Original Article

Greater consumption of noodle is associated with higher serum phosphorus levels: a cross-sectional study on healthy participants

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Higher serum phosphorus levels are associated with mortality and cardiovascular events, both in healthy individuals and those with chronic kidney disease. Owing to the increasing westernization of eating habits, a decrease in rice consumption and an increase in the intake of bread and noodle products were observed in Japan. This cross-sectional study investigated the influence of staple food (rice, bread, and noodle) consumption patterns on the serum levels of phosphorus and phosphate-regulating factors in 103 healthy young participants. Fasting blood and 24-h urine samples were collected; data about dietary habits were collected using a brief-type self-administered diet history questionnaire. Cluster analysis was conducted to assess subgroups classified according to staple food consumption patterns. Serum levels of phosphorus and phosphate-regulating factors did not significantly differ between subgroups classified based on the frequency of rice or bread consumption. However, the serum levels of phosphorus and fibroblast growth factor 23 were more significantly elevated in the higher than in the lower noodle consumption frequency subgroup. Cluster analysis defined three clusters, and the serum phosphorus levels in the high-noodle cluster were significantly higher than that in the high-bread and high-rice clusters. A high consumption of noodles was associated with elevated serum phosphorus levels. The trial was registered in the University Hospital Medical Information Network (UMIN) Center system (The name of the trial register: Hidekazu Arai, and UMIN accession number: UMIN000034352).

Key Words: **phosphorus, fibroblast growth factor 23, noodle, staple food, additive**

Hyperphosphatemia promotes arterial sclerosis and is associated with an increased risk of cardiovascular disease.[1,2] Hyperphosphatemia affects individuals with chronic renal failure. In several epidemiological studies, high serum phosphorus levels in patients with chronic renal failure were independently associated with mortality and cardiovascular events.[3–5] Interestingly, a similar association has been observed in participants with normal renal function who had serum phosphorus levels within the reference limits,[6,7] which indicates that the dietary intake of phosphorus must be controlled both in healthy individuals and those with kidney disease. Thus, the factors influencing serum phosphorus levels in healthy individuals must be explored.[8]

In Japan, rice is the major staple food (carbohydrate source), and it has a lower phosphorus content than breads and noodles.[9] In recent years, a decrease in rice consumption and an increase in the intake of bread and noodle products were observed in Japanese diets, which are significantly attributed to the westernization of eating habits and the growing market for instant and fast food.[10] Recent studies conducted in the US and Germany have revealed that breads are an important source of dietary phosphorus, although these foods are more likely to contain relatively low amount of phosphorus.[11,12] In several Asian countries, noodles are one of the staple food items.[13] Chinese yellow alkaline noodles contain a phosphorus-containing food additive, which is used as an alkalizing agent.[14] Instant noodles have additional phosphorus-containing food additives, which are used as thickeners, moisturizing agents, and colorants.[15] Furthermore, cereal processed foods may contain a phosphorus-containing modified starch.[16] Phosphorus in food additives exists as inorganic molecules and is more bioavailable than organic phosphorus occurring naturally.[17,18] In terms of characteristics, the Japanese steamed rice is cooked only with water without the addition of condiment or soup. Diets containing a high proportion of breads and noodles as the staple food instead of rice may be associated with greater intake of phosphorus, particularly food additive phosphate; however, the influence of these dietary habits on phosphorus intake and phosphate metabolism is not well characterized. Thus, this study aimed to evaluate the association between staple food consumption patterns as well as the levels of serum phosphorus and phosphate-regulating factors in a healthy young adult population.

Materials and Methods

Participants. A total of 109 healthy participants from the University of Shizuoka and the Yamagata Prefectural Yonezawa University of Nutrition Sciences were enrolled. All participants underwent physical measurements, blood sampling, and 24-h urine collection and were found to have normal renal function. Six participants had incomplete 24-h urine collection, and the ratio of 24-h urinary excretion of creatinine to the expected creatinine excretion in these participants, as calculated using Joossens and Geboers equations,[19] was <0.6. Therefore, they were excluded from the analysis. Finally, 103 participants were included in the analysis (20 men, 83 women; age range: 19–25 years). The clinical and biological characteristics of the participants are summarized in Table 1. All participants provided a written informed consent; the study protocol was approved by the Ethics Committee of the University of Shizuoka. The study protocol was in accordance with the Declaration of Helsinki.

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#This study was mainly carried out in University of Shizuoka. MS was transferred to Sugiyama Jogakuen University where present address.

