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The Positive Association of Total Protein Intake with Femoral Neck Strength (KNHANES IV)

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Abstract

Introduction—Despite the general belief that higher protein intake may be helpful for bone homeostasis, its impact on human bone health is still debated. Furthermore, the association of dietary protein intake with femoral neck (FN) strength, which can predict fracture risk independently of bone mineral density (BMD), has not been thoroughly studied.

Methods—This is a population-based, cross-sectional study from Korea National Health and Nutrition Examination Surveys, including 592 men aged 50 years or older and 590 postmenopausal women. The composite indices of FN strength, such as the compression strength index (CSI), bending strength index (BSI), and impact strength index (ISI), were generated by combining BMD, body weight, and height with the femoral axis length and width, which were measured by dual-energy x-ray absorptiometry.

Results—After adjustment for confounders, total protein intake (g/kg/d) positively correlated with all three FN composite indices in both genders ($P = 0.006$ to 0.035), except for BSI showing marginal significance in postmenopausal women ($P = 0.093$). Consistently, compared with subjects in lowest total protein intake quartile, those in the highest quartile showed markedly higher CSI, ISI, and ISI values ($P = 0.043$ to < 0.001), with a dose-response manner across increasing total protein intake quartile categories in both men and women (P for trend = 0.028 to < 0.001).

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Compliance with ethical standard

Informed consent

All participants in the KNHANES survey provided informed consent.

Conflict of interest

The authors declare that there is no conflict of interest.

Conclusions—These findings provide the clinical evidence that higher dietary protein intake can play a beneficial role on bone health through the increase of FN strength relative to load in adults.

Keywords

Protein intake; Bone strength; Femoral neck; Fracture

Introduction

As the life span of individuals continues to increase, osteoporotic fracture (OF) has become a worldwide public health problem. Among all types of OF, hip fracture is the most serious because of the high morbidity and mortality [1]. Although bone mineral density (BMD) is among the best available method for assessing future fracture risk, approximately two-thirds of individuals who suffer a fracture do not have BMD-defined osteoporosis [2]. In order to compensate for the limitation of BMD for prediction of hip bone health, Karlamangla *et al.* [3] developed the concept of composite indices of femoral neck (FN) strength. These indices integrate bone and body size with BMD, and represent the contribution of bone macroarchitecture to bone strength relative to an applied load. Indeed, recent epidemiologic studies demonstrated the usefulness of these indices for evaluating fracture risk [4–7]. The FN composite strength indices can be especially useful in case of assessing bone properties which are not explained by BMD. For example, the paradoxically increased fracture risk in subjects with diabetes, despite their higher BMD [8], is consistent with the lower composite indices seen in persons with diabetes relative to nondiabetics [5].

Protein constitutes one-third of total bone mass, of which type 1 collagen fibers make up the majority; in addition, amino acid precursors derived from dietary protein are required to maintain bone structure and quality [9,10]. Adequate protein intake is therefore likely to be essential for adult bone health. Surprisingly, the impact of dietary protein intake on osteoporosis-related phenotypes in human is a long-standing debate. Although high-protein diet has long been thought to have a negative influence on bone mass, possibly through its calciuric effect [11], other studies have reported its beneficial effects on bone metabolism by modulating bone-related hormones [12,13,10]. However, these epidemiologic studies have focused largely on the BMD values [14–17], which only partially explain bone strength [2], and clinical studies relating dietary protein intake to bone strength *per se* have been rare. Therefore, in our present study, to clarify the potential role of dietary protein intake on human bone health, we investigate its association with composite indices of FN strength using a representative cohort of the general Korean population.

Materials and methods

Study population

This cross-sectional study was based on data acquired in the Fourth Korea National Health and Nutrition Examination Survey (KNHANES IV) that was conducted between 2007 and 2009. This nationwide survey used a stratified, multistage, clustered probability sampling method to select a representative sample of the noninstitutionalized, civilian Korean population [18]. The survey consisted of a health interview survey, a nutrition survey, and a

health examination survey. All participants in this survey signed an informed consent form. The database of KNHANES is publicly available at the KNHANES website (<http://knhanes.cdc.go.kr>; available in Korean and English). Of the subjects who participated in the KNHANES IV, information regarding protein intake, hip geometry, and BMD was available for 604 men who were aged 50 years or older and 761 postmenopausal women. Subjects were excluded if they had taken drugs that could affect bone metabolism, such as bisphosphonate or hormone replacement therapy ($n = 183$). The remaining 1,182 subjects (592 men and 590 women) were eligible for this study. All participants in the KNHANES survey provided informed consent. The KNHANES was reviewed and approved by the Ethics Committee of the Korea Centers for Disease Control and Prevention.

