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Barrett's oesophagus and associated dysplasia are not equally distributed within the esophageal circumference

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ABSTRACT

Background: A careful endoscopic surveillance of Barrett's oesophagus is warranted to prevent esophageal cancer.
Aim: To identify the preferred location of non-circumferential Barrett's oesophagus and associated dysplasia within the esophageal circumference.
Methods: We retrospectively reviewed a prospectively maintained database of patients with non-circumferential lesions. The location of metaplastic lesions and dysplastic lesions within the esophageal circumference was identified as on a clock face, and their distribution in the 4 quadrants was compared.
Results: Of overall 443 patients with Barrett's oesophagus, 192 (43%) were eligible for our study. Multiple lesions were diagnosed in 110 (57%) of them, for a total amount of 352 metaplastic areas. Barrett's oesophagus lesions were located significantly more in the posterior wall of the oesophagus (38.4%), rather than in the right wall (28.8%), the anterior wall (22.6%), or the left wall (10.2%) ($P < 0.0001$). Among all metaplastic lesions, 28 were associated with dysplasia (7.9%), and one with adenocarcinoma (0.3%). Dysplastic lesions were significantly more common in the posterior wall (39.3%) than, respectively, in the anterior wall (35.8%), the right wall (21.4%) or the left wall (3.5%) ($P = 0.03$).
Conclusion: Our results show that the posterior wall of the oesophagus is the preferential location of both Barrett's oesophagus and associated dysplasia.

1. Introduction

Barrett's oesophagus (BE) is a premalignant condition that can lead to esophageal adenocarcinoma. It is defined as a replacement of the physiological squamous epithelium of the lower oesophagus by metaplastic columnar epithelium with the presence of goblet cells [1]. The prevalence of BE is estimated to be 1.6–1.7% in the general adult population, and increases to 5–10% in patients with gastro-esophageal reflux disease (GERD), especially in the case of severe esophagitis [2,3]. The sustained action of gastric refluxate (gastric acid and bile salts) on the esophageal squamous epithelium, that leads to chronic inflammation, represents a fundamental step in the pathogenesis of BE in predisposed subjects [4]. Furthermore, BE and GERD share multiple common risk factors, including obesity, smoke, or alcohol consumption [5–8].

In a subpopulation of subjects, BE may progress to dysplasia and eventually to esophageal adenocarcinoma [9]. The associated risk of cancer is estimated to be approximately 0.5% per year [1,2]. Endoscopic surveillance reduces the risk of mortality from esophageal adenocarcinoma [10], and is recommended in patients with BE [1,11]. The goal of endoscopic surveillance is to identify the areas of intestinal metaplasia and to assess the presence of dysplasia and cancer. Although advanced imaging modalities, such as chromoendoscopy or narrow-band imaging, increase significantly the diagnostic yield of endoscopic surveillance [12], their use is still not recommended for routine use [1]. Apart from the availability of advanced diagnostic equipment, a careful endoscopic examination is recommended to guarantee adequate quality of surveillance [13].

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The accurate identification, description and location of Barrett's segments represent therefore an essential step of the endoscopic examination and report. A higher frequency of BE lesions on the right side of the lower oesophagus was documented in a Japanese population undergoing endoscopic surveillance for short-segment BE [14]. To date, comparable data on Western patients have never been reported. Furthermore, few studies have suggested a spatial predilection of advanced lesions (high-grade dysplasia or intraepithelial carcinoma) for the 12–3 o'clock or 2–5 o'clock positions of the esophageal circumference, suggesting the enhanced scrutiny of such areas during the endoscopic exam [14–17].

The aim of this study is to identify, in a Western cohort of patients, the preferred location of BE and associated dysplasia within the esophageal circumference.

2. Patients and methods

2.1. Study design, data collection and selection criteria

This is a retrospective review of a prospectively maintained database of patients with histologically proven non-circumferential BE, who underwent upper endoscopy between July 2008 and July 2015 at the Endoscopy Center of the "A. Gemelli" University Hospital.

At the beginning, the electronic database of the Endoscopy Unit (ENDOBASE – Olympus) was reviewed by two authors (S.B. and G.I.) to retrieve pertinent endoscopic reports, videos and pictures for the identification of eligible subjects.

The following data were retrieved from our electronic database for the final analysis: patient demographics; endoscopic characteristic of BE (including the Prague C&M classification); presence of macroscopic markers suggestive for dysplasia or intraepithelial carcinoma (mucosal irregularities, nodules). All endoscopic reports describing the presence of esophageal lesions with non-squamous epithelial lining were considered for the analysis. We included both patients undergoing their regular follow-up of BE and patients at their first diagnosis of BE. If patients had undergone multiple exams at our Centre for the regular follow-up of BE, only their earliest endoscopic examination was considered for the final analysis.

