

## Weight Loss as a Nonpharmacologic Strategy for Erosive Esophagitis: A 5-Year Follow-up Study

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See editorial on page 607.

**Background/Aims:** Obesity is a risk factor for gastroesophageal reflux disease (GERD), with several studies demonstrating positive associations between body mass index (BMI) and GERD symptoms. However, little is known about the effect of BMI changes on erosive esophagitis (EE). In this study, we investigated whether BMI reduction could resolve EE. **Methods:** A retrospective cohort study was performed to assess the natural course of EE according to changes in BMI. Participants undergoing health check-ups from 2006 to 2012 were enrolled, and 1,126 subjects with EE were included. The degree of esophagitis was measured by upper endoscopy and serially checked over a 5-year follow-up. Logistic regression and Cox proportional hazards models were used to investigate the association between BMI reduction and EE resolution. **Results:** Substantial weight loss is associated with EE resolution. The adjusted odds ratio for EE resolution was 1.44 (95% confidence interval [CI], 1.09 to 1.92) among participants with a decrease in BMI compared to those with no decrease in BMI. The EE resolution rate was related to the degree of BMI reduction. The effect of weight loss on EE resolution was higher among subjects who lost more weight. Compared with subjects with no decrease in BMI, the hazard ratios for EE resolution were 1.09 (95% CI, 0.89 to 1.35), 1.31 (95% CI, 1.01 to 1.72) and 2.12 (95% CI, 1.44 to 3.12) in subjects with BMI reductions of  $\leq 1$ , 1–2, and  $>2$  kg/m<sup>2</sup>, respectively. **Conclusions:** EE resolution is associated with a decrease in BMI, and weight loss is potentially an effective GERD treatment. (*Gut Liver* 2018;12:633-640)

**Key Words:** Gastroesophageal reflux; Body mass index; Ero-

sive esophagitis; Weight loss

### INTRODUCTION

Gastroesophageal reflux disease (GERD) is a major upper gastrointestinal disease that has considerable implications for quality of daily life and represents an economic burden.<sup>1</sup> Endoscopically proven erosive esophagitis (EE) is also associated with Barrett's esophagus and an increased risk of esophageal adenocarcinoma.<sup>2</sup> The prevalence of GERD has increased during the past few decades in most of the world.<sup>3,4</sup> Prevalence estimates for GERD are approximately 10% to 30% in Western populations and 5% to 20% in Asia. Particularly low rates of GERD have been observed in East Asia compared to those in other geographic regions, ranging from 5.2% to 8.5%.<sup>5-7</sup>

However, an increase in the prevalence of GERD has been shown recently in East Asia, where the prevalence of GERD has generally been low. Environmental and lifestyle factors have been suggested as putative reasons for this phenomenon.<sup>5,6</sup> Several lifestyle-related factors such as a high body mass index (BMI), smoking, and consumption of specific foods, including alcohol, caffeine, fat and chocolate, are suggested as contributing factors for GERD. Lifestyle modifications including elevating the head of the bed, smoking cessation or adjustments to meal size and timing are reported to be useful measures for selected patients.<sup>8-11</sup>

Among the factors related to lifestyle, obesity has been considered as a major cause of the increasing prevalence of GERD.<sup>3,4</sup> Accumulating evidence indicates that obesity is an independent risk factor for GERD.<sup>12,13</sup> In addition, a dose-response relationship is suggested between an increase in BMI and the occurrence of GERD.<sup>14</sup> Such a strong association between GERD and obesity is not only limited to GERD symptoms but is also

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related to endoscopically proven EE.<sup>15-19</sup>

Considering the growing burden of GERD and concerns about complications of using proton pump inhibitors, weight loss could be an effective way of controlling GERD without complications.<sup>20,21</sup> However, there are not enough data regarding the usefulness of lifestyle modifications that include weight loss as the means of reducing GERD symptoms and/or EE. Moreover, conflicting results exist about the effects of lifestyle modifications on GERD symptoms and/or EE.<sup>8</sup> In this study, we investigated whether a decrease in BMI could resolve EE in a general population.

