Research Article

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High Salt Intake Is Associated with Atrophic Gastritis with Intestinal Metaplasia

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Abstract

Background: Although several studies have investigated excessive salt intake as a risk factor for gastric precancerous lesions, such as atrophic gastritis and intestinal metaplasia, the evidence is insufficient to make a conclusion. We evaluated the association between gastric precancerous lesions and salt intake.

Methods: From 2008 to 2015, the medical records of 728 subjects who underwent upper gastrointestinal endoscopy and sodium excretion in 24-hour urine tests were retrospectively reviewed. Sixty-six subjects were excluded due to diuretics use ($n = 55$), diagnosis with a gastric neoplasm ($n = 4$), or the cases of intestinal metaplasia in the absence of atrophy ($n = 7$), so 662 subjects were included. Atrophic gastritis and intestinal metaplasia were diagnosed by endoscopic findings. The subjects were grouped into three levels by tertiles of 24-hour urine sodium excretion.

Results: A total of 192 (29.0%) had atrophic gastritis without intestinal metaplasia and 112 (16.9%) had atrophic gastritis with intestinal metaplasia. A total of 276 subjects (61.5%) were infected with *Helicobacter pylori* (*H. pylori*). In multivariate analyses, *H. pylori* infection [OR = 14.17; 95% confidence interval (CI), 7.12–28.22) was associated with atrophic gastritis without intestinal metaplasia. Highest levels of sodium excretion (OR = 2.870; 95% CI, 1.34–6.14), heavy smoking (≥20 pack-years) (OR = 2.75; 95% CI, 1.02–7.39), and *H. pylori* infection (OR = 3.96; 95% CI, 2.02–7.76) were associated with atrophic gastritis with intestinal metaplasia.

Conclusions: Our endoscopy-based study suggested that high salt intake could be associated with an increased risk of atrophic gastritis with intestinal metaplasia.

Impact: Low salt diet might be helpful to prevent gastric carcinogenesis. *Cancer Epidemiol Biomarkers Prev; 26(7); 1133–8. ©2017 AACR.*

Introduction

Gastric cancer is a multifactorial disease that is associated with *Helicobacter pylori* (*H. pylori*) infection, genetic factors, and a number of environmental factors (1), including smoking, alcohol drinking, low socioeconomic status, and some dietary habits (2). Many studies on the associations between diet and gastric cancer have suggested that high salt consumption and a diet rich in nitrates and processed meat increase the risk of gastric cancer, whereas high consumption of fresh vegetables and fruits decreases the risk of gastric cancer (2–6).

Gastric cancer is the second most common cancer in Korea (7). The Korean National Cancer Screening Program has recommended regular 2-year interval gastric cancer screening by upper endoscopy or upper gastrointestinal barium study for individuals over 40 years of age.

According to the Korean National Health and Nutrition Examination Survey, the mean intake of sodium among Koreans is 3,889.9 mg/day, and 79.4% of the population has a higher intake than the WHO's recommended daily intake of 2,000 mg (8). A recent meta-analysis on diet and cancer risk in the Korean population showed that a high salt diet was associated with an increased risk of gastric cancer (9).

Gastric carcinogenesis has been considered as a multistep process: chronic gastritis, atrophic gastritis, intestinal metaplasia, dysplasia, and carcinoma (10). The study of the association between environmental factors and gastric precancerous lesions may contribute to clarifying the role of each factor in the different steps of gastric carcinogenesis (11). Although many studies have investigated excessive salt intake as a risk factor for gastric precancerous lesions, such as atrophic gastritis and intestinal metaplasia, the evidence is insufficient to make a conclusion (11–16). A recent meta-analysis showed a positive, but statistically nonsignificant, association between intestinal metaplasia and salt intake (11).

The aim of this study was to evaluate the association between salt intake measured by the excretion of sodium in urine over a 24-hour period and gastric precancerous lesions.

