

# World Journal of *Gastroenterology*

*World J Gastroenterol* 2019 July 7; 25(25): 3108-3282



**OPINION REVIEW**

- 3108 Advanced imaging in surveillance of Barrett's esophagus: Is the juice worth the squeeze?  
*Cerrone SA, Trindade AJ*
- 3116 Fate plasticity in the intestine: The devil is in the detail  
*Buczacki S*

**REVIEW**

- 3123 Revisiting the liver's role in transplant alloimmunity  
*Abrol N, Jadlowiec CC, Taner T*
- 3136 Hepatocellular carcinoma: Therapeutic advances in signaling, epigenetic and immune targets  
*Neureiter D, Stintzing S, Kiesslich T, Ocker M*
- 3151 Hepatocellular carcinoma: Mechanisms of progression and immunotherapy  
*Jiang Y, Han QJ, Zhang J*

**MINIREVIEWS**

- 3168 Epidemiology of hepatitis E in South-East Europe in the "One Health" concept  
*Mrzljak A, Dinjar-Kujundzic P, Jemersic L, Prpic J, Barbic L, Savic V, Stevanovic V, Vilibic-Cavlek T*
- 3183 Infections with *Helicobacter pylori* and challenges encountered in Africa  
*Smith S, Fowora M, Pellicano R*

**ORIGINAL ARTICLE****Basic Study**

- 3196 Sporamin suppresses growth of xenografted colorectal carcinoma in athymic BALB/c mice by inhibiting liver  $\beta$ -catenin and vascular endothelial growth factor expression  
*Yang C, Zhang JJ, Zhang XP, Xiao R, Li PG*
- 3207 Silicone-covered biodegradable magnesium stent for treating benign esophageal stricture in a rabbit model  
*Yang K, Cao J, Yuan TW, Zhu YQ, Zhou B, Cheng YS*
- 3218 Nuclear magnetic resonance-based metabolomics and metabolic pathway networks from patient-matched esophageal carcinoma, adjacent noncancerous tissues and urine  
*Liang JH, Lin Y, Ouyang T, Tang W, Huang Y, Ye W, Zhao JY, Wang ZN, Ma CC*

**Retrospective Study**

- 3231 Prevalence and risk factors for Barrett's esophagus in Taiwan  
*Chen YH, Yu HC, Lin KH, Lin HS, Hsu PI*
- 3242 Gut microbiota contributes to the distinction between two traditional Chinese medicine syndromes of ulcerative colitis  
*Zhang YL, Cai LT, Qi JY, Lin YZ, Dai YC, Jiao N, Chen YL, Zheng L, Wang BB, Zhu LX, Tang ZP, Zhu RX*

**Observational Study**

- 3256 Assessing significant fibrosis using imaging-based elastography in chronic hepatitis B patients: Pilot study  
*Park HS, Choe WH, Han HS, Yu MH, Kim YJ, Jung SI, Kim JH, Kwon SY*

**META-ANALYSIS**

- 3268 Botulinum toxin injections after surgery for Hirschsprung disease: Systematic review and meta-analysis  
*Roorda D, Abeln ZA, Oosterlaan J, van Heurn LW, Derikx JP*

**RETRACTION NOTE**

- 3281 Retraction Note: Construction of Gpm6a/ReelinGFP-CreERT2 by BAC recombination using a specific gene in hepatic mesothelial or stellate cells  
*Shi HB, Lou JL, Shi HL, Ren F, Chen Y, Duan ZP*

**ABOUT COVER**

Editorial board member of *World Journal of Gastroenterology*, Tatsuo Kanda, MD, PhD, Associate Professor, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Nihon University School of Medicine, Tokyo 173-8610, Japan

**AIMS AND SCOPE**

*World Journal of Gastroenterology* (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. The *WJG* Editorial Board consists of 701 experts in gastroenterology and hepatology from 58 countries.

The primary task of *WJG* is to rapidly publish high-quality original articles, reviews, and commentaries in the fields of gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, hepatobiliary surgery, gastrointestinal oncology, gastrointestinal radiation oncology, etc. The *WJG* is dedicated to become an influential and prestigious journal in gastroenterology and hepatology, to promote the development of above disciplines, and to improve the diagnostic and therapeutic skill and expertise of clinicians.