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Table 1. Characteristics of study participants

	All subjects (n = 103)
Age (years)	20.9 ± 1.3
Gender (% females)	80.6 (n = 83)
Height (cm)	161 ± 8
Body weight (kg)	54.4 ± 7.4
BMI (kg/m^2)	20.9 ± 2.1
Blood	
Urea nitrogen (mmol/L)	4.1 ± 1.0
Creatinine (μmol/L)	61.9 ± 10.6
Calcium (mmol/L)	2.35 ± 0.07
Phosphorus (mmol/L)	1.29 ± 0.16
iPTH (pg/ml)	34 ± 9
1,25(OH)$_2$VD$_3$ (pg/ml)	60.7 ± 16.0
iFGF-23 (pg/ml)	49.6 ± 41.4
cFGF-23 (RU/ml)	15.4 ± 13.5
Urine	
Creatinine (g/day)	1.16 ± 0.31
Urea nitrogen (g/day)	7 ± 3
Sodium (g/day)	2.83 ± 0.99
Potassium (g/day)	1.43 ± 0.53
Calcium (g/day)	0.10 ± 0.06
Phosphorus (g/day)	0.61 ± 0.18
CCr (ml/min)	127 ± 23
Diet	
Rice (g/1,000 kcal)	207 ± 76
Bread (g/1,000 kcal)	17 ± 17
Noodle (g/1,000 kcal)	26 ± 23
Protein (% Energy)	13.8 ± 2.5
Fat (% Energy)	27.3 ± 5.8
Carbohydrate (% Energy)	59.0 ± 7.6
Sodium (mg/1,000 kcal)	1,972 ± 421
Potassium (mg/1,000 kcal)	1,157 ± 296
Calcium (mg/1,000 kcal)	243 ± 78
Phosphorus (mg/1,000 kcal)	500 ± 85

Data presented as % or mean ± SD. BMI, body mass index; iPTH, intact parathyroid hormone; 1,25(OH)$_2$VD$_3$, 1α,25-dihydroxyvitamin D$_3$; iFGF-23, intact fibroblast growth factor 23; cFGF-23, C-terminal fibroblast growth factor 23; CCr, creatinine clearance.

Protocol. The participants underwent four examinations within a 1-week period, which were as follows: (1) collection of fasting blood samples in the morning, (2) 24-h urine collection, (3) anthropometric measurements, and (4) questionnaires about habitual diet (brief-type self-administered diet history questionnaire: BDHQ). The participants were instructed to follow their normal routine during the study period with no restrictions with respect to physical activity or dietary intake.

Anthropometric measurements and biochemical blood parameters. After measuring the body weight and height of each participant, body mass index (BMI) and body surface area (BSA) were calculated using the following formulas: BMI = body weight (kg)/body height (m)^2, and BSA = body weight$^{0.425}$ (kg) × body height$^{0.725}$ (cm) × 0.007184. Blood samples were collected in vacuum blood collection tubes and were centrifuged (4°C, 3,000 rpm, 10 min) immediately. The serum samples were separated and stored at –80°C until further processing. Serum levels of creatinine were measured by enzymatic method, urea nitrogen by ultraviolet absorption spectrophotometry, calcium and phosphorus by colorimetric method, intact parathyroid hormone (iPTH) by electro chemiluminescence immunoassay, and 1α,25-dihydroxyvitamin D$_3$ [1,25(OH)$_2$VD$_3$] by radioimmunoassay. These serum chemistry measurements were conducted by the analysis company, SRL Inc. (Tokyo, Japan). The serum intact fibroblast growth factor-23 (iFGF-23) and C-terminal fibroblast growth factor-23 (cFGF-23) levels were assessed using an FGF-23 enzyme-linked immunosorbent assay (ELISA) Kit (KAINOS Laboratories, Inc. Tokyo, Japan) and a Human FGF-23 (C-Term) ELISA Kit (Quidel, San Diego, CA), respectively, according to the manufacturer's instructions.

24-h urine collection. The participants were instructed to discard the first morning void and to collect all urine during the subsequent 24 h, including the first void in the next morning. After weighing the total volume of urine obtained from each individual, the samples were collected in the vessels for storage at −80°C until further processing. Urinary levels of creatinine and phosphorus were measured by enzymatic method, urea nitrogen by ultraviolet absorption spectrophotometry, sodium and potassium by electrode method, and calcium by colorimetric method. These urine chemistry measurements were conducted by the analysis company, BML Inc. (Tokyo, Japan). Creatinine clearance (CCr) was calculated using the following formula: CCr (ml/min) = [urine creatinine (mg/dl) × urine volume (ml/min)/serum creatinine (mg/dl)] × 1.73/BSA (m^2).

