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Serum Sodium and Areal Bone Mineral Density in American Adult's Population: A Secondary Analysis Based on the National Health and Nutrition Examination Survey

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1. Abstract

1.1. Background: Osteoporosis is a bone disease characterized by decreased Bone Mineral Density (BMD) and an increased risk of fracture. Hyponatremia has been found associated with osteoporosis and fractures. The dose-response relationship between serum sodium and bone mineral density remains unclear.

1.2. Aim: To determine the association between serum sodium and BMD at femoral neck and conclude the dose-response relationship.

1.3. Design: A cross-sectional study.

1.4. Methods: A second analysis based on the National Health and Nutrition Examination Survey.

1.5. Results: Overall 15822 participants were included in the analysis with average age 51 years of which 48.407% were female. In the weighted univariate and multivariate linear regression model, serum sodium was significantly associated with BMD at femoral neck(P<0.001).Furthermore, serum sodium(per 10 mmol/l) was negatively associated with BMD at femoral neck in the fully adjusted model(β = -0.019, 95% confidence interval: -0.028 to -0.010, P<0.001).Non-linear relationship was detected between serum sodium(per 10 mmol/l) and femoral neck BMD, whose inflection point was 13.7.In the left and right inflection points, the effect sizes and confidence intervals were 0.014 (-0.011, 0.040) and -0.028 (-0.040, -0.017), respectively. Subgroup analysis showed robust correlation between serum sodium and femoral neck BMD and there was a significant interaction for gender (P for interaction = 0.017).

1.6. Conclusion: The relationship between serum sodium and femoral neck BMD is significant and independent but non-linear. A serum sodium level larger than 13.7 per 10 mmol/l negatively correlates with femoral neck BMD.

2. Introduction

It is estimated that nearly 53 million Americans aged 15 years and older have low femoral neck bone mass [1].The resulting fracture has a significant morbidity and mortality impact on the public health system [2-4].Sodium in the bone accounts for half of the total sodium content in the body and is involved in the maintenance of homeostatic sodium balance and bone mineralization [5].Sodium-related electrolyte disorders are common in the clinical practice and has been found linked to falls and fractures [1, 6, 7].At present, most studies on the relationship between blood sodium concentration and bone mass conclude that hyponatremia (<135mmol/l) can lead to a decrease in bone density and an increased risk of osteoporosis [8-10]. Nevertheless, epidemiological studies produce conflicting results [11, 12] have reported an increased rate of osteoporosis with hyponatremia, another research reported no relationship in Bone Mineral Density (BMD) with serum sodium concentration [12]. Due to the heterogeneity of study design, study population and selected covariates, the results may be biased due to confoundings. Therefore, further large sample and multi-ethnic observational studies are necessary to detect the association and explore the dose-response relationship between serum sodium and bone mineral density.

We conducted a secondary data analysis based on the Nation-

al Health and Nutrition Examination Survey (NHANES) database. Accordingly, we hypothesized that serum sodium was independently associated with bone mineral density at the femoral neck in NHANES participants and calculated the effect value.

3. Methods

3.1. Study Population

NHANES is a representative cross-sectional survey that is commissioned by the National Center for Health Statistics(NCHS) [13].Study participants were selected from the periods 2005–2010,2013–2014 and 2017-2018.We did not obtain local institu-