Materials and Methods

Patients

We performed a cross-sectional study with asymptomatic subjects who collected 24-hour urine for the examination of sodium excretion for a health check-up at Seoul National University Hospital Healthcare System Gangnam Center (Seoul, Korea) from March 2008 to December 2015. Health check-ups have recently become very popular in Korea, because such examinations allow

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the general health to be checked in a few hours. Moreover, upper gastrointestinal endoscopy is performed as a part of a gastric cancer screening and health check-up program. A total of 769 subjects collected 24-hour urine completely, and 728 of them underwent upper gastrointestinal endoscopy. Medical records of these 728 subjects were retrospectively reviewed. A total of 66 subjects were excluded because of diuretics use ($n = 55$), a diagnosis of gastric neoplasm ($n = 4$; 1 tubular adenoma with low-grade dysplasia, 3 adenocarcinoma), or the cases of intestinal metaplasia in the absence of atrophy ($n = 7$). Thus, 662 subjects were included in the final analysis.

Subjects were instructed to void and discard the first urine in the morning and to collect up all voided urine until the first urine of the next day. After the volume of urine collection was measured, urinary sodium levels were measured using the ion selective electrode method by Toshiba 120FR chemistry automatic analyzer (Toshiba Medical System Corp.). If the urine collection was considered as incomplete or invalid, defined as the total volume <500 mL or more than one void missed, the subject was asked to redo the 24-hour urine collection. The values of 24-hour urine sodium excretion were divided into three levels by tertiles; ≤139, 140–194, and ≥195 mmol/d.

All subjects were requested to complete a self-administered, structured questionnaire on smoking history, alcohol intake, physical activity, and family history of gastric cancer. Smoking status was categorized into none, <20 pack-years, and ≥20 pack-years. Alcohol intake was measured by ascertaining the number of drinks per day, defined as beer (200 mL per glass), soju (50 mL per glass), wine (120 mL per glass), or liquor (30 mL per shot), each equivalent to approximately 10 g of alcohol per drink. The values of alcohol intake were divided into three levels by tertiles; ≤0.32, 0.33–6.86, and ≥6.87 g/day. Leisure time physical activity was evaluated with metabolic equivalent task (MET) hours. The MET values assigned to physical activity data were 3.3 for walking at a moderate pace, 3.8 for walking at a brisk speed, 7.0 for jogging, 8.0 for cycling, 7.0 for swimming, 6.0 for hiking, 4.5 for golf, 7.0 for tennis, and 5.5 for health club exercise. The MET hours per week were estimated by multiplying the reported time spent at each activity by the corresponding MET value. The values of physical activity were divided into three levels by tertiles; ≤11.55, 11.56–25.03, and ≥25.04 MET-hours/week.

Atrophic gastritis and intestinal metaplasia were diagnosed by endoscopic findings. Endoscopic atrophic gastritis was defined as thinning, whitish mucosal changes, or visible submucosal vascular patterns and endoscopic intestinal metaplasia as a white plaque-like elevation in the antrum and body (15). When a diagnosis of intestinal metaplasia was not clear or a suspicious neoplastic lesion was seen on endoscopy, an additional biopsy was conducted with several pieces of tissue samples from the most severe lesion. Histologic intestinal metaplasia was evaluated using the updated Sydney system (17). Histologic evaluation was performed in 132 subjects, and intestinal metaplasia was diagnosed in 62 subjects. All of the 62 subjects with histologically confirmed intestinal metaplasia were also endoscopically positive to intestinal metaplasia. Among the 70 subjects with histologically negative intestinal metaplasia, 65 subjects were also negative to intestinal metaplasia by endoscopy.

To minimize any interobserver variation, all endoscopic images were reviewed by one endoscopist with over 10 years of experience (J.H. Song).

All subjects underwent physical examinations by trained staff. The body mass index was calculated from measured weight and height as the weight (kg) divided by the height squared (m^2), and categorized into <23.0 (normal), 23.0–24.9 (over weight), and ≥25.0 kg/m^2 (obese).

