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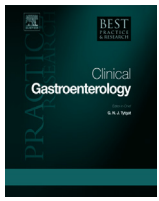

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Red flag imaging in Barrett's esophagus: Does it help to find the needle in the haystack?

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A B S T R A C T

Esophageal Adenocarcinoma (EAC) has suffered a sharp increase on its incidence for the last decades, and it is associated with a poor prognosis. Barrett's Esophagus (BE) is the most important identifiable risk factor for the progression to esophageal adenocarcinoma. The key to prevent and provide a curative treatment of esophageal adenocarcinoma is the detection and eradication of early neoplasia in patients with esophagus. Endoscopic surveillance is evolving from a blind or random four quadrant biopsies protocol (Seattle protocol) to a more targeted approach.

A detailed white light examination with high-resolution endoscopy is the cornerstone for recognition of early neoplastic lesions in BE. Additional imaging modalities may enhance targeting of lesions or provide more information at a focused level. There are emerging data that some of these new modalities can increase the yield of detecting dysplasia, although its routine use has yet to be validated.

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Introduction

Esophageal adenocarcinoma (EAC) has been increasing in the United States more than six-fold over the past three decades, faster than that of any other malignancy [1]. Barrett's Esophagus (BE) is a well-established precursor of EAC and increases the risk of developing EAC by greater than 40-fold compared with the general population [2].

The key of early diagnosis of oesophageal adenocarcinoma is the detection of early stage neoplasia arising in Barrett's Esophagus. Visible lesions in the setting of BE are at high risk of harboring neoplasia until proven otherwise [3]. The recognition of subtle lesions will therefore enable an early detection of disease. Traditionally, the detection of dysplasia is based upon random four-quadrant biopsies protocol obtained every 1–2 cm in the Barrett's segment, the so called Seattle protocol [4], which has shown to increase the detection of early neoplastic lesions when compared with randomly obtained biopsy specimens [5,6]. But this protocol is consuming, costly and subject to a considerable sampling error, as only a tiny fraction of the 'at risk' mucosa is sampled. Furthermore, adherence to this protocol in the general practice is poor (30%–79%) which significantly decreases the rate of detecting dysplasia [7–9].

Visible lesions in patients with dysplastic Barrett's esophagus are associated with higher risk of invasive carcinoma [10,11] and should be treated with a tissue-acquiring modality so these lesions can be appropriately resected and staged histologically [12].

The advent of endoscopic ablative therapies has rapidly changed the management of Barrett's esophagus. The rationale of these therapies resides in the risk of lymph node metastases when there is submucosal invasion. High grade dysplasia (HGD) and intramucosal carcinoma (IMC) are amenable for endoscopic treatment given the low risk of lymphatic spread in these stages, which increases substantially when submucosal invasion is present, from less than 5% for IMC to up to a 20% of risk of nodal involvement in submucosal cancer [11,13–18] and thus a surgical and/or systemic approach is required. Endoscopic therapy has emerged in this context as a minimally invasive approach for treatment of HGD or IMC as an alternative to oesophagectomy, which is associated with significant mortality and morbidity [19,20].

Given the importance of early detection of neoplasia and its clinical impact on management, several endoscopic imaging techniques have been developed and tested in order to improve the accuracy of endoscopic diagnosis (Table 1). Potential advantages of these imaging technologies include increased rates for the detection of high-risk lesions, the ability to target biopsies and resections, decreased total number of biopsies and costs for surveillance, and the ability to guide therapy in real-time.

Endoscopic techniques can be divided into primary detection and targeted imaging techniques. Detection techniques act as warning signs or *red flags*, drawing the attention of the endoscopist to a certain area. The greatest role for red flag techniques is to help identify neoplastic lesions for targeted biopsy and therapy while performing a surveillance careful inspection. Upon their detection, these areas can then be inspected in detail using targeted imaging techniques (e.g., magnification endoscopy or confocal endomicroscopy) or simply biopsied or resected for histologic evaluation.

A consensus methodological classification of endoscopic imaging proposed by Tajiri and Niwa in 2008 divides endoscopic techniques into five major categories: Conventional (WLE), image-enhancement (subdivided into digital, optical-digital, and chromoendoscopy methods), magnifying (optical and digital), microscopic (CLE and EC) and tomographic (endoscopic ultrasonography and optical coherence tomography) [21] (Table 2).

High resolution white light endoscopy (HRE) and magnification endoscopy

Detailed white light endoscopy (WLE) is the cornerstone in the detection of neoplasia in BE. High-resolution imaging improves the ability to discriminate detail, whereas magnification enlarges the image. Modern video endoscopes can be coupled with high-resolution technology, magnification devices and high definition screens. Signal images in these equipments can reach resolutions of more than one million pixels and zoom endoscopes can optically magnify images up to 150 times, while standard endoscopes magnify images 30 to 35 times of the monitor.

HRE appears to have higher sensitivity for detecting early neoplastic lesions in BE compared with standard endoscopy [22–25].