tional review board approval or participant consent for this analysis because it is a second analysis of publicly available identified data. The following exclusion criteria were used: a): participants without serum sodium concentration measurements and femoral bone mineral density; b) participants younger than 20 years; c) participants with eGFR<30 mL/min/1.73 m2; d) participants who were diagnosed as cancer or malignancy. The reason for excluding chronic kidney disease and cancer patient is to avoid confounding from renal osteodystrophy [14] or tomuo-related osteoporosis [15, 16]. Finally, 15822 participants were analysed (Figure 1).
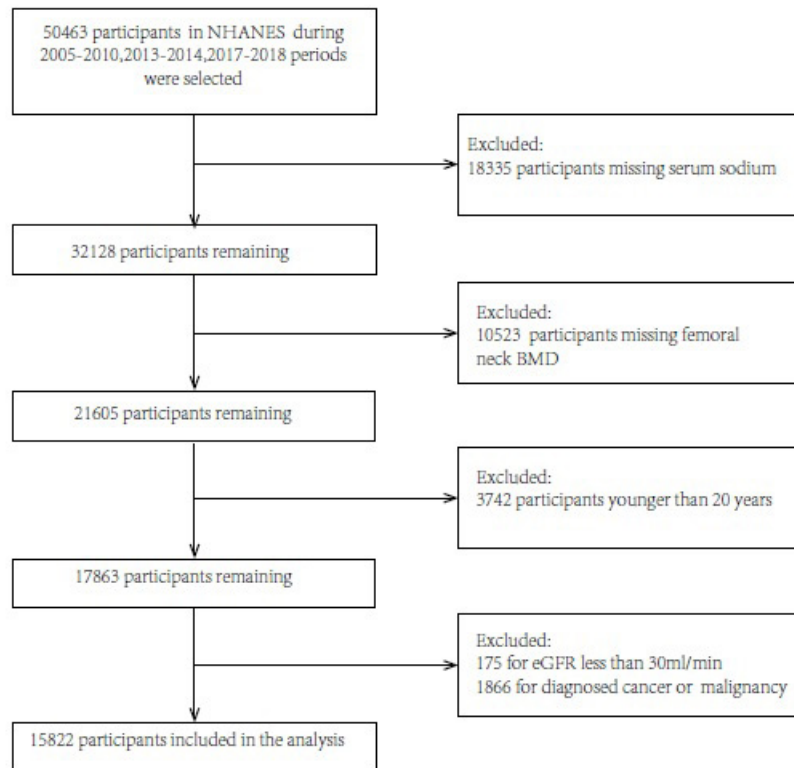

Figure 1: Study Population for Analysis

4. Acquirement of Serum Sodium, BMD and Other Covariates

Information on demographics (age, race, gender) were obtained via the demographic questionnaire. Based on the physical examination, the Body Mass Index (BMI) is calculated by dividing the weight in kilograms by the square of height in meters. Information on history of smoke status was obtained by a home interview. Laboratory data (serum albumin, sodium, glucose, calcium, phosphorous, creatinine) was measured on the Roche Cobas 6000(c501 module) analyzer. Diet information (energy, protein, total sugars, dietary fiber, cholesterol, calcium) was obtained from 24-h dietary recall. Information on awareness of comorbidities was obtained from the computer-assisted personal interview system. Bone densitometry indices at femoral neck were collected. For the assessment of Bone Mineral Density (BMD), special mobile examination centers equipped with dual energy X-ray absorption densitometers

(Hologic, Inc) were used. Details of the NHANES BMD examination protocols and quality controls have been published elsewhere [17, 18]. The chronic kidney disease-epidemiology collaboration equation [19] was used to calculate the estimated glomerular filtration rate (eGFR).

5. Statical Analysis

In our study, the mean and Standard Deviation (SD) of continuous variables are reported, whereas categorical variables are expressed as the percentage (%). The differences among different serum sodium concentrations in (Table.1) were detected using a weighted chi square test (categorical variables) and a weighted linear regression model (continuous variables). Following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline [20], the relationship between serum sodium and femoral neck BMD was tested using a weighted univariate and multivariate linear regression model. Model 1 is the non-ad-

justed model without covariates adjusted. Model 2 is the minimally-adjusted model, in which only sociodemographic variables are taken into account. Model 3 gives the full-adjusted model with covariates adjusted from Table 1. In this study, we examined the nonlinearity between serum sodium and femoral neck BMD using the Generalized Additive Model (GAM) and a smooth curve fitting method (penalized spline method) since linear regression models are often regarded for their inability to deal with nonlinear models. When no linearity was detected, a recursive algorithm was used to calculate the inflection point, which was then converted into a two-piecewise linear regression model on both sides of the inflection point [21]. A stratified linear regression model was used to analyze the subgroups. To test the interaction of continuous variables, we first converted them to categorical variables according to the clinical cut point. A likelihood ratio test was used to test for effect modification for subgroup indicators.

To determine the robustness of our results, we conducted a sensitivity analysis. For the purpose of verifying the results of serum sodium as the continuous variable as well as to examine the possibility of nonlinearity, we converted serum sodium into a categori-

cal variable according to the clinical cut point, and calculated the P for trend.

We used the statistical software packages R (http://www.r-project.org, The R Foundation) and Empowers tats (http://www. empowerstats.com, X&Y Solutions, Inc, Boston, MA) to analyze the data. Statistical significance was determined by P values less than 0.05 (two-sided).

