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***Prospective Study***

**Application of the Prague C and M criteria for endoscopic description of columnar-lined esophagus in South Korea**

Jung Wan Choe *et al.* Columnar-lined esophagus in South Korea

**Jung Wan Choe, Young Choon Kim, Moon Kyung Joo, Hyo Jung Kim, Beom Jae Lee, Ji Hoon Kim, Jong Eun Yeon, Jong-Jae Park, Jae Seon Kim, Kwan Soo Byun, Young-Tae Bak**

**Jung Wan Choe, Young Choon Kim, Moon Kyung Joo, Hyo Jung Kim, Beom Jae Lee, Ji Hoon Kim, Jong Eun Yeon, Jong-Jae Park, Jae Seon Kim, Kwan Soo Byun, Young-Tae Bak,** Department of Gastroenterology, Korea University Guro Hospital, Seoul 152-703, South Korea

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**Clinical trial registration:** Although this research is a prospective study, there is no need to register clinical trial. This study only analyzed the results of endoscopic features, not evaluated or compare the clinical outcome. So, we are so sorry not to provide the trial’s registry.

**Informed consent statement:** All study participants, or their legal guardian, provided written consent prior to study enrollment.

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**Correspondence to:** **Young-Tae Bak, MD,** Department of Gastroenterology, Korea University Guro Hospital, 148 Gurodong-ro, Guro-gu, Seoul 152-703, South Korea. drbakyt@korea.ac.kr

**Telephone:** +82-2-26261778

**Fax:** +82-505-1151778

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**Abstract**

**AIM:** To ascertain whether the Prague C (circumferential length) and M (maximal length) criteria for grading the extent of Barrett’s esophagus can be applied prior to its widespread application in South Korea.

**METHODS:** 213 consecutive cases with endoscopic columnar-lined esophagus (CLE) were included and classified according to the Prague C and M criteria.

**RESULTS:** Of 213 cases with CLE, the distribution of maximum CLE lengths was: 0.5-0.9 cm in 99 cases (46.5%); 1.0-1.4 cm in 63 cases (29.6%); 1.5-1.9 cm in 15 cases (7.0%); 2.0-2.4 cm in 14 cases (6.6%); 2.5-2.9 cm in 1 case (0.5%); and 7.0 cm in 1 case (0.5%). Twenty cases (9.4%) had columnar islands alone. Two hundred and eight cases (97.7%) lacked the circumferential CLE component (C0Mx). Columnar islands were found in 70 cases (32.9%), of which 20 cases (9.4%) had columnar islands alone.

**CONCLUSION:** In regions where most CLE patients display short or ultrashort tongue-like appearance, more detailed descriptions of CLE’s in < 1.0 cm lengths and columnar islands, as well as avoidance of repeating the prefix “C0” need to be considered in parallel with the widespread application of the Prague system in South Korea.

**Key words**: Barrett’s esophagus; Columnar-lined esophagus; Endoscopy; Prague criteria

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**Core tip:** This was a prospective study to assess the feasibility of the Prague C and M criteria for the endoscopic description of columnar-lined esophagus in South Korea. In regions like South Korea where the prevalence and endoscopic features of this condition are quite different from the West, we suggest possible modifications that may fit the characteristics of the South Korean source population more properly.

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**INTRODUCTION**

Barrett’s esophagus (BE) is defined as a histological change of the distal tubular esophagus, from squamous to columnar epithelium, which displays an intestinal metaplasia (IM) containing goblet cells[1,2]. Because BE is characterized by an upward shift of the squamocolumnar junction (SCJ) proximal to the gastroesophageal junction (GEJ), the resulting columnar-lined mucosa of the distal esophagus can be identified by its salmon-pink color during endoscopic examination[3,4]. Moreover,multiple endoscopic biopsies at the extended columnar-lined epithelium are needed to confirm BE diagnosis.

BE is associated with gastroesophageal reflux disease (GERD) and is considered a premalignant lesion for esophageal adenocarcinoma[5,6], the incidence of which is steadily rising in the United States and Europe[7,8]. Increasing GERD incidence in South Korea is considered to result from more consumption of westernized foods[9,10]. As patients with chronic GERD are at a higher risk of developing BE[11,12], the expected increase in BE and esophageal cancer incidence rates in the future is a matter of potential concern in South Korea.