## MATERIALS AND METHODS

### 1. Study population

A retrospective cohort study was conducted to examine the association between BMI and EE in relatively young, healthy Korean workers and their spouses participating in a medical health check-up program at the Healthcare Center of Kangbuk Samsung Hospital, Sungkyunkwan University, Seoul, Korea. Data from January 2006 to December 2012 were used. The study population consisted of 44,718 subjects who underwent upper endoscopy as part of a comprehensive health examination from January to December 2006. Participants who had a history of prior gastric surgery, gastric cancer, benign gastric or duodenal ulcer or who currently used proton pump inhibitors were excluded. A total 1,679 of participants with EE who completed a self-administered questionnaire were enrolled in this study. Of these, 1,126 subjects who had a follow-up period of more than 4 years were included in the final analysis (Fig. 1).

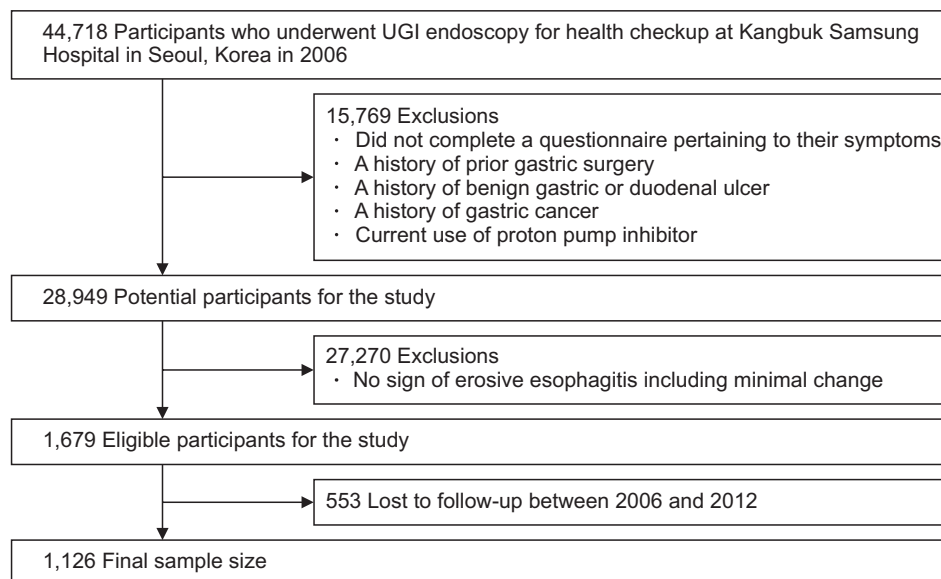
### 2. Clinical measurements and definitions

Clinical data about symptoms, medical history, medication

history, alcohol intake, smoking habits, physical activity, and educational status were obtained from a self-administered questionnaire. Anthropometric data were measured by trained staff during the examinations. BMI was calculated as weight in kilograms divided by the square of height in meters ( $\text{kg}/\text{m}^2$ ). Waist circumference (WC) was measured at the midpoint between the lower limit of the ribcage and the iliac crest. Abdominal obesity was defined as a WC  $\geq 80$  cm in females and  $\geq 90$  cm in males. Metabolic syndrome was defined according to the modified National Cholesterol Education Program Adult Treatment Panel III.<sup>22</sup> Systolic and diastolic blood pressure was measured using a standard mercury sphygmomanometer after at least 5 minutes of rest. The presence of fatty liver was evaluated on the basis of abnormal hepatic features from abdominal ultrasonography (USG).<sup>23</sup> Upper endoscopy was performed in all subjects and was performed at follow-ups annually. EE was categorized from A to D according to the LA classification.<sup>24</sup> A minimal change was not considered as EE.