6. Results

6.1. Baseline Characteristics of Participants

Approximately 51.59% of the participants were male, and their average age was 51.23±16.59 years. The weighted baseline characteristics are listed in (Table 1). The different serum sodium groups had statistically significant differences despite the energy intake and dietary fiber. Compared to the other subgroups, participants in the highest serum sodium group (145mmol/l or higher) were more likely to be women, non-hispanic black, patients ever suffered from angiocardiopathy (hypertension, heart failure) or arthritis, individuals with lower levels of serum albumin, serum phosphorus, protein, total sugars, calcium, femoral neck BMD and eGFR.

Table 1: Characteristics of Research Population Based On Serum Sodium Values(Weighted)

Serum sodium(mmol/l)	136 or lower	136 to 145	145 or higher	P value
Age(years)	51.59 ± 15.44	48.52 ± 15.60	58.73 ± 13.31	<0.001
Gender(%)				0.02
Male	45.32	50.74	48.33	
Female	54.68	49.26	51.67	
Race(%)				0.019
Mexican American	8.62	8.32	7.45	
Other Hispanic	4.31	5.04	4.7	
Non-Hispanic White	72.95	69.29	64.44	
Non-Hispanic Black	7.79	10.29	17.88	
Other Race - Including Multi-Racial	6.33	7.05	5.52	
Body mass index(kg/m2)	28.34 ± 5.84	28.15 ± 5.68	29.79 ± 7.17	<0.001
Smoke status(%)				<0.001
No	47.42	54	62.59	
Yes	52.58	46	37.41	
Laboratory data				
Serum albumin (g/dl)	4.19 ± 0.37	4.26 ± 0.31	4.11 ± 0.34	<0.001
Serum total calcium(mg/dl)	9.28 ± 0.42	9.45 ± 0.35	9.48 ± 0.48	<0.001
Serum creatinine(mg/dl)	0.85 ± 0.22	0.89 ± 0.20	0.90 ± 0.21	<0.001
Serum glucose(mg/dl)L.	129.36 ± 84.16	97.93 ± 28.19	105.96 ± 35.65	<0.001
Serum phosphorus(mg/dl)	3.71 ± 0.57	3.75 ± 0.56	3.71 ± 0.52	0.048
24-hour diet				
Energy(kcal)	1977.64 ± 924.48	2044.94 ± 926.06	2006.62 ± 876.23	0.218
Protein(g)	77.75 ± 40.41	82.03 ± 40.55	75.38 ± 36.70	0.007
Total sugars(g)	107.01 ± 75.69	109.92 ± 73.28	93.10 ± 54.98	0.01
Dietary fiber(g)	16.77 ± 10.22	16.88 ± 10.20	16.94 ± 9.36	0.966
Cholesterol (mg)	257.33 ± 207.64	279.73 ± 226.07	263.33 ± 185.83	0.049
Calcium (mg)	989.41 ± 701.60	943.69 ± 596.99	826.35 ± 514.06	0.009
Comorbidities(%)				
Hypertension				<0.001
No	54.85	69.89	45.02	
Yes	45.15	30.11	54.98	
Diabetes				<0.001
No	77.82	90.2	75.65	
Yes	20.04	7.82	21.31	
Borderline	2.13	1.98	3.05	
Liver disease				<0.001
No	92.31	96.39	97.24	
Yes	7.69	3.61	2.76	

Heart failure				<0.001
No	96.63	98.35	95.93	
Yes	3.37	1.65	4.07	
Arthritis				<0.001
No	67.78	74.23	60.77	
Yes	32.22	25.77	39.23	
Femoral neck BMD(g/cm2)	0.81 ± 0.15	0.83 ± 0.15	0.78 ± 0.14	<0.001
eGFR(mL/min/1.73 m2)	92.64 ± 21.00	92.49 ± 20.26	84.95 ± 19.68	<0.001

6.2. Univariate Analysis

(Table 2) shows the results of the univariate analysis, indicating that age, non-hispanic race, BMI, serum albumin, serum creatinine, energy, protein, total sugars, dietary fiber, cholesterol, calcium, and eGFR were positively associated with higher femoral neck BMD. We additionally found that serum total calcium and serum glucose were not correlated with the BMD, whereas female, americans except for blacks, smokers, serum phosphorus, serum sodium, hypertension, arthritis, diabetes, heart failure and liver disease were negatively associated with higher femoral neck BMD.

