Original Paper

Association of Bone Mineral Density with Albuminuria and Estimated Glomerular Filtration Rate : The Dong-gu Study

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Key Words

Albuminuria • Estimated glomerular filtration rate • Bone mineral density

Abstract

Background: Kidney dysfunction and albuminuria may be associated with BMD. However, little evidence has been reported on relationships between BMD and eGFR and albuminuria. **Methods:** A total of 8,992 subjects aged 50 years or older participated in a survey conducted. Participants had their lumbar spine and femoral neck BMD measured by a Lunar Prodigy bone densitometer (GE, Madison, WI). Kidney function was assessed using MDRD eGFR and diagnosis of albuminuria was based on albumin-creatinine ratio. **Results:** ACR was negatively associated with lumbar spine and femur neck BMD in females (lumbar spine: 1.001, 0.988, 0.974 and 0.979 g/cm², $p < 0.001$; femur neck: 0.796, 0.790, 0.783 and 0.782 g/cm², $p = 0.002$), but not in males, after adjusting for covariates. Additionally, eGFR was shown to be negatively associated with lumbar spine BMD after adjusting for covariates (male: 1.181, 1.166,

1.152 and 1.149 g/cm², $p = 0.001$; female: 0.997, 0.980, 0.979 and 0.982 g/cm², $p = 0.005$), but demonstrated no association with femur BMD. **Conclusions:** ACR in females was negatively associated with lumbar spine and femur neck BMD, but not in males. eGFR was negatively associated with lumbar spine BMD in both males and females.

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Introduction

Approximately 20% of people aged ≥ 65 years in the US exhibit moderate or severe kidney dysfunction [1]. Moreover, decreased renal function is associated with cardiovascular mortality and morbidity [2, 3] and is known to disturb bone and mineral metabolism [4]. Patients with end-stage kidney disease (ESKD) have both a lower bone mineral density (BMD) and a higher risk of osteoporotic fractures [5, 6]. Furthermore, individuals with renal insufficiency may also exhibit reduced BMD as a result of vitamin D-parathyroid hormone (PTH) homeostasis and metabolic acidosis [7]. Previous studies have reported that kidney dysfunction is associated with BMD [8-13]. However, because of small sample sizes and the result that the associations disappeared after adjusting for key confounders, such as sex, age and weight, the significance of those findings is uncertain.

Albuminuria is associated with atherosclerosis, which is mediated by vascular endothelial damage [14]. Moreover, endothelial dysfunction plays a key role in the initiation and progression of atherosclerosis [15]. Endothelial dysfunction of the glomerular basement membrane can modify glomerular barrier permeability in the kidneys, leading to excretion of albumin into the urine [16]. Atherosclerotic vascular disease may also directly impact bone metabolism and contribute to the development of osteoporosis [17]. Atherosclerosis severity is inversely correlated with BMD, independent of age and body mass index (BMI) [18, 19]. In addition, some medicines, including statins, concordantly enhance bone density and diminish atherogenesis [20]. However, little evidence has been reported on cause-and-effect relationships between BMD and albuminuria.

It is generally acknowledged that there are differences in the prevalence of osteoporosis between males and females [21]. Several studies have shown that postmenopausal women exhibit greater bone loss [22, 23] compared to men of the same age. Female gender is also considered a major risk factor for hip fracture in the general population [24].

Thus, in this study, BMD, the albumin-creatinine ratio (ACR) and estimated glomerular filtration rate (eGFR) were assessed and compared in Koreans aged ≥ 50 years to expose gender differences therein.

Materials and Methods

Study population

The Dong-gu Study is an ongoing prospective study designed to investigate the prevalence, incidence, and risk factors for chronic disease in an urban population. Details on the study subjects and measurements performed were published previously [25]. National resident registration records were used to identify potential participants in the study. From 2007 to 2010, 34,040 eligible subjects aged ≥ 50 years who resided in the Dong-gu district of Gwangju metropolitan city in South Korea were invited by telephone to participate in this study, and 9,260 subjects were enrolled (response rate: 27.2%; 3,713 males and 5,547 females). After excluding 268 respondents who did not provide urinary samples or did not have their BMD measured, 8,992 subjects (3,602 men, 5,390 women) were included in the present analyses.

