Detection and staging of esophageal cancers within Barrett's esophagus is improved by assessment in specialized Barrett's units

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Background: Identification and resection of mucosal abnormalities are critical in managing dysplastic Barrett's esophagus (BE) because these areas may harbor esophageal adenocarcinoma (EAC).

Objectives: To compare mucosal lesion and EAC detection rates in dysplastic BE in the community versus a BE unit and assess the impact of EMR on disease staging and management.

Design: Prospective cohort study.

Setting: Tertiary referral center.

Patients: Patients with dysplastic BE.

Interventions: Reassessment with high-definition white-light endoscopy (HD-WLE), narrow-band imaging (NBI), and Seattle protocol biopsies. EMR performed in lesions thought to harbor neoplasia. Review of referral histology and endoscopies.

Main Outcome Measurements: Mucosal lesion and EAC detection rates in a BE unit versus the community. Impact of EMR on management.

Results: Sixty-nine patients were referred (88% male; median age, 69 years). At referral, HD-WLE/NBI use was 57%/14%, and Seattle protocol adherence was 20%. Eighteen patients had intramucosal cancer. Lesions were detected in 65 patients in the BE unit versus 29 patients at referral ($P < .001$). EMR was performed in 47 patients. BE unit assessment confirmed EAC in all 18 patients and identified 10 additional patients (56% increased cancer detection, $P = .036$); all 10 had lesions identified in the BE unit (vs 3 identified at referral). EMR in these patients found submucosal cancer (n = 4) and intramucosal cancer (n = 6), resulting in esophagectomy (n = 4) and chemoradiotherapy (n = 1).

Limitation: Academic center.

Conclusion: BE assessment at a BE unit resulted in increased lesion and EAC detection. EMR of early cancers was critical in optimizing patient management. These data suggest that BE unit referral be considered in patients with dysplastic BE. (Gastrointest Endosc 2014;80:971-83.)

(footnotes appear on last page of article)

Until recently, surgical esophagectomy was the standard treatment for patients with early esophageal adenocarcinoma (EAC) and high-grade dysplasia (HGD) in Barrett's esophagus (BE). This was associated with mortality and morbidity rates as high as 5% and 30%, respectively.[1-3] A pivotal study that changed this approach to management was the AIM Dysplasia (Ablation of Intestinal Metaplasia Containing Dysplasia) trial, a sham-controlled study demonstrating that radiofrequency ablation (RFA) was highly effective for eradicating dysplastic BE.[4] Subsequent studies have found similar efficacy rates, and it is now widely accepted that combined endoscopic therapy using EMR in conjunction

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with RFA is a credible alternative to surgery for patients with early EAC and HGD in BE.[5]

Identification of mucosal abnormalities that may harbor advanced dysplasia or cancer, and removal by using EMR, is a critical aspect of BE assessment and staging. It is imperative to remove intramucosal cancer (IMC) and exclude submucosal cancer (SMC) before commencing RFA as they are not reliably ablated by this technique.[6-8] Furthermore, if cancer cells are found to extend into the submucosal layer, lymph node spread is reportedly as high as 30%.[1] These patients are usually referred for surgical resection or chemoradiotherapy.

Identification of these often subtle lesions requires careful, systematic assessment of the BE segment. Detection of mucosal abnormalities harboring HGD/EAC is shown to be improved by using high-definition white-light endoscopy (HD-WLE) and narrow-band imaging (NBI) modalities[9-11]; however, in a recently published survey in the United States, these modalities were used by only one-third of practicing gastroenterologists when assessing BE.[12] Additionally, studies show that rigorous endoscopic surveillance protocols result in significantly increased detection of HGD/EAC.[13,14] Conversely, without comprehensive sampling, detection of HGD/EAC is significantly decreased.[15] Despite this, adherence to the Seattle protocol by practicing community gastroenterologists is reportedly as low as 30% to 50%, and, notably, adherence rates vary inversely with the length of BE.[15,16] It is therefore highly likely that detection of mucosal abnormalities and cancers will be lower in the community setting than in a specialized BE unit, where use of HD-WLE and NBI and adherence to a rigorous biopsy protocol are consistently used.

AIMS

In a cohort of patients with dysplastic BE identified in the community setting, we aimed to determine the additional detection rate of mucosal abnormalities and EACs identified in a BE unit. We aimed to compare endoscopy methods used in the community versus those used in a BE unit to see which factors contributed to overall lesion and cancer detection rates. We also aimed to assess the impact of EMR on histopathological staging and subsequent patient management.

METHODS

Referrals

Consecutive patients referred to St. Vincent's Hospital Melbourne from November 2008 to September 2011 for management of dysplastic BE were prospectively entered into a central database. Patient demographic characteristics and the most advanced histology at and before referral and referral endoscopy details were recorded. These details, where provided, included BE extent, NBI use, presence and size of a hiatal hernia, and description of any mucosal abnormality.

Take-home Message

- Individuals with dysplastic Barrett's esophagus (BE) should be considered for referral to specialist centers for assessment before embarking on a definitive management course because assessment at a specialized BE unit results in improved detection of mucosal abnormalities and consequently improved detection of cancers.
- Specialist units also have expertise in performing EMR, which is critical in the adequate staging of dysplastic BE and in optimal treatment of early cancers before mucosal ablation therapy, such as radiofrequency ablation.

Assessment

Systematic assessment by using HD-WLE and then NBI was performed by 2 experienced endoscopists (A.T., C.J.) by using Olympus H-180 endoscopes (Olympus, Tokyo, Japan). BE extent was documented according to the Prague Classification[17] (Appendix 1, available online at www.giejournal.org). In 40 patients, confocal endomicroscopy (CEM) was also used at assessment. These patients were part of another study assessing the accuracy of predicting HGD/IMC in mucosa by using HD-WLE, NBI, and CEM. This study found that CEM was accurate in confirming suspected dysplasia/neoplasia seen with HD-WLE/NBI, but did not significantly add to the detection of HGD/IMC or impact on clinical outcome.[9] BE assessment by using HD-WLE/NBI without CEM was therefore considered the most efficacious approach in our unit.

Any mucosal abnormalities seen were described according to size, position (in centimeters from the mouth at an o'clock position), Paris Classification[18] (Appendix 2, available online at www.giejournal.org), and mucosal pattern (irregularity/loss).[19] Mapping biopsy specimens were taken according to the Seattle protocol[13] (Appendix 3, available online at www.giejournal.org) with targeted biopsies of any mucosal abnormalities. Biopsy specimens were labeled according to level and o'clock position in the neutral endoscope position to facilitate a more accurate location at subsequent endoscopy. Areas thought to harbor HGD or cancer, based on appearance characteristics or through biopsy confirmation, were removed with EMR. Initially, biopsy was performed on such lesions first, with EMR performed several weeks later. In later cases, EMR, where required, was often performed at the initial assessment.

Patients' subsequent management was dependent on the most advanced histology after assessment. Those with SMC were referred for esophagectomy or chemoradiotherapy as endoscopic therapy was not considered definitive. In those with IMC or nodular HGD, EMR was performed until we were confident that no cancer