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Discordance in Bone Mineral Density between the Lumbar Spine and Femoral Neck Is Associated with Renal Dysfunction

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Purpose: Bone mineral density (BMD) determined by dual-energy X-ray absorptiometry is considered a gold standard for diagnosing osteoporosis. Some people show discordance in BMD values measured at the femur and that at the lumbar spine (LS). The aim of the present study was to investigate whether differences in BMD T-scores between the LS and femur neck (FN) are associated with renal dysfunction in the general population of Korea.

Materials and Methods: We analyzed national data for 17306 adults from the Korean National Health and Nutrition Examination Survey conducted between 2008 and 2011. BMD T-score differences between LS and FN (termed BMD offset) were calculated by subtracting FN T-scores from LS T-scores. Diminished renal function was defined as estimated glomerular filtration rates (eGFR) less than 60 mL/min/1.73 m^2.

Results: Among those aged ≥50 years, BMD offset was negatively associated with eGFR levels. Additionally, eGFR levels decreased linearly across increasing BMD offset quartiles. Men and women with an offset of >1.5 showed a 4.79-times and 2.51-times higher risk of renal dysfunction, respectively, compared to individuals with an offset of ≤0, after adjusting for age, body mass index, educational level, current smoking, and physical activity. In contrast, there was little evidence of an association between renal dysfunction and BMD offset in subjects aged <50 years.

Conclusion: Discordance between LS and FN BMDs was significantly associated with renal dysfunction in subjects aged ≥50 years. When assessing bone health in older chronic kidney disease patients, physicians should consider the possibility of BMD discordance between LS and FN.

Key Words: Osteoporosis, renal insufficiency, absorptiometry, photon, aging

INTRODUCTION

Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing an individual to an increased risk of fracture.[1] Clinically, bone strength is estimated by non-invasive assessment of bone mineral density (BMD). BMD at the femur and lumbar spine (LS), as measured by dual-energy X-ray absorptiometry (DXA), is a fundamental measure with which to assess bone mass and is currently considered the gold standard for diagnosing osteoporosis among those without fragility fracture.[2]

Femoral cortical bone and LS trabecular bone have different characteristics,[3] and signals to bone, such as those initiated by hormones or medication, can differentially affect bone compartments.[3] Accordingly, it has been reported that diagnoses of osteoporosis are dependent on the sites used to take measurements.[4,5] Generally, menopause and glucocorticoid result in higher hip T-scores than LS T-scores,[6,7] whereas aging-associated processes, such as degenerative disc diseases, spondylo-

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sis, and aortic calcification, result in lower hip T-scores than LS T-scores.[7] Discordance in BMD between the LS and hip can be significant,[8] and a recent study that investigated the metabolic characteristics of subjects with BMD discordance reported that the prevalences of aging-associated diseases, such as diabetes and hypertension, were higher in subjects with a lower femur neck (FN) BMD than LS BMD.[9]

Reduced renal function is a marker of aging,[10,11] and renal dysfunction is associated with several degenerative diseases, including dementia and macular degeneration.[12,13] Thus, BMD discordance with higher LS T-score might be related with renal dysfunction. However, no study has evaluated a potential association between renal function and BMD discordance so far. Previously, offset (difference) between LS and FN T-score was used to represent BMD discordance and reported to enhance fracture risk prediction.[14] Thus, in this study, we aimed to determine whether renal dysfunction is associated with LS and FN T-score differences (termed BMD offset) in the Korean adult population.

MATERIALS AND METHODS

Data source and study population

This study was based on data obtained during the Korean National Health and Nutrition Examination Survey (KNHANES) conducted between July 2008 and May 2011. KNHANES is a nationally representative, population-based, cross sectional study that uses a complex, multi-stage probability sample design[15] and involves the collation of data obtained by physical examination, clinical and laboratory testing, personal interviews, and related measurement procedures. Body composition was measured by DXA only from July 2008 to May 2011 in the KNHANES. If there were vertebrae filled with a metallic implant or cement after surgery, those levels were excluded for measurement. Participants with only one analyzable vertebra or that had undergone bilateral femur surgery were excluded from spine and femur DXA testing, respectively.

Of the 21071 participants in KNHANES 2008–2011 that underwent DXA, we chose 19143 subjects aged ≥19 years. Subjects were excluded 1) if the subjects met exclusion criteria for DXA scan of LS or FN (n=964) as described above or 2) if clinical or laboratory values required for the present study were missing (n=873). In total, the study population comprised 17306 subjects.

All participants in the KNHANES provided written informed consent prior to participation. The Institutional Review Board of Dongguk University Ilsan Hospital approved the study protocol (IRB No: 2019-02-005-001).

