Endoscopic Diagnosis of Barrett esophagus and Barrett adenocarcinoma

Jun Haeng Lee
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Endoscopic diagnosis of GERD

- Mucosal Break
  - No
    - Non-erosive disease
      - Normal
      - Minimal change
  - Yes
    - Erosive esophagitis
      - A
      - B
      - C
      - D

Additional findings: Barrett esophagus, Stenosis, Ulcer, Bleeding, Sentinel fold
Definition of Barrett esophagus

1. Squamocolumnar junction displaced proximal to EG junction
2. Intestinal metaplasia
3. Alcian blue pH 2.5 positive
4. Goblet cells

Gastroenterology 2002;122:1569
To identify the distal extent of the BE, the most proximal end of stomach should be identified.

- It’s very important for (ultra)short segment Barrett’s esophagus.
Endoscopic EG junction?
Endoscopic anatomy of EGJ

Esophagogastric junction (EGJ) = Proximal margin of gastric folds = Distal end of palisade zone = Pinchcock action (PCA) = Squamocolumnar junction
Western view on EG junction

- Several linear gastric folds normally may be seen in the cardia. These folds terminate at the level of the normal location of the SCJ.
- The cephalad margins of these longitudinal gastric folds provide the best landmark for the EGJ (= muscular junction between esophagus and stomach) and as a marker for the normal location of the SCJ.
- These relationships to the EGJ can be demonstrated on surgical and autopsy specimens as well.
Hiatal hernia and determination of the EG junction

Ampulla

A-ring = muscular ring

Esophago-gastric junction

B-ring = mucosal ring

Diaphragm
Venous anatomy of distal esophagus
BE based on palisading zone

Normal  Barrett esophagus  Hiatal hernia  Hiatal hernia + BE

Choi DW. Korean J Gastroenterol 2002;17:245-248
Short-segment CLE with hiatal hernia

Hiatal opening

EG junction based on vascular pattern

Hernia sac

Squamocolumnar junction

ESEM
Is Biopsy Necessary for the Diagnosis of Barrett’s?
Recommended report form
- at least 2 biopsies

1) Columnar epithelium without intestinal metaplasia

2) Columnar epithelium with intestinal metaplasia, consistent with Barrett’s esophagus

2006. GI pathology study group, Korea
Diagnosis of Barrett’s esophagus

= ESEM + histological evidence of columnar metaplasia with goblet cells
Two key recommendations in the new BGS guideline for Barrett’s oesophagus

• BO is defined as an endoscopically apparent area above the oesophago-gastric junction that is suggestive of Barrett’s which is supported by the finding of columnar lined oesophagus on histology. The presence of areas of intestinal metaplasia (IM), although often present, is NOT a requirement for diagnosis.

• For patients with BO but without dysplasia, the recommended surveillance protocols are two yearly, for quadrant biopsies every 2 cm, but jumbo biopsies are NOT required.
理想: Seattle protocol

- Starting from the proximal margin of the gastric fold
- Four-quadrant biopsy
- 2 cm interval
- HGD: 1 cm interval
現實: How many biopsies would you take for this long segment Barrett’s esophagus?

Figure 6. Korean endoscopists’ opinion about the number of biopsies for an initially suspected long segment Barrett’s esophagus. Nearly 50% of responders answered that they would take three or four pieces of tissue, 12.1% would obtain one or two pieces, and 16.5% would take no biopsy. 

Endoscopic Findings of BE

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## Prevalence of BE in Asia

<table>
<thead>
<tr>
<th>Authors</th>
<th>Group</th>
<th>N-number</th>
<th>Prevalence of Barrett’s (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caygill (1999)</td>
<td>Europeans</td>
<td>44,721</td>
<td>1.6</td>
</tr>
<tr>
<td>Hirota (1999)</td>
<td>Americans</td>
<td>889</td>
<td>1.6</td>
</tr>
<tr>
<td>Cadour (1999)</td>
<td>Saud Arabians</td>
<td>2,572</td>
<td>0.31</td>
</tr>
<tr>
<td>Azuma (2000)</td>
<td>Japanese</td>
<td>650</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Park (2003)</strong></td>
<td>Koreans</td>
<td>1,553</td>
<td><strong>0.32</strong></td>
</tr>
</tbody>
</table>

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Park  HJ. J Gastroenterol 2003;38:23-27
## Risk factors of Barrett’s esophagus