**INDEXING/ABSTRACTING**

The *WJG* is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2019 edition of Journal Citation Report® cites the 2018 impact factor for *WJG* as 3.411 (5-year impact factor: 3.579), ranking *WJG* as 35<sup>th</sup> among 84 journals in gastroenterology and hepatology (quartile in category Q2). CiteScore (2018): 3.43.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Responsible Electronic Editor: *Yu-Jie Ma*  
 Proofing Production Department Director: *Yun-Xiaojuan Wu*

**NAME OF JOURNAL**

*World Journal of Gastroenterology*

**ISSN**

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

**LAUNCH DATE**

October 1, 1995

**FREQUENCY**

Weekly

**EDITORS-IN-CHIEF**

Subrata Ghosh, Andrzej S. Tarnawski

**EDITORIAL BOARD MEMBERS**

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

**EDITORIAL OFFICE**

Ze-Mao Gong, Director

**PUBLICATION DATE**

July 7, 2019

**COPYRIGHT**

© 2019 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjgnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjgnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjgnet.com/bpg/gerinfo/240>

**PUBLICATION MISCONDUCT**

<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Retrospective Study

## Prevalence and risk factors for Barrett's esophagus in Taiwan

Yan-Hua Chen, Hsien-Chung Yu, Kung-Hung Lin, Huey-Shyan Lin, Ping-I Hsu

**ORCID number:** Yan-Hua Chen (0000-0002-5241-258X); Hsien-Chung Yu (0000-0002-0261-0940); Kung-Hung Lin (0000-0003-2020-3756); Huey-Shyan Lin (0000-0003-4017-8359); Ping-I Hsu (0000-0003-3905-4674).

**Author contributions:** All authors helped to perform the research; Chen YH, Yu HC and Hsu PI designed the study and drafted the manuscript; Chen YH and Lin KH collected the data; Chen YH and Lin HS performed statistical analyses; Lin HS and Hsu PI revised the manuscript critically for important intellectual content.

**Supported by** the In-Hospital Research Project Funding of Kaohsiung Veterans General Hospital, No. VGHKS107-040.

**Institutional review board**

**statement:** This study was reviewed and approved by the Institutional Review Board of Kaohsiung Veterans General Hospital (VGHKS17-CT7-07).

**Informed consent statement:**

Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

**Conflict-of-interest statement:** All authors declare no conflicts-of-interest related to this article.

**Data sharing statement:** No additional data are available.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external

**Yan-Hua Chen, Hsien-Chung Yu, Kung-Hung Lin, Ping-I Hsu,** Division of Gastroenterology and Hepatology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung 81362, Taiwan

**Yan-Hua Chen, Hsien-Chung Yu, Kung-Hung Lin,** Health Evaluation Center, Kaohsiung Veterans General Hospital, Kaohsiung 81362, Taiwan

**Yan-Hua Chen, Kung-Hung Lin,** Department of Nursing, Meiho University, Neipu Township, Pingtung County 91202, Taiwan

**Hsien-Chung Yu,** Institute of Health Care Management, Department of Business Management, National Sun Yat-Sen University, Kaohsiung 80424, Taiwan

**Huey-Shyan Lin,** Department of Health-Business Administration, Fooyin University, Kaohsiung 83102, Taiwan

**Ping-I Hsu,** National Yang Ming University, Taipei 12221, Taiwan

**Corresponding author:** Ping-I Hsu, MD, Attending Doctor, Professor, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, No. 386, Ta-Chung 1<sup>st</sup> Rd, Zuoying Dist., Kaohsiung 81362, Taiwan.

[pihsu@vghks.gov.tw](mailto:pihsu@vghks.gov.tw)

**Telephone:** +886-7-3422121

**Fax:** +886-7-3468237

**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

reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Unsolicited manuscript

**Received:** January 8, 2019

**Peer-review started:** January 8, 2019

**First decision:** January 30, 2019

**Revised:** February 24, 2019

**Accepted:** March 1, 2019

**Article in press:** March 2, 2019

**Published online:** July 7, 2019

**P-Reviewer:** Friedel D, Mastracci L, Zhao J

**S-Editor:** Ma RY

**L-Editor:** A

**E-Editor:** Ma YJ



histological evaluation were judged as endoscopically suspected esophageal metaplasia (ESEM). BE was defined based on extension of the columnar epithelium  $\geq 1$  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,  $51.29 \pm 11.42$  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

©The Author(s) 2019. Published by Baishideng Publishing Group Inc. All rights reserved.