BMD measurements and assessment of T-score discordance

Areal BMD values (g/cm^2) at the LS and FN were measured using a DISCOVERY-W fan-beam densitometer (Hologic Inc., Bedford, MA, USA) by licensed, trained technicians. For quality control purposes, daily automatic calibration was performed using a phantom, and the examiners reviewed BMD results weekly. Acceptable BMD coefficients of variation for the L1–4 spine and FN by DXA were 1.9% and 2.6%, respectively. T-scores were calculated using the manufacturer's Japanese reference values. BMD offsets were calculated by subtracting FN T-scores from LS T-scores and used to examine the association between BMD discordance and renal dysfunction. In addition, the prevalences of major and minor discordances were calculated as previously described.[5,8] Briefly, major discordance was defined as an osteoporotic T-score at one site and a normal T-score at the other. Minor discordance was defined when, for example, one site was osteoporotic and the other osteopenic, or one site was osteopenic and the other normal.

Clinical and laboratory parameters

The participants' heights and weights were measured, and body mass indices (BMIs) were calculated by dividing weight by height squared (kg/m^2). The subjects were required to respond to a questionnaire that addressed age, sex, education level, smoking and alcohol consumption statuses, and physical activity. Education levels were classified into less than high school versus high school or higher. Subjects who had smoked at least 100 cigarettes during their lifetime and were smoking when they participated in KNHANES were classified as current smokers. Heavy drinkers were defined as those who drank >60 g of pure alcohol/occasion for men or >40 g of pure alcohol/occasion for women on more than two occasions per week. Physically active was defined as 1) ≥3 days of vigorous activity for ≥20 min/day per week or 2) ≥5 days of moderate intensity activity. Blood samples were collected by trained personnel after overnight fasting (for at least 8 h). Serum creatinine was measured using a Hitachi 7600 analyzer (Hitachi Co., Tokyo, Japan). Estimated glomerular filtration rates (eGFRs) were calculated using Chronic Kidney Disease-Epidemiology Collaboration formulae[16]: for women, $GFR=144\times(\text{serum creatinine}/0.7)^{-0.329}\times(0.993)^{Age}$ for a serum creatinine level of ≤0.7 mg/dL or $144\times(\text{serum creatinine}/0.7)^{-1.209}\times(0.993)^{Age}$ for a serum level >0.7 mg/dL, and for men, $GFR=141\times(\text{serum creatinine}/0.9)^{-0.411}\times(0.993)^{Age}$ for a serum creatinine level of ≤0.9 mg/dL or $141\times(\text{serum creatinine}/0.9)^{-1.209}\times(0.993)^{Age}$ for a level >0.9 mg/dL. Diminished renal function was defined as an eGFR of < 60 mL/min/1.73m^2.

Statistical analysis

KNHANES is a survey using a rolling sampling design that involves a complex, stratified, multistage, probability-cluster survey of a representative sample of the non-institutionalized civilian population in Korea.[17] To handle the multistage complex survey design, weights based on the sampling probabilities were assigned in all the analyses, of which the results were interpreted to the population. Continuous variables are present-

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ed as means±standard errors and categorial variables as numbers and proportions. For categorical variables, the weighted frequencies of categorical variables were normalized to the sample size, and Rao-Scott chi-square tests were performed to evaluate the significance of intergroup differences. Wald tests were used to analyze continuous variables. Multiple linear regression analysis was conducted to determine covariates significantly associated with eGFR, and to investigate the association between BMD offset and eGFR, analysis of covariance with adjustment for potential confounders was performed across quartiles of BMD offset. In addition, odds ratios (ORs) of diminished renal function according to BMD offset levels were estimated by multiple logistic regression analyses with adjustment for potential confounders. When analyzing ORs across BMD offset level, we classified BMD offset into five groups at 0.5 T-score intervals so that the result can be easily implemented in routine clinical practice. The analysis was performed on the total population and on two age groups (<50 or ≥50 years old) because hormonal changes that can affect bone physiology occur at around the age of 50. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA), and statistical significance was accepted for p values <0.05.

