Barrett’s Esophagus and Severe Reflux Esophagitis Share Common Pathophysiological Characteristics among Chinese in Taiwan

Teng-Yu Lee¹,³, Han-Chung Lien¹,², Chi-Sen Chang¹,³ and Mei-Chin Wen⁴

Abstract

Objective The pathophysiological data on Barrett’s esophagus are scant in Asia, so the purpose of this study was to compare and analyze the pathophysiological characteristics of Barrett’s esophagus and reflux esophagitis among Chinese in Taiwan.

Patients and Methods From November 2001 to January 2003, fifteen patients with Barrett’s esophagus were consecutively enrolled as the Barrett’s esophagus group. Fourteen patients with Los Angeles grade A/B esophagitis (mild esophagitis group) and fourteen patients with LA grade C/D esophagitis (severe esophagitis group) who were matched in age and gender with the Barrett’s esophagus group were enrolled. The data of esophageal manometry and ambulatory 24-hour pH monitoring were collected.

Results We found that the Barrett’s esophagus group had significantly weaker lower esophageal sphincter (LES) pressure and distal esophageal body contractions (p<0.05) than the mild esophagitis group. Both the Barrett’s esophagus group and severe esophagitis group had significantly higher esophageal acid reflux scores and frequency (p<0.05-0.01) compared to the mild esophagitis group. However, data on esophageal manometry and 24-hour pH monitoring in the Barrett’s esophagus and severe esophagitis groups did not significantly differ.

Conclusion We concluded that Barrett’s esophagus had significantly stronger acid reflux, lower LES pressure, and weaker distal esophageal peristalsis compared to mild esophagitis. Barrett’s esophagus and severe reflux esophagitis share common pathophysiological characteristics among Chinese in Taiwan.

Key words: Barrett’s esophagus, reflux esophagitis, intestinal metaplasia, Asian, pathophysiology

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Introduction

In Western countries, gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal disorders, and GERD contributes to reflux esophagitis and Barrett’s esophagus (BE). BE is a condition characterized by change in the esophageal epithelium of any length recognized at endoscopy, and the presence of specialized intestinal metaplasia confirmed by biopsy (1). Although the distal end of the lower-esophageal palisade vessels is used to define the gastroesophageal junction in Japan, the landmark is the upper end of the gastric longitudinal folds in most Western countries. Endoscopy is the technique of choice used to identify suspected BE, and biopsy must be performed to examine for dysplasia (2). The vast majority of adenocarcinomas of the esophagus are accompanied by intestinal metaplasia, and intestinal metaplasia of the esophagus is a premalignant lesion (3-6). Esophageal adenocarcinoma develops in approximately 0.5 percent of Caucasian patients with BE per year, and the rapidly rising incidence of adenocarcinoma of the esophagus in the United States has been attributed to...
the impact of BE (7-9).

Previous studies have suggested that the longer the duration of reflux symptoms, the higher the prevalence of BE at the time of upper gastrointestinal (UGI) endoscopy (10, 11). The degree and length of acid exposure in the esophagus are important factors in the pathogenesis of specialized intestinal metaplasia of the esophagus (12). Intestinal metaplasia develops when GERD damages the squamous esophageal mucosa and the injury heals through a metaplastic process in which columnar cells replace squamous cells (13). A preponderance of males have esophagitis and/or Barrett’s metaplasia, and Caucasian men overwhelmingly predominate (1, 3).