Measurements of clinical and laboratory parameters

All subjects underwent a thorough physical examination. Age, body weight, height, smoking, drinking and exercise habits were recorded. Smoking was divided into one of three categories (*e.g.*, never, past, or current), and alcohol use was listed as yes when the subject drank more than 3 units of alcohol per day. Exercise was indicated as yes when the subject exercised regularly at moderate levels (*e.g.*, for more than 20 minutes per session and more than three times per week). Height (cm) and weight (kg) were measured by using standardized protocols while the subject was dressed in light clothing without shoes. Body mass index (BMI; kg/m^2) was calculated from the height and weight.

After overnight fasting for 8 hours, blood samples were drawn from all participants during the survey, immediately refrigerated, and then transported to the Central Testing Institute (Neodin Medical Inc., Seoul, Korea). All blood samples were analyzed within 24 hours after transport. Serum 25-hydroxyvitamin D [25(OH)D] concentration was measured by radioimmunoassays (DiaSorin Inc., USA) using a 1470 Wizard Gamma Counter (PerkinElmer, Finland). Serum creatinine concentration was measured colorimetrically using an Automatic Analyzer 7600 (Hitachi, Japan). Glomerular filtration rate (GFR) was estimated using the Cockcroft-Gault formula [19].

Dietary assessment

Nutrient status, including total energy intake (Kcal/d), total protein intake (g/d), and calcium intake (mg/d), was assessed using a 24-hour dietary recall questionnaire administered by a trained dietitian. The results were generated using the Food Composition Table developed by the National Rural Resources Development Institute [20]. Weight-adjusted protein intake ($\text{g}/\text{kg}/\text{d}$) and energy from protein (%) meaning protein energy intake divided by total energy intake were calculated from total protein intake (g/d).

Dual-energy x-ray absorptiometry measurements

In the KNHANES, areal BMD (g/cm^2) was measured using whole-body dual-energy x-ray absorptiometry (DXA; QDR4500A; Hologic Inc., USA) at mobile examination centers operated by licensed, trained technicians. These DXA instruments were calibrated to a single standard as previously described [21] and reference values obtained [22]. DXA calibration was maintained via an internal referencing system and daily measured spine phantoms supplied by the manufacturers, which are bone and soft-tissue-equivalent

reference standards [23,24]. The quality control program for DXA also included training and monitoring of technologists, precision assessment and central review of all scans. The precision value of the equipment, in terms of the coefficient of variation (CV), was 1.2% for the FN. This value was obtained by scanning 30 randomly selected subjects who underwent two scans on the same day while getting off and back onto the examination table between their examinations.

The geometric bone structure was further analyzed using the hip structure analysis (HSA) program included in the APEX software from Hologic, as previously described [25]. The HSA program automatically set the region of interest, defined as the narrow neck, as traversing the narrowest width of the FN. The CV of the HSA indices, which was calculated from the same images used for the precision assessment of BMD, was approximately 2%.

Whole-body DXA has been used to assess body muscle distribution as well as bone density with minimal radiation exposure [26]. Appendicular skeletal muscle mass (ASM) was calculated as the sum of the fat-free soft tissue mass of the upper and lower limbs, according to the definition put forth by Heymsfield *et al.* [27].

Composite indices of femoral neck strength

To assess the ability of the FN to withstand loading during a fall, the indices of compression strength (CSI), bending strength (BSI), and impact strength (ISI) at the site of the FN were calculated from the mean FN width (FNW) and hip axis length (HAL), together with height, weight and FN BMD, as described by Karlamangla *et al.* [3]. The FNW is the smallest thickness of the FN along any line perpendicular to the FN axis. The HAL reflects the distance along the FN axis from the lateral margin at the base of the greater trochanter to the inner pelvic brim. The equations used were:

$$\begin{aligned} CSI &= (BMD \times FNW) / weight \\ BSI &= (BMD \times FNW^2) / (HAL \times weight) \\ ISI &= (BMD \times FNW \times HAL) / (height \times weight) \end{aligned}$$

CSI reflects the FN ability to withstand an axial compressive load, BSI reflects its ability to withstand bending forces, and ISI reflects the FN ability to absorb the energy of impact in a fall from standing height.

