Retrospective Study
Prevalence and risk factors for Barrett’s esophagus in Taiwan

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Abstract

BACKGROUND
Barrett’s esophagus (BE) is a pre-malignant condition associated with the development of esophageal adenocarcinoma. The prevalence of BE in the general populations of Asian countries ranges from 0.06% to 1%. However, with lifestyle changes in Asian countries and adoption of western customs, the prevalence of BE might have increased.

AIM
To determine the current prevalence of BE in Taiwan, and to investigate risk factors predicting the presence of BE.

METHODS
This retrospective study was conducted at the Health Evaluation Center of Kaohsiung Veterans General Hospital in Taiwan. Between January 2015 and December 2015, 3385 subjects undergoing routine esophagogastroduodenoscopy examinations as part of a health check-up at the Health Evaluation Center were included. Patient characteristics and endoscopic findings were carefully reviewed. Lesions with endoscopic findings consistent with BE awaiting histological confirmation were identified.
histological evaluation were judged as endoscopically suspected esophageal metaplasia (ESEM). BE was defined based on extension of the columnar epithelium ≥ 1 cm above the gastroesophageal junction and was confirmed based on the presence of specialized intestinal metaplasia (IM) in the metaplastic esophageal epithelium. Clinical factors of subjects with BE and subjects without BE were compared, and the risk factors predicting BE were analyzed.

RESULTS
A total of 3385 subjects (mean age, 51.29 ± 11.42 years; 57.1% male) were included in the study, and 89 among them were confirmed to have IM and presence of goblet cells via biopsy examination. The majority of these individuals were classified as short segment BE (n = 85). The overall prevalence of BE was 2.6%. Multivariate analysis disclosed that old age [odds ratio (OR) = 1.033; 95% confidence interval (CI): 1.012-1.055; P = 0.002], male gender (OR = 2.106; 95%CI: 1.145-3.872; P = 0.017), ingestion of tea (OR = 1.695; 95%CI: 1.043-2.754; P = 0.033), and presence of hiatal hernia (OR = 3.037; 95%CI: 1.765-5.225; P < 0.001) were significant risk factors predicting BE. The independent risk factor for the presence of IM in ESEM lesions was old age alone (OR = 1.029; 95%CI: 1.006-1.053; P = 0.014).

CONCLUSION
Current prevalence of BE among the general population in Taiwan is 2.6%. Old age, male gender, ingestion of tea and hiatal hernia are significant risk factors for BE.

Key words: Barrett’s esophagus; Prevalence; Risk factors; Intestinal metaplasia; Taiwan

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Core tip: The current prevalence of Barrett’s esophagus (BE), based on the diagnostic criteria of the American College of Gastroenterology, is 2.6% among the general population in Taiwan. Its prevalence in Taiwan is the highest among the general population in Asian countries. Significant risk factors for BE include old age, male gender, ingestion of tea and the presence of hiatal hernia. In clinical practice, more attention should be paid when endoscopically suspected esophageal metaplasia is observed in older individuals, as these lesions have a higher likelihood of bearing intestinal metaplasia.

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INTRODUCTION
Barrett’s esophagus (BE) is generally recognized as a pre-malignant condition and is associated with esophageal adenocarcinoma[4]. The American Gastroenterological Association defines BE as any extent of metaplastic columnar epithelium replacing the stratified squamous epithelium that normally lines the distal esophagus. Because intestinal metaplasia (IM) is the only type of esophageal columnar epithelium that clearly predisposes individuals to cancer development, its presence is a requirement for diagnosis[2]. However, the clinical guidelines of the American College of Gastroenterology (ACG) recommend that BE should be diagnosed only when the salmon-colored mucosa extend ≥ 1 cm into the tubular esophagus proximal to the gastroesophageal junction because of high inter-observer variability and the low risk for esophageal adenocarcinoma in cases of segments < 1 cm[3]. Periodic endoscopic surveillance for dysplastic or cancerous lesions is suggested for patients diagnosed with BE, although disagreement exists regarding the long-term survival benefit of such surveillance[4].