This study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the institutional review board of Chonnam National University Hospital, and informed consent was obtained from each subject.

Trained examiners interviewed patients using a questionnaire that included items to assess cigarette use, alcohol consumption, physical activity, use of diabetes medications, use of hypertension medications, and menopausal status. Weight was measured to the nearest 0.1 kg, with subjects dressed in light clothing, and height was measured to the nearest 0.1 cm in stocking feet. Venous blood samples and urinary specimens were collected from subjects following an overnight fast. Serum was separated on site and stored at -70°C until ready for use. Urinary albumin and creatinine concentrations were measured by turbidimetric immunoassay and the Jaffe method [26] using a Hitachi-7600 analyzer (Hitachi Ltd., Tokyo, Japan).

Kidney function

Kidney function was assessed according to eGFR, which was calculated using the MDRD formula [27] as follows: $175 \times (\text{serum creatinine}^{-1.154}) \times (\text{age}^{0.203}) \times 0.742$ [if female], expressing serum creatinine concentration in mg/dl. A diagnosis of albuminuria was based on ACR, which was calculated by dividing urinary albumin concentration (μg) by urinary creatinine concentration (mg).

BMD

Participants underwent measurement of lumbar spine and femoral neck BMDs with a Lunar Prodigy bone densitometer (GE, Madison, WI, USA). Lumbar spine BMD represented the average BMD of L1–L4. Daily phantom scans were performed each morning for proper quality control. All BMD scans were conducted by well-trained examiners using standardized procedures following the manufacturer's recommended protocols. Any scans comprising metal or other attenuating material in the region of interest as well as any scans of poor quality were discarded.

Statistical analysis

Data are presented as mean ± standard deviation (SD) or percentages for categorical variables. All analyses were stratified by sex. Models 1 and 2 were adjusted for age, height, and BMI in men and women, respectively. Model 3 included the Model 1 variables plus smoking, alcohol intake, physical activity regimen, diabetes medication, hypertension medication, and log transformed ACR or log transformed eGFR in men. Finally, Model 4 included all of the Model 3 variables plus menopausal status in women. Analysis of covariance by the models mentioned above was used to compare mean lumbar spine and right femoral neck BMD according to eGFR and ACR quartiles. Statistical significance was set at $p < 0.05$. Statistical analyses were performed using SPSS software package version 15.0 (SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics of the subjects

The baseline characteristics of the subjects are listed in Table 1. Age, height, weight, lumbar spine BMD, and femoral neck BMD were all higher in males than those in females. BMI was higher in females than that in males. Male subjects were more likely to smoke, drink alcohol, be physically active, and take diabetes medication than those in females.

Characteristics of the subjects according to ACR and eGFR quartiles

Table 2 shows the characteristics of the subjects according to ACR quartiles. Height and eGFR tended to be lower, whereas age and BMI tended to be higher with increased ACR in both male and female subjects. More males tended to report taking diabetes medication with increased ACR. More females tended to report taking hypertension medication and consuming relatively less alcohol, as well as being less physically active, and have postmenopausal status with increased ACR, as compared to male subjects.

Table 3 lists the subjects' characteristics according to eGFR quartiles. Age, BMI, and taking hypertension medication tended to be lower with increased eGFR in both male and female subjects. Height and weight tended to be lower in females than in males, whereas ACR tended to be lower with increased eGFR in males than occurred in females. Furthermore, more females tended to report consuming greater amounts of alcohol and fewer females tended to report taking diabetes medication and to be of postmenopausal status with increased eGFR.