Various studies have examined BE length as a risk factor for esophageal adenocarcinoma[13-15]. Results from a study showed that a doubling in BE length resulted in a 1.7-fold increase in the risk of developing esophageal adenocarcinoma[15], and others revealed that a significantly increased risk of dysplasia or adenocarcinoma was related to greater lengths of BE[13,14]. Therefore, accurate measuring of CLE lengths and describing in well-defined clinical terms are important in appropriate risk assessment and surveillance. Although previous diagnostic criteria for BE were based on the 3-cm length threshold of columnar-lined esophagus (CLE), by which BE was divided into 2 types, long (≥ 3 cm) and short (< 3 cm), this simple classification of variable endoscopic findings of CLE was a rather crude approach in describing BE. Furthermore, as considerable inter- and intra-observer variability in detecting and describing the CLE are common, the establishment of an accurate BE diagnosis and surveillance may be tricky[16-18].

Therefore, the Prague classification system that measures the circumferential (C) and maximal (M) extents for endoscopic standardization of BE lengths was developed and finally introduced by the International Working Group for the Classification of Oesophagitis (IWGCO) in 2004[19]. However, the overall reliability and validity of the Prague C and M Criteria for BE diagnosis continues to be challenged[20-22]. Moreover, its performance in South Korea where the incidence of BE is low and the short-segment BE is the predominant type remains unclear.

In the present study, we aimed to assess the feasibility of the Prague C and M criteria for the endoscopic description of CLE in South Korea where the prevalence and endoscopic features of this condition are quite different from the West and to suggest possible modifications that may fit the characteristics of the South Korean source population more properly.

**MATERIALS AND METHODS**

This prospective study was conducted from the endoscopy data of consecutive CLE patients who underwent esophagogastroduodenoscopy (EGD) at Endoscopy Center of the Korea University Guro Hospital, Seoul, South Korea. Exclusion criteria included the presence of esophageal varices, acute upper gastrointestinal bleeding, malignancy near GEJ, and history of gastric surgery. Before each EGD, written informed consent was obtained. All endoscopic procedures were performed by an experienced endoscopist (YTB).

GEJ and SCJ were carefully assessed during the insertion of the endoscope. The distal margin of the palisade blood vessels of the lower esophagus was used as a marker of GEJ[23]. If the palisade vessels could not be seen adequately, the proximal margins of the gastric folds were used to identify GEJ. SCJ was used as a marker for upper border of CLE. The length of CLE, that is the distance from GEJ to SCJ, was measured by the insertion depths with the centimeter markings on the endoscope. CLE’s shorter than 0.5 cm in length were ignored to avoid possible observation errors that may lead to overdiagnosis. Careful observation was done to look for any presence of islands of columnar mucosa.

The circumferential (C) and maximum (M) extents of CLE were recorded according to the Prague C and M criteria proposed by the IWGCO[19]. M lengths were divided into long (≥ 3 cm), short (1-2.9 cm), and ultrashort (< 1 cm) segments.

**RESULTS**

***Patient demographic characteristics***

A total of 213 CLE patients consisting of 154 men and 59 women, with 53.8 ± 12.3 years in age (mean ± SD) were enrolled.

***Distribution of CLE lengths and application of the Prague C and M criteria***

**Analysis of cases with CLE’s including ultrashort CLE’s:** Distribution of CLE’s according to their M values, including those with ultrashort CLE’s, is shown in Table 1. Among the total 213 cases, 99 (46.5%), 63 (29.6%), 15 (7.0%), 14 (6.6%), 1 (0.5%), and 1 (0.5%) had CLE’s of 0.5-0.9 cm, 1.0-1.4 cm, 1.5-1.9 cm, 2.0-2.4 cm, 2.5-2.9 cm, and ≥ 3.0 cm in lengths, respectively. The remaining 20 cases (9.4%) had columnar islands alone. Therefore, 99 cases (46.5%) had ultrashort CLE’s (CLE < 1.0 cm), 113 (53.1%) had short CLE’s (1-2 cm) and only one (0.5%) had a long CLE (≥ 3 cm), showing a CLE of 7.0 cm in length.

When the cases were classified by the Prague criteria, 208 (97.7%) had no C component (C0Mx). Two cases had C1M1 and the remaining three cases had either, C1M1.5, C1M1, or C1.5M2. Columnar islands were observed in 70 (32.9%) cases, of which 20 (9.4%) had columnar islands alone.

