ORIGINAL ARTICLE

The incidence of esophageal cancer and dysplasia in a Chinese population with nondysplastic Barrett’s esophagus

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Abstract

Aim: The aim of this study was to investigate the incidence of dysplastic transformation of Barrett’s esophagus (BE) in a Chinese population.

Method: Data from nondysplastic BE patients at Taichung Veterans General Hospital were collected from May 2008 to June 2017. The enrolled individuals received regular gastrointestinal (UGI) endoscopy during follow up. The pathological transformations, including low-grade dysplasia (LGD), high-grade dysplasia (HGD), or esophageal adenocarcinoma (EAC), were collected prospectively until June 2017. Rates of progression were calculated in cases with a diagnosis of dysplasia or EAC.

Results: There were 51 subjects who met the inclusion criteria, with a mean follow up of 3.71 years (SD, 1.61) and a total follow up of 189.1 patient-years. Eight cases (15.7%) developed LGD, with a calculated incidence rate of 2.9% per year. The mean time to development of LGD was 3.26 years (SD, 2.68–3.84). One subject (2%) developed EAC, with a calculated incidence rate of 0.4% per year. No case with HGD was detected.

Conclusion: In a Chinese population with nondysplastic BE, 15.7% of cases developed LGD, with an incidence rate of 2.9% per year, and 2% of cases developed EAC, with an incidence rate of 0.4% per year.

Background

Barrett’s esophagus (BE) is commonly defined as a change of any length in the distal esophageal epithelium that can be recognized as columnar-type mucosa on endoscopy, and intestinal metaplasia (IM) is confirmed by biopsy of the tubular esophagus.† BE is thought to underlie the increase in the incidence of esophageal adenocarcinoma (EAC).‡ The malignant transformation of BE into EAC is believed to occur through histopathological stages that are classified as no dysplasia, low-grade dysplasia (LGD), and high-grade dysplasia (HGD).§ The incidence rates of the transformation of BE to dysplasia or EAC have been well studied in Western countries.1–7 However, such data are limited in Asian populations.

The aim of our study was to investigate the incidence rates of dysplastic transformations of BE in a Chinese population.

Methods

Data from subjects with nondysplastic BE who visited the Medical Screening Center at Taichung Veterans General Hospital were collected from May 2008 to June 2013. BE was diagnosed by typical IM pattern according to American Gastroenterological Association (AGA) recommendations.1 The general data of enrolled patients, including age, gender, bodyweight, body mass index (BMI), and waist circumference, were recorded. The endoscopic findings, including hiatus hernia and the Prague C & M criteria,§ were collected. Patients were also tested for Helicobacter pylori infection.

The enrolled individuals received regular follow up at the outpatient clinic according to individual endoscopist’s suggestion, and repeated upper gastrointestinal (UGI) endoscopy with gastroesophageal junction (GEJ) biopsy was performed. The pathological appearances of LGD, HGD, and EAC were collected prospectively until June 2017. Rates of progression were calculated in cases with a diagnosis of dysplasia or EAC. Time-to-event analyses for progression to dysplasia and EAC were performed.

Exclusion criteria included dysplastic BE, total esophagectomy, severe cardiopulmonary deficiency, malignancy, other conditions that would contraindicate UGI endoscopy, and segments of metaplastic columnar epithelium <1 cm, which were classified as “specialized IM of the EGJ” or only one-time UGI endoscopy without follow-up pathological report.

Data are expressed as the standard deviation (SD) of the mean for each of the measured parameters. Gender and endoscopic findings of each stratified group are expressed as a percentage of the total patient number. Statistical comparisons were made using Pearson’s chi-square test or Fisher’s exact test to compare the effects of positive rate in each stratified group. An
independent $t$ test was used to analyze age, BW, BMI, and waist circumference. A $P$-value below 0.05 was considered statistically significant.

Product limit estimates of survival function were performed using the Kaplan–Meier method. Among the enrolled subjects who progressed, the mean, with SD, for the time (years) to dysplasia or EAC from the baseline endoscopy was calculated.

**Results**

From May 2008 to June 2013, there were 6837 cases that underwent endoscopies 9514 times; 77 subjects had a typical IM pattern at GEJ, but 11 and 15 cases were excluded due to “specialized IM of the EGJ” and “once UGI endoscopy only,” respectively. Finally, there were 51 subjects who met the inclusion criteria for this analysis. The mean age of this cohort was 64.37 years (SD, 14.62), and the vast majority of patients were male (40 cases, 78.4%). According to the Prague C & M criteria, the average C and M was 1.97 (SD, 0.70; range, 1–4) and 2.82 cm (SD, 0.99; range 2–5), respectively. The average number of biopsies during the initial endoscopy was 5.25 pieces (SD, 2.45; range, 2–12).

During the follow-up period, UGI endoscopy was performed an average of 2.78 times, and there were 40 and 11 cases that received UGI endoscopy twice and thrice, respectively. The mean duration from initial UGI endoscopy to follow-up UGI endoscopy was 2.28 years (SD, 1.04; range, 0.7–4.8), and the mean duration between first and second follow-up UGI endoscopy in those who underwent three endoscopies was 1.98 years (SD, 0.95; range, 0.5–4.2). The mean follow-up duration of our enrolled individuals was 3.71 years (SD, 1.61; range, 1.3–6.9), with a total duration of 189.1 patient-years.

As displayed in Table 1, during follow up, eight patients (15.7%) developed LGD, and thus, the calculated incidence rate was 2.9% per year. The mean time to development of LGD was 3.26 years (SD, 0.58). Only one subject (2%) developed EAC, so the calculated incidence rate was 0.4% per year. No cases of HGD were found. The Kaplan–Meier survival graph of LGD is shown in Figure 1.