Table 2: The Results of Univariate Analysis(Weighted)

Femoral neck BMD(g/cm2)	Statistics	β (95%CI) Pvalue
Age(years)	51.228 ± 16.591	0.042 (0.035, 0.050) <0.001
Gender		
Male	8163 (51.593%)	Ref
Female	7659 (48.407%)	-0.075 (-0.080, -0.071) <0.001
Race		
Mexican American	2865 (18.108%)	Ref
Other Hispanic	1529 (9.664%)	-0.015 (-0.028, -0.002) 0.021
Non-Hispanic White	7055 (44.590%)	-0.047 (-0.055, -0.038) <0.001
Non-Hispanic Black	3079 (19.460%)	0.052 (0.041, 0.063) <0.001
Other Race - Including Multi-Racial	1294 (8.178%)	-0.061 (-0.073, -0.050) <0.001
Body mass index(kg/m2)	28.351 ± 5.725	0.008 (0.007, 0.009) <0.001
Smoke status		
No	8443 (53.383%)	Ref
Yes	7373 (46.617%)	-0.005 (-0.010, -0.001) 0.0283
Serum albumin (g/dL)	4.226 ± 0.320	0.042(0.035, 0.050) <0.001
Serum total calcium(per10 mg/dl)	0.944 ± 0.036	-0.004 (-0.070, 0.062) 0.906
Serum creatinine(mg/dl).	0.890 ± 0.227	0.063 (0.051, 0.074) <0.001
Serum glucose(per 100 mg/dl)	1.030 ± 0.393	-0.001 ((-0.008, 0.006) 0.713
Serum phosphorus(mg/dl)	3.727 ± 0.554	-0.006 (-0.102, -0.019) 0.004
Serum sodium(per10 mmol/l)	13.945 ± 0.239	-0.038 (-0.048, -0.028) <0.001
Energy(per 100 kcal)	19.677 ± 9.230	0.002 (0.001, 0.003) <0.001
Protein(per 10 g)	7.890 ± 4.043	0.006 (0.005, 0.007) <0.001
Total sugars(per 10 g)	10.683 ± 7.177	0.002 (0.001, 0.003) <0.001
Dietary fiber (per 10 g)	1.677 ± 1.049	0.003 (0.001, 0.006) 0.013
Cholesterol (per 100 mg)	2.783 ± 2.268	0.007 (0.006, 0.008) <0.001
Calcium (per 100 mg)	8.962 ± 5.832	0.002 (0.001,0.003) <0.001
Hypertension		
No	10263 (64.956%)	Ref
Yes	5537 (35.044%)	-0.031 (-0.0360, -0.0260) <0.001
Arthritis		
No	11450 (72.533%)	Ref
Yes	4336 (27.467%)	-0.054 (-0.059, -0.049) <0.001
Diabetes		
No	13571 (85.833%)	Ref
Yes	1875 (11.859%)	-0.010 (-0.018, -0.002) 0.020
Borderline	365 (2.309%)	-0.013 (-0.029, 0.004) 0.136
Heart failure		
No	15389 (97.522%)	Ref
Yes	391 (2.478%)	-0.048 (-0.066, -0.030) <0.001
Liver disease		
No	15159 (96.046%)	Ref
Yes	624 (3.954%)	-0.037 (-0.049, -0.025) <0.001
eGFR(mL/min/1.73 m2)	92.310 ± 21.639	0.002 (0.001, 0.003) <0.001

6.3. The Results of Relationship Between Serum Sodium and Femoral Neck BMD

To determine the association between serum sodium and femoral neck BMD, we used a univariate linear regression model. We also presented the non-adjusted and adjusted models in (Table 3). In crude model, serum sodium showed negative correlation with femoral neck BMD (β = -0.038, 95% Confidence Interval (CI): -0.048 to -0.028, P < 0.001). In minimally adjusted model (adjusted age, sex, race), there were no obvious differences in the results (β = -0.015, 95%CI: -0.023 to -0.006, P < 0.001). We still detected the connection in fully adjusted model (β = -0.019, 95%CI: -0.028 to -0.010, P<0.001). To conduct sensitivity analysis, we also analyzed serum sodium as a categorical variable (according to clinical value), and found that the p for trend was not significant (p for trend was 0.271).