**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.

**Citation:** Chen YH, Yu HC, Lin KH, Lin HS, Hsu PI. Prevalence and risk factors for Barrett's esophagus in Taiwan. *World J Gastroenterol* 2019; 25(25): 3231-3241

**URL:** <https://www.wjgnet.com/1007-9327/full/v25/i25/3231.htm>

**DOI:** <https://dx.doi.org/10.3748/wjg.v25.i25.3231>

## INTRODUCTION

Barrett's esophagus (BE) is generally recognized as a pre-malignant condition and is associated with esophageal adenocarcinoma<sup>[1]</sup>. 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<sup>[2]</sup>. However, the clinical guidelines of the American College of Gastroenterology (ACG) recommend that BE should be diagnosed only when the salmon-colored mucosa extend  $\geq 1$  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<sup>[3]</sup>. 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<sup>[4]</sup>.

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<sup>[5-11]</sup>. 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<sup>[8,12]</sup>. An inverse association between the presence of *Helicobacter pylori* (*H. pylori*) infection and BE has also been reported<sup>[13,14]</sup>.

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%<sup>[15]</sup>. In Asia, the previously reported prevalence of BE is lower than that in western countries. Tseng *et al*<sup>[16]</sup> 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*<sup>[17]</sup> 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<sup>2</sup> (kg/m<sup>2</sup>), 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  $\geq 25$  in males or  $\geq 30$  in females, or (2) BMI  $\geq 27$ . Overweight was defined as a BMI of  $\geq 24$  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<sup>[18]</sup>. The

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<sup>[19]</sup>. 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  $\geq 3$  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  $\geq 1$  cm above the GEJ and was histologically confirmed by the presence of IM epithelium within the columnar-lined esophagus which contains goblet cells<sup>[20]</sup>.

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, *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,  $51.29 \pm 11.42$  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 goblets cells *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)<sup>[21]</sup>. Based on the definition, the prevalence of BE among the general population in Asia has been reported to range from 0.06% to 1%<sup>[16,17,22,23]</sup>. 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%<sup>[17]</sup>. Park *et al*<sup>[22]</sup> 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*<sup>[23]</sup> reported a 1% prevalence of histology-proven BE among the general population in China. The current study defined BE as ESEM  $\geq 1$  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<sup>[11,23,24]</sup>. 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<sup>[25]</sup>. 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<sup>[26,27]</sup>. Recently, Masaka *et al*<sup>[26]</sup> 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<sup>[26]</sup>. 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)<sup>[28,29]</sup>. Gudjonsson *et al*<sup>[28]</sup> 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)	
Age (yr) (mean ± SD)	55.63 ± 10.49	51.18 ± 11.43	< 0.001 <sup>a</sup>
Male gender	73 (82)	1859 (56.4)	< 0.001 <sup>a</sup>
Smoking	23 (25.8)	576 (17.5)	0.041 <sup>a</sup>
Consumption of alcohol	43 (48.3)	1080 (32.8)	0.002 <sup>a</sup>
Consumption of betel nuts	5 (5.6)	52 (1.6)	0.016 <sup>a</sup>
Ingestion of coffee	23 (25.8)	658 (20)	0.172
Ingestion of tea	26 (29.2)	624 (18.9)	0.015 <sup>a</sup>
Presence of hypertension	31 (34.8)	619 (18.8)	< 0.001 <sup>a</sup>
Presence of cardiovascular disease	33 (37.1)	742 (22.5)	0.001 <sup>a</sup>
Presence of pulmonary disease	3 (3.4)	100 (3.0)	0.752
Presence of diabetes	8 (9)	224 (6.8)	0.419
Reflux symptoms	3 (3.4)	163 (4.9)	0.801
Waist			< 0.001 <sup>a</sup>
Normal (< 90 cm for male, < 80 cm for female)	52 (58.4)	2566 (77.9)	
Obese (≥ 90 cm for male, ≥ 80 cm for female)	37 (41.6)	730 (22.1)	
Body fat percentage			0.072
Normal (< 25 cm for male, < 30 cm for female)	50 (56.8)	2163 (66)	
Obese (≥ 25 cm for male, ≥ 30 cm for female)	38 (43.2)	1113 (34)	
Body mass index			0.002 <sup>a</sup>
Normal (BMI < 24)	33 (37.1)	1818 (55.2)	
Overweight (24 ≤ BMI < 27)	34 (38.2)	960 (29.1)	
Obese (27 ≤ BMI)	22 (24.7)	518 (15.7)	
<i>H. pylori</i> infection	14 (15.7)	603 (18.3)	0.536
Endoscopic findings			
Reflux esophagitis	31 (34.8)	608 (18.4)	< 0.001 <sup>a</sup>
Hiatal hernia	71 (79.8)	1739 (52.8)	< 0.001 <sup>a</sup>
Gastritis	68 (76.4)	2263 (68.7)	0.119
Gastric ulcer	45 (50.6)	1345 (40.8)	0.065
Duodenal ulcer	5 (5.6)	218 (6.6)	0.709
Gastric and duodenal ulcer	47 (52.8)	1421 (43.1)	0.069
Inlet patch	8 (9)	167 (5.1)	0.137