Statistical analysis

Following the guideline of statistics from the Korea Centers for Disease Control and Prevention, all analyses were performed using the Complex Samples Plan (CSPLAN) which is available as the complex samples option in SPSS version 18.0 (SPSS Inc., USA). Survey sample weights were considered in all analyses to produce estimates that were representative of the non-institutionalized civilian population in Korea. Data are presented as means with standard deviation, or as numbers and percentages, unless otherwise specified. The baseline characteristics were calculated using an unpaired *t* test for continuous variables or the χ^2 test for categorical variables. To test our hypothesis that higher total protein intake might be associated with higher indices of FN strength, we performed multiple linear regression

analyses after adjustment for potential confounders. These confounding factors included age, smoking, drinking, and exercise habits, GFR, serum 25(OH)D level, and calcium intake, which were selected on the basis of clinical applicability. The beta values in this model indicates the nonstandardized regression coefficient, which signifies how much the mean of the dependent variable changes given a one-unit shift in the independent variable. To further analyze the changes in composite indices of FN strength according to total protein intake quartiles, multivariable-adjusted least-square means with 95% confidence intervals (CIs) were estimated and compared by analysis of covariance (ANCOVA) after adjustment for confounders. The trend of composite strength indices across increasing quartiles of total protein intake was checked by examining *P* values for the trends using multiple linear regression analyses. In the present study, *P* < 0.05 was considered to indicate statistical significance.

Results

The clinical characteristics of 592 men aged 50 years or older and 590 postmenopausal women are shown in Table 1. The mean age of the men was 61.1 years (range, 50–86 years), and the mean age of the women was 64.1 years (range, 45–89 years). Men had greater height, weight, percentages of current smoking, alcohol drinking, and regular exercise, GFR, serum 25(OH)D level, and calcium intake, whereas there was no difference of BMI between men and women. Total daily protein intake (g/d), weight-adjusted protein intake (g/kg/d), and energy from protein (%) were consistently higher in men than women. Men had markedly higher FN BMD, HAL, FNW, and all composite strength indices than women as well.

As a preliminary analysis, we first examined the possible associations of various indicators regarding protein intake with the composite indices of FN strength (Supplemental Table 1). After considering age, weight-adjusted total daily protein intake (g/kg/d) showed positive associations with CSI, BSI, and ISI in both men and women (*P* = 0.001 to 0.037), whereas simple total daily protein intake (g/d) and energy from protein (%) did not associate with any composite indices of FN strength, regardless of genders (*P* = 0.067 to 0.936). Therefore, we performed further analyses focusing on the effects of weight-adjusted total daily protein intake (g/kg/d) on bone strength.

Multiple linear regression analyses were performed to investigate whether total protein intake (g/kg/d) independently associated with the composite indices of FN strength (Table 2). In men, after adjustment for all potential confounders including age, smoking, drinking, and exercise habits, GFR, serum 25(OH)D level, and calcium intake, total protein intake (g/kg/d) positively correlated with CSI, BSI, and ISI (*P* = 0.006 to 0.024). Consistently, in women, total protein intake (g/kg/d) showed a significant positive association with the composite indices (*P* = 0.011 for CSI and 0.035 for ISI), except for BSI with marginal significance on the multivariable model (*P* = 0.093).

To find out whether the association between total protein intake (g/kg/d) and the composite strength indices is gradual or has a threshold effect, we divided the subjects into quartiles according to total protein intake levels in each gender (Fig. 1). In both men and women, all

three composite indices of FN strength linearly increased across increasing total protein intake quartiles (g/kg/d) after adjustment for age, smoking, drinking, and exercise habits, GFR, serum 25(OH)D level, and calcium intake (P for trend = 0.028 to < 0.001). Consistently, CSI, BSI, and ISI values were consistently higher in men in the third and/or highest total protein intake quartiles (g/kg/d) than in those in the lowest quartile group on the multivariable model ($P = 0.024$ to 0.043). In women, compared with subjects in the lowest total protein intake quartile (g/kg/d), those in the higher three quartiles and in the highest quartile had significantly higher CSI and ISI values ($P = 0.010$ to < 0.001), and BSI value ($P = 0.006$), respectively, after adjustment for confounders.