Table 1. Baseline characteristics of subjects

	Male	Female	<i>p</i>
<i>N</i> (%)	3602 (40.1)	5390 (59.9)	-
Age (years)	66.2±8.0	64.4±8.2	<0.001
Height (cm)	165.9±5.7	153.2±5.5	<0.001
Weight (kg)	65.9±9.1	57.8±8.0	<0.001
BMI (kg/m ²)	23.9±2.8	24.6±3.0	<0.001
ACR (μg/mg)	42.7±153.6	37.6±146.5	0.108
eGFR (mL/min per 1.73 m ²)	65.4±12.3	65.3±12.0	0.882
Lumbar BMD (g/cm ²)	1.2±0.2	1.0±0.2	<0.001
Femur neck BMD (g/cm ²)	0.9±0.1	0.8±0.1	<0.001
Smoking (%)	882(24.5)	98(1.8)	<0.001
Alcohol intake (%)	2893(80.5)	2004(37.3)	<0.001
Physically active (%)	1380(38.5)	1504(28.1)	<0.001
Diabetes Medication (%)	549(15.4)	595(11.1)	<0.001
Hypertension Medication (%)	1258(35.2)	1912(35.7)	0.635

Table 2. Characteristics of the subjects according to the ACR

All values are given as *n* (%) or mean ± standard deviation.
BMI, body mass index; ACR, albumin creatinine ratio; eGFR, estimated glomerular filtration rate; BMD, bone mineral density

ACR (μg/mg)	Q1	Q2	Q3	Q4	<i>P</i> *
Male					
<i>N</i> (%)	997(27.7)	819(22.7)	839(23.3)	947(26.3)	-
ACR (μg/mg)	5.0±1.7	9.9±1.5	17.4±3.4	133.5±280.3	<0.001
Age (years)	64.4±7.6	65.7±7.4	66.8±7.9	67.9±8.4	<0.001
Height (cm)	166.5±5.5	166.3±5.8	165.6±5.8	165.2±5.5	<0.001
Weight (kg)	66.0±8.8	65.6±9.4	65.6±9.3	66.4±9.2	0.223
BMI (kg/m ²)	23.8±2.7	23.7±2.8	23.9±2.9	24.3±2.9	<0.001
eGFR (mL/min per 1.73 m ²)	66.5±10.5	66.4±11.1	65.8±12.0	62.8±14.6	<0.001
Smoking (%)	240(24.1)	189(23.1)	240(28.7)	213(22.5)	0.012
Alcohol intake (%)	805(80.9)	630(77.0)	695(83.2)	763(80.7)	0.015
Physically active (%)	396(39.9)	308(37.7)	309(37.1)	367(39.0)	0.622
Diabetes Medication (%)	73(7.4)	90(11.1)	116(14.0)	270(28.8)	<0.001
Hypertension Medication (%)	300(30.2)	274(33.9)	265(32.0)	419(44.7)	<0.001
Female					
<i>N</i> (%)	1251(23.2)	1429(26.5)	1409(26.1)	1301(24.1)	-
ACR (μg/mg)	5.0±1.8	9.9±1.5	17.5±3.4	121.1±282.3	<0.001
Age (years)	61.3±7.3	63.5±7.7	65.4±8.0	67.3±8.5	<0.001
Height (cm)	154.3±5.2	153.7±5.4	152.7±5.7	152.1±5.6	<0.001
Weight (kg)	58.2±7.4	57.8±7.7	57.6±8.4	57.8±8.3	0.197
BMI (kg/m ²)	24.4±2.8	24.4±2.8	24.7±3.1	24.9±3.1	<0.001
eGFR (mL/min per 1.73 m ²)	66.1±10.5	66.4±11.1	65.4±11.6	63.3±14.3	<0.001
Smoking (%)	22(1.8)	23(1.5)	32(2.3)	22(1.7)	0.494
Alcohol intake (%)	511(41.0)	529(37.1)	517(36.9)	447(34.4)	0.008
Physically active (%)	422(33.9)	391(27.5)	374(26.7)	317(24.5)	<0.001
Diabetes Medication (%)	60(4.8)	106(7.5)	158(11.3)	271(21.0)	<0.001
Hypertension Medication (%)	320(25.7)	456(32.1)	510(36.5)	627(48.6)	<0.001
Postmenopause (%)	1164(93.6)	1369(96.7)	1363(97.6)	1256(97.4)	<0.001

All values are given as *n* (%) or mean ± standard deviation. ACR, albumin creatinine ratio; BMI, body mass index; eGFR, estimated glomerular filtration rate. **p* for trend.

