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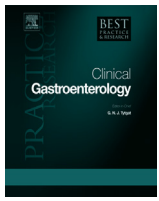

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Barrett's oesophagus: Frequency and prediction of dysplasia and cancer

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A B S T R A C T

The incidence of oesophageal adenocarcinoma is continuing to increase at an alarming rate in the Western world today. Barrett's oesophagus is a clearly recognized risk factor for the development of oesophageal adenocarcinoma, but the overwhelming majority of patients with Barrett's oesophagus will never develop oesophageal cancer. A number of endoscopic, histologic and epidemiologic risk factors identify Barrett's oesophagus patients at increased risk for progression to high-grade dysplasia and oesophageal adenocarcinoma. Endoscopic factors include segment length, mucosal abnormalities as seemingly trivial as oesophagitis and the 12 to 6 o'clock hemisphere of the oesophagus. Both intestinal metaplasia and low grade dysplasia, the latter only if confirmed by a pathologist with expertise in Barrett's oesophagus pathologic interpretation are the histologic risk factors for progression. Epidemiologic risk factors include ageing, male gender, obesity, and smoking. Factors that may protect against the development of adenocarcinoma include a diet rich in fruits and vegetables, and the use of proton pump inhibitors, aspirin/NSAIDs and statins.

Introduction

The incidence of oesophageal adenocarcinoma continues to rise at an alarming rate in the Western world, although the pace of this increase appears to have decreased in recent years [1]. Barrett's

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oesophagus is a clearly recognized risk factor for the development of oesophageal adenocarcinoma [2,3]. This has led to widespread endoscopic surveillance of Barrett's oesophagus patients in an effort to detect cancer at an earlier and potentially curable stage. However, the overwhelming majority of Barrett's oesophagus patients die of causes other than oesophageal adenocarcinoma, bringing into question the value of endoscopic surveillance programs as currently practiced [4]. Thus, it is important to identify risk factors for progression to adenocarcinoma and high-grade dysplasia. This review will explore the various endoscopic, histologic and clinical risk factors for the development of oesophageal adenocarcinoma among patients with Barrett's oesophagus.

Risk of progression to high-grade dysplasia & adenocarcinoma in Barrett's oesophagus without dysplasia

Despite the alarming increase in the incidence of oesophageal adenocarcinoma, the risk of adenocarcinoma in patients with Barrett's oesophagus without dysplasia is quite low. A number of studies have examined the risk of progression of nondysplastic Barrett's oesophagus to high-grade dysplasia/adenocarcinoma in recent years. Large contemporary studies clearly demonstrate a decreased risk of progression compared to earlier studies with small sample sizes [5]. Overall, the risk of progression to the endpoint of adenocarcinoma is approximately 0.12%–0.43%/year and for the combined endpoint of high-grade dysplasia/adenocarcinoma in the range of 0.26%–0.63%/year [5–9]. Furthermore, this risk appears to be stable over time [6].

Endoscopic features

Segment length

Oesophageal cancer develops in both short and long segments of Barrett's oesophagus. However, evidence from recent observational studies suggests that increasing segment length is a risk factor for progression to high-grade dysplasia/adenocarcinoma. A recent meta-analysis found a lower annual incidence of oesophageal adenocarcinoma in short segment Barrett's oesophagus patients when compared to all Barrett's oesophagus patients in the study (0.19% vs 0.33% per year) [8]. Work from the Northern Ireland Barrett's oesophagus register found the risk of progression to adenocarcinoma or high-grade dysplasia increased by seven fold in long segment compared to short segment Barrett's oesophagus (hazard ratio 7.1; 95% CI 1.74–29.04) [10]. A recent case control study from Berlin also found an association of segment length with progression of Barrett's oesophagus to high grade dysplasia/adenocarcinoma [11]. Compared to short segment Barrett's oesophagus, patients with long segment Barrett's oesophagus had an increased risk of progression (OR 2.69; 95% CI 1.48–4.88). Furthermore, for every increase in segment length by 1 cm, the risk of progression increased by 19% (OR 1.19; 95% CI 1.09–1.30). Similarly, work from a large United States multicenter cohort found that the risk for progression increased by 28% for every 1 cm increase in the length of the Barrett's segment [12]. Others have also reported an incremental increase in risk for progression with each cm increase in the segment length [13]. On the other hand, work from the Northern Ireland Barrett's oesophagus register found no relationship between segment length and risk of progression [6]. Taken together, it would appear that longer segments of Barrett's oesophagus are associated with an increased risk of progression to adenocarcinoma and high grade dysplasia.

Oesophagitis/Mucosal abnormalities

A number of mucosal changes within the Barrett's segment are associated with an increased risk for progression to high grade dysplasia/adenocarcinoma. A Dutch multicenter cohort study found an increased risk of progression to adenocarcinoma or high-grade dysplasia in Barrett's oesophagus patients with oesophagitis by the Los Angeles classification at baseline endoscopy (relative risk 3.5; 95% CI 1.3–9.5) [13]. The population based Northern Ireland Barrett's register found that patients with ulceration in the Barrett's segment but not elsewhere in the oesophagus were more likely to progress to cancer or high-grade dysplasia than non-progressors (hazard ratio 1.72; 95% CI 1.08–2.76) [10].