**Table 1** The incidence of esophageal adenocarcinoma and dysplasia in a population with nondysplastic Barrett’s esophagus

| Diagnosis | No. of incident cases | Incidence rate (%/year) | Mean (SD) time to development (years) |
|-----------|----------------------|-------------------------|---------------------------------------|
| LGD       | 8                    | 2.9                     | 3.26 (0.58)                           |
| EAC       | 1                    | 0.4                     | 1.3                                   |

EAC, esophageal adenocarcinoma; LGD, low-grade dysplasia; SD, standard derivation.

**Figure 1** Kaplan–Meier curve showing the percentage of subjects with Barrett’s esophagus free of low-grade dysplasia (LGD).

**Table 2** The general data and endoscopic appearances of each group

| No dysplasia (N = 42) | LGD (N = 8) | $P$-value $A$–$B$ |
|-----------------------|-------------|-------------------|
| Age (years) 64.25 ± 14.92 | 62.75 ± 13.31 | 0.781† |
| Gender (male) 30 (71.4%) | 5 (62.5%) | 0.619‡ |
| Waist (cm) 91.84 ± 10.20 | 88.43 ± 7.96 | 0.407† |
| BW (kg) 69.24 ± 12.31 | 63.16 ± 10.04 | 0.224† |
| BMI (kg/m²) 26.06 ± 4.19 | 23.93 ± 2.32 | 0.199† |
| Prague criteria C 1–2 | 41 (97.6%) | 7 (87.5%) | 0.847‡ |
| 3 | 1 (2.4%) | 1 (12.5%) |
| M | 1–2 | 32 (76.2%) | 5 (87.5%) | 0.479‡ |
| 3–4 | 10 (23.8%) | 1 (12.5%) |
| Hiatus hernia | 20 (47.6%) | 4 (50.0%) | 1.000‡ |
| H. pylori | 0 | 0 |

†Analyzed with Fisher’s exact test.
‡Analyzed with $t$ test.

BMI, body mass index; BW, body weight; M, mean; N, Number of patients; SD, standard derivation.
The general data and endoscopic appearances of the cases without dysplasia and those with LGD are listed in Table 2. There were no significant differences in age (mean 64.25 vs 62.75 years, \( P = 0.781 \)), gender (male ratio, 71.4% vs 62.5%, \( P = 0.619 \)), waist circumference (mean 91.84 vs 88.43 cm, \( P = 0.407 \)), BMI (mean 26.06 vs 23.93 kg/m\(^2\), \( P = 0.199 \)), hiatus hernia (47.6% vs 50%, \( P = 1.000 \)), and distribution of Prague C & M criteria between patients without dysplasia and those with LGD. None of our enrolled cases had \( H. pylori \) infection.

The case with EAC was male, and the endoscopic appearance revealed hiatus hernia and long segment BE (LSBE), which was defined as a >3 cm extension of the columnar mucosa into the esophagus,\(^9\) but owing to the low patient number in this subgroup (\( n = 1 \)), it was not possible to perform comparisons with other subgroups.

**Discussion**

The prevalence of BE is increasing in Western countries,\(^10\) and similar trends have recently emerged in Asian countries.\(^11\) BE is highly prevalent in people with gastroesophageal reflux disease (GERD), so the rising prevalence rates of GERD and obesity, combined with a decline in \( H. pylori \) infection, are thought to underlie the increased incidence of BE.\(^2,12\)

BE is the major risk factor for the development of EAC. The risk of EAC in patients with BE is highly variable, and the presence and grade of dysplasia are key predictors of the risk of progression to EAC.\(^1\) However, prior to 2000, the incidence of EAC in BE had been widely assumed to be higher due to the inclusion of cases with LSBE or dysplastic BE, an intermediate stage in the development of EAC.\(^13\) According to recent studies in Western populations, the annual incidence of EAC in baseline nondysplastic BE was around 0.4–0.6%.\(^3,4,7\) Our study showed that the incidence rate of EAC in nondysplastic BE was 0.4% per year, which was similar to the aforementioned studies.

One meta-analysis of nondysplastic BE included 11 434 patients and 58 547 patient-years of follow up, and the results showed that the pooled annual incidence of EAC was 0.33%.\(^14\) In patients with short-segment BE (SSBE), defined as a <3 cm extension into the esophagus,\(^9\) the annual incidence of EAC was only 0.19%.\(^14\) Our EAC case was classified as LSBE, which is traditionally considered to confer a higher risk of developing EAC.

Population-based studies estimated that the prevalence rate of BE-LGD ranged from 13 to 15%.\(^15,16\) A meta-analysis study enrolled 453 147 subjects, mainly from Eastern Asia. The pooled prevalence of histologically confirmed BE was 1.3%. Within BE cohorts, pooled prevalence rates of LGD, HGD, and EAC were 6.9%, 3.0%, and 2.0%, respectively.\(^17\) In our cases, 8 in 51 subjects (15.7%) developed LGD during a mean 3.71-year follow-up period.

There were several limitations in our study. First, diagnoses based on endoscopic and pathological appearance were confirmed by individual endoscopists and pathologists, but interobserver or intraobserver disagreement might have occurred. Second, this study was a hospital-based investigation of patients presenting to a single tertiary care center. Selection bias might therefore have existed. Third, some BE-associated variables, such as reflux symptoms and smoking, were not measured. Finally, most of our cases were classified as SSBE and may not reflect the prevalence seen in Western populations. Further research with the inclusion of more variables is needed.

In conclusion, our study found that, in 51 nondysplastic BE patients followed up for a total of 189.1 patient-years, eight cases (15.7%) developed LGD, with a calculated incidence rate of 2.9% per year. One subject (2%) developed EAC, with a calculated incidence rate of 0.4% per year.

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