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

gastric instillation of regular coffee and tea. The data for lower esophageal pH paralleled those for LESP<sup>[28]</sup>. Another single-blinded experimental study performed by Lohsiriwat *et al*<sup>[29]</sup> 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<sup>[29]</sup>. Additionally, tea consumption has been shown to increase gastric acid secretion<sup>[30]</sup>. Theophylline existing in black tea and green tea was also reported to induce esophageal acid reflux through inhibition of LESP<sup>[31]</sup>. It is therefore reasonable to expect that tea ingestion might be a risk factor for BE<sup>[32-34]</sup>. 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*<sup>[35]</sup>. An Italian study conducted by Filiberti *et al*<sup>[36]</sup> revealed that tea intake reduced the risk of BE and reflux esophagitis. A double-blind study performed by Pehl *et al*<sup>[37]</sup> 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*<sup>[38]</sup> 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

**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<sup>[21,39]</sup>. 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*<sup>[40]</sup> 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<sup>[40]</sup>. Moreover, the distribution of IM over the columnar-lined esophagus is markedly heterogeneous, which could cause sampling error. Chandrasoma *et al*<sup>[41]</sup> 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*<sup>[42]</sup> 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<sup>[43]</sup>. Second, the prevalence of hiatus hernia, which is a risk factor for acid reflux, increases with age<sup>[44]</sup>. 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<sup>[25]</sup>. 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		P value
	With specialized IM (BE) ( <i>n</i> = 89)	No specialized IM ( <i>n</i> = 334)	
Age (yr) (mean ± SD)	55.63 ± 10.49	51.36 ± 11.27	0.001 <sup>a</sup>
Male gender	73 (82)	226 (67.6)	0.008 <sup>a</sup>
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 <sup>a</sup>
Presence of cardiovascular disease	33 (37.1)	80 (24)	0.013 <sup>a</sup>
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			0.007 <sup>a</sup>
Normal (< 90 cm for male, < 80 cm for female)	52 (58.4)	244 (73.1)	
Obese (≥ 90 cm for male, ≥ 80 cm for female)	37 (41.6)	90 (26.9)	
Body fat percentage			0.275
Normal (< 25 cm for male, < 30 cm for female)	50 (56.8)	211 (63.2)	
Obese (≥ 25 cm for male, ≥ 30 cm for female)	38 (43.2)	123 (36.8)	
Body mass index			0.121
Normal (BMI < 24)	33 (37.1)	157 (47)	
Overweight (24 ≤ BMI < 27)	34 (38.2)	122 (36.5)	
Obese (27 ≤ BMI)	22 (24.7)	55 (16.5)	
<i>H. pylori</i> 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

<sup>a</sup>*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 <sup>a</sup>

<sup>a</sup>*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  $\geq 1$  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  $\geq 1$  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  $\chi^2$  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  $\pm$  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* = 0.002], 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). 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 hiatal 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.

