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Utility of Endoscopy for Diagnosis of Barrett in a Non-Western Society: Endoscopic and Histopathologic Correlation

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Barrett esophagus is metaplastic transformation of esophageal squamous epithelium to columnar cells. A total of 1370 patients who had undergone upper endoscopy because of dyspeptic complaints were enrolled in the study. Age, sex, alcohol and smoking habits, body mass index, type and duration of symptoms (heartburn, epigastric pain, nausea, vomiting), and use of proton pump inhibitors were evaluated in all patients and recorded on standardized forms. Patients were grouped as normal esophagogastric junction, long-segment Barrett esophagus, and short-segment Barrett. Biopsies were taken from at least 6 points and examined histopathologically. Of the 1370 patients involved in the study, 748 (54.6%) were female and 622 (45.4%) were male. Mean age was 47.2 ± 15.30 years. Short-segment Barrett esophagus was detected in 16 patients, and long-segment Barrett was detected in 11 patients. Although Barrett esophagus was detected in 11 cases that were suspected to have Barrett during endoscopy, histopathology was negative in all cases that were not suspected to have Barrett. Barrett esophagus prevalence was significantly higher in people who used alcohol and tobacco and who had hiatal hernia. Although Barrett esophagus was detected in 40% of cases that were suspected to have Barrett during endoscopy, histopathology was negative in all cases that were not suspected to have Barrett. Barrett was detected in 40.7% of cases that were suspected to have Barrett during endoscopy; histopathology was negative in all cases that were not suspected to have Barrett. Senstivity of endoscopy is questionable in detection of short-segment Barrett.

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Barrett esophagus (BE) is the metaplastic transformation of esophageal squamous epithelium into columnar cells.[1] This histologic alteration is an important complication of gastroesophageal reflux disease (GERD), and it sets the groundwork for adenocarcinoma.[2,3] Diagnosis is made by showing goblet cells and intestinal metaplasia in biopsy specimens taken from the lesions directly seen under endoscopy (Fig. 1).[4] It has an increasing incidence not only in the United States, New Zealand, and Australia, but also in the rest of the developed world.[5,6] Although there are conflicts about the prevalence of BE, reports have demonstrated 1.2% to 25% positivity of BE in endoscopy of asymptomatic patients,[7,8] and 8% to 20% positivity in patients who have GER symptoms.[9] Factors such as hiatal hernia, obesity, and *Helicobacter pylori* (HP) are responsible for BE because they provoke acid reflux.[10] Recently, BE incidence rates raised after the definition of short-segment BE was introduced.

The aim of this study was to compare endoscopic and histopathologic findings in patients who presented with dyspeptic complaints and had upper endoscopy.

Materials and Methods

A total of 1370 patients who had endoscopy for dyspeptic symptoms between February 2011 and March 2013 were enrolled in the study. Those who had gastric carcinoma, gastrointestinal bleeding during endoscopy, and coagulopathy disorder were excluded from the study. Age, sex, alcohol and smoking habits, heartburn, nausea, vomiting, use of proton pump inhibitors, and duration of symptoms were questioned and recorded on standard forms. Smoking more than 10 cigarettes a day was accepted as habitual smoking.[11] Alcohol abuse was identified according to the *Diagnostic and Statistical Manual of Mental Disorders 5*. Endoscopic examinations were carried out by gastroenterologists or certificated gastrointestinal surgeons using a standard endoscope (Fujinon EPX-4400, System WR, Fujifilm Turkey, Saitama, Japan) under sedation. During the course of endoscopy, esophagogastric junction (EGJ) was examined carefully. Squamocolumnar junction was defined as the line where squamous epithelium turns into salmon-colored columnar mucosa (Fig. 1). Patients were classified as normal EGJ, long-segment BE (intestinal metaplasia $\geq$3 cm beginning from EGJ), or short-segment BE (SSBE; intestinal metaplasia $<$3 cm beginning from EGJ; Fig. 2).[12–14] The presence of more than 2 cm of distance between EGJ and diaphragmatic notch was accepted as hiatal hernia. When normal EGJ was detected, at least 6 biopsies from different sites were taken and examined histopathologically. Of these 6 biopsies, 4 were taken from the squamocolumnar junction and 2 were taken from the gastric antrum. In BE suspected cases, extra biopsies were taken from all possible quadrants and columnar epithelium sites 1 cm distant from each other. All biopsy materials were stored in 10% formalin solution and stained with hematoxylin-eosin and Alcian Blue (Fig. 2). Pathology specimens were reviewed by senior pathologists.