Table 1. Clinical and Demographic Characteristics of the Study Population

	Men (n=7526)	Women (n=9780)	p value*
Age (yr)	43.9±0.3	45.8±0.3	<0.001
Weight (kg)	70.3±0.2	57.4±0.1	<0.001
Height (cm)	170.8±0.1	157.3±0.1	<0.001
BMI (kg/m^2)	24.06±0.049	23.22±0.051	<0.001
Serum creatinine (mg/dL)	0.96±0.004	0.70±0.002	<0.001
eGFR (mL/min/1.73 m^2)	96.8±0.3	101.7±0.3	<0.001
High education	5812 (77.22)	6220 (63.60)	<0.001
Current smoker	3556 (47.25)	649 (6.63)	<0.001
Heavy drinker	1698 (22.56)	519 (5.31)	<0.001
Physically active subjects	2067 (27.47)	2229 (22.79)	<0.001
LS BMD (T score)	-0.42±0.02	-0.75±0.02	<0.001
FN BMD (T score)	-0.16±0.02	-0.83±0.02	<0.001
LS osteoporosis	286 (3.80)	1338 (13.68)	<0.001
FN osteoporosis	117 (1.55)	945 (9.66)	<0.001

BMI, body mass index; eGFR, estimated glomerular filtration rate; LS, lumbar spine; BMD, bone mineral density; FN, femur neck.
Continuous variable results are shown as means±standard errors and categorical variable results as percentage weighted and relative frequencies.
Weighted frequencies of categorical variables are normalized to the sample size.
*Rao-Scott chi-square test for categorical variables and Wald test for continuous variables.

RESULTS

Characteristics of the study population

A total of 17306 subjects were included for analysis. Table 1 shows the baseline characteristics of the study subjects. Mean age was 43.85 years for men and 45.76 years for women. Height, weight, and BMI were significantly higher for men than women. Mean eGFR was greater for women (101.65 vs. 96.79), and the prevalence of osteoporosis was significantly higher in women than in men in the LS (13.68% vs. 3.80%) and in the FN (9.66% vs. 1.55%). When we analyzed baseline characteristics according to BMD offset levels, participants with BMD offset ≥0 were more likely to be old and have lower eGFR levels than those with BMD offset <0 (Supplementary Table 1, only online). Among those aged ≥50 years, BMD offset ≥0 was associated with higher BMI values. However, this association was not noticeable among those aged <50.

In our study, 29.2% (5061/17306) of the patients were classified as having BMD discordance (Supplementary Table 2, only online); of these, 55.62% (2815/5061) had lower LS BMD than FN BMD. Regarding the severity of discordance, 4968 (98.16%) exhibited minor discordance and 93 (1.84%) major discordance. When we conducted subgroup analysis on patients aged ≥50 years, 36.82% (3028/8223) were classified as having BMD discordance.

Association between BMD offset and eGFR

Multiple linear regression analysis was used to examine associations between eGFR and clinical parameters (Table 2). For subjects aged ≥50 years, eGFR was negatively associated with age, BMI, high education, and BMD offset in men and women, whereas eGFR was positively associated with heavy drinking. In subjects aged <50, eGFR was negatively associated with age and high education. However, the association between eGFR and BMD offset observed in those aged ≥50 was not observed in those <50.

To further examine the effect of BMD offset on renal function, we divided participants into BMD offset quartiles. After adjustment for age, education, BMI, educational level, current smoking, heavy drinking, and physical activity, eGFR levels were found to linearly decrease with increasing BMD offset in men and women aged ≥50 years (Table 3). In contrast, no significant difference in eGFR levels was observed between offset quartiles in subjects aged <50.

Risk of renal dysfunction according to BMD offset

In total, 2.60% (446/17306) of the study patients had renal dysfunction. Multiple logistic regression analysis was used to determine ORs of diminished renal function with respect to BMD offset (Table 4). We found that higher BMD offset was significantly more likely to diminish renal function in men [continuous variable; OR, 1.679; 95% confidence interval (CI), 1.455–1.936] and women (OR, 1.518; 95% CI, 1.291–1.785) aged ≥50 years. In addition, in this age group, individuals with a BMD offset of >0 consistently showed a higher risk of renal dysfunction, even after adjustment for age (Fig. 1). In men, the odds ratio for the risk of renal dysfunction was 4.785 times higher among participants with a BMD offset of ≥1.5 than among

Table 2. Multiple Linear Regression Analysis of Associations between Covariates and Renal Function

