Barrett's esophagus with low-grade dysplasia: True progression or missed lesions? A national tertiary referral evaluation

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***Background*:** Currently, there is no consensus on the management of Barrett's esophagus with low-grade dysplasia (LGD). This is mainly due to the variability in the progression rate of LGD reported in the literature and endoscopic diagnosis between community and expert centers.

***Aim*:** This multicenter study aimed to determine: (1) the proportion of prevalent high-grade dysplasia (HGD) or intramucosal carcinoma (IMC) diagnosed by endoscopic assessment in expert centers in individuals with a diagnosis of LGD in the community; and (2) the proportion of pathology upstage and downstage by expert gastrointestinal pathologists in patients diagnosed with Barrett's esophagus with LGD in the community.

***Methods*:** All consecutive patients referred to the six expert centers across Australia with a diagnosis of LGD from the community between 2010 and 2017 were included. Patient demographics and results from the community and expert centers were obtained from a Barrett's esophagus database from each individual expert center. The proportion of prevalent HGD or IMC at endoscopic assessment by expert centers and the proportion of community pathology upstage and downstage after assessment by an expert gastrointestinal pathologist were determined.

***Results*:** A total of 110 patients were referred to six expert centers from the community with a diagnosis of LGD (site 1, 42; site 2, 15; site 3, eight; site 4, 25; site 5, 12; site 6, eight). The majority of patients were male (74%), with a mean age of 66 years (SD, 16.4). Forty-seven patients (43%) had an expert gastrointestinal pathologist review of the original pathology slide, of which seven (15%) were upgraded to HGD and four (9%) were downgraded to indefinite for dysplasia (IND) or non-dysplastic Barrett's esophagus. All patients had an endoscopic assessment at an expert center (median time, 118 days [IQR, 67–229] after community assessment). After the expert center assessment, 22 patients (20%) had a diagnosis of HGD (n = 14) or IMC (n = 8); 59 had LGD, five had IND, and 24 had non-dysplastic Barrett's esophagus. Of the 110 patients, 27 had endoscopic mucosal resection (EMR) only, 47 had radiofrequency ablation (RFA) only, 13 had a combination of EMR and RFA, and 23 patients had surveillance only.

***Conclusion*:** Endoscopic assessment at expert centers resulted in detection of HGD and IMC in 20% of patients who had a recent diagnosis of LGD in the community. Expert gastrointestinal pathologist review resulted in an upgrade of histology in 15% of patients and downgrade of histology in 9% of patients. Those with more advanced dysplasia identified on expert assessment represent prevalent HGD or neoplasia rather than disease progression. The variation in findings between community and expert center assessments may partly explain the wide range of progression rates in the literature.

Diffuse endoscopically visible low-grade dysplasia in Barrett's esophagus: A new and more aggressive phenotype

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***Introduction*:** There has been significant technological advancement in endoscopic imaging over the past decade. This has led to reliable detection of high-grade dysplasia (HGD) and early esophageal adenocarcinomas (OAC) in Barrett's esophagus. However, low-grade dysplasia (LGD) is considered to be undetectable endoscopically in most cases, despite our best imaging modalities. The progression rate of LGD varies significantly in the literature, from 0.4% to 13.4%. Many studies have described risk factors for progression from LGD, such as multifocal dysplasia, persistent LGD, and use of biomarkers; however, the natural history of progression of LGD is still unpredictable.

***Aim*:** We aimed to describe a case series of a new phenotype of Barrett's esophagus, which may have a more aggressive potential for progression and can be identified on endoscopic examination with high-definition white light and narrow band imaging.

***Methods*:** This observational study was performed at a tertiary referral expert center for management of dysplastic Barrett's esophagus. We defined diffuse endoscopically visible LGD in Barrett's esophagus (DEVLB) as consisting of a large area of at least 6 cm^2: (1) with diffusely abnormal mucosa; (2) with variable loss of mucosal pattern; (3) often with widespread, subtle nodularity; (4) often with a clear demarcation with normal-looking smooth Barrett's mucosa; and (5) with histology showing predominantly multifocal LGD (sometimes with areas of HGD). A group of patients with DEVLB observed on their initial assessment endoscopy were included. The demographic, endoscopic, and histological data were extracted from a prospectively collected database.

***Results*:** Of a total of 419 patients referred to our expert center for assessment of dysplastic Barrett's esophagus during the period from January 2009 to March 2018, there were 10 patients (2.4%) with DEVLB identified on their initial assessment endoscopy. All were male (n = 10), with a median age of 70 years (IQR, 61–73). The median maximum length of Barrett's segment was 7.5 cm (IQR, 6–9). Six patients (60%) had DEVLB predominantly on the right wall of the esophagus only (12–6 o'clock position) and four patients (40%) had DEVLB on both the left wall (6–12 o'clock position) and the right wall of the esophagus. Patients were treated with a combination of endoscopic mucosal resection (EMR) of abnormal-looking tissue and post-EMR targeted biopsies of smooth or less abnormal Barrett's. A total of 75 EMRs were performed, with a median of six EMRs (IQR, 5–9) performed per patient. There were 97 post-EMR targeted biopsies performed, with a median of seven (IQR, 0–15) targeted biopsies performed per patient. Of the 75 EMRs performed, 43 (57%) contained LGD, 28 (38%) HGD, two non-dysplastic Barrett's esophagus, and one OAC. Of the 97 post-EMR targeted biopsies, 73 (75%) were non-dysplastic Barrett's esophagus, 20 (20%) were LGD, and four were HGD.

***Conclusion*:** This case series illustrates a subset of patients with a new phenotype of Barrett's esophagus consisting of DEVLB. The histology within this segment of Barrett's esophagus often contains widespread LGD and can be identified on endoscopy as a diffusely abnormal mucosal appearance over a large, defined area within a long Barrett's segment. In some cases, there is also focal HGD or OAC within this area, although more advanced disease is often difficult to identify within the large abnormal area. We believe that these patients may have a more aggressive phenotype and are best treated with extensive EMR of the DEVLB area.