### 3. Statistical analyses

Data are expressed as the mean  $\pm$  standard deviation (SD) for continuous variables and as percentages of the total number for categorical variables. Statistical analyses were conducted using a chi-square test for comparisons of discrete variables and an independent t-test for comparisons of continuous variables to identify significant differences among the characteristics of each group. Participants were subgrouped into the following categories according to the degree of change in BMI: 0 (no decrease in BMI, control),  $\leq 1$  (BMI reduction  $\leq 1 \text{ kg}/\text{m}^2$ ), 1-2 ( $1 \text{ kg}/\text{m}^2 < \text{BMI reduction} \leq 2 \text{ kg}/\text{m}^2$ ), and  $> 2$  (BMI reduction  $> 2 \text{ kg}/\text{m}^2$ ). Resolution rates of EE over time were assessed by the Kaplan-Meier method, and the differences among the different BMI groups were compared by a log-rank test. Logistic regression and Cox



**Fig. 1.** Flowchart of the enrolled study population. UGI, upper gastrointestinal.

proportional hazards models were used to evaluate the associations between changes in BMI and the resolution of EE. Multi-variable analysis was also done. Models were initially adjusted for age, sex, smoking, and alcohol consumption and further adjustments were made for potential confounding factors including fatty liver status on abdominal USG, physical activity, level of education, and metabolic syndrome status. For each variable, odds ratios (ORs) and hazard ratios (HRs) with 95% confidence intervals (CIs) are reported. Two-sided p-values <0.05 were considered statistically significant. Statistical analyses were performed using SPSS statistics version 21.0 (IBM Corp., Armonk, NY, USA).

## RESULTS

### 1. Characteristics of participants

Among the 1,679 participants, 553 were lost during follow-up between 2006 and 2012. During this period, changes in BMI and the status of endoscopically proven EE were observed. The mean follow-up period was 5.6±0.62 years, and the number of upper endoscopies performed was 4.61±1.51. The study population was relatively young (41±7.6 years), and 1,017 (90.3%) of the subjects were men. Mean BMI at baseline was 24.70±2.77. In addition, 3.1% of participants had a BMI ≥30 kg/m<sup>2</sup> in this study population. Of the 1,126 subjects, 645 (57.3%) showed resolution of EE, and 696 (61.8%) showed improvements in EE during the follow-up period. A total of 906 patients (80.5%) were classified as LA-A, 209 (18.6%) as LA-B, and 11 (1%) as LA-C or LA-D. Table 1 shows the baseline characteristics of the

subjects according to EE resolution status. Compared to subjects without EE, those with EE were more likely to be male (87.1% vs 94.6%, p<0.001) and current smokers (41.0% vs 49.6%, p<0.005), and statistically significant differences were observed in BMI (24.54±2.77 vs 24.92±2.77, p=0.021) and WC (86±9.3 vs 88±8.0, p=0.010). The proportion of subjects who achieved BMI reduction was significantly higher in the EE resolution group than in those without EE resolution (46.6% vs 53.5%, p=0.022). There were no significant differences in hypertension, alcohol intake, hiatal hernias, fatty liver status, frequency of regular exercise, level of education, and metabolic syndrome status between the subjects with resolution of EE and those without resolution of EE.

### 2. Resolution of EE according to a decrease in BMI

The resolution rates of EE were significantly different among the participants according to the changes in BMI. Participants with a reduced BMI have a significantly higher resolution rate of EE. The cases of resolution (53.5%) occurred in subjects with a decrease in BMI compared to 46.5% in those with no decrease in BMI (p=0.022). The crude OR for resolution of EE was 1.32 (95% CI, 1.04 to 1.67) among participants with a decrease in BMI compared to those with no decrease in BMI. In the multivariable analysis, the adjusted OR was 1.44 (95% CI, 1.09 to 1.92) after adjusting for sex, age, smoking status, alcohol intake, BMI, level of education, regular exercise, fatty liver status, and metabolic syndrome status (Table 2). Except for BMI, sex was the only other factor associated with resolution of EE. Males had an increased risk of persistence of EE (OR, 0.49; 95% CI, 0.27