All patients were notified about the procedures by physicians, and informed consent was taken. Patient data were analyzed using SPSS 15.0 (SPSS Inc, Chicago, Illinois). Student *t*-test and χ^2 tests were used where appropriate. $P < 0.05$ was accepted as statistically significant.

Results

Of the 1370 patients involved in the study 748 (54.6%) were female and 622 (45.4%) were male. Mean age was 47.2 $\pm$ 15.30 years. The demographic and clinical characteristics of patients are shown on Table 1. Alcohol use and smoking were significantly higher in male patients. A total of 19.2% of female and 22.6% of male patients were using proton pump inhibitors, and it was not statistically significant (Table 1). Female patients had more complaints of nausea, vomiting, and heartburn. Durations of symptoms were similar in both sexes. HP was positive in 64.8% of patients who had undergone endoscopy, and no significant difference was found between sexes. Endoscopic findings of patients using the classification described elsewhere[15] are listed in Table 2. A total of 27 patients had endoscopically diagnosed BE. Of these, 16 were reported as SSBE and 11 were reported as long-segment BE. Esophagitis was detected in 131 patients, of which 44 (33.5%) were female and 87 (66.5%) were male. The high rate of

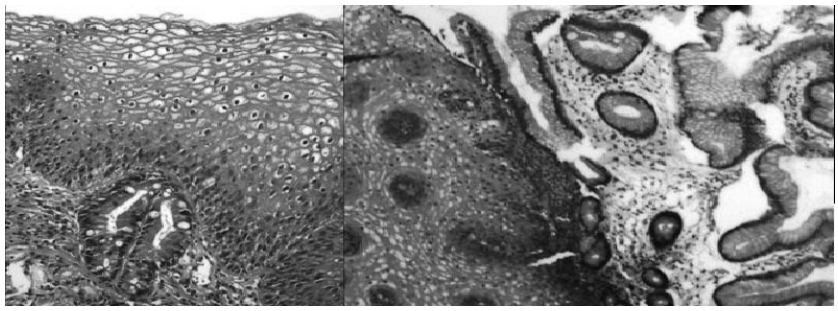

Fig. 1 Histopathology showing specialized intestinal metaplasia with glandular epithelium and characteristic goblet cells. Hematoxylin-eosin [×50 (left panel), ×100 (right panel)].

esophagitis in male patients was statistically significant ($P < 0.05$). Of the 11 patients (40.7%) with histopathologically diagnosed Barrett, 3 were female and 8 were male. There was not a statistically significant difference between sexes. Hiatal hernia was detected in 7 of 11 patients who were histopathologically identified as Barrett, and this was statistically significant ($P < 0.05$). Gastrointestinal symptoms, such as nausea, vomiting, and heartburn, were significantly higher in female sex. Alcohol use and smoking were more frequent among males and it was statistically significant ($P < 0.05$). Durations of symptoms were 46.1 ± 27.0 months in patients with histopathologically proven BE and 41.2 ± 27.8 months in patients who do not have BE, but the difference was not statistically significant. There was no statistically significant difference between sex groups on duration of symptoms (44.7 ± 27.7 months in female patients and 43.2 ± 27.2 months in male patients). When patients were grouped according to body mass index, 15 were underweight (1.1%), 434 (31.6%) were normal weight, 587 (42.9%) were overweight, and 334 (24.4%) were obese. Obesity frequency in our study population was similar to that of the Turkish population.[16] There was not a statistically significant association between body mass index and BE ($P > 0.05$).