Table 3: Relationship Between Serum Sodium (Per 10 Mmol/L) And Femoral Neck BMD(G/Cm2) In Different Models(Weighted)

Variable	Crude model (β, 95%CI, P)	Minimally adjusted model (β, 95%CI, P)	Fully adjusted model (β, 95%CI, P)
Serum sodium	-0.038 (-0.048, -0.028) <0.001	-0.015 (-0.023, -0.006) <0.001	-0.019 (-0.028, -0.010) <0.001
Serum sodium categories			
<13.6	Ref	Ref	Ref
13.6 to 14.5	0.205 (0.090, 0.321) 0.001	0.020 (-0.078, 0.117) 0.689	0.006 (-0.096, 0.107) 0.915
>=14.5	-0.286 (-0.529, -0.044) 0.021	-0.103 (-0.307, 0.101) 0.323	-0.223 (-0.433, -0.013) 0.037
P for trend	0.376	0.768	0.271

Crude model: we did not adjust other covariant Minimally adjusted model: we adjusted age, gender and race Fully adjusted model: we adjusted age,gender,race,body mass index, smoked at least 100 cigarettes in life, serum albumin, serum total calcium, serum creatinine, serum glucose, serum phosphorus, serum sodium, energy, protein, total sugars, dietary fiber, cholesterol, calcium, high blood pressure, arthritis, diabetes, heart failure, liver disease, eGFR.

CI: confidence interval; Ref: reference

6.4. The Analyses of Non-Linear Relationship

Due to serum sodium being a continuous variable, we also analysed the nonlinear relationship between serum sodium and femoral neck BMD ((Figure 2).We found that the relationship between serum sodium and femoral neck BMD was non-linear(adjusted for age, gender, race, serum albumin, serum total calcium, serum creatinine, serum glucose, serum phosphorus, body mass index, energy, protein, total sugars, dietary fiber, cholesterol, calcium, hypertension, diabetes, arthritis, heart failure, liver disease, smoke status, eGFR.)We calculated the inflection point as 13.7 by using a two-piecewise linear regression model. On the left of the inflection point, the effect size(β), 95%CI and P value were 0.014, -0.011 to 0.040 and 0.273, respectively. Additionally, our analysis found that serum sodium and femoral neck BMD were negatively correlated on the right side of the inflection point (-0.028, -0.040 to -0.017, <0.001) (Table 4).
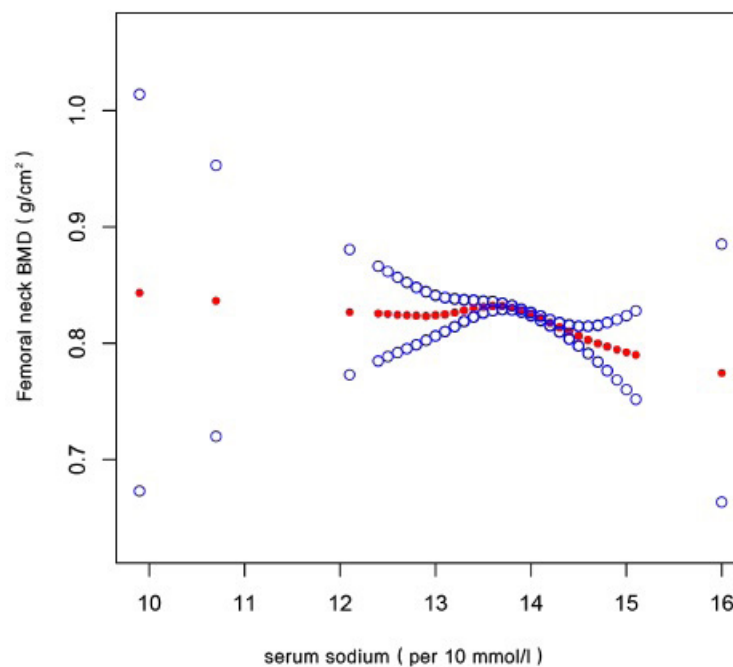

Figure 2: Dose–response relationship between serum sodium and femoral neck BMD. A nonlinear relationship between them was detected after adjusting for age, gender, race, serum albumin, serum total calcium, serum creatinine, serum glucose, serum phosphorus, body mass index, energy, protein, total sugars, dietary fiber, cholesterol, calcium, hypertension, diabetes, arthritis, heart failure, liver disease, smoke status, eGFR.