## REFERENCES

- 1 Sharma P. Clinical practice. Barrett's esophagus. *N Engl J Med* 2009; **361**: 2548-2556 [PMID: 20032324 DOI: 10.1056/NEJMcp0902173]
- 2 American Gastroenterological Association. Spechler SJ, Sharma P, Souza RF, Inadomi JM, Shaheen NJ. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. *Gastroenterology* 2011; **140**: 1084-1091 [PMID: 21376940 DOI: 10.1053/j.gastro.2011.01.030]
- 3 Shaheen NJ, Falk GW, Iyer PG, Gerson LB; American College of Gastroenterology. ACG Clinical

- Guideline: Diagnosis and Management of Barrett's Esophagus. *Am J Gastroenterol* 2016; **111**: 30-50; quiz 51 [PMID: 26526079 DOI: 10.1038/ajg.2015.322]
- 4 **ASGE Standards of Practice Committee**. Evans JA, Early DS, Fukami N, Ben-Menachem T, Chandrasekhara V, Chathadi KV, Decker GA, Fanelli RD, Fisher DA, Foley KQ, Hwang JH, Jain R, Jue TL, Khan KM, Lightdale J, Malpas PM, Maple JT, Pasha SF, Saltzman JR, Sharaf RN, Shergill A, Dornitz JA, Cash BD. Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy. The role of endoscopy in Barrett's esophagus and other premalignant conditions of the esophagus. *Gastrointest Endosc* 2012; **76**: 1087-1094 [PMID: 23164510 DOI: 10.1016/j.gie.2012.08.004]
  - 5 **Johansson J**, Håkansson HO, Mellblom L, Kempas A, Johansson KE, Granath F, Nyrén O. Risk factors for Barrett's esophagus: a population-based approach. *Scand J Gastroenterol* 2007; **42**: 148-156 [PMID: 17327933 DOI: 10.1080/00365520600881037]
  - 6 **Abrams JA**, Fields S, Lightdale CJ, Neugut AI. Racial and ethnic disparities in the prevalence of Barrett's esophagus among patients who undergo upper endoscopy. *Clin Gastroenterol Hepatol* 2008; **6**: 30-34 [PMID: 18063419 DOI: 10.1016/j.cgh.2007.10.006]
  - 7 **Kubo A**, Cook MB, Shaheen NJ, Vaughan TL, Whiteman DC, Murray L, Corley DA. Sex-specific associations between body mass index, waist circumference and the risk of Barrett's esophagus: a pooled analysis from the international BEACON consortium. *Gut* 2013; **62**: 1684-1691 [PMID: 23355549 DOI: 10.1136/gutjnl-2012-303753]
  - 8 **Steevens J**, Schouten LJ, Driessen AL, Huysentruyt CJ, Keulemans YC, Goldbohm RA, van den Brandt PA. A prospective cohort study on overweight, smoking, alcohol consumption, and risk of Barrett's esophagus. *Cancer Epidemiol Biomarkers Prev* 2011; **20**: 345-358 [PMID: 21173169 DOI: 10.1158/1055-9965.EPI-10-0636]
  - 9 **Forssell L**, Cnattingius S, Bottai M, Edstedt Bonamy AK, Lagergren J, Agrés L, Akre O. Increased risk of Barrett's esophagus among individuals born preterm or small for gestational age. *Clin Gastroenterol Hepatol* 2013; **11**: 790-794 [PMID: 23376800 DOI: 10.1016/j.cgh.2013.01.024]
  - 10 **Leggett CL**, Gorospe EC, Calvin AD, Harmsen WS, Zinsmeister AR, Caples S, Somers VK, Dunagan K, Lutzke L, Wang KK, Iyer PG. Obstructive sleep apnea is a risk factor for Barrett's esophagus. *Clin Gastroenterol Hepatol* 2014; **12**: 583-8.e1 [PMID: 24035775 DOI: 10.1016/j.cgh.2013.08.043]
  - 11 **Shiota S**, Singh S, Anshasi A, El-Serag HB. Prevalence of Barrett's Esophagus in Asian Countries: A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol* 2015; **13**: 1907-1918 [PMID: 26260107 DOI: 10.1016/j.cgh.2015.07.050]
  - 12 **Kubo A**, Levin TR, Block G, Rumore GJ, Quesenberry CP, Buffler P, Corley DA. Alcohol types and sociodemographic characteristics as risk factors for Barrett's esophagus. *Gastroenterology* 2009; **136**: 806-815 [PMID: 19111726 DOI: 10.1053/j.gastro.2008.11.042]
  - 13 **Corley DA**, Kubo A, Levin TR, Block G, Habel L, Zhao W, Leighton P, Rumore G, Quesenberry C, Buffler P, Parsonnet J. Helicobacter pylori infection and the risk of Barrett's esophagus: a community-based study. *Gut* 2008; **57**: 727-733 [PMID: 17895354 DOI: 10.1136/gut.2007.132068]