Independent variables	Dependent variable: eGFR					
	Men			Women		
	β	SE	*p* value*	β	SE	*p* value*
Age ≥50 years (n=8223)						
Age	-0.761	0.030	<0.001†	-0.923	0.025	<0.001†
BMI	-0.809	0.085	<0.001†	-0.160	0.065	0.014†
High education	-2.731	0.487	<0.001†	-2.136	0.511	<0.001†
Current smoker	1.276	0.497	0.011†	-1.155	0.944	0.222
Heavy drinker	2.294	0.632	<0.001†	3.772	1.020	<0.001†
Physically active subjects	0.826	0.546	0.131	0.149	0.449	0.741
LS BMD–FN BMD	-1.475	0.249	<0.001†	-1.564	0.219	<0.001†
Age <50 years (n=9083)						
Age	-0.723	0.029	<0.001†	-0.797	0.025	<0.001†
BMI	-0.221	0.073	0.003†	-0.007	0.052	0.888
High education	-2.271	0.858	0.008†	-1.181	0.557	0.034
Current smoker	1.388	0.441	0.002†	0.939	0.706	0.184
Heavy drinker	1.684	0.489	0.001†	0.938	0.731	0.200
Physically active subjects	-0.193	0.478	0.687	-0.467	0.417	0.264
LS BMD–FN BMD	-0.281	0.249	0.258	-0.229	0.224	0.307

BMI, body mass index; eGFR, estimated glomerular filtration rate; BMD, bone mineral density; LS, lumbar spine; FN, femur neck.
p value for difference in the effect of LS BMD–FN BMD according to sex=0.735.
*Wald test, †Statistically significant difference.

Table 3. Estimated Mean of eGFR Levels Across LS-FN T-Score Quartiles

Men						Women					
LS BMD–FN BMD Quartiles	eGFR EST (SE)	*p* value for pairwise difference				LS BMD–FN BMD Quartiles	eGFR EST (SE)	*p* value for pairwise difference			
		Q1	Q2	Q3	Q4			Q1	Q2	Q3	Q4
Age ≥50 years* (n=8223)											
Q1 (≤-0.621)	88.61 (±0.99)		0.005	0.003	<0.001	Q1 (≤-0.695)	92.07 (±1.47)		0.017	<0.001	<0.001
Q2 (<-0.621 to ≤0.019)	86.35 (±0.91)	0.005		0.618	0.136	Q2 (<-0.695 to ≤-0.091)	90.36 (±1.46)	0.017		0.278	0.020
Q3 (<0.019 to ≤0.654)	86.02 (±1.07)	0.003	0.618		0.352	Q3 (<-0.091 to ≤0.522)	89.64 (±1.47)	<0.001	0.278		0.278
Q4 (>0.654)	84.96 (±1.00)	<0.001	0.136	0.352		Q4 (>0.522)	88.68 (±1.50)	<0.001	0.020	0.278	
Overall *p* value	<0.0001						<0.0001				
Age <50 years† (n=9083)											
Q1 (≤-0.980)	105.13 (±0.71)		0.124	0.408	0.359	Q1 (≤-0.399)	111.43 (±0.98)		0.572	0.987	0.424
Q2 (<-0.980 to ≤-0.414)	103.66 (±0.74)	0.124		0.813	0.804	Q2 (<-0.399 to ≤0.173)	110.67 (±0.97)	0.572		0.526	0.978
Q3 (<-0.414 to ≤0.149)	104.07 (±0.67)	0.408	0.813		0.984	Q3 (<0.173 to ≤0.733)	111.42 (±0.92)	0.987	0.526		0.282
Q4 (>0.149)	104.05 (±0.66)	0.359	0.359	0.984		Q4 (>0.733)	110.56 (±0.94)	0.424	0.978	0.282	
Overall *p* value	0.0964						0.1026				

eGFR, estimated glomerular filtration rate; BMD, bone mineral density; EST, estimate; SE, standard error; LS, lumbar spine; FN, femur neck.
Overall results were derived by covariance analysis adjusted for age, body mass index (BMI), educational level, current smoking, heavy drinking, and physical activity.
*Estimated for a physically active subject of age 61.5 years, BMI 24.06 kg/m^2, high education, current smoker, and heavy drinker, †Estimated for a physically active subject of age 35.3 years, BMI 23.41 kg/m^2, high education, current smoker, and heavy drinker.

those with an offset of <0. Similarly, the risk was 2.507 times higher for women with an offset of ≥1.5. There was no significant difference in trends for renal dysfunction according to BMD offset between men and women (*p* interaction=0.654). This association between BMD offset and renal function was also seen in the analysis of the total study population (Supplementary Table 3 and Supplementary Fig. 1, only online). However, this association could not be analyzed for those aged <50 years because few in this age group exhibited diminished renal function (men, n=7; women, n=2).