**Table 1.** Characteristics of Subjects According to the Resolution of Erosive Esophagitis

| Characteristics                    | Overall<br>(n=1,126) | Resolution of EE         |                       | p-value |
|------------------------------------|----------------------|--------------------------|-----------------------|---------|
|                                    |                      | No resolution<br>(n=481) | Resolution<br>(n=645) |         |
| Age, yr                            | 41.02±7.63           | 41.14±7.71               | 40.86±7.52            | 0.54    |
| Male sex                           | 90.3                 | 94.6                     | 87.1                  | <0.001  |
| BMI, kg/m <sup>2</sup>             | 24.70±2.77           | 24.54±2.77               | 24.92±2.77            | 0.021   |
| Obesity, BMI ≥25 kg/m <sup>2</sup> | 42.6                 | 45.3                     | 40.6                  | 0.128   |
| Subjects with reduced BMI          | 50.5                 | 46.6                     | 53.5                  | 0.022   |
| Waist circumference, cm            | 86.62±8.83           | 85.97±9.26               | 87.66±7.99            | 0.010   |
| Smoking (current)                  | 44.7                 | 49.6                     | 41.0                  | 0.005   |
| Hypertension                       | 17.6                 | 17.5                     | 17.7                  | 0.947   |
| Alcohol, g/day                     | 14.38±15.2           | 13.85±15.02              | 15.08±15.42           | 0.182   |
| Hiatal hernia                      | 3.6                  | 3.4                      | 3.7                   | 0.497   |
| Fatty liver on USG                 | 44.9                 | 42.8                     | 47.8                  | 0.093   |
| Regular exercise                   | 19.4                 | 21.1                     | 17.1                  | 0.094   |
| Education (≥college)               | 81.5                 | 82.4                     | 80.4                  | 0.457   |
| Metabolic syndrome                 | 14.7                 | 16.2                     | 13.6                  | 0.235   |

Data are presented as the mean±SD or percentage.

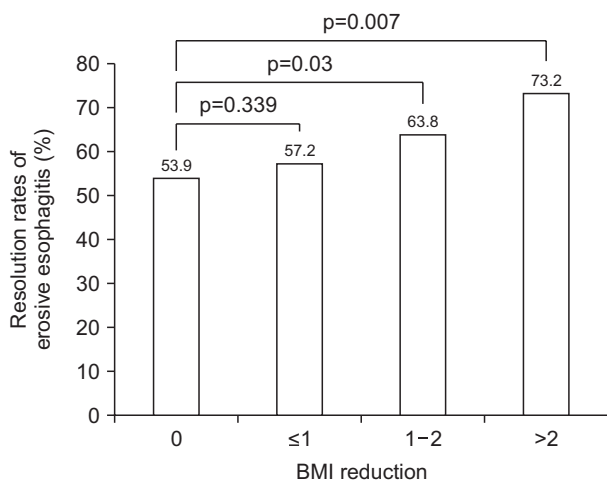
EE, erosive esophagitis; BMI, body mass index; USG, ultrasonography.

**Table 2.** Resolution of Erosive Esophagitis According to BMI Reduction

| Variable           | OR (95% CI)      |                  |                  |
|--------------------|------------------|------------------|------------------|
|                    | Unadjusted       | Adjusted 1       | Adjusted 2       |
| Decrease in BMI    | 1.32 (1.04–1.67) | 1.36 (1.06–1.73) | 1.44 (1.09–1.92) |
| Sex                | -                | 0.47 (0.28–0.78) | 0.49 (0.27–0.86) |
| Age                | -                | 1.00 (0.99–1.02) | 1.01 (0.99–1.03) |
| Smoking status     | -                | 0.82 (0.64–1.06) | 0.93 (0.69–1.26) |
| Alcohol intake     | -                | 1.00 (0.99–1.01) | 1.00 (0.99–1.01) |
| BMI                | -                | 0.97 (0.92–1.01) | 0.96 (0.90–1.02) |
| Education          | -                | -                | 1.31 (0.90–1.91) |
| Regular exercise   | -                | -                | 1.06 (0.72–1.55) |
| Fatty liver        | -                | -                | 1.05 (0.76–1.45) |
| Metabolic syndrome | -                | -                | 0.72 (0.46–1.11) |

Adjusted 1 was adjusted for sex, age, smoking status, alcohol intake and body mass index (BMI). Adjusted 2 was adjusted for all variables in adjusted 1 plus education status, regular exercise, fatty liver, and metabolic syndrome.

OR, odds ratio; CI, confidence interval.