Risk factors for BE have been extensively evaluated. White male individuals with gastroesophageal reflux disease (GERD), hiatal hernia, obesity, cigarette smoking, low
birth weight and obstructive sleep apnea are more likely to develop BE\cite{5-11}. Data concerning the role of alcohol intake in the development of BE are inconsistent. Additionally, some previous studies have found that wine consumption is inversely correlated with BE\cite{8,12}. An inverse association between the presence of Helicobacter pylori (H. pylori) infection and BE has also been reported\cite{13,14}.

The prevalence of BE in western countries is between 0.5% and 2% of unselected individuals; in individuals with acid reflux symptoms, the prevalence is higher ranging from 5% to 15%\cite{15}. In Asia, the previously reported prevalence of BE is lower than that in western countries. Tseng et al\cite{16} reported that the prevalences of endoscopically suspected esophageal metaplasia (ESEM) and BE between 2003 and 2006 in Taiwan were 0.28% and 0.06%, respectively. Chang et al\cite{17} showed that the prevalence of BE among subjects undergoing screening endoscopy in 2007 was 0.35%. However, with lifestyle changes in Asian countries such as increased western food consumption and adoption of western customs, the prevalence of BE might have increased.

The present study was conducted to (1) assess the current prevalence of BE among the general population in Taiwan, and (2) investigate independent risk factors predicting the development of BE in Taiwan.

**MATERIALS AND METHODS**

**Subjects**

Between January 2015 and December 2015, all consecutive outpatients who underwent routine esophagogastroduodenoscopy (EGD) examinations as part of a health check-up at their own expense at the Health Evaluation Center of the Kaohsiung Veterans General Hospital, Taiwan, were recruited into the present study. Exclusion criteria were (1) age less than 20 years, (2) refusal to undergo biopsy of suspicious gastrointestinal tract lesions, and (3) history of severe concomitant illness, including decompensated cirrhosis, uremia, and congestive heart failure.

**Questionnaire**

As a routine practice at the Health Evaluation Center, every subject was instructed to fill out a questionnaire detailing personal history, demographic data including age, gender, medical history, history of smoking, alcohol drinking, and coffee and tea consumption. Self-reported gastrointestinal discomforts including acid reflux symptoms or common upper gastrointestinal symptoms including epigastric pain or dyspepsia were also recorded.

**Body mass index and body fat percentage**

Personal data including body height, body weight, and body composition were readily accessible during routine physical examinations. They were recorded and transformed into body mass index (BMI) and body fat percentage (BFP) measurements, which were clinically important parameters for describing individuals as obese or overweight. BMI was calculated as weight/height$^2$ (kg/m$^2$), while BFP was determined with the bioelectrical impedance analysis method using the "X-Scan Plus II body composition analyzer (Jawon Medical Co., Ltd, Kyoungsan, South Korea)". The criteria of the Health Promotion Administration, Ministry of Health and Welfare of Taiwan, define obesity as (1) A percentage of body fat of ≥ 25 in males or ≥ 30 in females, or (2) BMI ≥ 27. Overweight was defined as a BMI of ≥ 24 and < 27. The participants were then classified into a normal or an obesity group based on BFP, and as normal, overweight, or obese based on BMI.

**Study design**

Clinical data including personal information from questionnaires, laboratory data, body weight, BMI, BFP, endoscopy reports and pathology report were collected through retrospective chart review. The endoscopes used for examination between January 2015 and August 2015 were GIF-XP260N, GIF-XQ260, GIF-Q260, and GIF-H260Z (Tokyo, Japan). New-generation endoscopes including GIF-H290Z and GIF-HQ290 had been introduced to our department for endoscopic examination since September 2015. All endoscopic examinations during this period were performed by seven experienced endoscopists. Most of the endoscopic procedures were performed under conscious sedation with the administration of sedative agents via the intravenous route by anesthesiologists. Among those not receiving conscious sedation, the attributed reasons were to old age, high risk in anesthesia due to underlying medical illness, or personal reasons. If more than one episode of endoscopic examination was performed in the same individual during the study period, the result of the first endoscopy was used as the index data. Lesions with endoscopic findings consistent with BE awaiting histological evaluation were judged as ESEM\cite{18}.
presence and extent of ESEM were diagnosed according to the Prague C & M Criteria. The length of ESEM was measured using the circumferential extent (C value) and the maximum extent (M value) above the anatomic gastroesophageal junction (GEJ) in centimeters\(^9\). The endoscopic landmark for the GEJ was defined as the proximal margin of the gastric folds. When the value of “M” in the Prague C & M criteria was ≥ 3 cm, the lesion was defined as long-segment BE (LSBE); if the value of “M” was < 3 cm, the lesion was classified as short-segment BE (SSBE). It was common practice for us to perform biopsies in all patients with LSBE in a random manner from four quadrants of the lesions, 2 cm-apart, throughout the columnar-lined esophagus per the Seattle protocol. Target biopsy was used for individuals with small tongues of columnar mucosa and for all patients with any suspicious IM and dysplastic lesions under NBI evaluation. All specimens acquired were embedded in paraffin, stained with hematoxylin and eosin and then reviewed by eight experienced general pathologists. BE was defined based on extension of the columnar epithelium ≥ 1 cm above the GEJ and was histologically confirmed by the presence of IM epithelium within the columnar-lined esophagus which contains goblet cells\(^20\).