DISCUSSION

This population-based study revealed that renal dysfunction is associated with BMD offset among Koreans older adults (aged

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Table 4. Multiple Logistic Regression Analyses and ORs of Diminished Renal Function (Estimated Glomerular Filtration Rate <60 mL/min/1.73 m^2)

Men			Women		
Variables	**OR (95% CI)**	***p* value**	**Variables**	**OR (95% CI)**	***p* value**
Age≥50 years* (n=8223)					
Age†	1.106 (1.082–1.130)	<0.001†	Age†	1.161 (1.137–1.185)	<0.001†
BMI†	1.136 (1.075–1.202)	<0.001†	BMI†	1.055 (1.006–1.108)	0.029†
Education	1.111 (0.786–1.571)	0.551	Education	1.067 (0.611–1.866)	0.819
Current smoking†	0.634 (0.418–0.962)†	0.032†	Current smoking	1.681 (0.900–3.141)	0.103
Heavy drinking	0.691 (0.326–1.466)	0.335	Heavy drinking	N/A	N/A
Physically active†	0.587 (0.365–0.942)	0.028†	Physically active	0.705 (0.429–1.159)	0.168
LS BMD–FN BMD (T score)†	1.679 (1.455–1.936)	<0.001†	LS BMD–FN BMD (T score)†	1.518 (1.291–1.785)	<0.001

OR, odds ratio; CI, confidence interval; BMI, body mass index; LS, lumbar spine; BMD, bone mineral density; FN, femur neck.
*The association in participants aged <50 years could not be analyzed due to a lack of patients with diminished renal function (men, n=7; women, n=2), †Statistically significant difference.

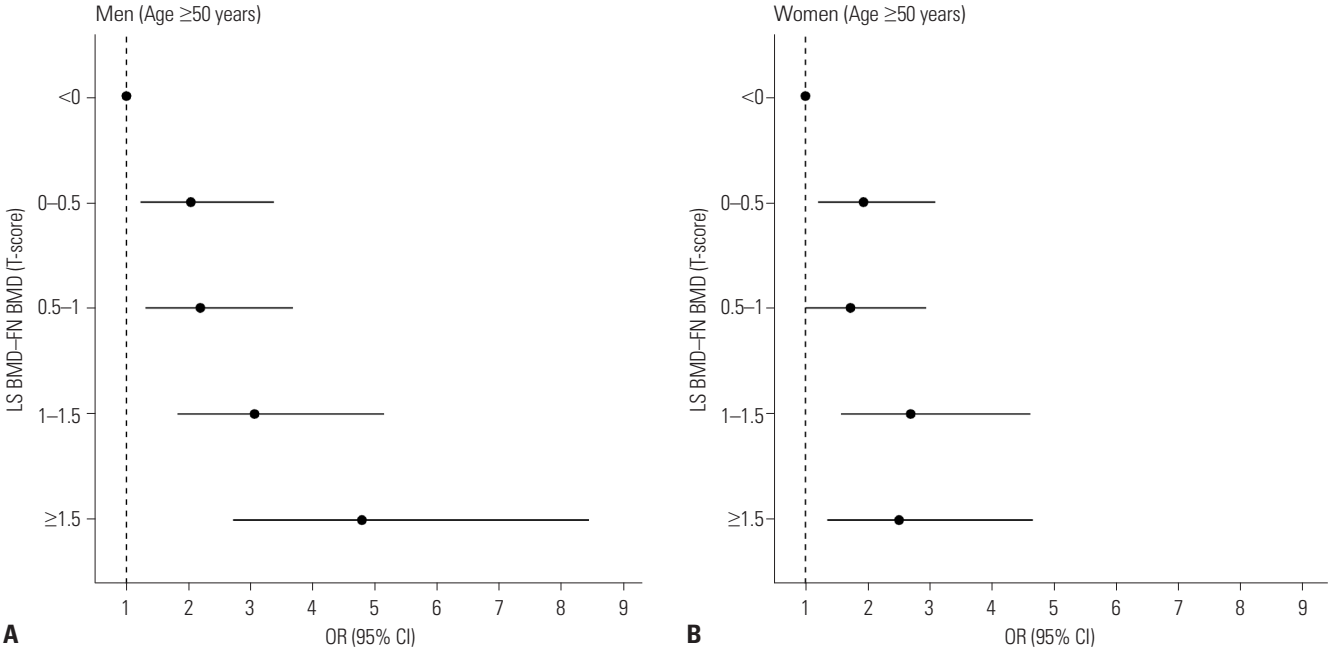

Fig. 1. ORs for diminished renal function according to BMD offset in men (A) and women (B) aged ≥50 years. BMD offset was calculated by subtracting FN T-scores from LS T-score and divided into five groups. A reference group had BMD offsets <0. ORs were obtained after adjustment for age, body mass index, education, smoking, drinking, and physical activity. OR, odds ratio; CI, confidence interval; LS, lumbar spine; BMD, bone mineral density; FN, femur neck.