Discussion

Barrett metaplasia is accepted as a precancerous lesion in the development of esophageal adenocarcinoma. In our study BE prevalence in dyspeptic patients who had endoscopy was found as 1.97% endoscopically and 0.8% histologically. Studies carried out in different countries have reached different results. A German study has found BE prevalence as 4.2%, and another study made in Japan reported this prevalence as 0.3% to 0.6%.[17] In studies conducted with Turkish patients, histopathologic BE prevalence has been found to be 1.7% and 7.4%.[15,18] In our study, most of the 11 patients with pathologically diagnosed BE were male, and the mean age was 46 years. These results are similar to the findings of other series in medical literature.[19,20]

SSBE could easily be missed when not carefully looked for during endoscopy, and biopsy could easily be taken from the wrong location. In a study by Padda and Ramirez,[21] histopathologic confirmation rates of SSBE and long-segment BE were 38% and 75%, respectively. As with Padda and Ramirez, in our study, only 36% of patients with a diagnosis of having SSBE during endoscopy had histopathologically confirmed BE, whereas most of the patients who were categorized as long-segment BE during endoscopy had histologic BE.

Hiatal hernia is an important factor in the development of GER, which is frequent in patients with BE. In a study by Cameron,[22] hiatal hernia was seen in 96% of patients with BE. In addition, hernia sac was longer and wider in patients with BE.[22] In our study, hiatal hernia was found in 7 of 11 patients (63.3%) who had histopathologically proven BE.

There are controversies regarding the correlation of esophagitis and BE.[23,24] There was no statistical-

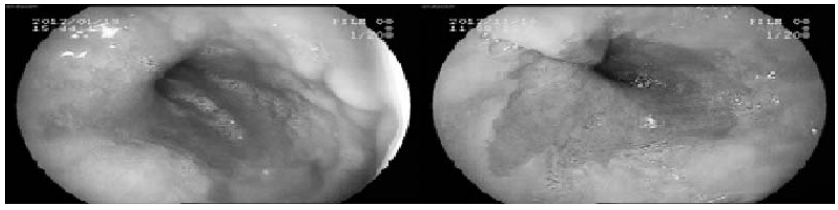

Fig. 2 Salmon-colored columnar mucosa.

Table 1 Demographic and clinical features

Characteristic	Male (n = 622)	Female (n = 748)	Total (n = 1370)
Age, y, mean ± SD (%)	46.4 ± 15.1 (24–90)	47.8 ± 15.4 (23–87)	47.2
Smoking, no. (%)*	237 (38.1)	162 (21.6)	399 (29.1)
Alcohol abuse, no. (%)*	122 (19.6)	13 (1.7)	135 (9.8)
Epigastric pain, no. (%)	219 (35.2)	288 (38.5)	507 (36.7)
Nausea, no. (%)*	154 (24.7)	360 (48.1)	514 (37.5)
Vomiting, no. (%)*	31 (4.9)	103 (13.7)	134 (9.7)
Heartburn, no. (%)*	67 (10.7)	113 (15.1)	180 (13.1)
HP positivity, no. (%)	392 (63)	486 (64.9)	878 (64)
Medical treatment, no. (%)	141 (22.6)	144 (19.2)	285 (20.8)
Duration of symptoms, mo, mean ± SD	44.7 ± 27.7	43.2 ± 27.2	43.9

*$P < 0.05$.

ly significant difference in esophagitis rates of patients who had BE and who did not have BE in our study. In addition, no relationship was found among dyspeptic symptoms (*e.g.*, nausea, vomiting, heartburn) or duration of symptoms and BE in our study. In studies carried out by Spechler *et al*[24] and Nandurkar *et al*,[25] a relation between SSBE and GER was not found. On the contrary, studies by Johnston *et al*[23] Pereira *et al*[26] showed a significant relation between SSBE and GER. Although we did not find a relation between the presence of esophagitis and BE, nonerosive GER disease that cannot be detected during endoscopic examination may be an important factor in the development of BE.