**Analysis of cases with CLE’s excluding ultrashort CLE’s:** Distribution of CLE’s according to their M values among those excluding ultrashort CLE’s is shown in Table 2. Among 139 cases, 63 (45.3%), 15 (10.8%), 14 (10.1%), 1 (0.7%), and 1 (0.7%) had CLE’s of 1.0-1.4 cm, 1.5-1.9 cm, 2.0-2.4 cm, 2.5-2.9 cm, and ≥ 3.0 cm in lengths, respectively. Therefore, 138 (99.3%) out of all 139 cases had short CLE’s, and only one showed an exceptionally long CLE.

When 139 cases were classified by the Prague criteria, 134 (96.4%) had CLE’s without C component (C0Mx). Two cases had C1M1 and the remaining three patients had either C1M1.5, C1M1, or C1.5M2. Columnar islands were found in 70 (50.4%) cases, of which 45 (32.4%) showing columnar islands alone.

**DISCUSSION**

BE is a very well known risk factor for the development of dysplasia and esophageal adenocarcinoma[24-26]. The risk of dysplasia and adenocarcinoma in metaplastic epithelium reportedly increases in parallel to the lengths of BE[13-15]. A recent multicenter study conducted by Gaddam *et al*[13] revealed that for every 1-cm extension in BE length, the risk of high-grade dysplasia and esophageal adenocarcinoma increased by 21%. The study demonstrated that the increase in BE lengths significantly widens the area of metaplasia, which is associated with the progression to high-grade dysplasia/esophageal adenocarcinoma[13]. Although a novel technique using a computer software program to create a two-dimensional image map of the esophagus has been introduced to accurately and reproducibly measure the extent of CLE[27], such a complicated approach is not suitable for a daily clinical practice. Therefore, assessment of BE extent by simple measurement of the height of metaplastic CLE remains as the most commonly used procedure to distinguish short- from long-segment BE[13-15]. However, the study of the clinical course and therapeutic response of BE has been limited because this classic method only provides gross estimates of the area. This system does not measure the surface areas of metaplastic mucosa, which may be more important than the endoscopic lengths[19]. The presence of an irregular border of columnar tissue or interspersed metaplastic mucosal islands can hamper the precise measurement of the extent of CLE[20].

The Prague C and M criteria, suggested by IWGCO, not only allows a more detailed description of the length of the endoscopically recognized CLE, using “C” and “M” values above the GEJ, but can also assist the objective calculation of the actual surface area, which may be more important in the risk assessment of the neoplastic transformation[19-21]. These advances in CLE description have facilitated the depiction and reporting of various circumferential and tongue-like longitudinal CLE lengths by using a method that can be understood easily and comprehensively. Importantly, high inter-observer reliability in the grading of endoscopically suspected CLE was demonstrated among gastroenterology experts and trainees[22].

In recent years, accelerated life style changes have increased the prevalence of GERD in Asian populations, including South Koreans[9,10,28,29], and BE incidence is also expected to increase[12]. BE prevalence in South Korea was 0.2%-3.6% in the year 2000[11,12,30], lower than in Western countries. Lengths and shapes of CLE’s as well as their prevalence in South Korea are quite different from those of the Western countries. Long-segment BE is more common in Western countries, wherein 14%-31% of BE patients show this type[31,32]. However, most cases of BE are short-segment type in South Korea, where long-segment type BE’s are extremely rare[11]. In our study, with the exception of the only one case, 212 (99.5%) out of 213 CLE cases were short-segment type (< 3 cm); and from these, 99 cases (46.5%) had ultrashort CLE (< 1 cm). Lee *et al*[33]reported that the reliability coefficients of the C and M values in the endoscopic recognition of short-segment type CLE were 0.90 (95%CI: 0.80%-1.00%) and 0.92 (95%CI: 0.87%-0.98%), respectively. However, the reliability of such coefficients for the recognition of the ultrashort (< 1 cm) CLE extent type was very low, with C and M coefficients of 0.18 (95%CI: 0.03%-0.32%) and 0.21 (95%CI: 0.00%-0.51%), respectively[33].