BDHQ. Habitual diet during the preceding month was assessed using the BDHQ.[20,21] The BDHQ includes questions about general dietary behavior and major cooking methods, frequency and amount of intake of five alcoholic beverages, and frequency of consumption of 50 selected food and nonalcoholic beverage items. The dietary intakes of energy, nutrients, and 55 foods from the BDHQ, which was based primarily on the Standard Tables of Food Composition in Japan,[9] were calculated using a commercial computer algorithm. The intake of macronutrients was expressed as percentage of the total energy intake. The intake of micronutrients and foods was energy-adjusted using the energy density model and was expressed as density (g or mg per 1,000 kcal energy intake). The BDHQ had a satisfactory ranking ability for the energy-adjusted intakes of several nutrients and food groups.[20,21]

Subgroup analyses based on the consumption frequency and pattern. To evaluate the association between staple food consumption pattern as well as serum levels of phosphorus and phosphate-regulating factors, the participants were categorized based on the consumption frequency of rice, bread, and noodle. The BDHQ comprised questions about the average amount of rice consumed per day (did not eat, <1 bowl, 1 bowl, 2 bowls, 3 bowls, 4 bowls, 5 bowls, 6–7 bowls, and ≥8 bowls) and consumption frequency of breads (including white bread and Japanese bread with a sweet filling), Chinese noodles (including instant products), Japanese wheat noodles (including instant products), and Buckwheat noodles (including instant products) (did not eat, <1 time/week, 1 time/week, 2–3 times/week, 4–6 times/week, 1 time/day, and ≥2 times/day). The participants were categorized into three or two subgroups based on the consumption frequency of rice (≤1 bowl, 2 bowls, and ≥3 bowls), bread, and noodles (<2 and ≥2 times/week). In the analysis of noodle intake, Chinese noodles, Japanese wheat noodles, and buckwheat noodles were considered as a single entity. BDHQ also comprised questions about the frequency of spaghetti/macaroni consumption. However, the intake of spaghetti/macaroni in our study population was too low to define it as a separate staple food category from noodles. Furthermore, in Japan, spaghetti/macaroni may be frequently consumed not only as a staple food but also as a side dish such as salad and soup; thus, spaghetti/macaroni was excluded from the analysis.

For further analysis, cluster analysis was performed to categorize participants based on staple food consumption patterns. The amount of rice, bread, and noodle intakes (g/1,000 kcal) were standardized to z-scores before cluster analysis to obtain equal weights when distances were calculated. Initially, the Ward's

Table 2. Characteristics of the participants disaggregated by the frequency of rice consumption

Rice	Consumption frequency			p
	≤1 bowl/day	2 bowl/day	≥3 bowl/day	
Rice (g/1,000 kcal)	109 (94, 131)	178 (164, 206)	256 (228, 298)	<0.001
Bread (g/1,000 kcal)	18 (4, 47)	20 (5, 34)	7 (4, 15)	0.005
Noodle (g/1,000 kcal)	32 (14, 60)	17 (12, 32)	17 (9, 28)	0.040
n (103)	22	34	47	
Gender (% females)	90.9 (*n* = 20)	85.3 (*n* = 29)	72.3 (*n* = 34)	
BMI (kg/m^2)	21.2 (19.9, 23.2)	20.2 (19.3, 20.9)	20.4 (19.5, 22.2)	0.100
Blood				
Urea nitrogen (mmol/L)	4.0 (3.2, 4.8)	3.8 (3.5, 4.6)	4.1 (3.5, 4.9)	0.828
Creatinine (μmol/L)	59.2 (53.0, 67.2)	59.2 (54.8, 65.4)	61.0 (54.8, 71.6)	0.430
Calcium (mmol/L)	2.35 (2.27, 2.40)	2.35 (2.32, 2.40)	2.40 (2.32, 2.42)	0.108
Phosphorus (mmol/L)	1.26 ± 0.16	1.29 ± 0.16	1.26 ± 0.13	0.737
iPTH (pg/ml)	35 (29, 42)	34 (28, 38)	35 (27, 40)	0.673
1,25(OH)$_2$VD$_3$ (pg/ml)	55.8 (43.6, 77.1)	55.8 (48.3, 70.2)	61.2 (49.8, 69.2)	0.779
iFGF-23 (pg/ml)	40.3 (31.3, 62.2)	38.2 (32.7, 54.9)	46.8 (31.4, 58.7)	0.728
cFGF-23 (RU/ml)	16.2 (9.0, 23.4)	11.6 (7.3, 16.1)	12.0 (7.8, 17.9)	0.153
Urine				
Creatinine (g/day)	1.06 (0.96, 1.22)	1.01 (0.86, 1.16)	1.13 (0.99, 1.15)	0.030
Urea nitrogen (g/day)	7 (5, 8)	7 (5, 9)	7 (6, 8)	0.768
Sodium (g/day)	2.82 ± 1.14	2.92 ± 0.94	2.78 ± 0.97	0.814
Potassium (g/day)	1.49 (0.95, 1.79)	1.31 (1.05, 1.65)	1.42 (1.02, 1.87)	0.809
Calcium (g/day)	0.10 (0.04, 0.12)	0.12 (0.07, 0.16)	0.09 (0.06, 0.13)	0.101
Phosphorus (g/day)	0.58 (0.45, 0.68)	0.52 (0.48, 0.74)	0.59 (0.50, 0.76)	0.391
CCr (ml/min)	129 ± 31	122 ± 19	129 ± 21	0.353
Diet				
Protein (% Energy)	14.6 (12.5, 17.1)	13.5 (11.7, 15.4)	12.9 (11.9, 14.3)	0.085
Fat (% Energy)	33.7 (27.7, 35.4)	27.9 (25.2, 31.0)	24.2 (21.1, 27.9)	<0.001
Carbohydrate (% Energy)	53.5 ± 9.6	58.0 ± 6.1	62.3 ± 5.7	<0.001†,‡,§
Sodium (mg/1,000 kcal)	2,353 ± 492	1,985 ± 319	1,784 ± 323	<0.001†,‡,§
Potassium (mg/1,000 kcal)	1,263 ± 313	1,182 ± 293	1,089 ± 278	0.061
Calcium (mg/1,000 kcal)	255 (215, 308)	260 (205, 310)	210 (157, 268)	0.021
Phosphorus (mg/1,000 kcal)	504 (456, 624)	521 (461, 567)	463 (425, 516)	0.015