The present study was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital (VGHKS17-CT7-07).

**Statistical analysis**

The primary endpoint of the study was the prevalence of BE. To determine the risk factors for BE, clinical and endoscopic parameters were examined using univariate analysis. These parameters included age, gender, history of smoking, history of alcohol consumption, ingestion of coffee, ingestion of tea, coexistence of an underlying disease, presence of diabetes, hypertension, cardiovascular disease, \textit{H. pylori} infection status, BFP, BMI, and endoscopic findings (including hiatal hernia, reflux esophagitis, peptic ulcer, and gastritis). The variables found to be statistically significant in univariate analysis were subsequently assessed using multivariate analysis to identify independent factors predicting BE. Categorical data were compared using the \(\chi^2\) test or Fisher’s exact test, as appropriate. The Student’s \(t\)-test was used for the comparison of continuous data. SPSS (version 12.0 for Microsoft Windows) was used for all statistical analyses. A \(P\) value less than 0.05 was considered statistically significant. The statistical methods of this study were reviewed by Huey-Shyan Lin, the consultant of Research and Development, Department of Health, Kaohsiung City Government, and research consultants of several hospitals, Taiwan.

**RESULTS**

Characteristics of participating subjects and endoscopic findings

During the study period, a total of 3387 subjects were recruited. The majority of these individuals (68.5%, \(n = 2321\)) were physically robust and underwent their health check-up to rule out physical disorders, particularly malignancy. The remaining individuals were either employees (21.9%, \(n = 741\)) who were undergoing a regular physical check-up arranged by their employers or those suffering from physical discomforts (9.6%, \(n = 325\)). Of these, two who were aged below 20 years were excluded from the study. Thus, 3385 individuals (mean age, 51.29 ± 11.42 years; 57.1% male) were included in further analyses.

A total of 639 subjects were found to have reflux esophagitis, with a prevalence of 18.8%. Among them, males were predominant (\(n = 519, 81.2\%\)). ESEM was found in 423 (12.5%) individuals, and 89 among them were confirmed to have IM and presence of goblet cells \textit{via} biopsy examination. Therefore, the overall prevalence of BE was 2.6%. The majority of these individuals were classified as SSBE cases (\(n = 85\)) whereas the remaining four patients were considered to be LSBE cases. No dysplasia or adenocarcinoma was detected in any of the patients. Concomitant reflux esophagitis was identified in 31 of the 89 BE patients (34.8%).

Risk factors for BE

The baseline characteristics of BE subjects and of individuals without BE were compared and shown in Table 1. The mean age was significantly higher in individuals with BE than in those without BE. Male gender, alcohol consumption, betel nut consumption, cigarette smoking, ingestion of tea, hypertension, history of cardiovascular disease, abnormal waist circumference and high BMI were more common among BE subjects. Endoscopic findings such as hiatal hernia and reflux esophagitis were discovered more frequently in the BE group. Multivariate analysis revealed that old age [odds ratio (OR) = 1.033; 95% confidence interval (CI): 1.012-1.055; \(P = 0.002\)],
male gender (OR = 2.106; 95%CI: 1.145-3.872; P = 0.017), ingestion of tea (OR = 1.695; 95%CI: 1.043-2.754; P = 0.033), and presence of hiatal hernia (OR = 3.037; 95%CI: 1.765-5.225; P < 0.001) were significant risk factors predicting BE (Table 2).