**Fig. 2.** Resolution rate of erosive esophagitis according to the decrease in body mass index (BMI).

to 0.86). When stratified by initial BMI ( $<25$  or  $\geq 25$  kg/m<sup>2</sup>), the OR (95% CI) for resolution of EE was 1.48 (1.01 to 2.16) in the participants with a BMI  $<25$  kg/m<sup>2</sup> in the multivariate analysis. However, no significant association between BMI reduction and resolution of EE was observed in the obese subjects (BMI  $\geq 25$  kg/m<sup>2</sup>; OR, 1.42; 95% CI, 0.92 to 2.18).

### 3. Resolution of EE according to different BMI categories

Further analysis was done to evaluate the effect of different degrees of BMI reduction on the resolution of EE. Fig. 2 shows the resolution rates of EE among the four different BMI groups, categorized as 0,  $\leq 1$ , 1–2, and  $>2$  kg/m<sup>2</sup>. Importantly, a greater decrease in BMI was associated with an increasing resolution rate of EE. The highest resolution rate was observed in participants achieving a decrease in BMI of  $>2$  kg/m<sup>2</sup> (73.2%,  $p=0.007$ ).

On the other hand, there was no significant improvement in resolution in subjects with a decrease in BMI of  $\leq 1$  kg/m<sup>2</sup>. In the crude analysis, ORs (95% CI) for resolution of EE were 1.15 (0.88 to 1.50), 1.51 (1.05 to 2.17), and 2.34 (1.27 to 4.33) among the subjects with  $\leq 1$ , 1–2, and  $>2$  kg/m<sup>2</sup> decreases in BMI, respectively. After adjustment, the association between the degree of BMI reduction and resolution of EE was not attenuated (Table 3). When the analysis was stratified by the existence of initial obesity, a dose-response relationship was observed in obese participants with a decrease in BMI of more than 1 kg/m<sup>2</sup>. In obese participants, ORs (95% CI) for the resolution of EE were 0.99 (0.60 to 1.62), 1.86 (1.01 to 3.44), and 2.89 (1.25 to 6.70) among the subjects with  $\leq 1$ , 1–2, and  $>2$  kg/m<sup>2</sup> decreases in BMI, respectively. However, no association was observed between the degree of BMI reduction and resolution of EE in non-obese participants (Table 3).

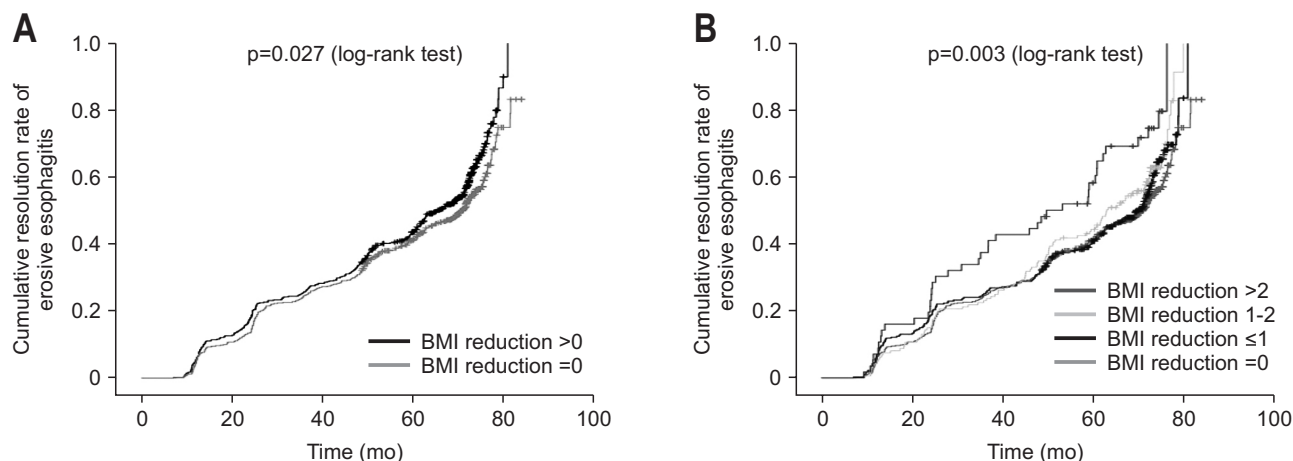
### 4. Cumulative resolution rate and hazard ratios of EE