Data presented as mean ± SD or median (25th–75th interquartile range). BMI, body mass index; iPTH, intact parathyroid hormone; 1,25(OH)$_2$VD$_3$, 1α,25-dihydroxyvitamin D$_3$; iFGF-23, intact fibroblast growth factor 23; cFGF-23, C-terminal fibroblast growth factor 23. †Tukey's post-hoc test, *p*<0.05, ≤1 bowl/day vs 2 bowl/day. ‡Tukey's post-hoc test, *p*<0.05, ≤1 bowl/day vs ≥3 bowl/day. §Tukey's post-hoc test, *p*<0.05, 2 bowl/day vs ≥3 bowl/day.

method using the squared Euclidean distance was used to establish the tree diagram, which was used to choose the number of clusters. The participants were then categorized via *K*-means cluster analysis.

Statistical analysis. The baseline and dietary characteristics of the study participants were presented as mean ± SD. Differences in sex with respect to serum levels of phosphorus and phosphate-regulating factors [iPTH, 1,25(OH)$_2$VD$_3$, iFGF-23, and cFGF-23] were assessed using the independent Student's *t* test and Mann–Whitney *U* test for normally and non-normally distributed variables, respectively. In the subgroup analyses based on the frequency of consumption of various staple food items and the staple food consumption pattern, data about all continuous variables were tested for normal distribution using the Shapiro–Wilk test. Data about normally distributed variables were presented as mean ± SD, and between-group differences were assessed using the parametric one-way analysis of variance (parametric ANOVA), followed by Tukey's post-hoc test or Student's *t* test. The Kruskal–Wallis ANOVA or Mann–Whitney *U* test was used to assess between-group differences with respect to non-normally distributed variables even in one subgroup, and the data were presented as median (25th–75th interquartile range). All analyses, including cluster analysis, were only repeated on women due to the small number of male participants. All statistical analyses were performed using the Statistical Package for the Social Sciences software ver. 22.0 for Windows (IBM SPSS, Inc., Chicago, IL). *P* values <0.05 were considered indicative of statistical significance.

Results

Characteristics of the participants. The characteristics of the participants are summarized in Table 1. The study population comprised 103 participants (mean age: 20.9 years); among them, 80.6% were women, and 87.4% had an ideal body weight (18.5≤BMI<25 kg/m^2). The mean serum phosphorus level was 1.29 mmol/L; approximately 10.7% of the participants had serum phosphorus levels above the reference levels (0.81–1.45 mmol/L), and none had serum phosphorus levels below the normal limits. We assessed the differences in sex with respect to serum levels of phosphorus and phosphate-regulating factors because sex was not distributed equally. The serum levels of phosphorus, iPTH, 1,25(OH)$_2$VD$_3$, iFGF-23, and cFGF-23 were not significantly different between male and female participants (data not shown). The mean 24-h urinary phosphorus excretion was 0.61 g/day. The

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Table 3. Characteristics of the participants disaggregated by the frequency of bread consumption