**Risk factors predicting the presence of IM in the ESEM lesions**

Of the 423 individuals with ESEM, IM was detected using histology examination in 89 subjects. The ESEM subjects were further divided into two groups based on the presence of IM and their baseline characteristics were compared (Table 3). Univariate analysis revealed that subjects with IM were more likely to be older in age, of male gender, have abnormal waist circumference, and have history of hypertension or cardiovascular disease. Multivariate analysis showed that old age (OR = 1.029; 95%CI: 1.006-1.053; P = 0.014) was the only significant risk factor predicting the presence of IM (Table 4).

**DISCUSSION**

The current study showed that the prevalence of reflux esophagitis and BE in subjects undergoing routine health check-up in Taiwan was 18.8% and 2.6%, respectively. The data indicate that the prevalence of BE among the general population in Taiwan is comparable with that in the western countries, ranging from 0.5% to 2%. Our study also demonstrated that old age, male gender, ingestion of tea, and hiatal hernia were the independent risk factors predicting the presence of BE. In the subjects with ESEM, old age was the only independent risk factor associated with the presence of specialized IM.

The Guidelines of the ACG define BE as any change in length of distal esophageal epithelium that can be recognized as columnar type mucosa in endoscopy and confirmed to have intestinal metaplasia via biopsy of the tubular esophagus. The updated ACG guideline recommends that biopsy is crucial to confirm the presence of IM, because esophageal or gastric cardia cancer risk in subjects with columnar lined epithelium of the esophagus was significantly elevated in those with IM over those without IM in a population-based cohort study (0.38% per year vs 0.07% per year, respectively)\(^{21}\). Based on the definition, the prevalence of BE among the general population in Asia has been reported to range from 0.06% to 1%\(^{21,22,23}\). A previous study in a medical center of Taiwan reported that the prevalence of BE among individuals undergoing routine health check-up was 0.06%\(^{24}\). Park et al\(^{25}\) conducted a nationwide study in South Korea and found a 0.84% prevalence of histology-proven BE in individuals undergoing routine health check-up. Peng et al\(^{26}\) reported a 1% prevalence of histology-proven BE among the general population in China. The current study defined BE as ESEM ≥ 1 cm with the presence of biopsy-proven IM, and demonstrated that the prevalence of BE among the general population was 2.6% in Taiwan, indicating that BE is not an uncommon disease in Taiwan currently.

Previously well-discussed risk factors for BE have included older age, male gender and hiatal hernia, consistent with our findings\(^{17,21,22}\). Individuals of old age and male gender might have a predisposition for the development of BE based on epidemiological data, but the underlying mechanisms accounting for the associations between the development of BE and the two risk factors need further investigations. Phenomena such as impaired esophageal motility or gastric emptying and decreased lower esophageal sphincter (LES) tone have been observed in many elderly individuals, and the risk of acid-related esophageal mucosal injury might increase subsequently\(^{26}\). Further, gender-related differences in physiology and pathophysiology of the alimentary tract might contribute to the preponderance of BE in males. Estrogen has been found to have anti-inflammatory activity, contributing to tissue resistance in females in animal models\(^{27,28}\). Recently, Masaka et al\(^{29}\) explored the role of estrogen (E2) in protecting esophageal damage in a chronic rat reflux esophagitis model. In addition, significant male-predominance in esophageal tissue damage due to exogenous nitric oxide (NO) has been found\(^{30}\). However, the detailed mechanism of estrogen action in controlling pathogenesis of the GERD spectrum remains unclear.

In the current study, tea ingestion was significantly associated with the development of BE. Such a finding has been rarely reported in previous studies. However, it undoubtedly poses a great impact on our daily clinical practice and care of the patient with BE, especially in Asian countries where the prevalence of tea ingestion is high. Several studies have shown that caffeine from coffee and tea induced or aggravated acid reflux by decreasing LES pressure (LESP)\(^{31,32}\). Gudjonsson et al\(^{33}\) conducted a blinded crossover study of 12 healthy subjects to evaluate the effect of coffee and tea upon LES function. LESP was significantly lower after intra-
### Table 1  Demographic data and endoscopic features of study groups, n (%)

