Best Practice & Research Clinical Gastroenterology 29 (2015) 533–544

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology

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Detection and characterization of early malignancy in the esophagus: What is the best management algorithm?

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Keywords:
Barrett's esophagus
Intestinal metaplasia
Seattle protocol
Image-enhanced endoscopy
Chromoendoscopy
Narrow band imaging
Autofluorescence imaging
Confocal laser endomicroscopy
Early esophageal adenocarcinoma
Radiofrequency ablation
Argon plasma coagulation
Endoscopic mucosal resection

A B S T R A C T

Barrett's esophagus is a known precursor for esophageal adenocarcinoma. Early detection of dysplasia provides a window of opportunity for curative intervention. Several image-enhanced technologies have been developed to improve visualization of neoplasia. These however have not been found to be superior to the standard four quadrant random biopsy protocol. Patients are risk-stratified based on the degree of dysplasia found on biopsies and undergo either surveillance or treatment. Endoscopic therapy has become the mainstay of treatment for early neoplasia.

Introduction

Barrett's esophagus (BE) is a known premalignant condition which predisposes to the development of esophageal adenocarcinoma (EAC). The incidence of EAC reported in a recent large prospective study in patients with BE undergoing surveillance endoscopy was 0.45% per annum [1]. Long term endoscopic surveillance of BE remains controversial as not all patients with EAC have a preceding diagnosis of BE and most patients with BE do not develop EAC. The diagnosis of BE itself is also debatable. BE is defined as a

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http://dx.doi.org/10.1016/j.bpg.2015.06.004
1521-6918/

change in the distal esophagus of any length to columnar epithelium with identifiable intestinal metaplasia on biopsy [2]. Unlike American, European and Australian guidelines, guidelines from the UK and Japan exclude the need for intestinal metaplasia (IM) from their diagnostic criterion [3,4]. Recent studies have found similar neoplastic risk in patients who have columnar lined epithelium but without IM [5,6].

Early detection and appropriate management of BE are crucial to halt the increasing incidence of EAC. Despite improvement in short and long term survival over the last 25 years (1 and 5-yr survival rates were 34% and 5% during 1973–1977 and 44% and 13% during 1993–1997 respectively ($p < 0.05$)), prognosis for EAC remains dismal [7]. There are well-established risk factors for BE such as age above 50, male, white race, hiatus hernia, chronic gastroesophageal reflux disease (GORD), obesity and high waist-to-hip ratio but there is no concrete data that surveillance will reduce deaths and thereby prolong survival [8]. It is also difficult to develop an effective screening strategy based on symptoms as 40% who have EAC have no history of chronic GORD [9]. This article examines the best diagnostic and management algorithm for BE. The grade of dysplasia determines the surveillance interval and treatment. Consideration of a surveillance program with clear clinical end-points should be discussed with patient to improve adherence whilst also taking into consideration the patients comorbidities, expected life expectancy and potential limitation in cancer detection.

Diagnosis of Barrett's esophagus

Endoscopic diagnosis

On endoscopy, BE appears as a salmon-pink tongue of mucosa extending into the esophagus from the gastroesophageal junction. The validated Prague's Circumferential (C) & Maximum (M) classification should be used for endoscopic landmarks of the upper end of gastric folds and is a useful tool to follow progress [10]. The current mainstay for diagnosis is random four-quadrant every 2 cm biopsies on high resolution white light endoscopy (HR-WLE). This strategy samples only a small fraction (<5%) of the columnar lined epithelium and could potentially miss inconspicuous areas harbouring dysplasia. Intestinal metaplasia itself can be patchy in BE. One observational study suggested at least 8 random biopsies needs to be taken to diagnose IM in long segment BE [11]. Using a jumbo forceps has not been found to be superior to large-capacity forceps in obtaining adequate tissue samples [12].

For patients with known dysplasia, the Seattle protocol of random four-quadrant every 1 cm biopsy is recommended as some studies suggested that standard biopsy of quadrantic 2 cm may cause a miss rate of up to 50% [13]. Gupta et al. recommends spending approximately 1 min/cm inspecting the BE segment which may increase the yield of detecting dysplasia in BE [14]. Meticulous attention should be paid to the distal margin of the CLE especially between the 2–5 o'clock position as these areas have been identified in studies as the preferential location where neoplasia is located [15,16]. Targeted biopsies should be performed on visible mucosal abnormalities (ulcer, nodules, erythema or areas of friability) as they could represent advanced lesion [17]. This should be done initially before random biopsies of the rest of the mucosa are undertaken as biopsy-related bleeding may impair endoscopic views.

Image-enhanced endoscopy

The prospect of advanced imaging modalities such as dye-spray or electronic chromoendoscopy, autofluorescence imaging (AFI) and confocal laser endomicroscopy (CLE) is promising but they have not been demonstrated to be superior to the current strategy of random four-quadrant biopsies in detecting neoplasia in BE [18]. In cases where there is doubt or for purposes of delineating the lesion further prior to resection, these technologies may be utilised in conjunction with HR-WLE.

1) Chromoendoscopy.

Chromoendoscopy uses stains such as methylene blue and acetic acid to improve visualisation of neoplastic lesions. A meta-analysis of 9 studies revealed that there is no incremental yield in the detection of neoplasia using methylene blue chromoendoscopy [19]. Acetic acid is easily available but results have not been consistent in providing additional value over HR-WLE [20,21]. Additionally many endoscopists find the application of dye time-consuming and cumbersome hence it is not a popular technique.