  - 14 **Wang C**, Yuan Y, Hunt RH. Helicobacter pylori infection and Barrett's esophagus: a systematic review and meta-analysis. *Am J Gastroenterol* 2009; **104**: 492-500; quiz 491, 501 [PMID: 19174811 DOI: 10.1038/ajg.2008.37]
  - 15 **Runge TM**, Abrams JA, Shaheen NJ. Epidemiology of Barrett's Esophagus and Esophageal Adenocarcinoma. *Gastroenterol Clin North Am* 2015; **44**: 203-231 [PMID: 26021191 DOI: 10.1016/j.gtc.2015.02.001]
  - 16 **Tseng PH**, Lee YC, Chiu HM, Huang SP, Liao WC, Chen CC, Wang HP, Wu MS, Lin JT. Prevalence and clinical characteristics of Barrett's esophagus in a Chinese general population. *J Clin Gastroenterol* 2008; **42**: 1074-1079 [PMID: 18360296 DOI: 10.1097/MCG.0b013e31809e7126]
  - 17 **Chang CY**, Lee YC, Lee CT, Tu CH, Hwang JC, Chiang H, Tai CM, Chiang TH, Wu MS, Lin JT. The application of Prague C and M criteria in the diagnosis of Barrett's esophagus in an ethnic Chinese population. *Am J Gastroenterol* 2009; **104**: 13-20 [PMID: 19098843 DOI: 10.1038/ajg.2008.43]
  - 18 **Vakil N**, van Zanten SV, Kahrilas P, Dent J, Jones R; Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol* 2006; **101**: 1900-1920; quiz 1943 [PMID: 16928254 DOI: 10.1111/j.1572-0241.2006.00630.x]
  - 19 **Sharma P**, Dent J, Armstrong D, Bergman JJ, Gossner L, Hoshihara Y, Jankowski JA, Junghard O, Lundell L, Tytgat GN, Vieth M. The development and validation of an endoscopic grading system for Barrett's esophagus: the Prague C & M criteria. *Gastroenterology* 2006; **131**: 1392-1399 [PMID: 17101315 DOI: 10.1053/j.gastro.2006.08.032]
  - 20 **Haggitt RC**, Reid BJ, Rabinovitch PS, Rubin CE. Barrett's esophagus. Correlation between mucin histochemistry, flow cytometry, and histologic diagnosis for predicting increased cancer risk. *Am J Pathol* 1988; **131**: 53-61 [PMID: 3354644]
  - 21 **Bhat S**, Coleman HG, Yousef F, Johnston BT, McManus DT, Gavin AT, Murray LJ. Risk of malignant progression in Barrett's esophagus patients: results from a large population-based study. *J Natl Cancer Inst* 2011; **103**: 1049-1057 [PMID: 21680910 DOI: 10.1093/jnci/djr203]
  - 22 **Park JJ**, Kim JW, Kim HJ, Chung MG, Park SM, Baik GH, Nah BK, Nam SY, Seo KS, Ko BS, Jang JY, Kim BG, Kim JW, Choi YS, Joo MK, Kim JI, Cho MY, Kim N, Park SH, Jung HC, Chung IS; H. pylori and GERD Study Group of Korean College of Helicobacter and Upper Gastrointestinal Research. The prevalence of and risk factors for Barrett's esophagus in a Korean population: A nationwide multicenter prospective study. *J Clin Gastroenterol* 2009; **43**: 907-914 [PMID: 19417682 DOI: 10.1097/MCG.0b013e318196bd11]
  - 23 **Peng S**, Cui Y, Xiao YL, Xiong LS, Hu PJ, Li CJ, Chen MH. Prevalence of erosive esophagitis and Barrett's esophagus in the adult Chinese population. *Endoscopy* 2009; **41**: 1011-1017 [PMID: 19967617 DOI: 10.1055/s-0029-1215291]
  - 24 **Kuo CJ**, Lin CH, Liu NJ, Wu RC, Tang JH, Cheng CL. Frequency and risk factors for Barrett's esophagus in Taiwanese patients: a prospective study in a tertiary referral center. *Dig Dis Sci* 2010; **55**: 1337-1343 [PMID: 19557516 DOI: 10.1007/s10620-009-0872-7]
  - 25 **Tack J**, Vantrappen G. The aging esophagus. *Gut* 1997; **41**: 422-424 [PMID: 9391234 DOI: 10.1136/gut.41.4.422]
  - 26 **Masaka T**, Iijima K, Endo H, Asanuma K, Ara N, Ishiyama F, Asano N, Koike T, Imatani A, Shimosegawa T. Gender differences in esophageal mucosal injury in a reflux esophagitis model of rats. *Gut* 2013; **62**: 6-14 [PMID: 22287598 DOI: 10.1136/gutjnl-2011-301389]
  - 27 **Velders M**, Schleipen B, Fritzscheier KH, Zierau O, Diel P. Selective estrogen receptor- $\beta$  activation