The serum *H. pylori* IgG antibody test was performed using a commercially available ELISA (*H. pylori*-EIA-Well, Radim) on the same day of endoscopy. An IgG value ≥15 U/mL was defined as a positive result and <15 U/mL as a negative result. If there was a gastric or duodenal ulcer, tissues from the antrum and body were obtained for a rapid urease test (CLOtest; Delta West) and/or histologic evaluation of *H. pylori* infection by modified Giemsa staining. The subjects were considered to be infected with *H. pylori* if any one of the tests (serology, rapid urease test, histology) was positive.

The study protocol was approved by the ethics committee of the Seoul National University Hospital (Seoul, Korea; Institutional Review Board number: H-1604-005-751) and was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

Descriptive analyses included calculation of rates and proportions for categorical data and means and SDs for continuous data.

Subjects without mucosal atrophy were defined as controls and were compared with those with atrophic gastritis without intestinal metaplasia and atrophic gastritis with intestinal metaplasia. Statistical significance was evaluated with a Pearson χ^2 test for categorical variables and a one-way ANOVA test for continuous variables. *Post hoc* analyses were performed using Bonferroni correction.

Associations of the risk factors for atrophic gastritis without intestinal metaplasia and atrophic gastritis with intestinal metaplasia were evaluated by multinomial logistic regression analysis in terms of the OR and the corresponding 95% confidence interval (CI). The results were considered statistically significant if the two-sided *P* value was <0.05 or if the 95% CI did not include unity. All statistical analyses were performed using Statistical Package for the Social Science (SPSS) version 21 software (SPSS Inc.).

Results

Of the 662 subjects, 358 subjects (54.1%) had gastric mucosa without atrophy, 192 (29.0%) had atrophic gastritis without intestinal metaplasia, and 112 (16.9%) had atrophic gastritis with intestinal metaplasia.

A total of 276 subjects (61.5%) were infected with *H. pylori*; 224 were positive in serology only, 20 in histology only, 28 in serology and histology, 3 in serology and rapid urease test, and 1 in serology, histology, and rapid urease test.

The associations of lifestyle factors with atrophic gastritis and intestinal metaplasia are shown in Table 1. The mean ages of both the atrophic gastritis without intestinal metaplasia and the atrophic gastritis with intestinal metaplasia groups were significantly higher than that of the control group. Twenty-four–hour sodium excretion, smoking, and alcohol intake were significantly increased in atrophic gastritis with intestinal metaplasia compared with that in the controls. *H. pylori* infection was high in atrophic gastritis without intestinal metaplasia group.

Table 2 shows the associations of the risk factors for atrophic gastritis and intestinal metaplasia. In age-adjusted univariate analyses, male and *H. pylori* infection showed an increased risk

Table 1. Associations of lifestyle factors with atrophic gastritis and intestinal metaplasia