To investigate whether the effects of protein intake on bone may be mediated through skeletal muscle, which is mechanically and functionally linked with bone, the ASM was additionally adjusted in the multivariable model (Table 3). In men, the positive associations of total daily protein intake (g/kg/d) with CSI and ISI remained significant ($P = 0.032$ and 0.022 , respectively), while the statistical significance for BSI became marginal ($P = 0.083$). In women, the associations of total daily protein intake (g/kg/d) with the FN composite indices following the additional adjustment for ASM were markedly attenuated, leading to no statistical significances for BSI and ISI ($P = 0.156$ and 0.101 , respectively), and marginal significance for CSI ($P = 0.052$).

Finally, the association of total protein intake (g/kg/d) with the composite strength indices was evaluated after classifying the participants into two groups according to their age (Table 4). Multiple linear regression analyses showed the positive correlation of total protein intake (g/kg/d) with CSI and ISI in men under 65 years old ($P = 0.031$ and 0.028 , respectively), whereas there was no significant relationship between these parameters in men aged 65 years or older ($P = 0.075$ and 0.050 , respectively). On the other hand, in women, the positive association of total protein intake (g/kg/d) with CSI and ISI was observed only in the group with 65 years or older ($P = 0.010$ and 0.038 , respectively), but not in those under 65 years old ($P = 0.212$ and 0.298 , respectively).

Discussion

In this nationally representative population-based cohort of men 50 years or older and postmenopausal women, we observed that total protein intake positively correlated with all three FN composite indices in both genders, except for BSI showing marginal significance in postmenopausal women, after adjustment for potential confounders. Consistently, compared with subjects in lowest total protein intake quartile, those in the highest quartile showed markedly higher CSI, ISI, and ISI values in a dose-response manner across increasing total protein intake quartile categories in both men and women. These findings provide the clinical evidence that higher dietary protein intake can play a beneficial role on bone health through the increase of FN strength relative to load in adults.

Despite the general belief that higher protein intake may be helpful to maintain bone homeostasis in adults, whether dietary protein has an anabolic, catabolic or neutral effect on bone mass remains a controversial issue. For example, among the two representative longitudinal studies, the Framingham Osteoporosis Study reported that low dietary protein

intake associated with higher rates of bone loss [14], whereas Rapuri *et al.* [28] showed no statistically significant association. Because of the importance and uncertainty of this issue, the National Osteoporosis Foundation recently performed a systemic review and meta-analysis, and suggested that higher protein intake may have a protective effect of BMD on lumbar spine but no effect on BMD on total hip, FN, or total body [29]. However, they discussed that conclusions were limited due to the heterogeneity of studies and uncontrolled confounders. Furthermore, most of clinical studies have linked protein intake only to BMD value [14–17,28], which is not the sole driver of bone strength, due to its convenient availability. Therefore, these preceding studies, although important, have not been sufficient to fully assess the role of dietary protein on bone properties.

The composite indices of FN strength, easily measured through DXA, are concepts that combine the size and areal BMD of FN with body size to estimate the bone strength relative to the load (impact forces) during a fall [3]. There is evidence that analysis of FN strength can predict fracture risk independently of BMD [30], and combining the strength indices with BMD makes the prediction even more accurate compared to BMD alone [31]. Moreover, a recent study in postmenopausal women revealed that 2D DXA-derived hip geometry and the analyzed simple strength indices correlated well with results from 3D quantitative computed tomography [32]. In fact, these composite strength indices improve the ability to predict fracture in both women [3,4] and men [6]. When we employed these effective indices in our study, we showed that higher dietary protein intake significantly associated with higher FN strength. Although the effect of dietary protein on fractures is still inconclusive [33,34,29], our results suggest that higher dietary protein intake may contribute, at least in part, to the lower OF risk by improving bone quality including bone macrostructure, regardless of the effect on BMD.

For a long period of time, the role of dietary protein intake on bone has been mainly considered in terms of interaction with calcium metabolism [12]. In brief, although earlier studies suggested that protein intake might be harmful for bone health due to the calciuric effect [11], there is accumulating evidence that it can be beneficial when calcium intake is optimal [35,36]. However, in the present study, we controlled GFR, serum 25(OH)D level, and calcium intake as confounding factors in order to appropriately investigate the pure physiologic effects of protein intake on bone strength, and there are several possible mechanisms that may explain their positive association, independent of calcium metabolism. First, collagen and noncollagen proteins, such as proteoglycans, provide the structural backbone of bone matrix [37], and thus adequate dietary protein intake is critical to obtain and maintain the optimal bone strength. Second, the anabolic drive of protein intake could be mediated through the stimulation of growth factors for bone, such as insulin-like growth factor I (IGF-I) [38,39]. Third, there is molecular evidence that sufficient amino acids resulting from higher protein intake can directly affect bone metabolism by increasing osteoblastic differentiation and suppressing osteoclastic activity [10,40,41]. Fourth, muscle and bone are known to have common genetic, nutritional, lifestyle, and hormonal determinants, and to be tightly coupled during growth, development, and aging [42]. Furthermore, interactions between muscle and bone may affect bone strength [43]. In fact, when the skeletal muscle mass was additionally adjusted in the multivariable model, the associations of total protein intake with the composite strength indices were attenuated in