Comparison of mean BMD according to ACR quartiles

Table 4 lists the mean values (± standard error, SE) for lumbar spine and femoral neck BMD according to ACR quartiles. Lumbar spine and right femoral neck BMD values in male

Table 3. Characteristics of the subjects according to the eGFR

eGFR (mL/min per 1.73 m ²)	Q1	Q2	Q3	Q4	P*
Male					
N (%)	905(24.9)	915(25.2)	892(24.6)	908(25.0)	-
eGFR (mL/min per 1.73 m ²)	4937±7.8	60.8±1.8	67.9±2.1	79.7±6.7	<0.001
Age (years)	68.2±8.1	66.4±8.7	66.2±7.9	64.3±7.0	<0.001
Height (cm)	166.2±5.6	166.1±5.5	166.0±5.7	165.4±5.8	0.014
Weight (kg)	67.4±8.6	66.3±9.2	65.7±9.3	64.6±9.2	<0.001
BMI (kg/m ²)	24.4±2.6	24.0±2.9	23.8±2.9	23.6±2.8	<0.001
ACR (μg/mg)	68.4±239.5	31.7±88.8	38.7±146.6	33.2±90.1	<0.001
Smoking (%)	197(23.0)	178(23.3)	234(24.0)	273(27.2)	0.129
Alcohol intake (%)	678(79.3)	624(81.8)	779(80.1)	812(81.0)	0.595
Physically active (%)	334(39.2)	290(38.0)	393(40.5)	363(36.4)	0.281
Diabetes Medication (%)	156(18.4)	104(13.7)	137(14.2)	152(15.2)	0.035
Hypertension Medication (%)	402(47.4)	269(35.5)	313(32.4)	274(27.5)	<0.001
Female					
N (%)	1353(24.9)	1359(25.1)	1351(24.9)	1346(24.8)	-
eGFR (mL/min per 1.73 m ²)	50.7±7.3	62.3±1.8	70.1±2.6	80.4±7.4	<0.001
Age (years)	67.5±8.0	65.2±7.5	64.9±8.0	59.3±6.9	<0.001
Height (cm)	152.9±5.6	153.2±5.4	152.9±5.8	153.9±5.3	<0.001
Weight (kg)	58.4±8.1	57.7±8.0	57.3±8.0	57.9±7.7	0.007
BMI (kg/m ²)	24.9±3.0	24.6±3.0	24.5±2.9	24.4±2.9	<0.001
ACR (μg/mg)	65.5±248.0	30.1±93.5	27.6±78.7	25.5±79.2	<0.001
Smoking (%)	33(2.4)	24(1.8)	18(1.4)	21(1.7)	0.375
Alcohol intake (%)	446(33.6)	545(37.0)	487(38.0)	506(41.2)	0.001
Physically active (%)	371(26.7)	415(28.3)	361(28.3)	357(29.0)	0.601
Diabetes Medication (%)	224(16.2)	168(11.4)	135(10.6)	68(5.6)	<0.001
Hypertension Medication (%)	664(48.0)	512(34.9)	434(34.0)	302(24.7)	<0.001
Postmenopause (%)	1367(99.2)	1439(98.3)	1217(95.5)	1129(91.9)	<0.001
All values are given as n (%) or mean ± standard deviation. eGFR, estimated glomerular filtration rate; BMI, body mass index; ACR, albumin creatinine ratio. *p for trend.					

subjects were not different according to ACR. Mean lumbar spine and right femoral neck BMD values in females decreased significantly with increasing ACR after adjusting for age, height, and BMI (Model 3) (lumbar spine: 0.999, 0.985, 0.973, and 0.984 g/cm²; $p < 0.001$; femoral neck: 0.796, 0.789, 0.782, and 0.784 g/cm²; $p = 0.002$). These significant differences did not disappear after additionally adjusting for other covariates (Model 4) (lumbar spine: 1.001, 0.988, 0.974, and 0.979 g/cm²; $p < 0.001$; femoral neck: 0.796, 0.790, 0.783, and 0.782 g/cm², $p = 0.002$).