Bread	Consumption frequency		p
	<2 times/week	≥2 times/week	
Rice (g/1,000 kcal)	233 ± 80	182 ± 62	0.001
Bread (g/1,000 kcal)	5 (3, 7)	28 (18, 38)	<0.001
Noodle (g/1,000 kcal)	23 (11, 34)	15 (10, 33)	0.138
n (103)	51	52	
Gender (% females)	88.2 (n = 45)	73.1 (n = 38)	
BMI (kg/m^2)	20.4 (19.1, 21.8)	20.6 (19.5, 22.2)	0.520
Blood			
Urea nitrogen (mmol/L)	4.0 (3.3, 5.0)	3.9 (3.5, 4.6)	0.851
Creatinine (μmol/L)	61.0 (53.9, 66.3)	59.2 (54.8, 68.1)	0.979
Calcium (mmol/L)	2.37 ± 0.07	2.35 ± 0.07	0.646
Phosphorus (mmol/L)	1.29 ± 0.16	1.26 ± 0.13	0.188
iPTH (pg/ml)	35 (28, 40)	34 (27, 40)	0.450
1,25(OH)$_2$VD$_3$ (pg/ml)	65.0 (51.2, 69.7)	54.3 (47.7, 74.3)	0.192
iFGF-23 (pg/ml)	47.9 (33.9, 59.4)	40.1 (31.3, 54.7)	0.227
cFGF-23 (RU/ml)	13.1 (8.8, 19.9)	11.6 (7.8, 18.4)	0.382
Urine			
Creatinine (g/day)	1.02 (0.90, 1.18)	1.13 (0.95, 1.53)	0.036
Urea nitrogen (g/day)	7 (5, 8)	7 (6, 9)	0.080
Sodium (g/day)	2.92 ± 1.00	2.74 ± 0.99	0.330
Potassium (g/day)	1.41 (1.06, 1.68)	1.45 (1.02, 1.84)	0.747
Calcium (g/day)	0.10 (0.05, 0.14)	0.11 (0.06, 0.14)	0.642
Phosphorus (g/day)	0.53 (0.45, 0.68)	0.61 (0.51, 0.80)	0.027
CCr (ml/min)	122 ± 23	132 ± 22	0.038
Diet			
Protein (% Energy)	13.0 (11.5, 15.2)	13.8 (12.2, 15.1)	0.166
Fat (% Energy)	26.3 ± 6.6	28.2 ± 4.8	0.096
Carbohydrate (% Energy)	60.2 ± 8.6	57.8 ± 6.4	0.102
Sodium (mg/1,000 kcal)	1,955 (1,655, 2,252)	1,911 (1,660, 2,214)	0.553
Potassium (mg/1,000 kcal)	1,097 (907, 1,264)	1,153 (974, 1,422)	0.227
Calcium (mg/1,000 kcal)	222 (169, 274)	245 (181, 311)	0.156
Phosphorus (mg/1,000 kcal)	490 ± 89	509 ± 82	0.270

Data presented as mean ± SD or median (25th–75th interquartile range). BMI, body mass index; iPTH, intact parathyroid hormone; 1,25(OH)$_2$VD$_3$, 1α,25-dihydroxyvitamin D$_3$; iFGF-23, intact fibroblast growth factor 23; cFGF-23, C-terminal fibroblast growth factor 23.

mean phosphorus intake estimated from the BDHQ was 500 mg/1,000 kcal.

Association between the frequency of rice consumption and phosphate metabolism. We compared the characteristics of the participants between subgroups classified according to the frequency of rice consumption (≤1, 2, and ≥3 bowls/day, Table 2). No significant difference was observed among the three subgroups in terms of serum levels of phosphorus or phosphate-regulating factors and 24-h urinary phosphorus excretion. Similar results were observed among female participants (Supplemental Table 1*). Bread intake significantly differed among the three subgroups (Kruskal–Wallis ANOVA, $p = 0.005$); the subgroup who consumed ≥3 bowls of rice per day had the lowest bread intake. In addition, the intake of noodles differed significantly among the three subgroups (Kruskal–Wallis ANOVA, $p = 0.040$); the subgroup who consumed ≤1 bowl of rice per day had the highest noodle intake. Moreover, the percentage of energy intake from fats and intakes of sodium and phosphorus differed significantly among the three subgroups (Kruskal–Wallis ANOVA, $p<0.001$, parametric ANOVA, $p<0.001$, and Kruskal–Wallis ANOVA, $p = 0.015$, respectively), and the subgroup who consumed ≥3 bowl of rice per day had the lowest intake. These associations were also observed among female participants (Supplemental Table 1*).

Association between the frequency of bread consumption and phosphate metabolism. We compared the characteristics of the participants between subgroups classified according to the frequency of bread consumption (<2 and ≥2 times/week, Table 3). The serum levels of phosphorus and phosphate-regulating factors did not differ between these two subgroups. The subgroup with a higher frequency of bread consumption had a significant increase in 24-h urinary phosphorus excretion compared with the subgroup with a lower frequency of bread consumption (Mann–Whitney U test, $p = 0.027$); however, this difference was not observed among female participants (Supplemental Table 2*).

Association between the frequency of consumption of noodle and phosphorus metabolism. We compared the characteristics of the participants between subgroups classified according to the frequency of noodle consumption (<2 times/week and ≥2 times/week, Table 4). Serum phosphorus levels in the higher noodle consumption frequency subgroup were significantly higher than those in the lower noodle consumption frequency subgroup (Student's t test, $p = 0.049$). In addition, serum levels of iFGF-23 and cFGF-23 were significantly higher in the higher noodle consumption frequency subgroup than in the lower noodle consumption frequency subgroup (Mann–Whitney U test, $p = 0.013$

*See online. https://doi.org/10.3164/jcbn.20-23

Table 4. Characteristics of the participants disaggregated by the frequency of noodle consumption