- stimulates skeletal muscle growth and regeneration. *FASEB J* 2012; **26**: 1909-1920 [PMID: 22278942 DOI: 10.1096/fj.11-194779]
- 28 **Gudjonsson H**, McAuliffe TL, Kaye MD. [The effect of coffee and tea upon lower esophageal sphincter function.]. *Laeknabladid* 1995; **81**: 484-488 [PMID: 20065484]
- 29 **Lohsirawat S**, Puengna N, Leelakusolvong S. Effect of caffeine on lower esophageal sphincter pressure in Thai healthy volunteers. *Dis Esophagus* 2006; **19**: 183-188 [PMID: 16722996 DOI: 10.1111/j.1442-2050.2006.00562.x]
- 30 **Ruggiero P**, Rossi G, Tombola F, Pancotto L, Lauretti L, Del Giudice G, Zoratti M. Red wine and green tea reduce H pylori- or VacA-induced gastritis in a mouse model. *World J Gastroenterol* 2007; **13**: 349-354 [PMID: 17230601 DOI: 10.3748/wjg.v13.i3.349]
- 31 **Berquist WE**, Rachelefsky GS, Kadden M, Siegel SC, Katz RM, Mickey MR, Ament ME. Effect of theophylline on gastroesophageal reflux in normal adults. *J Allergy Clin Immunol* 1981; **67**: 407-411 [PMID: 7229228 DOI: 10.1016/0091-6749(81)90087-7]
- 32 **Bhatia SJ**, Reddy DN, Ghoshal UC, Jayanthi V, Abraham P, Choudhuri G, Broor SL, Ahuja V, Augustine P, Balakrishnan V, Bhasin DK, Bhat N, Chacko A, Dadhich S, Dhali GK, Dhawan PS, Dwivedi M, Goenka MK, Koshy A, Kumar A, Misra SP, Mukewar S, Raju EP, Shenoy KT, Singh SP, Sood A, Srinivasan R. Epidemiology and symptom profile of gastroesophageal reflux in the Indian population: report of the Indian Society of Gastroenterology Task Force. *Indian J Gastroenterol* 2011; **30**: 118-127 [PMID: 21792655 DOI: 10.1007/s12664-011-0112-x]
- 33 **Winters C**, Spurling TJ, Chobanian SJ, Curtis DJ, Esposito RL, Hacker JF, Johnson DA, Cruess DF, Cotelingam JD, Gurney MS. Barrett's esophagus. A prevalent, occult complication of gastroesophageal reflux disease. *Gastroenterology* 1987; **92**: 118-124 [PMID: 3781178 DOI: 10.1016/0016-5085(87)90847-X]
- 34 **Burgess JN**, Payne WS, Andersen HA, Weiland LH, Carlson HC. Barrett esophagus: the columnar-epithelial-lined lower esophagus. *Mayo Clin Proc* 1971; **46**: 728-734 [PMID: 5128394]
- 35 **Sajja KC**, El-Serag HB, Thrift AP. Coffee or Tea, Hot or Cold, Are Not Associated With Risk of Barrett's Esophagus. *Clin Gastroenterol Hepatol* 2016; **14**: 769-772 [PMID: 26681488 DOI: 10.1016/j.cgh.2015.12.007]
- 36 **Filiberti RA**, Fontana V, De Ceglie A, Bianchi S, Grossi E, Della Casa D, Lacchin T, De Mattheis M, Ignomirelli O, Cappiello R, Rosa A, Foti M, Laterza F, D'Onofrio V, Iaquinto G, Conio M. Association between coffee or tea drinking and Barrett's esophagus or esophagitis: an Italian study. *Eur J Clin Nutr* 2017; **71**: 980-986 [PMID: 28488688 DOI: 10.1038/ejcn.2017.64]