≥50 years). We observed that lower eGFR level was associated with higher BMD offset. When we divided BMD offsets into five groups at intervals of 0.5, participants with a BMD offset of ≥1.5 showed a significantly higher risk of developing renal dysfunction than those with an offset <0, even after adjustment for age. However, these associations were not seen in younger adults (age <50 years).

Previous studies have reported prevalences of LS and hip T-score discordance ranging from 41.69% to 57.51%[5,18-22] in which the proportions of subjects with a lower LS BMD than FN BMD ranged from 43.80%[5] to 92.13%.[20] In the present study, only 29.2% (5061/17306) of the study subjects exhibited BMD discordance (Supplementary Table 2, only online), and of these, 55.62% had lower LS BMD than FN BMD. The lower prevalence of BMD discordance observed in the present study is considered to be mainly attributable to differences in the characteristics of study populations, including age and ethnicities. In the present study, the mean ages of men and women were 43.85 and 45.76 years, respectively, whereas mean ages in previous studies were above 53 years.[15-17] When we conducted subgroup analysis on patients at aged ≥50 years, 36.82% (3028/8223) was classified as having BMD discordance, and 56.4% of these had a lower LS BMD than FN BMD (Supplementary Table 2, only online). Because subgroup analysis of patients aged ≥50 years could not fully explain the high BMD concordance in our study, we cannot exclude the possibility of an ethnic difference regarding BMD discordance. Future studies from other Asian countries are needed to clarify this difference.

Several different reasons have been proposed to explain BMD discordance.[5] In addition to technical reasons, such as artifacts and improper patient positioning, physiologic and pathologic factors may contribute. For example, differences in exposure to weight bearing between skeletal sites can result in physiologic discordances. Indeed, unloaded skeletons have been reported to show excessive bone loss,[23] whereas weight bearing exercise has been shown to significantly improve BMD.[24] Meanwhile, estrogen deficiency in postmenopausal women is known to accelerate trabecular bone loss[7] and, thus, dominantly reduces LS BMD, which results in BMD discordance. Pathologic discordance mainly arises from aging-related diseases, such as osteophytosis, vertebral sclerosis, and aortic calcification. These conditions overestimate T-score of LS BMD, which results in higher LS BMD than FN BMD.[5]

Studies have recently focused on higher fracture risk among subjects with BMD discordance.[14,25] Because LS T-score is not incorporated into the fracture risk assessment tool (FRAX®), individuals with a lower LS BMD than FN BMD can be underestimated by the FRAX system. Thus, studies in which estimated fracture risk was adjusted for BMD offset showed improvements in fracture risk assessment and demonstrated that lower offset coincided with higher fracture risk.[14,26] However, in another study, subjects with BMD offset ≥1.5 were found to be at higher risk of major osteoporotic fractures than those with a BMD offset of 0.5 to 1.5,[25] which suggested that a higher LS BMD is not always good for bone health. Indeed, in the present study, a higher LS BMD was associated with renal dysfunction, and patients with renal insufficiency have been shown to be at increased risk of osteoporotic fractures.[27,28]

Previously, BMD testing was not recommended in patients with chronic kidney disease (CKD) due to the lack of evidence that BMD predicts fractures in patients with renal dysfunction.[29] However, 2017 clinical practice guidelines on CKD-mineral and bone disorders recommended that BMD testing be performed to assess fracture risk in patients with renal dysfunction,[30] based on prospective cohort studies.[31,32] Notably, those studies demonstrated that hip BMD was associated with fracture risk, and Iimori, et al.,[31] reported that LS BMD was not associated with fracture risk. Given that the recorded association between BMD discordance and renal dysfunction in our study, it would seem prudent not to assess bone health solely based on LS BMD in older CKD patients.

Regarding a mechanism linking BMD discordance and renal dysfunction, we consider changes in parathyroid hormone (PTH) levels a possible cause. Serum PTH levels are elevated in patients with decreased renal function and cause cortical bone loss, but preserved bone mass at trabecular sites,[33] which increases BMD offset. However, in the present study, the association between renal dysfunction and a high BMD offset was preserved in subjects with normal renal function (eGFR ≥60 mL/min/1.73 m^2; data not shown), which suggests that PTH does not have a significant role. Aging processes could be other possible explanations for this association. Aging is related with clinically diagnosed or undiagnosed degenerative changes at the spine level[34] which can result in BMD discordance through overestimation of LS BMD. Given that the eGFR also declines with aging,[35] renal dysfunction could coincide with BMD discordance. Recently, biological age was reported to be an important factor for assessing health and aging status and for predicting mortality and the incidences of major age-related diseases.[36] BMD T-score as well as renal function were reported to vary among people of the same age.[36,37] Thus, the noted significant association between BMD offset and renal dysfunction in this study, even after adjustment for actual age, suggests that BMD offset is related to renal dysfunction possibly attributed to biological aging.