| Characteristics                      | Barrett's esophagus | P value |
|--------------------------------------|----------------------|---------|
|                                      | Yes (n = 89)         | No (n = 3296) |
|                                       | 55.63 ± 10.49        | 51.18 ± 11.43 |
| Age (yr) (mean ± SD)                 | 55.63 ± 10.49        | 51.18 ± 11.43 |
| Male gender                          | 73 (82)              | 1859 (56.4) |
| Smoking                              | 23 (25.8)            | 576 (17.5) |
| Consumption of alcohol               | 43 (48.3)            | 1080 (32.8) |
| Consumption of betel nuts            | 5 (5.6)              | 52 (1.6) |
| Ingestion of coffee                  | 23 (25.8)            | 658 (20) |
| Ingestion of tea                     | 26 (29.2)            | 624 (18.9) |
| Presence of hypertension             | 31 (34.8)            | 619 (18.8) |
| Presence of cardiovascular disease   | 33 (37.1)            | 742 (22.5) |
| Presence of pulmonary disease        | 3 (3.4)              | 100 (3.0) |
| Presence of diabetes                 | 8 (9)                | 224 (6.8) |
| Reflux symptoms                      | 3 (3.4)              | 163 (4.9) |
| Waist                                | 52 (58.4)            | 2566 (77.9) |
| Normal (< 90 cm for male, < 80 cm for female) | 37 (41.6) | 730 (22.1) |
| Normal (< 25 cm for male, > 30 cm for female) | 50 (56.8) | 2163 (66) |
| Normal (< 25 cm for male, > 30 cm for female) | 38 (43.2) | 1113 (34) |
| Obese (≥ 90 cm for male, ≥ 80 cm for female) | 37 (41.6) | 730 (22.1) |
| Body fat percentage                  |                      | 0.072 |
| Endoscopic findings                  |                      | 0.002a |
| Reflux esophagitis                   | 31 (34.8)            | 608 (18.4) |
| Hiatal hernia                        | 71 (79.8)            | 1739 (52.8) |
| Gastritis                            | 68 (76.4)            | 2263 (68.7) |
| Gastric ulcer                        | 45 (50.6)            | 1345 (40.8) |
| Duodenal ulcer                       | 5 (5.6)              | 218 (6.6) |
| Gastric and duodenal ulcer           | 47 (52.8)            | 1421 (43.1) |
| Inlet patch                          | 8 (9)                | 167 (5.1) |

*P < 0.05. BMI: Body mass index; H. pylori: Helicobacter pylori; SD: Standard deviation.

The data for lower esophageal pH paralleled those for LESP[28]. Another single-blinded experimental study performed by Lohsiriwat et al[29] evaluated the effect of caffeine on LES and esophageal peristaltic contractions in healthy Thai adults. The result indicated that caffeine affected esophageal function, resulting in a decrease in basal LESP and distal esophageal contraction, which is known to promote esophageal reflux[29]. Additionally, tea consumption has been shown to increase gastric acid secretion[30]. Theophylline existing in black tea and green tea was also reported to induce esophageal acid reflux through inhibition of LESP[31]. It is therefore reasonable to expect that tea ingestion might be a risk factor for BE[32-34]. However, only a few studies have examined the relationship of coffee or tea with BE, and their data have been inconsistent. No association between risk of BE and consumption of coffee or tea was found by Sajja et al[35]. An Italian study conducted by Filiberti et al[36] revealed that tea intake reduced the risk of BE and reflux esophagitis. A double-blind study performed by Pehl et al[37] compared the impact of regular and decaffeinated coffee on esophageal acidity in terms of esophageal pH measurements, and reported that the fraction of time for which esophageal pH was less than 4 was reduced in the decaffeinated coffee-consuming group potentially via a reduction in esophageal reflux. Chang et al[38] have recently studied the effect of reflux-provoking diets on acid reflux in Taiwan, and found that frequent tea consumption increased the risk of asymptomatic erosive