Comparison of mean BMD according to eGFR quartiles

Table 5 lists the mean values (± SE) for lumbar spine and femoral neck BMD according to eGFR quartiles. Lumbar BMD decreased significantly with increased eGFR after adjusting for age, height, and BMI in male subjects (Model 1) (1.182, 1.166, 1.152, and 1.147 g/cm²; $p < 0.001$), and this significant difference did not disappear after further adjusting for other confounding factors (Model 2) (1.181, 1.166, 1.152, and 1.149 g/cm²; $p = 0.001$). Mean lumbar BMD values in female subjects decreased significantly with increased eGFR after adjusting for age, height, and BMI (Model 3) (0.998, 0.978, 0.982, and 0.971 g/cm²; $p = 0.002$). This significant difference also did not disappear after further adjusting for other confounding factors (Model 4), (0.997, 0.980, 0.979, and 0.982 g/cm²; $p = 0.015$). However, femoral neck BMD values did not significantly differ between eGFR quartiles.

Table 4. Comparison of mean BMD according to the ACR

	ACR ($\mu\text{g}/\text{mg}$)	Male		Female	
		Model 1*	Model 2†	Model 3**	Model 4††
Lumbar (L1-L4)	Q1	1.161 (0.006)	1.163 (0.006)	0.999 (0.004)	1.001 (0.004)
	Q2	1.157 (0.007)	1.161 (0.007)	0.985 (0.004)	0.988 (0.004)
	Q3	1.155 (0.006)	1.158 (0.006)	0.973 (0.004)	0.974 (0.004)
	Q4	1.168 (0.006)	1.161 (0.006)	0.984 (0.004)	0.979 (0.004)
	<i>p</i>	0.469	0.953	<0.001	<0.001
Femur neck	Q1	0.884 (0.004)	0.884 (0.004)	0.796 (0.003)	0.796 (0.003)
	Q2	0.877 (0.004)	0.880 (0.004)	0.789 (0.003)	0.790 (0.003)
	Q3	0.880 (0.004)	0.882 (0.004)	0.782 (0.003)	0.783 (0.003)
	Q4	0.882 (0.004)	0.880 (0.004)	0.784 (0.003)	0.782 (0.003)
	<i>p</i>	0.724	0.834	0.002	0.002

All values are given as Mean (Standard Error). BMD, bone mineral density; ACR, albumin creatinine ratio. * Adjusted by age, height, and BMI. †Adjusted by age, height, BMI, smoking, alcohol intake, physically active, diabetes medication, hypertension medication, and $\ln(\text{eGFR})$. ** Adjusted by age, height, and BMI. ††Adjusted by age, height, BMI, smoking, alcohol intake, physically active, diabetes medication, hypertension medication, $\ln(\text{eGFR})$, and postmenopause.

Table 5. Comparison of mean BMD according to the eGFR

	eGFR (mL/min per 1.73m^2)	Male		Female	
		Model 1*	Model 2†	Model 3**	Model 4††
Lumbar (L1-L4)	Q1	1.182 (0.006)	1.181 (0.007)	0.998 (0.004)	0.997 (0.004)
	Q2	1.166 (0.007)	1.166 (0.007)	0.978 (0.004)	0.980 (0.004)
	Q3	1.152 (0.006)	1.152 (0.006)	0.982 (0.004)	0.979 (0.004)
	Q4	1.147 (0.006)	1.149 (0.006)	0.971 (0.004)	0.982 (0.004)
	<i>p</i>	<0.001	0.001	0.002	0.005
Femur neck	Q1	0.887 (0.004)	0.889 (0.004)	0.788 (0.003)	0.788 (0.003)
	Q2	0.876 (0.004)	0.876 (0.004)	0.786 (0.003)	0.786 (0.003)
	Q3	0.883 (0.004)	0.883 (0.004)	0.789 (0.003)	0.787 (0.003)
	Q4	0.877 (0.004)	0.878 (0.004)	0.788 (0.003)	0.788 (0.003)
	<i>p</i>	0.170	0.126	0.888	0.884