- 992 consecutive patients in 4 university hospitals

<table>
<thead>
<tr>
<th></th>
<th>BE</th>
<th>Non-BE</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M:F)</td>
<td>24:12</td>
<td>499:457</td>
<td>0.12</td>
</tr>
<tr>
<td>Age</td>
<td>51.1</td>
<td>45.5</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>22.8</td>
<td>22.6</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>13 (36%)</td>
<td>318 (33.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Alcohol</td>
<td>18 (50%)</td>
<td>336 (35.1%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Reflux symptoms</td>
<td>7 (19%)</td>
<td>157 (16.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>Reflux esophagitis</td>
<td>9 (25%)</td>
<td>82 (8.6%)</td>
<td>0.00</td>
</tr>
<tr>
<td>hernia ≥ 2cm</td>
<td>8 (22%)</td>
<td>85 (8.9%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Kim JY. J Gastroenterol Hepatol 2005;20:633-636
**Prevalence and risk factors of Barrett’s esophagus in SMC**

Jeong Hwan Kim, Poong-Lyul Rhee, Jun Haeng Lee, Hyuk Lee, Yong Sung Choi, Hee Jung Son, Jae J Kim and Jong Chul Rhee

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**Key words**
Barrett’s esophagus, columnar-lined esophagus, prevalence, risk factors, specialized intestinal metaplasia.

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**Abstract**

**Background and Aim:** Barrett’s esophagus (BE) is diagnosed when specialized intestinal metaplasia (SIM) is detected histologically in endoscopically suspected columnar-lined esophagus (CLE). It is a premalignant condition and plays a pivotal role in the development of esophageal adenocarcinoma. It has traditionally been believed to affect Asians less frequently. The aim of this study was to determine the prevalence of BE and possible associated risk factors in Korea.

**Methods:** A retrospective analysis of 70103 patients who had undergone their first upper endoscopies was performed using computerized medical records. Of these, 696 (1%) patients had suspected CLE. After screening by telephone, 480 were enrolled. The clinical and endoscopic characteristics of histologically identifiable BE and endoscopically suspected CLE not confirmed by biopsy (suspected CLE without SIM) were investigated.

**Results:** Barrett’s esophagus was present in 151 patients (0.22%) with a mean age of 53.8 ± 10.9 years. BE was more commonly found in men. BE was associated with a set of features distinct from suspected CLE without SIM; older age, greater predominance of male sex, more frequent smoking history, and more frequent acid regurgitation symptom.

**Conclusions:** Barrett’s esophagus remains less common in Korea than in Western countries. Old age, male sex, smoking, and acid regurgitation symptom were significant risk factors.
Prevalence of BE in SMC

EGD 70,103

Suspected CLE 696

CLE, SIM (-) 545

BE, SIM (+) 151 (0.22%)

No CLE 69,407

Kim JH. J Gastroenterol Hepatol 2007;22:908-912
Changing prevalence of upper gastrointestinal disease in 28 893 Koreans from 1995 to 2005
Jin Il Kim\textsuperscript{a}, Sang Gyun Kim\textsuperscript{b}, Nayoung Kim\textsuperscript{b}, Jae Gyu Kim\textsuperscript{c}, Sung Jae Shin\textsuperscript{d}

Prevalence of Barrett’s esophagus

P=0.031

Barrett’s esophagus
Barrett’s esophagus
Length of Barrett esophagus

- **M**: maximum length
- **C**: circumference length
- 표기 예: C3M5

Sharma. Gastroenterology 2006;131:1392-1399
Short segment Barrett esophagus
Tongue-like projection in BE
New imaging techniques

- Additional merit of advanced techniques needs further confirmation.