both men and women. These results suggest that the possible effects of dietary protein intake on muscle may indirectly contribute to the changes in bone properties.

A particularly interesting observation in the present study is that the positive correlation of total protein intake with the strength indices was more dominant in men under 65 years old and in women aged 65 years or older, respectively, raising the possible presence of different association according to gender and age. We speculate that the results in women may be explained by abrupt loss of estrogen in middle-aged women (ages 50–64 y), compared with older women (ages over 65 y) having less significant hormone alterations. In detail, the rapid decrease in estrogen levels during and early after menopause is the most important biological event that causes enormous changes in homeostasis in women. Regarding bone metabolism, substantial evidence indicates that estrogen deficiency not only directly affects bone cells [44], but also involves diverse, indirect mechanisms, such as ROS, cytokines, and growth factors, that result in adverse outcomes of bone remodeling [45]. Therefore, we assume that the effects of tremendous changes caused by estrogen deficiency in middle-aged women may be strong enough to countervail those of protein intake on bone metabolism. However, we cannot apply these explanations to the association by age in men. Therefore, further studies focusing on how male and female hormones interact with protein metabolism in relation to bone may help to explain the differences depending on the gender and age group in the association between protein intake and FN strength.

The major strength of our study is that it is a large population-based study using well-collected national data, which enhances the statistical reliability of the results and the generalizability of the data. Despite this, several limitations should be considered when interpreting our data. Most importantly, 24-hour dietary recall method, despite the usefulness especially in a large study, inevitably has some level of recall or misreporting bias with the risk of limited accuracy for the measurement of absolute intakes. Second, because it was a cross-sectional study, we could not determine whether there was a causal relationship between dietary protein and the composite indices. Third, although the effects of dietary protein on bone can be various depending on the subclasses of amino acids and the protein source (animal vs vegetable), this information was unavailable in KNHANES. The role of specific amino acid or protein source on bone strength should be clarified in further clinical studies. Lastly, the composite indices in our study are based on macroscopic measurements from DXA scans; they do not reflect microscopic features such as the quality of cancellous mineralization and the microarchitecture, which can be measured by quantitative computed tomography, both of which are important determinants of bone strength.

In summary, data gathered from a nationally representative cohort demonstrate that higher dietary protein intake was positively associated with the composite indices of FN strength in both men and women. The data presented here may have clinical implications in that they provide the evidence that higher protein intake may contribute to lower risk of hip fracture through the improvement of bone strength.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

The composite indices of femoral neck strength according to total protein intake quartiles in men (A) and women (B). Values are presented as the estimated mean with 95 % confidence intervals (CIs) after adjustment for confounding factors using analysis of covariance (ANCOVA). Confounding variables include age, smoking, drinking, and exercise habits, glomerular filtration rate, 25-hydroxyvitamin D, and calcium intake.

Table 1

Baseline characteristics of the study population

Variables	Men (n = 592)	Women (n = 590)	P value
Age (years)	61.1 ± 8.5	64.1 ± 9.9	< 0.001
Weight (kg)	66.0 ± 9.7	55.6 ± 8.0	< 0.001
Height (cm)	166.6 ± 6.0	152.9 ± 5.7	< 0.001
Body mass index (kg/m ²)	23.8 ± 3.0	23.8 ± 2.9	0.997
Current smoker (%)	36.7	7.3	< 0.001
Alcohol drinker (%)	38.4	4.3	< 0.001
Regular exercise (%)	22	13.9	0.002
GFR (mL/min)	72.8 ± 18.1	65.3 ± 19.4	< 0.001
25(OH)D (ng/mL)	24.7 ± 7.4	20.7 ± 7.6	< 0.001
Calcium intake (mg/d)	517.7 ± 350.6	391.7 ± 333.3	< 0.001
Protein intake (g/d)	70.9 ± 33.2	49.7 ± 26.7	< 0.001
Protein intake (g/kg/d)	1.08 ± 0.50	0.90 ± 0.48	< 0.001
Energy from protein (%)	14.0 ± 4.1	13.1 ± 3.8	0.001
FN BMD (g/cm ²)	0.760 ± 0.125	0.608 ± 0.112	< 0.001
HAL (cm)	11.30 ± 0.60	10.04 ± 0.63	< 0.001
FNW (cm)	3.67 ± 0.23	3.22 ± 0.24	< 0.001
Composite strength indices			
CSI (g/kg-m)	4.25 ± 0.68	3.54 ± 0.59	< 0.001
BSI (g/kg-m)	1.38 ± 0.25	1.14 ± 0.23	< 0.001
ISI (g/kg-m)	0.289 ± 0.048	0.232 ± 0.039	< 0.001