All values are given as Mean (Standard Error). BMD, bone mineral density; eGFR, estimated glomerular filtration rate. * Adjusted by age, height, and BMI. †Adjusted by age, height, BMI, smoking, alcohol intake, physically active, diabetes medication, hypertension medication, and $\ln(\text{ACR})$. ** Adjusted by age, height, and BMI. ††Adjusted by age, height, BMI, smoking, alcohol intake, physically active, diabetes medication, hypertension medication, $\ln(\text{ACR})$, and postmenopause.

Discussion

We investigated whether lumbar spine and femoral neck BMD were associated with ACR and eGFR in Koreans aged ≥ 50 years. The data suggest that ACR was negatively associated with lumbar spine and femoral neck BMD in females, but not in males, after adjusting for age, weight, and other covariates.

Only one other study has examined the relationship between ACR and BMD in the general population. In the Tromsø study, Jørgensen *et al.* [28] followed 4,497 subjects aged 55–74 years old for an average of 8.4 years and examined whether elevated ACRs were associated with non-vertebral fractures. Those researchers measured initial BMD at the wrist by single X-ray absorptiometry and analyzed the associations between BMD and log transformed ACR. They reported that BMD was negatively associated with log transformed ACR, similar to the data presented in our study.

Endothelial dysfunction of the glomerular basement membrane can modify glomerular barrier permeability in the kidneys, leading to excretion of albumin into the urine [16]. Therefore, albuminuria is a marker of endothelial dysfunction, plays a key role in the initiation and progression of atherosclerosis [15], and is associated with increased levels of inflammatory markers [29]. One of the explanations that has been proposed for the association between albuminuria and osteoporosis is that albuminuria is associated with reduced bone blood flow, resulting in a decreased rate of bone remodeling and the development of osteoporosis [30]. Moreover, some investigators have found a positive relationship between ACR and PTH [28]. When serum calcium level is low, PTH level rises, which may promote osteoclast-mediated bone resorption.

In this study, ACR was associated with BMD in female subjects only. It is well-known that there are gender differences in bone density. Furthermore, BMD decreases linearly in women with age after menopause at a 1.7-fold faster rate than in their male counterparts [31]. Gender differences in BMD are multifactorial, but hormones seem to play an important role. Estrogens exert beneficial effects on plasma lipid and lipoprotein concentrations and reduce atherosclerosis [32]. Estrogen deficiency in females following menopause contributes to a relatively higher presence of osteoporosis in women compared with men [33]. In addition, estrogen was negatively correlated with ACR among females with type 2 diabetes [32]. Therefore, ACR might be associated with mediation of BMD by estrogen in females.

According to the present data, eGFR was not associated with femoral neck BMD and was negatively associated with lumbar spine BMD. Previous studies have investigated the associations between renal insufficiency and BMD, but the results were conflicting [8-13, 34-36]. A few small studies have indicated that renal insufficiency is related to low bone mass [8-13], but data from more extensive studies have indicated that such an association could be explained by confounding factors, primarily sex, age, and weight [34-36].

Hsu et al. [35] analyzed 13,848 adults aged ≥ 20 years who took part in the Third National Health and Nutrition Examination Survey. Proximal femoral BMD was measured using dual energy X-ray absorptiometry (DXA), and kidney function was assessed according to serum creatinine, blood urea nitrogen and Cockcroft-Gault equation creatinine clearance. They reported that chronic renal insufficiency was not associated with femoral BMD after adjusting for confounding factors. In the Cardiovascular Health Study (1,519 participants), researchers investigated whether kidney function, as assessed by cystatin-C levels, was associated with BMD, and reported that cystatin-C is related to annual changes in BMD, but not with initial femur or total hip BMD [34]. However, as a critical limitation of their study, cystatin-C level was determined 2 years prior to the BMD measurements. In the Osteoporotic Fractures in Men (MrOS) study [36], investigators followed 404 elderly male subjects for an average of 4.4 years and observed a significant association between cystatin-C and annual change in total hip BMD. However, no difference in baseline total hip BMD was observed according to quartiles of cystatin-C concentration ($p = 0.90$). In these studies, kidney function was not associated with BMD, similar to the present study.