Therefore, the routine applicability of the Prague C and M criteria as a standardized validated method for the detailed endoscopic description of ultrashort BE and short-segment BE, the most dominant BE types in South Korea, requires further analysis. As our study showed, all ultrashort CLE and almost all short-segment CLE cases lacked the C component and were classified as C0Mx. Therefore, it appears appropriate for us to propose to omit of the prefix “C0” from all C0Mx cases in order to avoid needless repetitions when describing most cases in regions like South Korea. Because the presence of columnar islands is a frequent finding as we have observed in this study and they also may change to dysplasia[34], we propose to add this to the Prague system, which currently does not include this category. Resultant examples following our proposals are: C2M5, if 2.0 cm of C component with 5.0 cm of M component; M2, if 2.0 cm of M component without C component; C2M5i or M2i, if columnar island(s) is/are found in addition to C2M5 or M2 CLE; and M0i, if only columnar island(s) is/are found.

In summary, the Prague C and M system is simple and useful in daily description of endoscopic feature of CLE’s. However, in regions like South Korea where most cases with CLE display only short or ultrashort types without C component, we propose to omit the needless repetition of “C0” prefix from C0Mx and to add i component to describe the presence of columnar islands which also may have a potential to be dysplastic.

**COMMENTS**

***Background***

The Prague C (circumferential length) and M (maximal length) criteria have been adopted widely for grading the extent of Barrett’s esophagus (BE). However, its validity in regions with low prevalence of BE, remains unclear. This study was designed to ascertain whether these criteria can be applied prior to its widespread application in South Korea.

***Research frontiers***

The Prague C and M system is simple and useful in daily description of endoscopic feature of BE’s. But, the overall reliability and validity of the Prague C and M Criteria for BE diagnosis continues to be challenged. In this study, there are some suggestions of possible modifications that may fit the characteristics of the South Korean source population more properly.

***Innovations and breakthroughs***

In regions like South Korea where most cases with columnar-lined esophagus display only short or ultrashort types without C component, we propose to omit the needless repetition of “C0” prefix from C0Mx and to add “I” component to describe the presence of columnar islands which also may have a potential to be dysplastic.

***Applications***

This study serves as additional evidence supporting the investigation in parallel with the widespread application of the Prague system in South Korea.

***Terminology***

Barrett’s esophagus: A histological change of the distal tubular esophagus, from squamous to columnar epithelium, which displays an intestinal metaplasia (IM) containing goblet cells. The Prague classification criteria: A system to measure the circumferential (C) and maximal (M) extents for endoscopic standardization of BE lengths.

***Peer-review***

The study is has clear defined inclusion and exclusion criteria and is well conducted despite the lack of a control group. I think this study is innovative and would be interesting to see if the findings are reproducible in other countries where BE is not as common as in the West.

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**Table 1 Application of Prague C and M criteria in cases with ultrashort, short, and long columnar-lined esophagus (*n* = 213)**

|  |  |  |
| --- | --- | --- |
| Lengths of CLE (cm) | *n* (%) | C0Mx cases (%) |
| 0 (islands only) | 20 (9.4) | 20 (100) |
| 0.5-0.9 | 99 (46.5) | 99 (100) |
| 1.0-1.5 | 63 (29.6) | 61 (96.8) |
| 1.5-1.9 | 15 (7.0) | 14 (93.3) |
| 2.0-2.4 | 14 (6.6) | 12 (85.7) |
| 2.5-2.9 | 1 (0.5) | 1 (100) |
| ≥ 3.0 | 1 (0.5) | 1 (100) |
| Total | 213 (100) | 208 (97.7)1 |

1Exceptions: 2 cases with C1M1 and 3 cases with either C1M1.5, C1M2, or C1.5M2. CLE: Columnar-lined esophagus.

**Table 2 Application of Prague C and M criteria in cases with short and long columnar-lined esophagus (*n* = 139)**

|  |  |  |
| --- | --- | --- |
| Lengths of CLE (cm) | *n* (%) | C0Mx cases (%) |
| 0 (islands only) | 45 (32.4) | 45 (100) |
| 1.0-1.4 | 63 (45.3) | 61 (96.8) |
| 1.5-1.9 | 15 (10.8) | 14 (93.3) |
| 2.0-2.4 | 14 (10.1) | 12 (85.7) |
| 2.5-2.9 | 1 (0.7) | 1 (100) |
| ≥ 3.0 | 1 (0.7) | 1 (100) |
| Total | 139 (100) | 134 (96.4)1 |

1Exceptions: 2 patients with C1M1 and 3 patients with either C1M1.5, C1M2, or C1.5M2. CLE: Columnar-lined esophagus