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Table 2 Multivariate analysis of risk factors predicting Barrett's esophagus

| Clinical factor | Coefficient | Standard error | Odds ratio (95%CI) | P value |
|-----------------|-------------|----------------|-------------------|---------|
| Age             | 0.033       | 0.011          | 1.033 (1.012-1.055)| 0.002   |
| Male gender     | 0.745       | 0.311          | 2.106 (1.145-3.872)| 0.017   |
| Tea consumption | 0.528       | 0.248          | 1.695 (1.043-2.754)| 0.033   |
| Hiatal hernia   | 1.111       | 0.277          | 3.037 (1.765-5.225)| < 0.001 |

CI: Confidence interval.

esophagitis in Taiwanese men. Therefore, with increased acid exposure over the esophageal mucosa, probably by decreasing LES pressure, tea ingestion is still a reasonable risk factor for BE. In the results of the present study, the proportion of subjects with reflux esophagitis was indeed higher in the BE group than in the non-BE group (34.8% vs 13.4% respectively, \( P < 0.001 \), Table 1), although the association was not significant in multivariate analysis.

The importance of IM, which is diagnosed as identification of goblet cells in the columnar-lined esophagus, could be explained based on higher risk of developing adenocarcinoma in such cases compared with cases of columnar metaplasia without goblet cells, as previously reported\[21,39\]. Of the 423 subjects labeled as ESEM in this study, IM was detected in 89 individuals. The detection rate of IM in metaplastic epithelium was 21% only. Many factors may lead to false negative detection of IM in daily practice. For example, the number of endoscopic biopsies taken may directly affect the yield rate of IM. Harrison et al\[40\]. found that the diagnostic yield of IM was 34.7% when four biopsies were taken, which increased to 67.9% with eight biopsies, and would have reached 100% if more than 16 biopsies were taken\[40\]. Moreover, the distribution of IM over the columnar-lined esophagus is markedly heterogeneous, which could cause sampling error. Chandrasoma et al\[41\] demonstrated that the prevalence and density of goblet cells between the most proximal and most distal levels were markedly different, and the probability of finding IM was highest when the biopsies were focused in the most proximal area of the columnar-lined esophagus.

In this study, we adopted the Seattle protocol with four quadrant biopsies, 2 cm-apart, throughout the columnar-lined esophagus. Additionally, target biopsy was used for individuals with small tongues of columnar mucosa and for all patients with any suspicious IM and dysplastic lesions under NBI evaluation. Although obtaining 4-quadrant biopsy specimens at interval of every 1 cm throughout the columnar-lined esophagus might increase the yield rate of IM, the procedure time, the dose of anesthetic agents and biopsy-related bleeding rate would increase. Our Health Evaluation Center therefore used the Seattle protocol with 4-quadrant biopsies at interval of every 2 cm for ESEM. Furthermore, the esophageal biopsy specimens were interpreted by eight pathologists. Mastracci et al\[42\] revealed that the overall agreement rate of the diagnostic category of “BE with IM” between pathologists is moderate, with a K value of 0.599. This phenomenon might also be one of the confounding factors responsible for the different detection rates between ESEM and BE.

The results of the present study demonstrated that old age significantly increased the likelihood of discovering IM, with a 1.029-fold increase in odds ratio per year of age increase. There are some postulated reasons which might explain this phenomenon. First, the density and surface area of IM might increase over time, due to prolonged gastric acid stimulation\[43\]. Second, the prevalence of hiatus hernia, which is a risk factor for acid reflux, increases with age\[44\]. Third, many older individuals, as a result of underlying medical illness and medication, may experience decreases in salivary flow, esophageal motility, gastric emptying, and LES tone\[25\]. In clinical practice, more attention should be paid when ESEM is observed in older individuals, as these lesions have a higher likelihood of bearing IM.

The present study also had some limitations. First, it was conducted using a retrospective observational method, and was subject to confounding due to other unmeasured variables. Second, in real-world clinical practice, there may exist conditions affecting the detection rate such as poor compliance with standard biopsy protocol or insufficient observation over the E-C junction area.