The prevalence of EE decreased over time. This change was more prominent in participants with a reduced BMI (Fig. 3A). A significantly higher resolution rate was observed in participants with a decrease in BMI of more than 2 kg/m<sup>2</sup> than in the other BMI groups (Fig. 3B). In a multivariate adjusted model that accounted for potential confounders, including sex, age, BMI, smoking status, alcohol intake, fatty liver status, level of education, physical activity, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and homeostatic model assessment for insulin resistance scores, the HR (95% CI) for resolution of EE was 1.22 (1.01 to 1.46,  $p=0.39$ ) among the participants with a decrease in BMI compared to those with no decrease in BMI. Table 4 represents the HRs and 95% CIs for the resolution of EE according to the degree of BMI reduction. The adjusted HRs (95% CI) for resolution of EE were 1.09 (0.89 to 1.35), 1.31 (1.01 to

**Table 3.** Resolution of Erosive Esophagitis According to Obesity Status

| Variable           | OR (95% CI)                          |                                      |                      |
|--------------------|--------------------------------------|--------------------------------------|----------------------|
|                    | BMI <25 kg/m <sup>2</sup><br>(n=646) | BMI ≥25 kg/m <sup>2</sup><br>(n=480) | Overall<br>(n=1,126) |
| Decrease in BMI    |                                      |                                      |                      |
| 0                  | 1.00 (reference)                     | 1.00 (reference)                     | 1.00 (reference)     |
| ≤1                 | 1.38 (0.91–2.10)                     | 0.99 (0.60–1.62)                     | 1.19 (0.87–1.63)     |
| 1–2                | 1.65 (0.88–3.09)                     | 1.86 (1.01–3.44)                     | 1.76 (1.14–2.71)     |
| >2                 | 2.53 (0.63–10.22)                    | 2.89 (1.25–6.70)                     | 2.86 (1.41–5.81)     |
| Sex                | 0.42 (0.22–0.81)                     | 0.55 (0.14–2.14)                     | 0.44 (0.25–0.78)     |
| Age                | 1.02 (0.99–1.04)                     | 1.01 (0.97–1.04)                     | 1.01 (0.99–1.03)     |
| Smoking status     | 0.93 (0.61–1.40)                     | 0.95 (0.61–1.48)                     | 0.94 (0.69–1.27)     |
| Alcohol intake     | 1.00 (0.99–1.02)                     | 1.00 (0.99–1.02)                     | 1.00 (0.99–1.01)     |
| Education          | 1.39 (0.84–2.28)                     | 1.17 (0.64–2.15)                     | 1.30 (0.89–1.90)     |
| Regular exercise   | 0.94 (0.57–1.54)                     | 1.33 (0.71–2.47)                     | 1.06 (0.73–1.56)     |
| Fatty liver        | 0.99 (0.63–1.55)                     | 0.89 (0.56–1.42)                     | 0.93 (0.69–1.26)     |
| Metabolic syndrome | 0.79 (0.30–2.09)                     | 0.66 (0.40–1.10)                     | 0.64 (0.42–0.98)     |

OR, odds ratio; CI, confidence interval; BMI, body mass index.



**Fig. 3.** Cumulative resolution rate of erosive esophagitis according to a decrease or no decrease in body mass index (BMI) (A) and according to changes in BMI of 0, ≤1, 1–2, and >2 kg/m<sup>2</sup> (B).

**Table 4.** Resolution of Erosive Esophagitis According to Change in BMI

| Variable        | HR (95% CI)      |                  |                  |
|-----------------|------------------|------------------|------------------|
|                 | Unadjusted       | Adjusted 1       | Adjusted 2       |
| Decrease in BMI |                  |                  |                  |
| 0               | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| ≤1              | 1.10 (0.92–1.31) | 1.10 (0.92–1.32) | 1.09 (0.89–1.35) |
| 1–2             | 1.23 (0.98–1.54) | 1.23 (0.98–1.56) | 1.31 (1.01–1.72) |
| >2              | 1.81 (1.30–2.51) | 2.07 (1.48–2.91) | 2.12 (1.44–3.12) |

Adjusted 1 was adjusted for sex, age, body mass index (BMI), smoking status, and alcohol intake. Adjusted 2 was adjusted for all variables in adjusted 1 plus fatty liver, education status, regular exercise, total cholesterol, triglycerides, low-density lipoprotein cholesterol, homeostatic model assessment for insulin resistance.