### Table 1. Advanced Imaging Techniques for Barrett’s Esophagus.

<table>
<thead>
<tr>
<th>Technique</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-resolution, white-light endoscopy</td>
<td>Uses a charge-coupled device with up to 1 million pixels and high-resolution components</td>
<td>Becoming the default standard, given improvements in the quality, clarity, and resolution of white-light imaging</td>
</tr>
<tr>
<td>Magnification endoscopy</td>
<td>Uses optical magnification (up to x70–100) to visualize subtle mucosal patterns and lesions within the Barrett's segment</td>
<td>Evaluated in case series; not directly compared with standard endoscopy and tedious to use, since it allows visualization of very focal areas</td>
</tr>
<tr>
<td>Chromoendoscopy</td>
<td>Sprays various stains (e.g., methylene blue, indigo carmine), over the esophageal mucosa to accentuate the contrast between the metaplastic and nonmetaplastic epithelium</td>
<td>Has been tested in randomized, controlled trials with varying results; relatively inexpensive to use; challenges include variability in use of stains and spray catheter, and lack of standardization of technique</td>
</tr>
<tr>
<td>Narrow-band imaging (electronic chromoendoscopy)</td>
<td>Uses spectral narrow-band optical filters with predominance of blue light rather than the complete white-light spectrum; this highlights mucosal and vascular patterns indicative of neoplastic tissue</td>
<td>Relatively easy to use and tested in randomized, controlled trials showing yield that is similar to that of routine biopsies; difficulty with pattern recognition and learning curve</td>
</tr>
<tr>
<td>Autofluorescence imaging</td>
<td>Detects change in fluorescence from alteration in the content of cellular molecules such as NADPH and collagen, with neoplastic tissue showing differential fluorescence (color)</td>
<td>Allows broad-based imaging; high false positive rates, subjective color interpretation, and lack of commercial availability</td>
</tr>
<tr>
<td>Confocal microscopy</td>
<td>Uses a single plane of focus with laser microscopes, allowing for real-time viewing of cellular details</td>
<td>High-quality and detailed imaging of Barrett’s glands and cells; challenges include imaging of very focal areas, intravenous fluorescence agent, and image interpretation</td>
</tr>
</tbody>
</table>
OCT findings of BE

- Absence of the layered structure of normal squamous epithelium and the vertical “pit and crypt” morphology of gastric mucosa
- Disorganized architecture with inhomogeneous tissue contrast and an irregular mucosal surface
- Presence of submucosal glands
- A trend toward more irregular glandularity with increasing degrees of dysplasia.

Chak (Cleveland U). Endoscopy 2005;37:587-590
Early Barrett’s Cancer

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Esophageal adenocarcinoma
- Age-specific incidence in the USA (1977-1996)
Esophageal cancer in the US

Fig. 2. Histology and esophageal cancer incidence (1975–2001). Data from the National Cancer Institute’s Surveillance, Epidemiology, and End Results program with age-adjustment using the 2000 U.S. standard population. **Solid black line** = adenocarcinoma; **dashed line** = squamous cell carcinoma; **dotted line** = not otherwise specified.
A Single Center's 30 Years' Experience of Esophageal Adenocarcinoma

Juk Son, M.D., Hyo Jin Park, M.D., Kee Sup Song, M.D., Ki Joong Kim, M.D., Chang Youl Lee, M.D., Sang In Lee, M.D. and In Suh Park, M.D.

Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Background: Adenocarcinoma of the esophagus has been reported to be increasing in incidence in a number of regions throughout the world, while the incidence of squamous cell carcinoma (SCCA) of the esophagus is mostly stable or decreasing. To evaluate the increasing tendency of adenocarcinoma of the esophagus.

Methods: We studied retrospectively the records of patients with histologically proven esophageal cancer between 1970 and 1999 at the Yonsei Medical Center.

Results: Total cases of esophageal cancer were 969 patients of which the cases of adenocarcinoma and SCCA were 27 patients and 918 patients, respectively. The ratio of esophageal adenocarcinoma to SCCA was 0.0375 in the 1970s, 0.0241 in the 1980s and 0.0292 in the 1990s. There was no statistical difference (p=0.811) in the ratios of adenocarcinoma of the esophagus between the three consecutive 10-year groups.

Conclusion: In conclusion, unlike the US and other western countries, it seems that the ratio of esophageal adenocarcinoma compared to SCCA has not increased among patients with esophageal carcinoma at the Yonsei Medical Center.

Key Words: esophageal adenocarcinoma, squamous cell carcinoma
Esophageal adenocarcinoma in Korea
- a single center experience

<table>
<thead>
<tr>
<th></th>
<th>Adenocarcinoma</th>
<th>SCCA*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>3 (3.75%)</td>
<td>77 (96.25%)</td>
</tr>
<tr>
<td>Group 2</td>
<td>6 (2.41%)</td>
<td>243 (97.59%)</td>
</tr>
<tr>
<td>Group 3</td>
<td>18 (2.92%)</td>
<td>598 (97.08%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>27</strong></td>
<td><strong>918</strong></td>
</tr>
</tbody>
</table>

