Directional distribution of neoplasia in Barrett's esophagus is not influenced by distance from the gastroesophageal junction

Lisa Cassani, MD,[1] Eric Sumner, MD,[1] James C. Slaughter, PhD,[2] Patrick Yachimski, MD, MPH[1]

Nashville, Tennessee, USA

Background: Accurate endoscopic detection and staging are critical for appropriate management of Barrett's esophagus (BE)–associated neoplasia. Prior investigation has demonstrated that the distribution of endoscopically detectable early neoplasia is not uniform but instead favors specific directional distributions within a short BE segment; however, it is unknown whether the directional distribution of neoplasia differs with increasing distance from the gastroesophageal junction, including in patients with long-segment BE.

Objective: To identify whether directional distribution of BE-associated neoplasia is influenced by distance from the gastroesophageal junction.

Design: Retrospective cohort study.

Setting: Tertiary-care referral center.

Patients: Patients with either short-segment or long-segment BE undergoing EMR.

Intervention: EMR.

Main Outcome Measurements: Directional distribution of BE-associated neoplasia stratified by distance from gastroesophageal junction.

Results: EMR was performed on 60 lesions meeting study criteria during the specified time period. Pathology demonstrated low-grade dysplasia in 22% (13/60), high-grade dysplasia in 38% (23/60), intramucosal (T1a) adenocarcinoma in 23% (14/60), and invasive (≥T1b) adenocarcinoma in 17% (10/60). Directional distribution of lesions was not uniform ($P < .001$), with 62% of lesions (37/60) located between the 1 o'clock and 5 o'clock positions. When circular statistics methodology was used, there was no difference in the directional distribution of neoplastic lesions located within 3 cm of the gastroesophageal junction compared with ≥3 cm from the gastroesophageal junction.

Limitations: Single-center study may limit external validity.

Conclusion: The directional distribution of neoplastic foci within a BE segment is not influenced by distance of the lesion from the gastroesophageal junction. Mucosa between the 1 o'clock and 5 o'clock locations merits careful attention and endoscopic inspection in individuals with both short-segment BE and long-segment BE. (Gastrointest Endosc 2013;77:877-82.)

Endoscopic therapy has emerged as a viable alternative to surgical esophagectomy for treatment of Barrett's esophagus (BE) and intraepithelial neoplasia. A recent international consensus statement recommended that endoscopic therapy should be preferred over surgery for most patients with BE containing high-grade dysplasia (HGD).[1] A rationale for endoscopic therapy for such patients is predicated not only on the presumed efficacy of

Abbreviations: BE, Barrett's esophagus; HGD, high-grade dysplasia; LGD, low-grade dysplasia.

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Current affiliations: Division of Gastroenterology, Hepatology and Nutrition (1), Department of Biostatistics (2), Vanderbilt University Medical Center, Nashville, Tennessee, USA.

Reprint requests: Patrick Yachimski, MD, MPH, Division of Gastroenterology, Hepatology and Nutrition, Vanderbilt University Medical Center, 1660 The Vanderbilt Clinic, Nashville, TN 37232-5280.

If you would like to chat with an author of this article, you may contact Dr Yachimski at patrick.yachimski@vanderbilt.edu.

EMR or ablation techniques but also the ability to accurately and confidently stage disease before therapy. Optimal disease staging is necessary to identify patients with (1) HGD or intramucosal (T1a) adenocarcinoma who may achieve endoscopic remission of disease with appropriate treatment and after-treatment surveillance and (2) invasive disease who may instead opt for surgical or systemic treatment modalities.