HR, hazard ratio; CI, confidence interval.



1.72), and 2.12 (1.44 to 3.12), in groups showing BMI reductions of  $\leq 1$ , 1–2, and  $> 2$  kg/m<sup>2</sup>, respectively ( $p=0.001$ ). The beneficial effect of BMI reduction was not apparent in subjects with a decrease in BMI of  $\leq 1$  kg/m<sup>2</sup>.

## DISCUSSION

In this study population, EE was observed in approximately 6% of subjects who underwent upper endoscopy and completed the questionnaire. BMI was associated with a significantly increased prevalence of EE.<sup>25</sup> In the current study, significantly higher resolution rates of EE were observed among the participants with a decrease in BMI during the 5-year follow-up period. A dose-response relationship was observed between the resolution of EE and BMI reduction. The resolution rate was significantly higher in subjects with a decrease in BMI of more than 2 kg/m<sup>2</sup> than that in the other BMI reduction groups. These findings showed not only a strong association between the BMI and EE but also the positive effect of BMI reduction on EE resolution. The current study suggests that efforts to reduce BMI can provide an effective measure to resolve EE.

Underlying this association between obesity and GERD, several physiologic changes have been observed, providing clues about this association. An increase in intra-gastric pressure and esophageal acid exposure was reported in subjects with obesity.<sup>26–28</sup> Obesity is also related to a decrease in lower esophageal sphincter (LES) pressure and abnormal transient LES relaxation.<sup>29,30</sup> In addition to this, hormonal factors related to adiposity such as adiponectin or leptin are suspected to be linked to the pathogenesis leading to the development of GERD.<sup>31</sup>

Because obesity is a potentially modifiable risk factor, several studies have been conducted to investigate the effect of BMI reduction on the improvement of GERD symptoms. However, there were conflicting results about the effect of weight loss in the early studies. Several studies failed to find an association between GERD symptoms and weight reduction.<sup>32,33</sup> In the population-based study of Olmsted County including 637 participants, weight loss of more than 10 pounds did not result in improvement in GERD symptoms.<sup>33</sup> However, in recent prospective studies, beneficial effects of weight reduction on GERD symptoms have been reported. In the large cohort study with 10,545 subjects, as a part of the Nurses' Health study, women with a decrease in BMI of more than 3.5 kg/m<sup>2</sup> reported reductions in GERD symptoms compared to symptoms in women without a change in BMI (OR, 0.64; 95% CI, 0.42 to 0.97).<sup>14</sup> In another large-scale study with 29,610 participants, weight loss was significantly associated with resolution of GERD symptoms among the subjects with  $> 3.5$  kg/m<sup>2</sup> of decrease in BMI compared to participants with  $< 0.5$  kg/m<sup>2</sup> of change in BMI (OR, 1.98; 95% CI, 1.45 to 2.72).<sup>34</sup> Moreover, in prospective study including 332 subjects with overweight and/or obesity (BMI 25 to 39.9 kg/m<sup>2</sup>), participants with weight loss of 5% to 10% (women)

and  $\geq 10\%$  (men) showed significant improvements in symptoms during the 6 months of a structured weight loss program.<sup>35</sup>

According to the existing evidence, weight loss is thought to be associated with improvements of GERD symptoms. However, little is known regarding the resolution of endoscopically proven EE after weight loss. In the current study, weight loss was associated with resolution of EE. Significantly increased resolution rates were observed among the subjects with a decrease in BMI. In addition, resolution of EE was dose-dependently associated with BMI reduction among the subjects with a decrease in BMI. The current study suggests that not only GERD symptoms but also endoscopically proven EE could be improved by weight reduction.