In conclusion, the current prevalence of BE among the general population in Taiwan is 2.6%. Its prevalence in Taiwan is the highest in Asian countries, and is comparable with that in western countries. Old age, male gender, ingestion of tea and the presence of hiatal hernia are significant risk factors for the development of BE in Taiwan.
### Table 3  Univariate analysis of risk factors in relation to presence of intestinal metaplasia in the subjects with columnar lined epithelium of the esophagus, n (%)

| Characteristics                  | ESEM                      | With specialized IM (BE) (n = 89) | No specialized IM (n = 334) | P value |
|----------------------------------|---------------------------|-----------------------------------|-----------------------------|---------|
| **Age (yr) (mean ± SD)**         | 55.63 ± 10.49             | 51.36 ± 11.27                     | 0.001*                      |
| **Male gender**                  | 73 (82)                   | 226 (67.6)                        | 0.008*                      |
| **Smoking**                      | 23 (25.8)                 | 66 (19.8)                         | 0.211                       |
| **Consumption of alcohol**       | 43 (48.3)                 | 124 (37.1)                        | 0.055                       |
| **Consumption of betel nuts**    | 5 (5.6)                   | 6 (1.8)                           | 0.059                       |
| **Ingestion of coffee**          | 23 (25.8)                 | 90 (26.9)                         | 0.834                       |
| **Ingestion of tea**             | 26 (29.2)                 | 90 (26.9)                         | 0.67                        |
| **Presence of hypertension**     | 31 (34.8)                 | 72 (21.6)                         | 0.010*                      |
| **Presence of cardiovascular disease** | 33 (37.1)             | 80 (24)                           | 0.013*                      |
| **Presence of pulmonary disease** | 3 (3.4)                   | 10 (3.0)                          | 0.741                       |
| **Presence of diabetes**         | 8 (9)                     | 26 (7.8)                          | 0.710                       |
| **Reflux symptoms**              | 3 (3.4)                   | 20 (6.0)                          | 0.437                       |
| **Waist**                        |                           |                                   |                             |
| Normal (< 90 cm for male, < 80 cm for female) | 52 (58.4)           | 244 (73.1)                        | 0.007*                      |
| Obese (≥ 90 cm for male, ≥ 80 cm for female) | 37 (41.6)           | 90 (26.9)                         |                             |
| Body fat percentage              |                           |                                   |                             |
| Normal (< 25 cm for male, < 30 cm for female) | 50 (56.8)           | 211 (63.2)                        | 0.275                       |
| Obese (≥ 25 cm for male, ≥ 30 cm for female) | 38 (43.2)           | 123 (36.8)                        |                             |
| **Body mass index**              |                           |                                   |                             |
| Normal (BMI < 24)                | 33 (37.1)                 | 157 (47)                          | 0.121                       |
| Overweight (24 ≤ BMI < 27)       | 34 (38.2)                 | 122 (36.5)                        |                             |
| Obese (27 ≤ BMI)                 | 22 (24.7)                 | 55 (16.5)                         |                             |
| **H. pylori infection**          | 14 (15.7)                 | 68 (20.4)                         | 0.326                       |
| Endoscopic findings              |                           |                                   |                             |
| Reflux esophagitis               | 31 (34.8)                 | 112 (33.5)                        | 0.818                       |
| Hiatal hernia                    | 71 (79.8)                 | 289 (86.5)                        | 0.112                       |
| Gastritis                        | 68 (76.4)                 | 245 (73.4)                        | 0.56                        |
| Gastric ulcer                    | 45 (50.6)                 | 143 (42.8)                        | 0.191                       |
| Duodenal ulcer                   | 5 (5.6)                   | 25 (7.5)                          | 0.542                       |
| Gastric and duodenal ulcer       | 47 (52.8)                 | 152 (45.5)                        | 0.22                        |
| Inlet patch                      | 8 (9)                     | 30 (9)                            | 0.998                       |
| Length of ESEM (cm)              | 1.42 ± 0.84               | 1.31 ± 0.48                       | 0.243                       |

*P < 0.05. BE: Barrett’s esophagus; BMI: Body mass index; ESEM: Endoscopically suspected esophageal metaplasia; H. pylori: Helicobacter pylori; IM: Intestinal metaplasia; SD: Standard deviation.

### Table 4  Multivariate analysis of risk factors in relation to presence of specialized intestinal metaplasia

| Clinical factor   | Coefficient | Standard error | Odds ratio (95%CI) | P value |
|-------------------|-------------|----------------|--------------------|---------|
| Age               | 0.029       | 0.012          | 1.029 (1.006-1.053) | 0.014*  |

*P < 0.05. CI: Confidence interval.