	Total ($N = 662$)	Control ($n = 358$)	AG without IM ($n = 192$)	AG with IM ($n = 112$)	*P*
Age	52.76 ± 10.74	49.33 ± 10.75	56.01 ± 9.34[a]	58.13 ± 8.97[a]	<0.001[b]
Sex					
Female	341 (51.5)	220 (61.5)	93 (48.4)	28 (25.0)	<0.001[c]
Male	321 (48.5)	138 (38.5)	99 (51.6)	84 (75.0)	
24-h urine Na (mmol/d)	174.96 ± 74.61	167.89 ± 73.36	178.22 ± 74.97	191.96 ± 75.50[a]	0.009[b]
T1 (≤139)	223 (33.7)	127 (35.5)	67 (34.9)	29 (25.9)	0.003[c]
T2 (140–194)	220 (33.2)	130 (36.3)	61 (31.8)	29 (25.9)	
T3 (≥195)	219 (33.1)	101 (28.2)	64 (33.3)	54 (48.2)	
Smoking (pack-year)	7.97 ± 14.12	5.54 ± 11.84	7.23 ± 13.12	16.75 ± 18.35[a]	<0.001[b]
0	367 (60.8)	227 (69.4)	105 (61.0)	35 (33.3)	<0.001[c]
<20	132 (21.9)	64 (19.6)	40 (23.3)	28 (26.7)	
≥20	105 (17.4)	36 (11.0)	27 (15.7)	42 (40.0)	
Alcohol (g/d)	8.29 ± 13.76	7.41 ± 12.91	7.99 ± 13.41	11.59 ± 16.42[a]	0.021[b]
T1 (≤0.32)	183 (28.6)	96 (27.7)	60 (32.4)	27 (25.0)	0.026[c]
T2 (0.33–6.86)	243 (38.0)	147 (42.5)	63 (34.1)	33 (30.6)	
T3 (≥ 6.87)	213 (33.3)	103 (29.8)	62 (33.5)	48 (44.4)	
Leisure PA (MET-hr/wk)	22.93 ± 23.24	21.05 ± 19.40	24.27 ± 22.36	26.68 ± 33.53	0.060[b]
T1 (≤11.55)	235 (37.1)	136 (39.8)	62 (33.3)	37 (34.9)	0.597[c]
T2 (11.56–25.03)	188 (29.7)	100 (29.2)	56 (30.1)	32 (30.2)	
T3 (≥25.04)	211 (33.3)	106 (31.0)	68 (36.6)	37 (34.9)	
BMI (kg/m^2)	23.86 ± 2.96	23.38 ± 3.05	24.30 ± 2.77[a]	24.50 ± 2.80[a]	0.004[b]
<23	140 (37.2)	87 (43.9)	31 (29.0)	22 (31.0)	0.072[c]
23–24.9	111 (29.5)	54 (27.3)	36 (33.6)	21 (29.6)	
≥25	125 (33.2)	57 (28.8)	40 (37.4)	28 (39.4)	
FHx of GC					
No	592 (89.7)	323 (90.2)	175 (92.1)	94 (83.9)	0.070[c]
Yes	68 (10.3)	35 (9.8)	15 (7.9)	18 (16.1)	
H. pylori infection					
No	173 (38.5)	123 (56.9)	19 (13.1)	31 (35.2)	<0.001[c]
Yes	276 (61.5)	93 (43.1)	126 (86.9)	57 (64.8)	

NOTE: Data represent means ± SDs for continuous variables and numbers (%) for categorical variables

Abbreviations: AG, atrophic gastritis; BMI, body mass index; FHx, family history; GC, gastric cancer; IM, intestinal metaplasia; PA, physical activity.

[a]$P < 0.05$.

[b]Statistical analysis was performed by one-way ANOVA.

[c]Statistical analysis was performed by Pearson χ^2 test.

of atrophic gastritis without intestinal metaplasia. Male, high level of sodium excretion, smoking, alcohol, and *H. pylori* infection showed an increased risk of atrophic gastritis with intestinal metaplasia.

In multivariate analyses, *H. pylori* infection (OR = 14.17; 95% CI, 7.12–28.22) was associated with an increased risk of atrophic gastritis without intestinal metaplasia. Highest levels of sodium excretion (OR = 2.87; 95% CI, 1.34–6.14), heavy smoking (≥20 pack-years; OR = 2.75; 95% CI, 1.02–7.39), and *H. pylori* infection (OR = 3.96; 95% CI, 2.02–7.76) were associated with an increased risk of atrophic gastritis with intestinal metaplasia. When the interaction between *H. pylori* infection and 24-hour urine sodium excretion was analyzed by multinomial logistic regression, the results were statistically insignificant.