Noodle	Consumption frequency		p
	<2 times/week	≥2 times/week	
Rice (g/1,000 kcal)	214 ± 77	196 ± 72	0.243
Bread (g/1,000 kcal)	15 (6, 32)	7 (3, 22)	0.028
Noodle (g/1,000 kcal)	12 (7, 18)	37 (27, 56)	<0.001
n (103)	63	40	
Gender (% females)	87.3 (*n* = 55)	70.0 (*n* = 28)	
BMI (kg/m^2)	20.3 (19.3, 21.7)	20.7 (19.7, 22.7)	0.304
Blood			
Urea nitrogen (mmol/L)	4.0 ± 0.9	4.3 ± 1.1	0.261
Creatinine (μmol/L)	59.2 (54.8, 66.3)	61.9 (53.9, 71.6)	0.496
Calcium (mmol/L)	2.35 ± 0.07	2.35 ± 0.07	0.992
Phosphorus (mmol/L)	1.26 ± 0.13	1.32 ± 0.16	0.049
iPTH (pg/ml)	34 (28, 40)	36 (28, 40)	0.836
1,25(OH)$_2$VD$_3$ (pg/ml)	59.8 ± 16.0	62.0 ± 16.1	0.499
iFGF-23 (pg/ml)	39.3 (28.3, 54.6)	48.9 (36.8, 60.9)	0.013
cFGF-23 (RU/ml)	11.0 (7.4, 16.0)	15.7 (10.4, 22.1)	0.008
Urine			
Creatinine (g/day)	1.05 (0.89, 1.23)	1.15 (1.01, 1.50)	0.012
Urea nitrogen (g/day)	7 (5, 8)	7 (6, 9)	0.248
Sodium (g/day)	2.65 ± 0.94	3.13 ± 1.01	0.020
Potassium (g/day)	1.30 (1.02, 1.67)	1.51 (1.07, 1.84)	0.159
Calcium (g/day)	0.10 (0.06, 0.14)	0.10 (0.06, 0.14)	0.946
Phosphorus (g/day)	0.58 (0.46, 0.68)	0.60 (0.50, 0.78)	0.144
CCr (ml/min)	124 ± 21	132 ± 25	0.075
Diet			
Protein (% Energy)	13.4 (11.7, 15.0)	13.4 (12.1, 15.3)	0.645
Fat (% Energy)	27.2 ± 6.0	27.3 ± 5.5	0.937
Carbohydrate (% Energy)	59.1 ± 8.1	58.9 ± 7.0	0.893
Sodium (mg/1,000 kcal)	1,862 ± 378	2,145 ± 432	0.001
Potassium (mg/1,000 kcal)	1,130 (966, 1,307)	1,092 (929, 1,397)	0.612
Calcium (mg/1,000 kcal)	248 ± 83	235 ± 70	0.429
Phosphorus (mg/1,000 kcal)	500 ± 89	499 ± 81	0.953

Data presented as mean ± SD or median (25th–75th interquartile range). BMI, body mass index; iPTH, intact parathyroid hormone; 1,25(OH)$_2$VD$_3$, 1α,25-dihydroxyvitamin D$_3$; iFGF-23, intact fibroblast growth factor 23; cFGF-23, C-terminal fibroblast growth factor 23.

and $p = 0.008$, respectively). Although 24-h urinary phosphorus excretion was not significantly different between these two subgroups, the 24-h urinary sodium excretion was significantly higher in the subgroup with a higher frequency of noodle consumption (Student's t test, $p = 0.020$). Similar results were observed in female participants (Supplemental Table 3*).

Association between staple food consumption pattern and phosphorus metabolism. The tree diagram established using the Ward's method of cluster analysis indicated that the three clusters were the most appropriate groupings. We then categorized the participants into three subgroups via *K*-means clustering analysis using the amount of rice, bread, and noodle intake (g/1,000 kcal) and compared the characteristics of the participants between these subgroups (Table 5). Clusters 1, 2, and 3 had a significantly higher intake of noodle, bread, and rice than the other clusters. Clusters 1, 2, and 3 were labeled high-noodle, high-bread, and high-rice clusters, respectively. The high-noodle cluster had a significant increase in serum phosphorus levels compared with the high-bread and high-rice clusters (parametric ANOVA, $p = 0.036$; Tukey's post-hoc test, high-noodle vs high-bread, $p = 0.034$; Tukey's post-hoc test, high-noodle vs high-rice, $p = 0.043$). The cluster analysis and comparison of female participants only did not substantially change these results (serum phosphorus levels in the high-noodle cluster vs high-bread or high-rice cluster; Tukey's post-hoc test, $p = 0.020$ and $p = 0.053$, respectively, Supplemental Table 4*). The serum levels of phosphate-regulating factors and 24-h urinary phosphorus excretion was not significantly different between these three subgroups. The 24-h urinary sodium excretion was significantly higher in the high-noodle cluster than in the high-bread cluster in only female participants (Tukey's post-hoc test, $p = 0.036$, Supplemental Table 4*). The percentage of energy intake from fats differed significantly among the three subgroups (parametric ANOVA, $p = 0.013$); the high-rice cluster had the lowest.