The present study is limited by its cross-sectional nature, and thus, we could not determine whether there is a causal relationship or simply an association between T-score offset and renal dysfunction. In addition, we could not exclude subjects with spine pathology other than surgery-related (e.g., osteophyte, aortic calcification, fracture) on DXA scans. Furthermore, important clinical information, such as glucocorticoid use or PTH levels, were not collected. Finally, because the data used in this study included only Korean individuals, our results cannot be generalized to other ethnicities. Despite these limitations, the major strength of our study is that it was conducted using data collected during a well-designed survey of a nationally representative sample, which considerably enhances the statistical reliability of our results.

In summary, data gathered from a nationally representative cohort demonstrated that T-score discordance with higher LS BMD is significantly associated with renal dysfunction. When assessing the bone health of older CKD patients, physicians should consider the possibility of BMD discordance between LS and FN.

DATA AVAILABILITY STATEMENT

Original data are publicly available for free from the KNHANES website (http://knhanes.cdc.go.kr) for purposes such as academic research.

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AUTHOR CONTRIBUTIONS

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REFERENCES

1. NIH Consensus Development Panel on osteoporosis prevention, diagnosis, and therapy, March 7-29, 2000: highlights of the conference. South Med J 2001;94:569-73.
2. Morgan SL, Prater GL. Quality in dual-energy X-ray absorptiometry scans. Bone 2017;104:13-28.
3. Ott SM. Cortical or trabecular bone: what's the difference? Am J Nephrol 2018;47:373-5.
4. Lu YC, Lin YC, Lin YK, Liu YJ, Chang KH, Chieng PU, et al. Prevalence of osteoporosis and low bone mass in older Chinese population based on bone mineral density at multiple skeletal sites. Sci Rep 2016;6:25206.
5. Woodson G. Dual X-ray absorptiometry T-score concordance and discordance between the hip and spine measurement sites. J Clin Densitom 2000;3:319-24.
6. Briot K, Roux C. Glucocorticoid-induced osteoporosis. RMD Open 2015;1:e000014.
7. Hunter DJ, Sambrook PN. Bone loss. Epidemiology of bone loss. Arthritis Res 2000;2:441-5.
8. El Maghraoui A, Mouinga Abayi DA, Rkain H, Mounach A. Discordance in diagnosis of osteoporosis using spine and hip bone densitometry. J Clin Densitom 2007;10:153-6.
9. Hong AR, Kim JH, Lee JH, Kim SW, Shin CS. Metabolic characteristics of subjects with spine-femur bone mineral density discordances: the Korean National Health and Nutrition Examination Survey (KNHANES 2008-2011). J Bone Miner Metab 2019;37:835-43.
10. Glassock RJ, Winearls C. Ageing and the glomerular filtration rate: truths and consequences. Trans Am Clin Climatol Assoc 2009;120:419-28.
11. Musso CG, Oreopoulos DG. Aging and physiological changes of the kidneys including changes in glomerular filtration rate. Nephron Physiol 2011;119 Suppl 1:1-5.
12. Sasaki Y, Marioni R, Kasai M, Ishii H, Yamaguchi S, Meguro K. Chronic kidney disease: a risk factor for dementia onset: a population-based study. The Osaki-Tajiri Project. J Am Geriatr Soc 2011;59:1175-81.
13. Liew G, Mitchell P, Wong TY, Iyengar SK, Wang JJ. CKD increases the risk of age-related macular degeneration. J Am Soc Nephrol 2008;19:806-11.
14. Leslie WD, Lix LM, Johansson H, Oden A, McCloskey E, Kanis JA. Spine-hip discordance and fracture risk assessment: a physician-friendly FRAX enhancement. Osteoporos Int 2011;22:839-47.
15. Kim Y. The Korea National Health and Nutrition Examination Survey (KNHANES): current status and challenges. Epidemiol Health 2014;36:e2014002.
16. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12.
17. Kim Y, Park S, Kim NS, Lee BK. Inappropriate survey design analysis of the Korean National Health and Nutrition Examination Survey may produce biased results. J Prev Med Public Health 2013;46:96-104.