### ARTICLE HIGHLIGHTS

**Research background**

Barrett’s esophagus (BE) is generally recognized as a pre-malignant condition and is associated with the development of esophageal adenocarcinoma. The presence of intestinal metaplasia (IM) is generally required for diagnosis because it is the only type of esophageal columnar epithelium that clearly predisposes individuals to cancer development. The updated guidelines of the
American College of Gastroenterology recommend that BE should be diagnosed when there is extension of salmon-colored mucosa into the tubular esophagus extending ≥ 1 cm proximal to the gastroesophageal junction with biopsy confirmation of IM. The prevalence of BE in the general populations of Asian countries ranges from 0.06% to 1%, which is lower than that in western countries. However, with adoption of western customs and lifestyle changes in Asian countries, the prevalence of BE might have increased.

**Research motivation**
Currently, there is a lack of universal diagnostic criteria for BE because the definition varies among different countries and is updated as time goes by. Nevertheless, the most updated guidelines from the American College of Gastroenterology provide a pragmatic framework for our daily clinical practice. We wished to update the current prevalence of BE in Taiwan based on these criteria strictly.

**Research objectives**
To determine the current prevalence of BE in Taiwan, and to investigate risk factors predicting the presence of BE.

**Research methods**
Subjects undergoing routine esophagogastroduodenoscopy examinations as part of a health check-up at the Health Evaluation Center of Kaohsiung Veterans General Hospital in Taiwan were included. Subjects aged below 20 years or refused biopsy examination were excluded. Endoscopic findings consistent with BE awaiting histological evaluation were judged as endoscopically suspected esophageal metaplasia (ESEM). The diagnosis of BE requires an extension of the columnar epithelium ≥ 1 cm above the gastroesophageal junction and the presence of specialized IM in the metaplastic esophageal epithelium. To determine the risk factors for BE, clinical and endoscopic parameters were examined using univariate analysis. The variables found to be statistically significant in univariate analysis were subsequently assessed using multivariate analysis to identify independent factors predicting BE. Categorical data were compared using the χ² test or Fisher’s exact test, as appropriate. The Student’s t-test was used for the comparison of continuous data. A P value less than 0.05 was considered statistically significant.

**Research results**
A total of 3387 subjects were recruited in the study. Of these, two who were aged below 20 years were excluded from the study. Thus, 3385 individuals (mean age, 51.29 ± 11.42 years; 57.1% male) were included in further analyses. ESEM was found in 423 individuals, and 89 among them were confirmed to have IM and presence of goblet cells via biopsy examination. Therefore, the overall prevalence of BE was 2.6%. Factors that were significantly associated with a higher risk for BE via multivariate analysis included old age [odds ratio (OR) = 1.033; 95% confidence interval (CI): 1.012-1.055; P = 0.017], ingestion of tea [OR = 1.695; 95% CI: 1.043-2.754; P = 0.033], and presence of hialtal hernia [OR = 3.037; 95% CI: 1.765-5.225; P < 0.001]. Old age alone was the only independent risk factor for the presence of IM in ESEM lesions (OR = 1.029; 95% CI: 1.006-1.053; P = 0.014).

**Research conclusions**
The current prevalence of BE among the general population in Taiwan is 2.6%. Its prevalence in Taiwan is not only the highest in Asian countries but also comparable with that in western countries. Adoption in western customs and foods might have contributed to this phenomenon substantially. From this study, we confirmed that old age, male gender, and presence of hialtal hernia were solid risk factors for BE. Besides, ingestion of tea, a common habit of Asian people, is also significantly associated with the development of BE in Taiwan. Such a finding has been rarely reported in previous studies. The results of the present study demonstrated that old age significantly increased the likelihood of discovering IM in ESEM lesions, with a 1.029-fold increase in odds ratio per year of age increase. From this point, more attention should be paid when ESEM is observed in older individuals in clinical practice, as these lesions have a higher likelihood of bearing IM.

**Research perspectives**
As this is a retrospective observational study and was subject to confounding due to other unmeasured variables, the true prevalence of BE might have been underestimated. Well-designed prospective clinical trials are needed to reveal the real prevalence of BE in the future. The exact mechanism responsible for the impact of tea ingestion on the development of BE is not clear. Further studies focusing on this topic are required.

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