- 37 **Pehl C**, Pfeiffer A, Wendl B, Kaess H. The effect of decaffeination of coffee on gastro-oesophageal reflux in patients with reflux disease. *Aliment Pharmacol Ther* 1997; **11**: 483-486 [PMID: 9218070 DOI: 10.1046/j.1365-2036.1997.00161.x]
- 38 **Chang CH**, Wu CP, Wang JD, Lee SW, Chang CS, Yeh HZ, Ko CW, Lien HC. Alcohol and tea consumption are associated with asymptomatic erosive esophagitis in Taiwanese men. *PLoS One* 2017; **12**: e0173230 [PMID: 28264069 DOI: 10.1371/journal.pone.0173230]
- 39 **Bandla S**, Peters JH, Ruff D, Chen SM, Li CY, Song K, Thoms K, Little VR, Watson T, Chapurin N, Lada M, Pennathur A, Luketich JD, Peterson D, Dulak A, Lin L, Bass A, Beer DG, Godfrey TE, Zhou Z. Comparison of cancer-associated genetic abnormalities in columnar-lined esophagus tissues with and without goblet cells. *Ann Surg* 2014; **260**: 72-80 [PMID: 24509200 DOI: 10.1097/SLA.0000000000000424]
- 40 **Harrison R**, Perry I, Haddadin W, McDonald S, Bryan R, Abrams K, Sampliner R, Talley NJ, Moayyedi P, Jankowski JA. Detection of intestinal metaplasia in Barrett's esophagus: an observational comparator study suggests the need for a minimum of eight biopsies. *Am J Gastroenterol* 2007; **102**: 1154-1161 [PMID: 17433019 DOI: 10.1111/j.1572-0241.2007.01230.x]
- 41 **Chandrasoma PT**, Der R, Dalton P, Kobayashi G, Ma Y, Peters J, Demeester T. Distribution and significance of epithelial types in columnar-lined esophagus. *Am J Surg Pathol* 2001; **25**: 1188-1193 [PMID: 11688579 DOI: 10.1097/0000478-200109000-00010]
- 42 **Mastracci L**, Piol N, Molinaro L, Pitto F, Tinelli C, De Silvestri A, Fiocca R, Grillo F; ABRAM Study Group. Interobserver reproducibility in pathologist interpretation of columnar-lined esophagus. *Virchows Arch* 2016; **468**: 159-167 [PMID: 26563401 DOI: 10.1007/s00428-015-1878-5]
- 43 **Smout AJ**, Breedijk M, van der Zouw C, Akkermans LM. Physiological gastroesophageal reflux and esophageal motor activity studied with a new system for 24-hour recording and automated analysis. *Dig Dis Sci* 1989; **34**: 372-378 [PMID: 2920643 DOI: 10.1007/bf01536258]
- 44 **Roman S**, Kahrilas PJ. The diagnosis and management of hiatus hernia. *BMJ* 2014; **349**: g6154 [PMID: 25341679 DOI: 10.1136/bmj.g6154]



Published By Baishideng Publishing Group Inc  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA  
Telephone: +1-925-2238242  
Fax: +1-925-2238243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