GERD has been traditionally considered less common in Asia, especially in East Asia, where a prevalence as low as 2.4% in the general population was reported in the 1970s (14). Hiatal hernia, one of the most important risk factors for GERD, was reported to be less than 1% in East Asia in the 1970s (15). However, a study (16) conducted in 1997 reported a GERD prevalence of 5%, and the overall incidence of reflux esophagitis in the general population is increasing. Moreover, in a study (17) which included 464 consecutive patients who underwent UGI endoscopy for a variety of UGI symptoms between July 1991 and June 1992, erosive esophagitis was found in 14.5% of patients, and 2% of cases were identified as BE. In recent years, the incidence of reflux esophagitis was reported to be from 9% to 24.6% in patients who underwent a health check-up in Taiwan (18-20). The prevalence of GERD appears to be rapidly increasing in the Asian-Pacific region, possibly due to the influence of western lifestyle and increased awareness among doctors and patients (21). Although BE appears to affect Asians less frequently (1, 22), reports of the pathophysiological characteristics of BE in the Chinese population are scant. Our aim therefore was to access and compare pathophysiological characteristics of BE and reflux esophagitis among Chinese in Taiwan, and then compare our findings with those in Caucasians.

**Patients and Methods**

**Patients**

We prospectively collected data on consecutive patients with suspected BE who underwent UGI endoscopy at Taichung Veterans General Hospital (TCVGH; a tertiary hospital in Taiwan) from November 2001 to January 2003. A total of twenty-one patients (mean age 62.4; male-to-female ratio: 17:4; and 15 patients with hiatal hernia) were diagnosed with BE, which was confirmed by specialized intestinal metaplasia in biopsy samples. However, only 15 patients agreed to undergo esophageal manometry and 24-hour pH monitoring and these patients were classified as the BE group in this study. Among patients who were referred to our laboratory for esophageal manometry and 24-hour pH assessment because of GERD and reflux esophagitis, fourteen patients with Los Angeles (LA) grade A/B esophagitis (mild esophagitis group) and fourteen patients with LA grade C/D esophagitis (severe esophagitis group) who were matched in age and gender with the BE group were enrolled in a prospective manner (23). UGI endoscopy was repeated to rule out underlying BE in patients with severe esophagitis after three months of medical therapy. These volunteers were required to abstain from medications known to affect gastrointestinal motility or gastric acid secretion (7 days for proton pump inhibitors, 72 hours for prokinetics, 24 hours for H2 receptor antagonists, and 24 hours for antacids) before their participation in this study. None of the patients had undergone previous anti-reflux surgery, and patients with malignancy or named motility disorder were also excluded. The ethics committee of our hospital approved this study.

**Esophageal manometry**

After patients fasted overnight, they underwent esophageal manometry, which was performed using an eight-lumen, water-perfused, esophageal manometric catheter (Dent Sleeve, Synectics, Stockholm, Sweden) consisting of a multi-lumen silicone tube (5.0 mm OD). The data were displayed continuously on a monitor and stored on a computer system (Polygram Upper GI 6.30, Gastrosoft, Inc., Synectics Medical).

With the patient in the supine position, the manometric catheter was introduced through the patient’s nose into the stomach and was withdrawn through the lower esophageal sphincter (LES) using the station pull-through technique at 1-cm increments every 10 seconds. The resting LES pressure was defined as the difference between the end-expiratory gastric baseline pressure and the highest end-expiratory pressure just distal to the respiratory inversion point. Contractions in the esophageal body were measured with the sensors in the esophagus (located at 3, 8, and 13 cm from the midpoint of the sleeve sensor), and the esophageal pressure of 1, 6, and 11 cm above the LES was recorded. At least fifteen wet swallows (5 mL water) were taken, separated by 30-second intervals, but only the last 10 were analyzed. Esophageal motility abnormalities were defined according to previously published criteria, and LES pressure less than 10 mmHg was considered as incompetent LES (24, 25). Ineffective esophageal motility (IEM) was defined as the occurrence of more than 30% hypotensive (< 30 mmHg) or failed contractions of the standard 10 wet swallows (26).