We estimated kidney function according to MDRD eGFR, rather than by using cystatin-C. MDRD eGFR is based on serum creatinine levels, which are influenced, in part, by muscle mass, whereas cystatin-C level does not depend on age, sex, or muscle mass. While it is recognized that serum cystatin-C is superior to serum creatinine as a marker of kidney function [37], whether cystatin-C is a better predictor of GFR than MDRD eGFR remains controversial [38, 39]. We reanalyzed the present data after adjusting for lean body mass, but there was little effect on previously observed outcomes (data not shown).

In this study, decreased eGFR was associated with increased lumbar spine BMD. This is contrary to the previous notion that patients with chronic renal insufficiency may have reduced BMD as a result of abnormalities in acid-base and vitamin D- PTH homeostasis [35]. The reason why eGFR is negatively associated with lumbar spine BMD remains unclear, although several explanations have been proposed. First, the previous notion that patients with chronic renal insufficiency may have reduced BMD as a result of abnormalities in acid-base and vitamin D- PTH homeostasis arose from a study on patients with ESRD. Advanced

kidney dysfunction in patients with ESRD is associated with reduced BMD; patients with ESRD also exhibit elevated PTH, chronic acidosis, and bone turnover abnormalities [6, 9]. However, an association between renal insufficiency and BMD was not shown in mild or moderate patients with chronic kidney disease (CKD) [34-36]. Interestingly, in the study that utilized data from NHANES III [40], individuals with osteoporosis (BMD T-score > 2.5 SD) had a much higher prevalence of mild to moderate CKD, whereas osteopenia (BMD T-score 1-2.5 SD) was observed in patients with severe CKD. Second, findings should be interpreted in the context of the study design. The subjects of the present study underwent measurement of lumbar spine and femoral neck BMD, whereas the subjects of the NHANES III, Cardiovascular Health, and MrOS studies underwent measurements of femoral neck and/or total hip BMD [34-36]. Third, measuring BMD using DXA entails certain limitations, as the technique utilizes attenuation of radiation in bone or soft tissue. Thus, anything within the radiation path can lead to an overestimation of BMD, such as arthritic conditions, scoliosis, aortic calcification, or peritoneal fluid [41]. Moreover, patients with CKD have poor bone quality, which cannot be measured by absorptiometry, including abnormal micro-architecture, mineralization density, crystal deposition in the bone matrix or abnormalities in the matrix itself [41].

It is well-known that BMI is associated with osteoporosis [42, 43]. In the present study, BMD was positively associated with BMI (data not shown). Two hypotheses have been proposed to explain the relationship between BMI and osteoporosis. First, body fat provides indirect protection from bone loss by mediating the peripheral conversion of adrenal steroids to metabolically active estrogen [44]. Second, heavy individuals in early adulthood tend to reach a higher peak BMD than thinner individuals, leading to the development of higher BMD [45].

This study had several limitations. First, no direct measurement of GFR was obtained, the gold standard of which is insulin clearance, but this was not feasible in a large epidemiologic study. Second, levels of drugs known to influence bone metabolism (such as estrogens, bisphosphonates, glucocorticoids, and thiazides) were not measured. Some medicines, including statins, concordantly enhance bone density and diminish atherogenesis [20]. Third, levels of potential mediators of bone loss, such as calcium, phosphorus, vitamin D, or PTH, were not determined.

Despite these limitations, this study contributes greatly to the current knowledge concerning the associations between ACR or eGFR and BMD in a large, community-based population.

Conclusion

In conclusion, ACR was negatively associated with lumbar spine and femoral neck BMD in females, but not in males, after adjusting for age, height, BMI and other covariates. In addition, eGFR was negatively associated with lumbar spine BMD in both males and females after adjusting for the same confounding factors, but showed no association with femoral BMD.

Conflict of Interests

None declared.

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