Discussion

Serum phosphorus levels of >1.26 mmol/L, even if within the normal limit, may be a risk factor for coronary artery atherosclerosis in healthy young adults.[22] A previous study including 441 young Japanese women (aged 18–22 years) reported mean (± SD) serum phosphorus levels of 1.29 ± 0.13 mmol/L,[23] which is similar to the levels reported in our study population (1.29 ± 0.16 mmol/L). Furthermore, 53.4% of the participants in the present study had serum phosphorus levels of >1.26 mmol/L, and these high levels were associated with a high consumption

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Table 5. Characteristics of the participants disaggregated by the staple food consumption pattern using cluster analysis

Staple food consumption pattern	Cluster 1: high-noodle	Cluster 2: high-bread	Cluster 3: high-rice	*p*
Rice (g/1,000 kcal)	155 ± 83	147 ± 37	241 ± 66	<0.001‡,§
Bread (g/1,000 kcal)	3 (0, 10)	37 (32, 47)	7 (4, 15)	<0.001
Noodle (g/1,000 kcal)	84 (72, 92)	18 (10, 33)	17 (9, 28)	<0.001
n (103)	10	28	65	
Gender (% females)	100 (*n* = 10)	79 (*n* = 22)	78 (*n* = 51)	
BMI (kg/m^2)	21.0 (20.1, 23.4)	20.7 (19.6, 21.9)	20.3 (19.2, 22.0)	0.426
Blood				
Urea nitrogen (mmol/L)	4.3 ± 1.3	3.9 ± 0.8	4.2 ± 1.0	0.378
Creatinine (μmol/L)	57.7 (49.7, 65.0)	58.3 (52.6, 66.1)	61.9 (55.3, 68.1)	0.128
Calcium (mmol/L)	2.38 ± 0.08	2.34 ± 0.07	2.36 ± 0.07	0.372
Phosphorus (mmol/L)	1.39 ± 0.17	1.25 ± 0.15	1.27 ± 0.14	0.036†,‡
iPTH (pg/ml)	31 (27, 39)	34 (28, 40)	35 (28, 40)	0.706
1,25(OH)$_2$VD$_3$ (pg/ml)	56.5 ± 17.7	59.3 ± 17.4	61.9 ± 15.2	0.532
iFGF-23 (pg/ml)	44.6 (34.9, 60.4)	40.1 (30.4, 58.5)	45.5 (31.8, 58.8)	0.691
cFGF-23 (RU/ml)	12.9 (11.7, 27.0)	14.3 (10.1, 19.4)	11.7 (7.4, 17.9)	0.246
Urine				
Creatinine (g/day)	1.02 (0.95, 1.21)	1.06 (0.88, 1.45)	1.11 (0.95, 1.30)	0.769
Urea nitrogen (g/day)	6 (5, 8)	8 (5, 9)	7 (6, 8)	0.556
Sodium (g/day)	3.12 ± 1.34	2.59 ± 0.99	2.89 ± 0.93	0.254
Potassium (g/day)	1.52 (1.10, 1.79)	1.41 (1.05, 1.75)	1.42 (1.02, 1.70)	0.890
Calcium (g/day)	0.11 (0.04, 0.13)	0.09 (0.05, 0.14)	0.11 (0.06, 0.14)	0.522
Phosphorus (g/day)	0.51 (0.46, 0.61)	0.60 (0.47, 0.78)	0.59 (0.48, 0.71)	0.373
CCr (ml/min)	130 ± 35	131 ± 24	125 ± 20	0.454
Diet				
Protein (% Energy)	15.4 (12.8, 17.1)	13.7 (11.9, 15.2)	13.2 (11.7, 14.6)	0.092
Fat (% Energy)	28.7 ± 7.4	29.7 ± 5.2	26.0 ± 5.5	0.013§
Carbohydrate (% Energy)	56.0 ± 9.2	56.4 ± 7.1	60.5 ± 7.2	0.024§
Sodium (mg/1,000 kcal)	2,513 ± 483	2,015 ± 317	1,870 ± 388	<0.001†,‡
Potassium (mg/1,000 kcal)	1,335 (1,096, 1,449)	1,102 (1,001, 1,435)	1,098 (902, 1,285)	0.118
Calcium (mg/1,000 kcal)	292 (192, 330)	261 (194, 304)	221 (167, 279)	0.142
Phosphorus (mg/1,000 kcal)	551 ± 93	507 ± 87	489 ± 81	0.085

Data presented as mean ± SD or median (25th–75th interquartile range). BMI, body mass index; iPTH, intact parathyroid hormone; 1,25(OH)$_2$VD$_3$, 1α,25-dihydroxyvitamin D$_3$; iFGF-23, intact fibroblast growth factor 23; cFGF-23, C-terminal fibroblast growth factor 23. †Tukey's post-hoc test, *p*<0.05, high-noodle vs high-bread. ‡Tukey's post-hoc test, *p*<0.05, high-noodle vs high-rice. §Tukey's post-hoc test, *p*<0.05, high-bread vs high-rice.

of noodles.