**Ambulatory esophageal pH monitoring**

A catheter containing a mono-crystalline antimony pH electrode was introduced through the nostril into the esophagus and placed 5 cm above the proximal border of the LES, which was manometrically identified. The pH values were recorded with a portable monitor (Digitrapper MK III, Synectics Medical AB, Stockholm, Sweden). Patients received meals as usual, which were recorded during the test
Table 1. Demographics and Endoscopic Findings of Patients in the Three Groups

<table>
<thead>
<tr>
<th></th>
<th>Barrett’s esophagus (n=15)</th>
<th>Esophagitis C/D (n=14)</th>
<th>Esophagitis A/B (n=14)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>64.0 ± 4.3</td>
<td>67.4 ± 3.9</td>
<td>61.5 ± 4.6</td>
<td>0.627</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td>0.876</td>
</tr>
<tr>
<td>Male</td>
<td>12/15 (80.0%)</td>
<td>11/14 (78.6%)</td>
<td>12/14 (85.7%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>3/15 (20.0%)</td>
<td>3/14 (21.4%)</td>
<td>2/14 (14.3%)</td>
<td></td>
</tr>
<tr>
<td>Hiatal hernia</td>
<td>10/15 (66.7%)</td>
<td>10/14 (71.4%)</td>
<td>6/14 (42.9%)</td>
<td>0.251</td>
</tr>
</tbody>
</table>

Results

The demographics and endoscopic findings are shown in Table 1. There were no significant differences among the three groups (BE, severe esophagitis, and mild esophagitis groups) with regard to mean age, gender (male/female ratio), and presence of hiatal hernia.

The data obtained from esophageal manometry are shown in Table 2. The basal pressure of LES (p<0.05) and peristaltic wave amplitude at 1 cm (p<0.05) and 6 cm (p<0.05) proximal to the upper border of the LES in the BE group seemed to be lower than those in the mild esophagitis group. However, the length of the LES, patient percentage of incompetent LES, peristaltic wave amplitude at 13 cm proximal to the upper border of the LES, and patient percentage of IEM were not significantly different between the two groups. In addition, there was no significant difference between the data on esophageal manometry of the BE group and the severe esophagitis group.

The data obtained from esophageal 24-hour pH monitoring are shown in Table 3. The total 24-hour time percentage of pH<4 (p = 0.001), time percentage of pH<4 in upright position (p = 0.002), time percentage of pH<4 in supine position (p = 0.012), time percentage of pH<4 during postprandial 2 hours (p = 0.004), DeMeester score (p = 0.007), number of 24-hour total reflux episodes (p = 0.002), duration of the longest reflux episode (p = 0.020), and the number of reflux episodes longer than 5 minutes (p = 0.030) in the BE group were significantly different than those in the mild esophagitis group. These results indicated that longer and more frequent acid reflux episodes occurred in the BE group. In addition, the total 24-hour time percentage of pH<4 (p<0.001), time percentage of pH<4 in upright position (p = 0.001), time percentage of pH<4 in supine position (p = 0.001), DeMeester score (p = 0.029), number of 24-hour total reflux episodes (p<0.001), and duration of the longest reflux episode (p = 0.001) in the severe esophagitis group were significantly different than those in the mild esophagitis group.
Table 2. Data on Esophageal Manometry of Patients in the Three Groups

<table>
<thead>
<tr>
<th></th>
<th>Barrett’s esophagus (n=15)</th>
<th>Esophagitis C/D (n=14)</th>
<th>Esophagitis A/B (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LES</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal pressure (mmHg)</td>
<td>8.9 ± 2.0*</td>
<td>11.1 ± 2.3</td>
<td>15.5 ± 2.4</td>
</tr>
<tr>
<td>Incompetent LES</td>
<td>10/15 (66.7%)</td>
<td>9/14 (64.3%)</td>
<td>4/14 (28.6%)</td>
</tr>
<tr>
<td>Sphincter length (cm)</td>
<td>2.3 ± 0.1</td>
<td>2.4 ± 0.1</td>
<td>2.4 ± 0.2</td>
</tr>
<tr>
<td>Esophageal body contractions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amplitude 1 (mmHg)</td>
<td>33.3 ± 4.5*</td>
<td>34.6 ± 5.0</td>
<td>51.9 ± 6.6</td>
</tr>
<tr>
<td>Amplitude 6 (mmHg)</td>
<td>33.7 ± 4.9*</td>
<td>36.8 ± 6.1</td>
<td>54.1 ± 6.7</td>
</tr>
<tr>
<td>Amplitude 13 (mmHg)</td>
<td>38.0 ± 3.8</td>
<td>37.1 ± 5.8</td>
<td>48.5 ± 7.2</td>
</tr>
<tr>
<td>Ineffective esophageal motility</td>
<td>7/8 (46.7%)</td>
<td>9/14 (64.3%)</td>
<td>5/14 (35.7%)</td>
</tr>
</tbody>
</table>