The associations of the risk factors for histologically confirmed intestinal metaplasia ($n = 62$) were evaluated by multinomial logistic regression analysis. In multivariate analyses, heavy smoking (≥20 pack-years; OR = 3.51; 95% CI, 1.12–11.03) was associated with an increased risk of histologically confirmed intestinal metaplasia. Highest level of sodium excretion was also showed increased risk, but was statistically insignificant (OR = 1.42; 95% CI, 0.564–3.564).

Discussion

This cross-sectional study suggested that high salt intake was associated with an increased risk of atrophic gastritis with intestinal metaplasia. This study was conducted on Koreans who tend to have a high salt intake, and its results have important implications because it is the first large-scale study to show the association between gastric precancerous lesions and objective salt intake, which was measured by 24-hour sodium excretion.

In a study conducted in Japan, dietary habits of eating traditional Japanese food, such as cod roe and miso soup, have been reported to increase the occurrence of atrophic gastritis (13). As cod roe and miso soup are usually salt-rich foods, it has been assumed that high salt intake is associated with atrophic gastritis (13). In a study on diet and precancerous lesions of the stomach, which was published by the European Cancer Prevention (ECP)-EURONUT-intestinal metaplasia study group, daily urinary excretion of sodium and potassium was analyzed using 24-hour urine samples (16). This study showed that the Na/K ratio was increased in the intestinal metaplasia group compared with that in the control group (16). According to a retrospective study that analyzed the risk factors of metaplastic gastritis in Koreans, old age, male sex, *H. pylori* seropositivity, and smoking were evaluated as risk factors, but salt intake did not show a statistically significant association (12). This study evaluated salt intake through dietary assessment, and it was a diet survey using an unvalidated questionnaire (12). Therefore, it is difficult to determine that an accurate assessment was conducted.

There are many ways to estimate salt intake, including dietary and urinary assessment. Although dietary assessment such as a diet food record or dietary recall is most commonly used, it is

Table 2. Risk factors for atrophic gastritis and intestinal metaplasia

	AG without IM		AG with IM	
	OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)
Sex				
Female	Reference	Reference	Reference	Reference
Male	1.50 (1.04–2.17)	0.97 (0.41–2.29)	4.08[c] (2.49–6.69)	2.17 (0.79–6.01)
24-h urine Na (mmol/d)				
T1 (≤139)	Reference	Reference	Reference	Reference
T2 (140–194)	0.99 (0.64–1.55)	1.23 (0.64–2.37)	1.16 (0.63–2.12)	1.05 (0.48–2.28)
T3 (≥195)	1.50 (0.95–2.36)	1.53 (0.76–3.05)	3.39[c] (1.92–5.99)	2.87 (1.34–6.14)
P_{trend}[d]	0.086	0.228	<0.001	0.005
Smoking (pack-year)				
0	Reference	Reference	Reference	Reference
<20	1.27 (0.79–2.04)	0.99 (0.44–2.27)	2.64[c] (1.46–4.78)	1.29 (0.51–3.31)
≥20	1.24 (0.70–2.19)	0.90 (0.35–2.30)	5.46[c] (3.01–9.91)	2.75[c] (1.02–7.39)
P_{trend}[d]	0.323	0.932	<0.001	0.016
Alcohol (g/d)				
T1 (≤0.32)	Reference	Reference	Reference	Reference
T2 (0.33–6.86)	0.76 (0.48–1.21)	0.74 (0.36–1.52)	0.92 (0.51–1.67)	0.46 (0.20–1.09)
T3 (≥6.87)	1.13 (0.70–1.81)	0.96 (0.38–2.45)	2.09[c] (1.17–3.74)	0.39 (0.14–1.08)
P_{trend}[d]	0.584	0.948	0.008	0.081
Leisure PA (MET-hr/wk)				
T1 (≤11.55)	Reference	—	Reference	—
T2 (11.56–25.03)	1.26 (0.79–2.00)		1.22 (0.69–2.16)	
T3 (≥25.04)	1.23 (0.79–1.92)		1.09 (0.63–1.89)	
P_{trend}[d]	0.358		0.736	
BMI (kg/m^2)				
<23	Reference	—	Reference	—
23–24.9	1.48 (0.79–2.76)		1.18 (0.57–2.45)	
≥25	1.59 (0.86–2.92)		1.52 (0.76–3.04)	
P_{trend}[d]	0.139		0.227	
FHx of GC				
No	Reference	—	Reference	—
Yes	0.71 (0.37–1.35)		1.58[c] (0.83–3.00)	
H. pylori infection				
No	Reference	Reference	Reference	Reference
Yes	12.20 (6.67–22.33)	14.17 (7.12–28.22)	3.49[c] (1.97–6.17)	3.96[c] (2.02–7.76)