Reports were considered eligible only if: patients had no history of gastric and/or esophageal surgical or endoscopic treatment (including endoscopic mucosal resection and/or radiofrequency ablation for BE); the circumferential location of the lesion, as on a clock face, was described in the endoscopic report; endoscopic pictures and/or videos (caught with the endoscope in the neutral position) were available; the biopsy sampling was performed according to the Seattle biopsy protocol [18]; each biopsy specimen was stored in a separate bin containing formalin, for further histological analysis; lesions were classified as C0 with any M, according to the Prague C&M classification [18] (lesions > C0 were instead excluded).

Afterwards, two authors (D.A. and S.B.) retrieved the corresponding histology reports of all previously collected endoscopic reports, to confirm or reject the diagnosis of BE with or without associated dysplasia, by searching the database of the Histopathology Unit of the "A. Gemelli" University Hospital. If a histology report was not available, we excluded the corresponding endoscopic report from the final analysis. BE was defined as the presence of intestinal metaplasia (specialized columnar epithelium with goblet cells) in the oesophagus, including the squamocolumnar junction. Dysplasia was defined as the presence of a non-invasive neoplastic epithelial proliferation [19].

Patients with non-squamous epithelial lining devoid of intestinal metaplasia in the distal oesophagus were excluded from the analysis.

2.2. Assessment of the endoscopic location of lesions

Two endoscopists (G.C. and S.B.) reviewed separately each report and compared them with related endoscopic videos and/or images to confirm presence and location of each lesion described earlier by the single examining operator; any disagreement was resolved by consensus.

In the case of multiple BE lesions, each tongue was counted individually. The location of the lesions within the esophageal circumference was determined with the scope in a neutral position, and the subject in the left lateral decubitus position. Lesions were located within the esophageal lumen according to the numbers of a clock face, with, respectively, the 12 o'clock position corresponding to the centre the anterior (ventral) wall of oesophagus, the 3 o'clock position to the centre of the right wall (contiguously to the lesser curvature of the stomach), the 6 o'clock position to the centre of the posterior (dorsal) wall and the 9 o'clock position to the centre of the left wall of the oesophagus.

Subsequently, the esophageal lumen was divided into four quadrants, corresponding to the four walls of the oesophagus (anterior wall: 11 to 1 o'clock; right wall: 2–4 o'clock; posterior wall: 5–7 o'clock; left wall: 8 and 10 o'clock), and into two hemi-circumferences (right hemi-circumference: 1–6 o'clock; left hemi-circumference: 7–12 o'clock).

If a lesion crossed over 2 or more o'clock positions, quadrants or hemi-circumferences, the central part of the segment was identified to assess its predominant location.

All reviewed procedures had been performed by highly experienced endoscopists (G.C., L.P., C.S., A.L., M.E.R., G.C.), with the patient under conscious or deep sedation, and were carried out with high-definition endoscopes (EG-2990i by Pentax Medical, Japan; GIF-H180 by Olympus, Japan), without chromoendoscopy or any other magnification technique.

2.3. Histology assessment

Haematoxylin and eosin staining was routinely used for histologic examinations, and only in uncertain cases p53 was evaluated. Two expert histopathologists (R.R. and D.A.) reviewed the tissue slides of all retrieved histology reports to confirm the presence of BE and, in case, of associated dysplasia of each lesion; any disagreement was resolved by consensus.

2.4. Statistical analysis

Patient data were retrieved from a prospectively maintained electronic database (ENDOBASE-Olympus). Statistical analyses were performed with an online calculator (http://www.graphpad.com/quickcalcs/) and with Microsoft Excel for Mac (Microsoft Excel. Redmond, Washington: Microsoft, 2011). Clinical parameters and data of patients are expressed as means and ranges. Inter-observer agreement between the two reviewers of available endoscopic images and videos (G.C. and S.B.) was evaluated using Cohen's kappa statistics. Inter-observer agreement between the two reviewers of available histology reports (R.R. and D.A.) was evaluated using Cohen's kappa statistics.

Student's t-test was performed to compare the frequency of metaplastic lesions in the right and in the left hemi-circumference; P value <0.05 was considered statistically significant.

Virtually, in the absence of background data, we can presume that all the four quadrants of the esophageal circumference share the same odds to contain a lesion. Therefore, Chi-square test was performed to compare the expected frequency of metaplastic areas for each quadrant (that is 25%) along the esophageal circumference with the observed ones; P value <0.05 was considered statistically significant. The position of dysplastic lesions was compared with