* p < 0.05 versus Esophagitis A/B

Abbreviations: LES: lower esophageal sphincter. Amplitude 1, 6, or 11 cm: Pressure of wave amplitude at 1, 6, or 11 cm proximal to upper border of LES.

esophagitis group, but the time percentage of pH<4 during postprandial 2 hours (p = 0.104) and the number of reflux episodes longer than 5 minutes (p = 0.095) were not significantly different. Acid clearance time was not significantly different among these three groups (p = 0.691). In addition, there was no significant difference in the data on esophageal 24-hour pH monitoring between the BE group and the severe esophagitis group.

Discussion

In our clinical practice, we do not often see patients with BE, so collecting a sufficient number of BE cases was the most difficult part of this study. Of the 21 patients with BE in this study (6 patients declined to participate in this study), the mean age was 62.38 ± 4.01 (mean ± standard error) with a range of 29 to 83 years, and there were 17 male patients (male-to-female ratio = 4.25: 1). In addition, hiatal hernia was found in 15 patients (71.4%). These data seem to suggest that older age, male gender, and presentation of hiatal hernia are characteristics found in most cases of BE, and thus are compatible with findings on Caucasians (1).

With regard to the results of the esophageal motility study, the basal pressure of the LES and peristaltic wave amplitude in the distal esophagus in the BE group seemed to be significantly lower than those in the mild esophagitis group, but there was no significant difference between the data of esophageal manometry of the BE group and those of the severe esophagitis group. Incompetent LES and esophageal peristaltic dysfunction can exacerbate gastroesophageal reflux, but neither one seemed to play a key role in subsequent BE formation. These findings were basically compatible with those of previous studies on Caucasians (27, 28).

In general, with regard to the results of pH studies, almost all of the parameters for acid reflux in the BE group and the severe esophagitis group were significantly higher than those in the mild esophagitis group, and these findings were predictable. However, all of the parameters for acid reflux in the BE group were as severe as those in the severe esophagitis group. These results showed significantly longer and more frequent acid reflux in both groups, but they did not explain the causes leading to BE formation. In studies (12, 28, 29) about long- and short-segment BE, long-segment BE seemed to result in more pronounced acid reflux than short-segment BE, but there was no significant difference between long-segment BE and severe esophagitis. On the other hand, Coenraad et al (27) reported a higher number of reflux episodes longer than 5 minutes in the BE group compared to that of the severe esophagitis group. In addition, they reported a lower acid clearance time in the BE group and severe esophagitis group compared to that of the mild-moderate esophagitis group. In the present study,
Table 3. Data of Esophageal 24-hour pH Monitoring of Patients in the Three Groups