Technological and procedural advances that have improved the accuracy of endoscopic detection and staging include enhanced optics with high-definition white light endoscopy and narrow-band imaging, EUS, and EMR. Historical cohorts describing occult cancer in 33% to 73% of surgical resection specimens among patients undergoing esophagectomy for HGD[2-9] are no longer applicable. In the current era of rigorous endoscopic staging, the presence of occult invasive malignancy in patients undergoing esophagectomy for HGD is no more than 5%.[10]

Accurate endoscopic staging of BE is not purely a function of the technical tools in an endoscopist's armamentarium, however, but also may be influenced by subjective variables in how an endoscopist chooses to inspect a BE segment. One recent study suggested that inspection time longer than 1 minute per centimeter of BE was associated with increased detection of endoscopically suspicious lesions.[11]

In addition, prior studies have identified that the directional (in other instances termed circumferential, spatial, or radial) distribution of endoscopic lesions within BE is not random,[12,13] suggesting that particular attention to certain locations within a circumferential extent of BE will result in a higher yield for detection of advanced neoplasia than random endoscopic inspection and sampling. One study reported that greater than 50% of lesions were located within a 2 o'clock to 5 o'clock arc (with 3 o'clock defined as alignment with the lesser curvature of the proximal stomach) in patients with BE <5 cm in length.[13]

What remains unknown, however, is whether this finding is relevant only for patients with short segment BE or whether it is also applicable to patients with long-segment BE and lesions not in close proximity to the gastroesophageal junction. The aim of this study, therefore, was to identify whether the directional distribution of endoscopically detected neoplasia within BE is influenced by distance from the gastroesophageal junction, with the hypothesis that the directional distribution of neoplasia would differ for lesions at increased distance from the gastroesophageal junction compared with lesions in close proximity to the gastroesophageal junction.

Take-home Message

- The distribution of early neoplasia in Barrett's esophagus is not uniform but instead exhibits a directional tendency, irrespective of distance of the lesion from the gastroesophageal junction.
- Careful endoscopic inspection of mucosa located between the 1 o'clock and 5 o'clock locations is warranted in patients with short-segment Barrett's esophagus and long-segment Barrett's esophagus.

METHODS

Approval to conduct this retrospective study was granted by the Vanderbilt University Institutional Review Board. The cohort consists of patients with BE who had been referred to the Vanderbilt Barrett's Esophagus Endoscopic Treatment Program (V-BEET) and who had undergone EMR between September 2009 and August 2012. Demographic, clinical, and endoscopic data were obtained from review of the electronic medical record. Study data were collected and managed by using REDCap electronic data capture tools hosted at Vanderbilt University. REDCap (Research Electronic Data Capture) is a secure, Web-based application designed to support data capture for research studies.[14]

Candidates for EMR included patients with prior biopsies documenting the presence of low-grade dysplasia (LGD), HGD, and/or adenocarcinoma. In all cases, visual inspection of the BE segment was performed using high definition white light and narrow-band imaging as previously described.[15] Length of BE was defined as the distance between the top of the gastric folds and the visible squamocolumnar junction. Areas of nodularity, superficial erosion, or those with a hypervascular mucosal appearance were targeted for EMR using a cap-assisted mucosectomy device (Duette Multi-Band Mucosectomy; Cook Medical, Limerick, Ireland) as previously described.[15] EMR was targeted to focal endoscopically visible abnormalities; wide-field EMR was not performed. Anatomic location of the resected lesion with respect to distance from the gastroesophageal junction was documented before resection.

For the purposes of this study, orientation of endoscopically visible lesions within a BE segment was as previously described[13]: with the patient in a left lateral decubitus position and the endoscope in a neutral position, the 3 o'clock position was defined as alignment with the lesser curvature of the stomach. Photodocumentation of the lesion was obtained before attachment of the endoscopic resection device to the endoscope. In order to identify directional distribution of the lesion, an experienced endoscopist who had not performed the initial endoscopy and who was unaware of the study design and hypothesis reviewed the endoscopic images of the lesions.

Resected specimens were retrieved and submitted to pathology in formalin solution. Formalin-fixed and paraffin-embedded specimens were reviewed by two expert GI pathologists, with grading of dysplasia and assessment of depth of adenocarcinoma invasion (pT1a or pTab) performed as previously described.[15] Expert pathology review and endoscopic mucosal resection alters the diag-