18. Moayyeri A, Soltani A, Tabari NK, Sadatsafavi M, Hossein-Neghad A, Larijani B. Discordance in diagnosis of osteoporosis using spine and hip bone densitometry. BMC Endocr Disord 2005;5:3.
19. El Maghraoui A, Mouinga Abayi DA, Ghozlani I, Mounach A, Nouijai A, Ghazi M, et al. Prevalence and risk factors of discordance in diagnosis of osteoporosis using spine and hip bone densitometry. Ann Rheum Dis 2007;66:271-2.
20. Singh M, Magon N, Singh T. Major and minor discordance in the diagnosis of postmenopausal osteoporosis among Indian women using hip and spine dual-energy X-ray absorptiometry. J Midlife Health 2012;3:76-80.
21. Singh T, Ghosh A, Khandelwal N, Singla V, Gupta M. Major and minor discordance in dual-energy X-ray absorptiometry diagnosis of osteoporosis–A cross-sectional, population-based, observational study in Indian women. J Midlife Health 2020;11:12-6.
22. Mounach A, Abayi DA, Ghazi M, Ghozlani I, Nouijai A, Achemlal L, et al. Discordance between hip and spine bone mineral density measurement using DXA: prevalence and risk factors. Semin Arthritis Rheum 2009;38:467-71.
23. Beaupre GS, Lew HL. Bone-density changes after stroke. Am J Phys Med Rehabil 2006;85:464-72.
24. Kim SJ, Kim SN, Yang YN, Lee IS, Koh SE. Effect of weight bearing exercise to improve bone mineral density in children with cerebral palsy: a meta-analysis. J Musculoskelet Neuronal Interact 2017;17:334-40.
25. Leslie WD, Kovacs CS, Olszynski WP, Towheed T, Kaiser SM, Prior JC, et al. Spine-hip T-score difference predicts major osteoporotic fracture risk independent of FRAX®: a population-based report from CAMOS. J Clin Densitom 2011;14:286-93.
26. Johansson H, Kanis JA, Odén A, Leslie WD, Fujiwara S, Glüer CC, et al. Impact of femoral neck and lumbar spine BMD discordances on FRAX probabilities in women: a meta-analysis of international cohorts. Calcif Tissue Int 2014;95:428-35.
27. Nickolas TL, McMahon DJ, Shane E. Relationship between moderate to severe kidney disease and hip fracture in the United States. J Am Soc Nephrol 2006;17:3223-32.
28. Isaia GC, Tamone C, Ravazzoli M. [Fractures and chronic renal insufficiency]. G Ital Nefrol 2008;25:57-65.
29. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl 2009;113:S1-130.
30. Ketteler M, Block GA, Evenepoel P, Fukagawa M, Herzog CA, McCann L, et al. Executive summary of the 2017 KDIGO chronic kidney disease-mineral and bone disorder (CKD-MBD) guideline update: what's changed and why it matters. Kidney Int 2017;92:26-36.
31. Iimori S, Mori Y, Akita W, Kuyama T, Takada S, Asai T, et al. Diagnostic usefulness of bone mineral density and biochemical markers of bone turnover in predicting fracture in CKD stage 5D patients--a single-center cohort study. Nephrol Dial Transplant 2012;27:345-51.
32. Yenchek RH, Ix JH, Shlipak MG, Bauer DC, Rianon NJ, Kritchevsky SB, et al. Bone mineral density and fracture risk in older individuals with CKD. Clin J Am Soc Nephrol 2012;7:1130-6.
33. Silverberg SJ, Shane E, de la Cruz L, Dempster DW, Feldman F, Seldin D, et al. Skeletal disease in primary hyperparathyroidism. J Bone Miner Res 1989;4:283-91.
34. Tenne M, McGuigan F, Besjakov J, Gerdhem P, Åkesson K. Degen-

erative changes at the lumbar spine--implications for bone mineral density measurement in elderly women. Osteoporos Int 2013;24:1419-28.
35. Eriksen BO, Palsson R, Ebert N, Melsom T, van der Giet M, Gudnason V, et al. GFR in healthy aging: an individual participant data meta-analysis of iohexol clearance in European population-based cohorts. J Am Soc Nephrol 2020;31:1602-15.
36. Kang YG, Suh E, Lee JW, Kim DW, Cho KH, Bae CY. Biological age as a health index for mortality and major age-related disease incidence in Koreans: National Health Insurance Service-health screening 11-year follow-up study. Clin Interv Aging 2018;13:429-36.
37. Mussolino ME, Gillum RF. Low bone mineral density and mortality in men and women: the Third National Health and Nutrition Examination Survey linked mortality file. Ann Epidemiol 2008;18:847-50.

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