In a recent study involving health check-ups of 15,295 subjects, weight loss was associated with an improvement of GERD symptoms (OR, 1.32; 95% CI, 1.05 to 1.76), but, EE was not improved after weight loss.<sup>36</sup> These results do not correspond with the findings of our study. This disparity could be explained by the short follow-up duration of less than 2 years and the inclusion of minimal change esophagitis in the prior study. The severity of esophagitis can change and fluctuate over time. In a large cohort study of 3,894 patients with GERD, the progression and regression of esophagitis were observed over a 2-year follow-up period. Importantly, 25% of non-EE cases progressed to LA-A or LA-B after 2 years.<sup>37</sup> In the present study, we excluded non-EE and minimal-change esophagitis at baseline, and our follow-up duration was quite long. These factors could have led to different results from those of the previous study.

Interestingly, our data indicate that a substantial BMI reduction is required to induce resolution of EE, especially in obese participants. The resolution rate was twice as high in subjects who achieved a BMI reduction of more than 2 kg/m<sup>2</sup> (Table 4) than in the other groups. However, no association was observed in subjects with a decrease in BMI of  $\leq 1$  kg/m<sup>2</sup>. On the other hand, in the non-obese participants, the degree of BMI reduction was not associated with the resolution of EE even though weight loss was significantly associated with resolution of EE. This result is consistent with previous large population studies.<sup>34,35</sup> In the Olmsted County cohort, moderate weight loss ( $> 4.5$  kg, mean BMI change  $1.3 \pm 3.2$  kg/m<sup>2</sup>) was not associated with improvements of GERD symptoms.<sup>33</sup> In a prospective study involving a weight loss program,  $< 5\%$  weight loss did not result in GERD symptom improvement.<sup>35</sup> Our data suggest that an increase in BMI might predispose an individual to the development of anatomic or hormonal changes, and substantial weight loss is required to offset the effects of longstanding pathophysiologic changes induced by obesity over a significant period of time.

To the best of our knowledge, this is the first study that shows the association between a decrease in BMI and resolution of EE. However, there are several limitations to the current study. First, due to the observational nature of this study, the degrees of

weight loss were not balanced among the participants. Participants with higher degrees of obesity and more unfavorable metabolic profiles tend to experience more weight loss. Individual effort to promote their own health might be responsible for this. In this regard, there were not enough participants with a normal BMI and having a BMI reduction of more than 2 kg/m<sup>2</sup>. Only 2% of non-obese participants achieved a BMI reduction of >2 kg/m<sup>2</sup>, compared with 9% of obese participants. Thus, the observed effect of BMI reduction might be weakened by the relatively small number of participants who had substantial weight loss in the normal body weight group. Second, the use of proton pump inhibitors during the follow-up period was not evaluated in this study. This is a major limitation of our study and requires a careful interpretation of the findings. However, the baseline LA classification among the different BMI reduction groups was not significantly different (p=0.845). It is difficult to consider the effects of the prevalence of proton pump inhibitor use, particularly in participants with greater levels of BMI reduction. Third, the resolution of GERD symptoms was not evaluated in this study. The follow-up data for reflux symptoms before 2012 could not be obtained. However, the resolution of EE is regarded as a reliable end point for successful therapy and correlates well with symptom improvement.<sup>38</sup> It is highly probable that endoscopically proven resolution of EE could result in the resolution of GERD symptoms as well. Based on the limited symptom data in our study, acid regurgitation was reported in 15.6% (71/454) of the participants with resolution of EE compared to 21.8% (82/376) of those without resolution of EE (p=0.025). The resolution rates of acid regurgitation were not significantly different among the BMI groups (78.9%, 83.8%, 82.8% and 89.5% in subjects with BMI reductions of 0, ≤1, 1–2, and >2 kg/m<sup>2</sup>, respectively, p=0.214).

The population in this study was relatively healthy and was not restricted to those with overweight or obesity, who are generally expected to benefit from weight loss. Our study's population might reflect the real world. In the current study, weight loss in non-obese people was also associated with resolution of EE. The results of this study might provide reliable evidence that BMI reduction is an effective option for the treatment of GERD in general practice. To ensure this, further studies evaluating the effects of weight loss in non-obese populations is required.

In conclusion, the current study is in accordance with previous studies and provides evidence supporting an association between BMI and EE. Our results suggest that resolution of EE is significantly and independently associated with a decrease in BMI. Interestingly, beneficial effects of weight loss were higher in participants who achieved substantial weight loss. Weight loss has a potential role in the treatment of EE as a nonpharmacologic strategy.

## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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