The relationship between HP infection and BE has not been fully identfied yet. Moreover, some authors argue that HP infection is an inhibitor of BE development by reducing acid secretion.[27] On the contrary, no relation between HP infection and BE was found in several studies.[28,29] In a such a high-prevalence area as Turkey, it may be difficult to document a relationship between HP infection and BE. In fact, no significant association was found between HP infection and BE in our study.

Table 2 Classification of cases that were diagnosed as Barrett with endoscopy

Endoscopic appearance	Male (n)	Female (n)	Total (n)
Short segment Barrett's			
A	1	1	2
B	5	4	9
C	1	2	3
D	1	0	1
E	1	0	1
Long segment Barrett's	6	5	11
Total (n)	15	12	27

A, Barrett appearance on squamocolumnar junction; B, tonguelike Barrett appearance; C, isletlike Barrett appearance; D, tonguelike Barrett appearance and irregularity on squamocolumnar junction; and E, isletlike Barrett appearance and irregularity on squamocolumnar junction.

There are studies reporting that alcohol use provokes GER and thus indirectly reduces BE, but on the other hand there are studies showing no relation between the two.[30,31] Although some previous studies have shown inverse correlation with wine use[32,33] but positive correlation with liquor use[34] and BE development, some authors have argued that alcohol itself, not the type of the different drinks, was directly related to GERD.[35] Our study found a significant relationship between BE and alcohol abuse and tobacco use, and demonstrates that BE development increases with alcohol abuse and smoking. Further studies are needed to show the mechanisms and results of risks between foods and drinks and BE.

There are certain reports indicating that there exists a discordance between clinical and pathologic diagnosis of BE among endoscopists in different countries.[36] Some authors suggest that the definition of BE should actually be columnar lined esophagus. These further justify the aim of our study.

Conclusion

Patients with dyspeptic or GERD complaints are candidates for BE screening. It is important to raise awareness about SSBE, although it may yield overdiagnosis of SSBE, which may be another problem for beginners in endoscopy. Although BE was detected 40.7% of cases that were suspected to have BE during endoscopy, histopathology was negative in all cases that were not suspected to have BE, thus proving the importance of a careful endoscopic evaluation. Our study points out the fact that senstivity of endoscopy is questionable in detection of SSBE.

Table 3 Comparison of clinical and endoscopic features of patients with and without histopathologic Barrett diagnosis

Characteristic	Pathologic Barrett	No pathologic Barrett
Age, y, mean ± SD (%)	48.6 ± 14.8 (20–71)	47.1 ± 15.3 (23–90)
Female/male, no.	3/8	745/614
Smoking, no. (%)*	9 (81)	390 (29)
Alcohol abuse, no. (%)*	8 (72)	127 (9)
Heartburn, no. (%)	1 (9)	179 (13)
Nausea, no. (%)	4 (36)	510 (36)
Vomiting, no. (%)	0	134 (10)
Epigastric pain, no. (%)	5 (45)	502 (37)
Duration of symptoms, mo, mean ± SD	46.1 ± 27.0	41.2 ± 27.8
Hiatal hernia, no. (%)*	7 (64)	161 (12)
HP positivity, no. (%)	7 (64)	871 (64)
Endoscopic esophagitis, no. (%)	1 (9)	130 (10)
Endoscopic Barrett, no. (%)*	11 (40.7)	16 (59.2)
Endoscopic LES floppiness, no. (%)	0	30 (2)

LES, lower esophageal sphincter.
*$P < 0.05$.