<table>
<thead>
<tr>
<th></th>
<th>Barrett’s esophagus (n=15)</th>
<th>Esophagitis C/D (n=14)</th>
<th>Esophagitis A/B (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time pH &lt; 4 (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% total reflux</td>
<td>20.8 ± 4.4**</td>
<td>16.4 ± 2.3**</td>
<td>5.4 ± 1.2</td>
</tr>
<tr>
<td>% upright reflux</td>
<td>20.2 ± 3.6**</td>
<td>16.1 ± 2.2**</td>
<td>6.3 ± 1.2</td>
</tr>
<tr>
<td>% supine reflux</td>
<td>21.3 ± 6.1*</td>
<td>16.2 ± 3.9**</td>
<td>4.0 ± 1.8</td>
</tr>
<tr>
<td>% postprandial</td>
<td>33.5 ± 5.9**</td>
<td>24.7 ± 4.0</td>
<td>10.3 ± 3.0</td>
</tr>
<tr>
<td>DeMeester Score</td>
<td>77.3 ± 15.7**</td>
<td>68.2 ± 11.4*</td>
<td>21.2 ± 4.9</td>
</tr>
<tr>
<td>Reflux episodes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number/24 hr</td>
<td>228.9 ± 40.6**</td>
<td>268.5 ± 72.5**</td>
<td>73.9 ± 13.7</td>
</tr>
<tr>
<td>Longest episode (min)</td>
<td>42.9 ± 11.0*</td>
<td>30.9 ± 6.1**</td>
<td>14.0 ± 4.1</td>
</tr>
<tr>
<td>&gt; 5 Min duration (N)</td>
<td>9.6 ± 2.4*</td>
<td>8.4 ± 1.3</td>
<td>3.1 ± 0.9</td>
</tr>
<tr>
<td>Acid clearance time (min)</td>
<td>1.4 ± 0.2</td>
<td>1.2 ± 0.1</td>
<td>1.0 ± 0.1</td>
</tr>
</tbody>
</table>

* p < 0.05 versus Esophagitis A/B
** p < 0.01 versus Esophagitis A/B

Definition: Acid clearance time: duration (minutes) of esophageal pH <4 / number of reflux episodes.

the acid clearance time was not significantly different among the three groups. We believe these differences are minor, and they cannot alter the conclusion that acid reflux in severe reflux esophagitis can be as severe as that in BE.

Numerous studies have reported that BE is related to GERD, but BE usually only develops in a small number of patients with GERD. Pronounced gastroesophageal acid reflux might play a central role in BE development, and this theory is supported by previous studies (30, 31). Bile reflux may also contribute to the formation of Barrett’s esophagus (29, 30), although bile reflux was not analyzed in this study due to limited facilities in our hospital. However, in several other studies (27-29), there were no significant differences in the pathophysiological characteristics of gastroesophageal reflux between patients with BE and patients with severe esophagitis, and these results did not help to clarify the etiology of BE. Gene expression studies have contributed to an understanding of the process of metaplasia that leads to BE, and exposure to acid and bile might activate some gene expression (32, 33). However, it is still not clear whether ethnic differences alter the pathophysiological presentation. Our data on esophageal manometry and 24-hour pH monitoring of the BE and severe esophagitis groups were not significantly different. In a study by Hirota et al (34), the average duration of GERD symptoms in patients with long-segment BE was as long as 20 years. Although duration of GERD symptoms does not predict the occurrence of BE, it is an important risk factor for BE. Chronic GERD with acid, bile acids, pepsin reflux, and possibly other complicating causes such as different gene expression, social and environmental factors contribute to the formation of BE.

GERD has been traditionally considered less common in Asia, and BE is still infrequently reported in Taiwan even though the prevalence of reflux esophagitis is increasing (14-20). Less awareness and less powerful diagnostic tools might cause underestimation of BE. The presence of intestinal metaplasia within the esophagus is often intermittent, and it is easy to miss during standard endoscopy with random biopsy examinations. However, some new diagnostic tools such as narrow band imaging, chromoendoscopy, and magnification endoscopy may improve the detection rate of BE (35-37). Although these tools have only recently been
adopted in clinical practice, we expect that they will make the diagnosis of BE easier.

In conclusion, we found that the clinical characteristics of patients with BE in our study were essentially similar to those in studies on Caucasians: older age, male gender predominance, and high percentage of hiatal hernia. Our findings were also similar to those of studies on Caucasians showing significantly stronger acid reflux, lower LES pressure, and weaker distal esophageal peristalsis in BE compared to LA grade A/B (mild) esophagitis. BE and severe reflux esophagitis share common pathophysiological characteristics among the Chinese in Taiwan.

Acknowledgement

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References

associated adenocarcinoma cell lines after acid or bile salt exposure. BMC Gastroenterol 7: 24, 2007.


