Cdx2 Immunohistochemical Positivity Confirms Barrett Esophagus in the Absence of Goblet Cells and Confers Significant Risk for High Grade Dysplasia and Esophageal Adenocarcinoma: A Pilot Study

Parth M Patel MD, Hassan Zreik MD, Merritt Bern MD, Douglas Grider MD

HENRY FORD HEALTH SM

❖ Introduction:

- Barrett's esophagus (BE) is a premalignant condition defined by intestinal metaplasia (IM) and can develop into esophageal adenocarcinoma (EAC).
- The standard tool for diagnosing BE is esophagogastroduodenoscopy (EGD).
- Based on American College of Gastroenterology (ACG) guidelines, patients that do not have goblet cells GCs on the initial or subsequent biopsies do not qualify for surveillance EGDs.
- The absence of GCs on subsequent biopsy could be due to tissue sampling error, medication effects, or true goblet cells loss over time.
- The caudal-related homeobox transcription factor 2 (CDX2) is a well-established marker for intestinal mucosa and is present in BE mucosa, consistent with IM.
- In this paper, we examine the role of CDX2 staining as a marker for BE IM when patients do not have GCs on subsequent biopsies and determine the risk for high-grade dysplasia (HGD) or EAC.

❖ Methods:

- Serial biopsies of the esophagus were obtained during surveillance EGDs, with the initial biopsy set confirming BE with GCs and a second set that did not show GC.
- The CDX2 stains were prepared from paraffin blocks.

❖ Methods:

- 35 patients met all inclusion criteria and had initial biopsies that were positive for CDX2.
- Of those 35 patients, 34 were positive for CDX2 on subsequent slides.
- Of these 34 patients, one had HGD, and one had HGD and EAC.
- One patient was negative for GCs and CDX2 on the subsequent slides; this patient had HGD.
- In total, 3 of 35 patients (9%) had HGD or EAC on subsequent slides.

❖ Discussion:

- This study, while small, shows that CDX2 may be an important adjunctive test for the surveillance of BE.
- Our results demonstrate that BE patients with proven GCs IM on initial biopsy, but not subsequent biopsies, are overwhelmingly positive for CDX2 and still have a significant risk of HGD or EAC.
- Our study has important limitations, including the small sample size due to strict inclusion criteria required by the IRB.
- Despite this, our study provides valuable information concerning CDX2 and the development of HGD and EAC in BE patients, especially those without GCs on subsequent biopsies.
- Our study supports the use of CDX2 as an adjunctive test for the initial diagnosis of BE.
- More importantly, the patients with previously diagnosed BE who no longer have GCs on subsequent biopsies but are CDX2 positive continue to have a significant risk for HGD or EAC and warrant continued surveillance. We believe that CDX2 can help identify this at-risk group