References

1. Spechler SJ, Lee E, Ahnen D, Goyal RK, Hirano I, Ramirez F *et al*. Long-term outcome of medical and surgical therapies for gastroesophageal reflux disease: follow-up of a randomized controlled trial. *JAMA* 2001;**285**(18):2331–2338
2. Banerjee R, Reddy DN. Enhanced endoscopic imaging and gastroesophageal reflux disease. Indian J Gastroenterol 2011; **30**(5):193–200
3. Shaheen NJ, Crosby MA, Bozymski EM, Sandler SM, Spechler SJ. Is there publication bias in the reporting of cancer risk in Barrett's esophagus. *Gastroenterology* 2000;**119**(2):333–338
4. Sivri B. Low prevalence of Barrett esophagus in Turkey. *Turk J Gastroenterol* 2008;**19**(3):143–144
5. Blot WJ, Devesa SS, Kneller RW, Fraumeni JF. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1991;**265**(10):1287–1289
6. Botterweck AA, Schouten LJ, Volovics A, Dorant E, Brandt PA. Trends in incidence of adenocareinoma of the oesophagus and gastric cardia in ten European countries. *Int J Epidemiol* 2000; **29**(4):645–654
7. Lehmann FS, Renner EL, Meyer-Wyss B, Wilder-Smith CH, Mazzucchelli L, Ruchti C *et al. Helicobacter pylori* and gastric erosions: results of a prevalence study in asymptomatic volunteers. *Digestion* 2000;**62**(2–3):82–86
8. Ecclissato C, Carvalho AF, Ferraz JG, Nucci G, Souza CA, Pedrazoli J. Prevalence of peptic lesions in asymptomatic, healthy volunteers. *Dig Liver Dis* 2001;**33**(5):403–406
9. Spechler SJ, Goyal RK. Barrett's esophagus. *N Engl J Med* 1986; **315**(6):362–371
10. Kim JH, Rhee PL, Lee JH, Lee H, Choi YS, Son HJ *et al*. Prevalence and risk factors of Barrett's esophagus in Korea. *J Gastroenterol Hepatol* 2007;**22**(6):908–912
11. Alcedo J, Ferrández A, Arenas J, Sopeña F, Ortego J, Sainz R *et al*. Trends in Barrett's esophagus diagnosis in Southern Europe: implications for surveillance. *Dis Esophagus* 2009; **22**(3):239–248
12. Gerson LB, Shetler K, Triadafilopoulos G. Prevalence of Barrett's esophagus in asymptomatic individuals. *Gastroenterology* 2002;**123**(2):461–467
13. Azuma N, Endo T, Arimura Y, Motoya S, Itoh F, Hinoda Y *et al*. Prevalence of Barrett's esophagus and expression of mucin antigens detected by a panel of monoclonal antibodies in Barrett's esophagus and esophageal adenocarcinoma in Japan. *J Gastroenterol* 2000;**35**(8):583–592
14. Hirato WK, Loughney TM, Lazas DJ, Maydonovitch CL, Rohl V, Wong RK. Specialized intestinal metaplasia, dysplasia, and cancer of the esophagus and esophagogastric junction: prevalence and clinical data. *Gastroenterology* 1999;**116**(2): 277–285
15. Toruner M, Soykan I, Ensari A, Kuzu I, Yurdaydin C, Ozden A. Barrett's esophagus: prevalence and its relationship with dyspeptic symptoms. *J Gastroenterol Hepatol* 2004;**19**(5):535–540
16. Health Ministry of Republic of Turkey. *Obesity Report: Perception of Body Mass Index. Ankara 2012; Report no. 894*. Ankara, Turkey: Health Ministry of Republic of Turkey; 2012
17. Sharma P, McCallum RW, Lundell L. The geoprevalence of Barrett's esophagus. Presented at: Sixth OESO World Congress; September 2000; Paris, France
18. Dincer D, Besisik F, Sahin E, Demir K, Tuncer I, Cevikbas U *et al*. Intestinal metaplasia of the gastric cardia: a study form Turkey. *Hepatogastroenterology* 2002;**49**(46):1153–1156
19. Gerson LB, Edson R, Lavori PW, Triadafilopoulos G. Use of a simple symptom questionnaire to predict Barrett's esophagus in patients with symptoms of gastroesophageal reflux. *Am J Gastroenterol* 2001;**96**(7):2005–2012
20. Voutilainen M, Farkkila M, Juhola M, Nuorva K, Mauranen K, Mäntynen T *et al*. Specialized columnar epithelium of the esophagogastric junction: prevalence and associations. *Am J Gastroenterol* 1999;**94**(4):913–918