Values are presented as mean with standard deviation unless otherwise specified. *P* values were determined using the Student's *t* test for continuous variables and the χ^2 test for categorical variables. Bold values indicate statistically significant values. GFR, glomerular filtration rate; 25(OH)D, 25-hydroxyvitamin D; FN BMD, femoral neck bone mineral density; HAL, hip axis length; FNW, femoral neck width; CSI, compression strength index; BSI, bending strength index; ISI, impact strength index.

Table 2

Multiple linear regression analysis to determine whether total protein intake associates independently with composite indices of femoral neck strength

Dependent variables	Protein intake (g/kg/d)		
	Multivariable model		
	β	SE	P value
Men			
CSI (g/kg-m)	0.219	0.080	0.008
BSI (g/kg-m)	0.071	0.031	0.024
ISI (g/kg-m)	0.016	0.006	0.006
Women			
CSI (g/kg-m)	0.169	0.065	0.011
BSI (g/kg-m)	0.043	0.025	0.093
ISI (g/kg-m)	0.010	0.005	0.035

Multivariable model was adjusted for age, smoking, drinking, and exercise habits, glomerular filtration rate, 25-hydroxyvitamin D, and calcium intake. β , non-standardized regression coefficient; SE, standard error; CSI, compression strength index; BSI, bending strength index; ISI, impact strength index. Bold values indicate statistically significant values.

Table 3

Multiple linear regression analysis to determine whether total protein intake associates independently with composite indices of femoral neck strength after additional adjustment for appendicular skeletal muscle mass

Dependent variables	Protein intake (g/kg/d)		
	Multivariable model		
	β	SE	P value
Men			
CSI (g/kg-m)	0.164	0.075	0.032
BSI (g/kg-m)	0.052	0.030	0.083
ISI (g/kg-m)	0.012	0.005	0.022
Women			
CSI (g/kg-m)	0.140	0.071	0.052
BSI (g/kg-m)	0.038	0.027	0.156
ISI (g/kg-m)	0.009	0.005	0.101

Multivariable model was adjusted for appendicular skeletal muscle mass as well as age, smoking, drinking, and exercise habits, glomerular filtration rate, 25-hydroxyvitamin D, and calcium intake. β , non-standardized regression coefficient; SE, standard error; CSI, compression strength index; BSI, bending strength index; ISI, impact strength index. Bold values indicate statistically significant values.

Table 4

Multiple linear regression analysis to determine whether total protein intake associates independently with composite indices of femoral neck strength according to their age

Protein intake (g/kg/d)					
Multivariable model					
Age < 65 y (n = 317 men, 278 women)			Age 65 y (n = 275 men, 312 women)		
Dependent variables	β	SE	P value	β	SE
Men					
CSI (g/kg-m)	0.170	0.077	0.031	0.287	0.159
BSI (g/kg-m)	0.048	0.031	0.125	0.106	0.061
ISI (g/kg-m)	0.012	0.005	0.028	0.021	0.011
Women					
CSI (g/kg-m)	0.110	0.088	0.212	0.247	0.093
BSI (g/kg-m)	0.033	0.032	0.302	0.049	0.045
ISI (g/kg-m)	0.007	0.006	0.298	0.015	0.007
				0.038	

Multivariable model was adjusted for age, smoking, drinking, and exercise habits, glomerular filtration rate, 25-hydroxyvitamin D, and calcium intake. β , non-standardized regression coefficient; SE, standard error; CSI, compression strength index; BSI, bending strength index; ISI, impact strength index. Bold values indicate statistically significant values.