has several limitations. First, it was a retrospective cross-sectional analysis from a single center. Second, the number of subjects was rather small. Third, other markers of CKD-MBD, including vitamin D or fibroblast growth factor-23, were not available. Fourth, the residual renal function calculated from 24 h urine collection was not assessed because of missing data. Instead, we used the equation proposed by Shafi et al. which uses the serum urea and creatinine concentrations [21].

In conclusion, measurement of the TBS in ESKD patients revealed poor cancellous bone connectivity. The TBS was positively correlated with BMD, and renal function and inflammation were significantly associated with a low TBS. These findings support the use of the TBS as a tool to identify the risk of osteoporosis and fracture, and may reflect ESKD patients with high levels of inflammation. Additional studies with a larger sample size are needed to clarify the association identified herein.

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Compliance with ethical standards

Conflict of interest The authors have no competing interests to declare.

Human and animal rights and informed consent For this type of study, formal consent is not required.

Ethical approval The study was approved by the ethics committee at Incheon Saint Mary's Hospital (OC16TISI0057), and conducted in accordance with the principles of the Declaration of Helsinki.

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