# Who Deserves Endoscopic Screening for Esophageal Neoplasia?

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**KEYWORDS**

• Barrett's esophagus • Screening • Esophageal adenocarcinoma • Endoscopy

**KEY POINTS**

- Barrett's esophagus (BE) is regarded as the precursor to most esophageal adenocarcinomas (EAC).
- EAC that is diagnosed while in a BE surveillance program (constituting <10% of all EAC) likely has better outcomes compared with EAC diagnosed after the onset of symptoms (constituting >90% of all cases).
- Most BE in the community remains undetected despite increasing endoscopy volumes, likely due to the absence of widespread targeted screening.
- Given the prevalence of BE in the population is likely less than 10%, many BE risk assessment scores have been proposed, using known risk factors for BE. Most have not been validated in independent cohorts, and threshold for recommending screening is not yet defined.
- Validation of these scores in independent populations, defining the threshold for proceeding with screening followed by their utilization for targeting those at risk may help in making BE/EAC screening more efficient and effective.

## INTRODUCTION

Barrett's esophagus (BE) was first described more than 60 years ago as a change in the esophageal mucosa from a squamous-type to a columnar-type that was associated with esophageal ulcers.[1] Today, this largely asymptomatic change in the esophageal lining is regarded as the precursor lesion to most esophageal adenocarcinoma (EAC). Even after understanding this association for the last several decades, the incidence of EAC continues to increase with an estimated 6-fold increase since 1975.[2]

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Once EAC is diagnosed after the onset of symptoms, the prognosis is grim with an estimated 20% survival at 5 years.[3] On the other hand, survival of early stage EA (T1a: mucosally confined) is far superior: greater than 80% at 5 years.[4,5] Given the rising incidence of this lethal cancer that has a known precursor lesion, there is mounting interest in finding a cost-effective, patient and provider acceptable, easily applicable and accurate means by which the population at risk for developing BE can be screened followed by enrollment in a surveillance program. However, this seemingly logical rationale has several limitations, which include the lack of an accurate risk assessment tool and a suitable widely applicable screening tool. This article reviews and summarizes the emerging data regarding the development and validation of BE risk assessment tools.

## ACCURATELY DIAGNOSING THE PRECURSOR LESION

Before addressing screening, being able to define BE is critical. Although this metaplastic change in the esophageal mucosa was described several decades ago, an unambiguous and universally acceptable definition remains elusive. Diagnosing BE requires an endoscopic assessment and histologic evaluation. Under direct white-light endoscopy, the metaplastic columnar epithelium of BE is differentiated from the surrounding squamous epithelial lining by its salmon color appearance. In order to diagnose BE, columnar epithelium must be located at least 1 cm proximal to the gastroesophageal junction (GEJ), which is defined by all major gastrointestinal (GI) societies as being located at the top of the gastric folds.[6–9] This diagnostic criteria is supported by studies that have shown that intestinal metaplasia (IM) at the GEJ (<1 cm in length of esophageal columnar metaplasia) does not appear to increase the risk of developing EAC.[10,11] In addition, the interobserver agreement in documenting columnar segments less than 1 cm is low.[12]

Once endoscopically defined, metaplasia has to be histologically confirmed. There remains controversy regarding the type of metaplasia that qualifies as diagnostic for BE.[13] Currently, although almost all major GI societies accept that only intestinal-type epithelium with goblet cells (denoting the presence of IM) constitutes a diagnosis of BE, the British Society of Gastroenterology recommends that goblet cells need not be present to make the diagnosis, that is, any type of columnar metaplasia in the esophagus satisfies the diagnostic criteria for BE.

The British Society of Gastroenterology's recommendations are based on the argument that columnar metaplasia (irrespective of the presence of IM) increases the risk of developing EAC. Supporting data for this view come from a population study of 319 patients over a median of 12 years showing that they developed EAC at a similar rate as those with IM.[14] There are data to suggest that columnar mucosa without IM has similar DNA abnormalities as well as cytokeratin (CK7/CK20, which are markers of ductal and intestinal differentiation) and DAS-1 staining patterns as BE with IM.[15–18] However, these data are contradicted by a large population-based study of 8522 patients that showed the rate for developing EAC in the setting of IM was 0.38% per year when compared with those without IM, which progressed at a rate of 0.07% per year ($P<.001$).[19] There are also data to suggest that follow-up biopsies in those without IM at initial endoscopy may reveal IM in 29% of cases.[20]

Beyond just making the diagnosis of BE, challenges exist when attempting to determine the degree of dysplasia at the time of diagnosis. An accurate diagnosis is important, because dysplasia, despite limitations, remains the best available and clinically used marker for predicting cancer risk. Most challenging is being able to differentiate BE with low-grade dysplasia (LGD) from nondysplastic BE (NDBE).[21] Worryingly, in a