Abbreviations: AG, atrophic gastritis; BMI, body mass index; FHx, family history; GC, gastric cancer; IM, intestinal metaplasia; PA, physical activity.
[a]Adjusted for age.
[b]Adjusted for age, sex, 24-hour urine Na excretion, smoking, alcohol, and *H. pylori* infection.
[c]$P < 0.05$, the differences between AG without IM and AG with IM.
[d]P values for the linear trend test across categories were calculated with the median value of each category as a continuous variable.

difficult to quantify the concentration of sodium contained in various recipes and to assess the exact salt intake in cases of underreporting or arbitrarily adding salt (18). Although food frequency questionnaires are advantageous in overcoming the problems related to day-to-day variability by estimating the intake over a longer period than the diet record or recall, it is also very difficult to accurately quantify the daily intake (18).

The gold standard method for evaluating salt intake measures the amount of sodium excreted through 24-hour urine (19). As about 90% of salt consumed is excreted through urine, 24-hour urine collection reliably reflects salt intake (18). Incomplete and/or undercollection of urine due to missed urine voids can result in inaccurate results (20). Moreover, people vary in their daily consumption of sodium. For an accurate representation of regular salt intake, urine collections during a timed, consecutive 24-hour period would be necessary. Previous studies reported that testing of 3 to 14 collections was helpful to minimize variation (21–23). However, repetitive collection and handling of urine voids for 24 hours is burdensome in a field survey setting, particularly when resources are constrained (24). In this study, salt intake was assessed using one-time 24-hour urine excretion of sodium. Urine collection was reconducted when the urine collection was determined to be incomplete or invalid (such as cases in which the total volume of urine collection was less than 500 mL or one void or more of urine was missed). The values were categorized by tertiles and compared by setting the lowest level as the reference to analyze the OR of 24-hour urine sodium excretion. Although the atrophic gastritis risk was increased by 50% when there was a high salt intake, there was no statistically significant association (OR = 1.53; 95% CI, 0.76–3.05). On the other hand, the intestinal metaplasia risk was increased by approximately three times when there was a high salt intake (OR = 2.87; 95% CI, 1.34–6.14).

There have been many studies on the mechanisms through which salt contributes to gastric carcinogenesis. Salt affects the occurrence of gastric cancer by increasing the effect of carcinogens such as N-methyl-N-nitro-N-nitrosoguanidine (25). In addition, a high concentration of salt causes gastric epithelial hyperplasia and parietal cell loss and increases *H. pylori* colonization (26). A high salt diet is also effective in enhancing the carcinogenic effect of cagA-positive *H. pylori* strains (27).

In this study, the OR of *H. pylori* was lower in intestinal metaplasia than in atrophic gastritis. When intestinal metaplasia develops in the gastric mucosa, the gastric mucus and acidity change and *H. pylori* colonization is decreased, which results in the *H. pylori* serology changing to negative (28, 29). Because of this, it is believed that the positivity rate for *H. pylori* serology was lower

in the intestinal metaplasia group than in the atrophic gastritis group. According to a recent cohort study published in Japan, *H. pylori*–associated chronic gastritis or the resulting gastric atrophy has been followed up for 16 years, and the risk of gastric cancer development was analyzed. The risk of gastric cancer development was reported to be the highest in the *H. pylori*–negative and atrophic gastritis–positive group (30). This group represents a more advanced stage of *H. pylori*–associated atrophic gastritis, which is gastric atrophy together with intestinal metaplasia.