Table 4: Nonlinearity Addressing of Serum Sodium (Per 10 Mmol/L) And Femoral Neck BMD(G/Cm2)

femoral neck BMD	β (95%CI) Pvalue
Model I Fitting model by standard linear regression	-0.019 (-0.028, -0.010) <0.001
Model II Fitting model by two-piecewise linear regression	
Inflection point	13.7
< 13.7	0.014 (-0.011, 0.040) 0.273
< 13.7	-0.028 (-0.040, -0.017) <0.001
P for log likelyhood ratio test	0.006

Note: Above modes all adjusted for age, gender, race, serum albumin, serum total calcium, serum creatinine, serum glucose, serum phosphorus, body mass index, high blood pressure, diabetes, energy, protein, total sugars, dietary fiber, cholesterol, calcium, arthritis, heart failure, liver disease, smoke at least 100 cigarettes in life, eGFR.

6.5. The Results of Subgroup Analyses

As is shown in (Table 5), serum sodium was positively associated with femoral neck BMD in participants with heart failure (β:0.001, 95%CI: -0.004, 0.006, p=0.766), although the difference was not statistically significant. The results in other subgroups corresponded with each other which reveal the robustness of the negative trend of serum sodium on femoral neck BMD. There was a significant interaction for gender (P for interaction = 0.017), however no interactions were found for age, race, BMI, smoke status, hypertension, arthritis, diabetes, heart failure and liver disease. (P for integration>0.05).

Table 5: Effect Size of Serum Sodium (Per 10 Mmol/L) On Femoral Neck BMD in Subgroups

Characteristics	N	β (95%CI) Pvalue	P for interaction
Age(years)			0.375
<60	10257	-0.017 (-0.030, -0.005) 0.008	
>=60	5563	-0.008 (-0.022, 0.007) 0.298	
Gender			0.017
Male	8161	-0.014 (-0.027, -0.001) 0.036	
Female	7659	-0.020 (-0.033, -0.008) 0.001	
Race			0.711
Mexican American	2865	-0.020 (-0.040, -0.001) 0.046	
Other Hispanic	1529	-0.045(-0.076, -0.014) 0.004	
Non-Hispanic White	7054	-0.017(-0.029, -0.004) 0.012	
Non-Hispanic Black	3079	-0.018(-0.042, 0.005) 0.131	
Other Race - Including Multi-Racial	1293	-0.027 (-0.061, 0.008) 0.128	
Body mass index(kg/m2)			0.834
<18.5	225	-0.001 (-0.007, 0.001) 0.837	
>=18.5, <25	4427	-0.003 (-0.005, -0.001) 0.001	
>=25, <30	5745	-0.003 (-0.004, -0.001) <0.001	
>=30	5353	-0.001 (-0.003, 0.001) 0.174	
Smoke status			0.159
No	8441	-0.022 (-0.035, -0.010) 0.001	
Yes	7373	-0.010 (-0.023, 0.003) 0.118	
Hypertension			0.241
No	10262	-0.022 (-0.034, -0.010) <0.001	
Yes	5536	-0.007 (-0.022, 0.007) 0.304	
Arthritis			0.294
No	11448	-0.020 (-0.030, -0.009) <0.001	
Yes	4336	-0.009 (-0.026, 0.007) 0.265	
Diabetes			0.472
No	13570	-0.020 (-0.029, -0.010) <0.001	
Yes	1875	-0.011(-0.038, 0.015) 0.377	
Broderline	364	-0.005 (-0.068, 0.058) 0.870	
Heart failure			0.623
No	15388	-0.002 (-0.003, -0.001) <0.001	
Yes	390	0.001 (-0.004, 0.006) 0.766	
Liver disease			0.135
No	15157	-0.002 (-0.003, -0.001) <0.001	
Yes	624	-0.006 (-0.010, -0.001) 0.013	

Note1: Above model adjusted for age, gender, race, body mass index, smoked at least 100 cigarettes in life, serum albumin, serum total calcium, serum creatinine, serum glucose, serum phosphorus, serum sodium, energy, protein, total sugars, dietary fiber, cholesterol, calcium, high blood pressure, arthritis, diabetes, heart failure, liver disease, eGFR.

Note2:In each case, the model is not adjusted for the stratification variable.