$p = 0.811$

SCCA*, squamous cell carcinoma
Siewart type I adenocarcinoma is not increasing in Japan (NCC, Tokyo hospital)

**Figure 2**  Trend in type of esophagogastric junction (EGJ) adenocarcinoma according to Siewert’s classification. (▲), Siewert Type 1; (○), Siewert Type 2; (■) Siewert Type 3.
Clinicopathologic Characteristics of Barrett’s Cancer in Korea

Jun-Won Chung*, Gin Hyug Lee*, Hwoon-Yong Jung*, Kee Don Choi*, Ho June Song*, Kwi-Sook Choi*, Hyung Chul Oh*, Kee Wook Jung*, Jae Won Choe†, Jeong Won Kim†, Eunsil Yu†, and Jin-Ho Kim*

Departments of *Internal Medicine, †Health Medicine and ‡Pathology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea

Fig. 1. Endoscopy images of surgically treated Barrett’s cancer. (A) A type 0-IIa hyperemic elevated lesion on the right side. (B) A type 0-IIc+IIa rectangular lesion that developed from the short-segment Barrett’s esophagus, accompanied by reflux esophagitis (arrowhead). A whitish squamous island was also evident (arrow). (C) A round hyperemic 0-IIb lesion similar to deep erosion.
Fig. 2. Case of mucosal Barrett’s cancer treated by endoscopic submucosal dissection. (A) A hyperemic depressed lesion above the esophagogastric junction. A whitish squamous island was evident in the middle of the Barrett’s cancer (arrow). (B) Histopathologic view of the endoscopically resected specimen. The esophageal gland (arrow) was evident under the Barrett’s cancer (H&E stain, ×40). (C) Dysplastic epithelial cells mixed with glands containing sparse goblet cells (H&E stain, ×400).
Fig. 3. Type 0-IIa Barrett’s cancer invading the mucosa that was treated by endoscopic submucosal dissection. (A) Hyperemic elevated lesion above the esophagogastric junction. (B) Histopathologic view of the endoscopically resected specimen. The esophageal gland (arrow) was evident under the columnar lined esophagus (H&E stain, ×40).

Fig. 4. Type 0-I+IIb Barrett’s cancer invading the mucosa that was treated by endoscopic submucosal dissection. (A) A hyperemic polypoid lesion with exudates just above the esophagogastric junction. (B) Image obtained after endoscopic submucosal resection. A protruding lesion (arrow) was detected around Barrett’s epithelium, which had an irregular fine mucosal pattern. (C) Histopathologic view of the endoscopically resected specimen. The esophageal gland (arrow) was evident beneath the disrupted squamous epithelium (H&E stain, ×100).
The Clinical Characteristics and Outcomes of Barrett’s Cancer at a Single Institution in Korea

Sang-Jung Kim, M.D., Jun Haeng Lee, M.D., Beom Jin Kim, M.D., Poong-Lyul Rhee, M.D., Jae J. Kim, M.D., Jong Chul Rhee, M.D., Kyoung Mee Kim, M.D.* and Yong Mog Shim, M.D.†

Departments of Medicine *Pathology and †Thoracic Surgery, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea

Table 1. Summary of 11 Patients with Barrett’s Cancer

<table>
<thead>
<tr>
<th>Sex/Age</th>
<th>Presenting symptom</th>
<th>BMI (kg/m²)</th>
<th>Smoking</th>
<th>Tumor location</th>
<th>Gross type</th>
<th>Type of operation</th>
<th>Size (cm)</th>
<th>Dep.</th>
<th>LNM</th>
<th>Stage</th>
<th>FU (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/55</td>
<td>Dysphagia</td>
<td>23.9</td>
<td>Yes</td>
<td>35 cm from UI</td>
<td>I</td>
<td>Transhphagectomy</td>
<td>2.1</td>
<td>SM</td>
<td>0/20</td>
<td>I</td>
<td>8</td>
</tr>
<tr>
<td>M/64</td>
<td>Epigastric pain</td>
<td>24.8</td>
<td>Yes</td>
<td>34 cm from UI</td>
<td>IIb</td>
<td>Transphagectomy</td>
<td>1.5</td>
<td>IM</td>
<td>0/15</td>
<td>I</td>
<td>5</td>
</tr>
<tr>
<td>M/76</td>
<td>Epigastric pain</td>
<td>21.4</td>
<td>No</td>
<td>40 cm from UI</td>
<td>IIb+IIc+IIa</td>
<td>Transphagectomy</td>
<td>7.2</td>
<td>IM</td>
<td>0/8</td>
<td>I</td>
<td>2</td>
</tr>
<tr>
<td>M/64</td>
<td>Weight loss</td>
<td>23.9</td>
<td>Yes</td>
<td>35 cm from UI</td>
<td>IIa+IIc</td>
<td>Transphagectomy</td>
<td>3.5</td>
<td>SM</td>
<td>0/60</td>
<td>I</td>
<td>4</td>
</tr>
<tr>
<td>M/56</td>
<td>Epigastric pain</td>
<td>21.7</td>
<td>Yes</td>
<td>Cardia</td>
<td>IIb+IIc</td>
<td>Total gastrectomy</td>
<td>1.2</td>
<td>SM</td>
<td>0/39</td>
<td>I</td>
<td>4</td>
</tr>
<tr>
<td>F/54</td>
<td>Acid reflux symptoms</td>
<td>25.4</td>
<td>No</td>
<td>40 cm from UI</td>
<td>IIb</td>
<td>Total gastrectomy</td>
<td>0.4</td>
<td>IM</td>
<td>0/21</td>
<td>I</td>
<td>3</td>
</tr>
<tr>
<td>M/67</td>
<td>None</td>
<td>21.7</td>
<td>No</td>
<td>40 cm from UI</td>
<td>IIb+IIc</td>
<td>Proximal gostrectomy</td>
<td>0.9</td>
<td>SM</td>
<td>0/5</td>
<td>I</td>
<td>2</td>
</tr>
<tr>
<td>M/38</td>
<td>Acid reflux symptoms</td>
<td>29.9</td>
<td>Yes</td>
<td>30 cm from UI</td>
<td>IIa</td>
<td>Transphagectomy</td>
<td>2.2</td>
<td>SM</td>
<td>1/32</td>
<td>IIB</td>
<td>2</td>
</tr>
<tr>
<td>M/36</td>
<td>None</td>
<td>20.7</td>
<td>No</td>
<td>40 cm from UI</td>
<td>IIa</td>
<td>Total gastrectomy</td>
<td>0.8</td>
<td>IM</td>
<td>0/22</td>
<td>I</td>
<td>0</td>
</tr>
<tr>
<td>M/72</td>
<td>Indigestion</td>
<td>16.3</td>
<td>No</td>
<td>40 cm from UI</td>
<td>IIa</td>
<td>Total gastrectomy</td>
<td>0.4</td>
<td>IM</td>
<td>0/36</td>
<td>I</td>
<td>0</td>
</tr>
<tr>
<td>M/68</td>
<td>None</td>
<td>21.0</td>
<td>No</td>
<td>38 cm from UI</td>
<td>IIa</td>
<td>Endoscopic submucosal dissection</td>
<td>0.5</td>
<td>IM</td>
<td>-</td>
<td>I</td>
<td>0</td>
</tr>
</tbody>
</table>

BMI, body mass index; UI, upper incisor; Dep., depth of invasion; IM, intramucosal; SM, submucosal; LNM, lymph node metastasis; -, no lymph node dissection; FU, follow-up.
Endoscopically defined esophagogastric juction = proximal margin of gastric folds

Upward deviated squamocolumnar juction

Cancer
Barrett adenocarcinoma
- Histologically confirmed true Barrett esophagus
Tongue-like projection (very short)

Elevated lesion with top erosion

Endoscopically defined SCJ
Distribution of dysplasia and cancer in resection specimens

- Barrett’s, no dysplasia
- Low-grade dysplasia
- High-grade dysplasia
- Cancer

Cameron. Am J Gastroenterol 1997;92:586-91
Barrett cancer at SMC

The number of patients who diagnosed first on SMC

Year at diagnosis
Barrett adenocarcinoma (F/71)
- additional case after the report
Barrett adenocarcinoma (SMC #15)
- the only one case in 2011
Where are we now?

Squamous cell carcinoma, esophagus

Adenocarcinoma, esophagus
Take home message

- Endoscopic determination of EG junction is the most important factor for the accurate diagnosis of Barrett’s esophagus.
- Histological confirmation of goblet cell metaplasia is necessary in 2012 in Korea.
- The epidemiology of Barrett’s adenocarcinoma should be carefully monitored.
Thank you for your attention.