Kemi *et al.*[24] examined the association between mineral metabolism and habitual consumption of two types of dairy products, mainly including natural phosphate (milk and cheese, excluding processed cheese) and phosphate additives (processed cheese). A higher consumption of processed cheese was associated with a higher mean serum parathyroid hormone concentrations, whereas the effects of milk and cheese consumption on serum parathyroid hormone concentrations were contradictory. Karp *et al.*[17] investigated the acute effects of dietary phosphorus from different food sources on bioavailability. Despite the similar amount of phosphorus intake, urinary phosphate excretion in the supplement session in which the main phosphorus sources were inorganic phosphate was higher than that in the grain session in which the main phosphorus sources were oatmeal porridge and non-fermented rye bread. These results indicate that the effect of food including phosphate additives on the mineral metabolism differs from that of foods containing natural phosphorus. A randomized controlled trial of patients with end-stage renal disease showed that nutritional care emphasized via education about avoiding foods with phosphorus additives led to a significant decrease in serum phosphorus levels after 3 months compared with regular nutritional care.[25]

Moore *et al.*[26] determined the dietary intake of foods mainly containing organic phosphorus (without phosphate additives) and those containing inorganic phosphorus (processed food with phosphate additives) using dietary intake data from the National Health and Nutrition Examination Survey 2003–2006. Moreover, they evaluated the association between the source of dietary phosphorus intake and serum phosphorus levels. Results showed that cereal and grain products containing inorganic phosphate additives (including ready-to-eat cereals, quick breads, cakes, cookies, crackers, and tortilla) significantly increase serum phosphorus concentration, even though it is consumed less frequently than foods without phosphate additives. Inorganic phosphates are primarily incorporated into cereal products, which are used as quality improvers for certain types of noodles to enhance texture, appearance, and flavor. By modifying starch gelatinization and acting as a chelating agent, phosphates effectively improve dough processing behaviors and noodle structure and inhibit the discoloration of fresh noodles.[27,28] Furthermore, instant noodles have additional phosphorus-containing food additives, which are used as thickeners, moisturizing agents, and colorants.[15] A survey of the ingredient and nutrition labels of commercially available processed food in Indonesia showed that 77% of cereals and cereal products (including instant noodle) had phosphate-based food additive.[29]

In the present study, high noodle consumption was associated with elevated serum phosphorus levels but not with 24-h urinary phosphorus excretion. A possible reason for this could be that urinary phosphorus excretion reflects the short-term phosphorus intake state, whereas fasting serum phosphorus levels reflect the long-term phosphorus intake state. We previously observed that 24-h urinary phosphorus excretion reflected phosphorus intake over a single day and that morning fasting serum phosphorus levels were not responsive to changes in the total amount of dietary phosphorus intake in the previous day.[30]

Foley *et al.*[22] showed that serum phosphorus levels >1.26 mmol/L in young adults, even if within the normal limits, may be a risk factor for coronary artery atherosclerosis. In this study, the mean serum phosphorus level in the high-noodle cluster was 1.39 mmol/L. Furthermore, in our study, the frequent consumption of noodles was associated with habitual high sodium intake. High sodium intake is a well-known risk factor for hypertension.[31–33] A high consumption of instant noodles is associated with a higher risk of various cardiovascular risk factors.[34–36] Collectively, these results indicate that the frequent consumption of noodles may increase cardiovascular risk in an additive manner.

Our study had some limitations. First, the study cohort was relatively small. Second, data about dietary habits were obtained using the BDHQ, which can be affected by reporting bias. Finally, this was a cross-sectional study; thus, causality cannot be examined. Further studies must be conducted to determine if the habitual consumption pattern of staple food affects serum phosphorus levels.

In conclusion, a high consumption of noodles was associated with elevated serum phosphorus levels. However, further studies must be performed to determine whether this relationship is causal.

Author Contributions

The authors' contributions to manuscript were as follows: conceptualization, MS, TY, HK, and HA; methodology, MS and HA; investigation, YS, MS, YN, and HA; formal analysis, YS and YN; writing-original draft, YS; writing-review & editing, MS, TY, HK, and HA; funding acquisition, MS; supervision, HA.

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Abbreviations

ANOVA	analysis of variance
BDHQ	brief-type self-administered diet history questionnaire
BMI	body mass index
BSA	body surface area
CCr	creatinine clearance
cFGF-23	C-terminal fibroblast growth factor-23
ELISA	enzyme-linked immunosorbent assay
iFGF-23	intact fibroblast growth factor-23
iPTH	intact parathyroid hormone
$1,25(OH)_2VD_3$	1α,25-dihydroxyvitamin D_3

Conflict of Interest

No potential conflicts of interest were disclosed.

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