7. Discussion

In the present study, we assessed the effect of serum sodium on femoral neck BMD among participants from the NHANES database. As is shown in fully adjusted model, serum sodium was negatively associated with femoral neck BMD(p<0.001). Whereas we handled serum sodium as a categorical variable, inverse trend was observed. Accordingly, we further analysed the non-linear relationship between serum sodium and femoral neck BMD. The different correlations of serum sodium on BMD were found on the left and right sides of inflection point (Serum sodium per 10 mmol/l=13.7). The assessment of serum sodium in baseline was negatively associated with femoral neck BMD on the right side of the inflection point, but it was not significantly associated with BMD on the left side. These results showed reliability in prespecified subgroups.

There were inconsistent results reported in previous studies investigating the relationship between serum sodium and BMD. According to one previous study [11] based on an animal model, rats with hyponatremia experienced a 30% reduction in bone mineral density measured by DXA compared to rats without hyponatremia. In order to provide clinical context to the observation, they also analysed data from adults in NHANES III using linear regression models. The results showed that mild hyponatremia (T-score -2.5 or less) is associated with greater odds of osteoporosis (OR = 2.85) at the hip. However, other studies failed to replicate the results of the in vitro trials. Based on a study of 1408 female participants, [22] found that those with a serum sodium level of <135 mmol/L had significantly lower bone density and a significantly higher rate of OP than reference group participants (8.7% versus 3.2 %, P<0.001). In a prospective cohort study [12] reported hyponatremia (serum sodium concentration < 136 mmol/L) had increased risk of vertebral fractures in the fully adjusted model but found no association with BMD. These studies focused on hyponatremia as a risk factor for fracture or osteoporosis.

In fully adjusted model, we show serum sodium was statistically significant with BMD at femoral neck(p<0.001). Our results showed a positive correlation between serum sodium and bone mineral density at femoral neck when serum sodium concentrations less than 13.7 per 10 mmol/ L in the U.S. adults population, suggesting that elevated serum sodium inhibits bone loss, whereas no statistically significance was found(p=0.273). A negative correlation was observed when serum sodium concentration was higher than 13.7 per 10 mmol/ L, suggesting that higher blood sodium level may cause decreased bone mass. This phenomenon may be related to high sodium intake. [23] ovariectomized adult rats with low calcium intake were given NaCl supplement to observe the effect of sodium supplement on urinary calcium and bone mass and found that the urine excretion of calcium was significantly higher in the rats provided with additional NaCl intake, and the contents of mineral ash, calcium and phosphate were lower per unit bone

volume, suggesting that NaCl intake promoted bone loss and affected calcium balance in ovariectomized rats. Similarly, [24] fed male rats with high sodium diet for 8 weeks and detected the bone mineral density, cortical bone width and bone strength in the high sodium group decreased significantly, and the higher the concentration of sodium, the more obvious the decrease of bone mineral density.

Our study has some strengths. We use both the generalized additive model and the generalized linear model to examine the nonlinear relationship between serum sodium and femoral neck BMD. The advantage of GAM in dealing with non-linear relationships is obvious, and it can deal with the non-parametric smoothing as well as fit the data with a regression spline. In using GAM, we will be able to better understand the relationship between exposure and outcome. We also applied strict statistical adjustment to minimize residual confounding in this study, since it is an observational study with unavoidable confounding. We also noted a nonlinear relationship in our study after adjusting for age, gender, race, and other confounding factors not reported by previous studies.

It is important to note that our study has some limitations. First, this study is an analytical cross-sectional study and, as such, provides only weak evidence about exposure and outcome, which makes it difficult to distinguish between cause and effect. Second, because the study population consists of only American citizens, it may not be generalizable to other ethnic groups. Third, our study was limited to a single site at the neck of the femur, so the relationship between serum sodium and BMD at other sites, such as the lumbar spine and the trochanter of the femur, was not explored. Forth, since detailed data on long-term sodium intake in the study population were not available, so the association between sodium intake and bone mineral density in the study population remained unclear. Although our study confirmed that serum sodium was correlated with bone mineral density at femoral neck, the effect value was weak, so the effect of serum sodium on bone mineral density and osteoporosis still needs further study.

8. Conclusion

The association between serum sodium and BMD is significant and independent but non-linear and the association is modified by gender. Serum sodium is negatively correlated with femora neck BMD when serum sodium is larger than 13.7 per 10 mmol/l.

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