There were several limitations in this study. First, most cases of atrophic gastritis and intestinal metaplasia in this study were diagnosed using an endoscope. When a diagnosis of intestinal metaplasia was not clear by endoscopy, an additional biopsy was performed and metaplasia was histologically confirmed. Of the 112 cases of atrophic gastritis with intestinal metaplasia, biopsy-proven intestinal metaplasia occurred in 62 cases. The associations of the risk factors for histologically confirmed intestinal metaplasia were evaluated, and heavy smoking ($\geq$20 pack-years; OR = 3.51; 95% CI, 1.12–11.03) was associated with an increased risk of intestinal metaplasia. Highest level of sodium excretion, however, was shown to be statistically insignificant (OR = 1.42; 95% CI, 0.564–3.564). These inconsistent results could be attributed to the selection bias that the cases of definite intestinal metaplasia by endoscopy were not included in the histologically confirmed intestinal metaplasia group, that is, an additional biopsy was conducted only when a diagnosis of intestinal metaplasia was not clear or a suspicious neoplastic lesion was seen on endoscopy. On the other hand, the misclassification of atrophic gastritis and intestinal metaplasia would be possible if some cases of intestinal metaplasia were not diagnosed as intestinal metaplasia histologically due to sampling error, and this misclassification would dilute differences between intestinal metaplasia and controls, thus underestimating the associations. An accurate endoscopic diagnosis of intestinal metaplasia is a clinical challenge (31). Biopsy is the gold standard method for the diagnosis of atrophic gastritis and intestinal metaplasia; however, multiple biopsies for accurate diagnosis are invasive and time consuming (32). Moreover, multiple random biopsies might not be effective to detect intestinal metaplasia because of the significant sampling error (31). Even though improved endoscopic techniques, such as chromoendoscopy, magnifying endoscopy, narrow-band imaging technique, and confocal laser endomicroscopy, have been shown to improve detection and diagnosis of intestinal metaplasia during endoscopy in several studies (31), we need more data for these issues. When comparing the consistency between endoscopic and histologic diagnosis for the atrophic gastritis evaluation in a recent study, a relatively good correlation has been shown (32). In this study, one expert with an endoscopic career of more than 10 years reviewed all of the endoscopic pictures to minimize interobserver variation.

Second, this study was conducted under the assumption that the dietary habits would not be changed significantly without any health problem. Atrophic gastritis is usually not associated with upper gastrointestinal symptoms. Indeed, one-point measurements of salt intake by 24-hour sodium excretion may not be representative of the exposure at the time of atrophic gastritis initiation or progression. This could be a limitation in this study.

Third, to eliminate other factors affecting sodium excretion, we excluded the subjects taking diuretics in this study population. However, some medications other than diuretics may also affect sodium excretion. This could be another limitation of this study.

In conclusion, our endoscopy-based study suggested that high salt intake could be associated with an increased risk of atrophic gastritis with intestinal metaplasia, implying that low salt diet might be helpful to prevent gastric carcinogenesis. However, large-scale further studies are warranted to elucidate the association between salt intake and real gastric intestinal metaplasia.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: J.H. Song, Y.S. Kim, J.H. Lim, S.Y. Yang
Development of methodology: J.H. Song, Y.S. Kim, N.J. Heo, J.H. Lim
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): J.H. Song, J.H. Lim, S.Y. Yang, G.E. Chung
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): J.H. Song, N.J. Heo, J.H. Lim, G.E. Chung
Writing, review, and/or revision of the manuscript: J.H. Song, Y.S. Kim
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): J.H. Song, J.H. Lim, S.Y. Yang, G.E. Chung, J.S. Kim
Study supervision: Y.S. Kim, J.S. Kim

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