21. Padda S, Ramirez F. Accuracy in the diagnosis of SSBE: the role of endoscopic experience. *Gastrointest Endosc* 2001;**54**(5): 605–608
22. Cameron AJ. Barrett's esophagus: prevalence and size ofhiatal hernia. *Am J Gastroenterol* 1999;**94**(8):2054–2059.
23. Johnston MH, Hammond AS, Laskin WL, Jones MD. The prevalence and clinical characteristics of short segments of specialized intestinal metaplasia in the distal esophagus on routine endoscopy. *Am J Gastroenterol* 1996;**91**(8):1507–1511
24. Spechler SJ, Zeroogian JM, Antonioli DA, Wang HH, Goyal RK. Prevalence of metaplasia at the gastroesophageal junction. *Lancet* 1994;**344**(8936):1533–1536
25. Nandurkar S, Talley NJ, Martin CJ, Adams TH. Short segment Barrett's esophagus: prevalence, diagnosis and associations. *Gut* 1997;**40**(6):710–715
26. Pereira AD, Suspiro A, Chaves P, Saraiva A, Glória L, de Almeida JC *et al*. Short segments of Barrett's epithelium and intestinal metaplasia in normal appearing esophagogastric junctions: the same or two different entities? *Gut* 1998;**42**(5): 659–662
27. Goldblum JR, Vicari JJ, Falk GW, Rice TW, Peek RM, Easley K *et al*. Inflammation and intestinal metaplasia of gastric cardia: the role of gastroesophageal reflux and *H. pylori* infection. *Gastroenterology* 1998;**114**(4):633–639
28. Abbas Z, Hussainy AS, Ibrahim F, Jafri W, Shaikh H, Kahn HA. Barrett's esophagus and *Helicobacter pylori*. *J Gastroenterol Hepatol* 1995;**10**(3):331–333
29. Newton M, Bryan R, Burnham WR, Kamm MA. Evaluation of *Helicobacter pylori* in reflux esophagitis and Barrett's esophagus. *Gut* 1997;**40**(1):9–13
30. Johansson J, Hakansson HO, Mellblom L, Kempas A, Johansson KE, Granath F *et al*. Risk factors for Barrett's oesophagus: a population-based approach. *Scand J Gastroenterol* 2007;**42**(2):148–156
31. Conio M, Filiberti R, Blanchi S, Ferraris R, Marchi S, Ravelli P *et al*. Risk factors for Barrett's esophagus: a case-control study. *Int J Cancer* 2002;**97**(2):225–229
32. Kubo A, Levin TR, Block G, Rumore GJ, Quesenberry CP Jr, Buffler P *et al*. Alcohol types and sociodemographic characteristics as risk factors for Barrett's esophagus. *Gastroenterology* 2009;**136**(3):806–815
33. Anderson LA, Cantwell MM, Watson RG, Johnston BT, Murphy SJ, Ferguson HR *et al*. The association between alcohol and reflux esophagitis, Barrett's esophagus, and esophageal adenocarcinoma. *Gastroenterology* 2009;**136**(3): 799–805
34. Veugelers PJ, Porter GA, Guernsey, Casson AG. Obesity and lifestyle risk factors for gastroesophageal reflux disease, Barrett esophagus and esophageal adenocarcinoma. *Dis Esophagus* 2006(5);**19**:321–328
35. Ronkainen J, Aro P, Storskrubb T, Johansson SE, Lind T, Bolling-Sternevald E *et al*. Prevalence of Barrett's esophagus in the general population: an endoscopic study. *Gastroenterology* 2005;**129**(6):1825–1831
36. Takubo K, Vieth M, Aida J, Sawabe M, Kumagai Y, Hoshihara Y *et al*. Differences in the definitions used for esophageal and gastric diseases in different countries: endoscopic definition of the esophagogastric junction, the precursor of Barrett's adenocarcinoma, the definition of Barrett's esophagus, and histologic criteria for mucosal adenocarcinoma or high-grade dysplasia. *Digestion* 2009;**80**(4):248–257