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A REVIEW OF BARRETT'S ESOPHAGUS

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Abstract

Barrett's Esophagus is a premalignant condition that predisposes patients to the development of esophageal adenocarcinoma.

- Esophageal adenocarcinoma dramatically rising over several decades; survival rates of less than 17% in a five year period.
- Management and treatment continues to evolve: use of radio-frequency ablation effective to treat low grade dysplasia
- Studies of risk factors and treatment options explored: Efficacy and durability of endoscopic radiofrequency ablation for treatment of low grade dysplasia as option for metaplasia eradication
 - Gastrointestinal pathologist expert reviews ensure identification of dysplasia prior to treatment
 - Appropriate endoscopic surveillance intervals
 - Gastroenterology guidelines for screening and surveillance for long term management
 - Lifelong endoscopic surveillance individualized to monitor for recurrence of metaplasia

Introduction

- Barrett's Esophagus (BE) is a pre-malignant, dysplastic condition of the distal esophagus that predisposes patients to the development of esophageal adenocarcinoma
- Gastroesophageal reflux disease is the precursor to the development of BE, up to 15% of adults in the United States have Barrett's Esophagus.

Statement of the Problem

- Recommendations for the management and treatment of Barrett's esophagus continue to evolve, now expanding the use of radio-frequency ablation (RFA) for the treatment of low grade dysplasia BE, previously observed with endoscopic surveillance until advancement to high grade dysplasia.
- Risk factors associated with the development of Barrett's esophagus need to be studied due to the increasing burden of conditions associated with the progression to esophageal adenocarcinoma.
- More studies are needed to evaluate the long term efficacy and durability of early endoscopic RFA and the appropriate surveillance intervals to further determine successful treatment of dysplastic BE and reduction of EAC.

Research Question

- In adult patients with non-dysplastic or low grade dysplasia BE, as compared to high grade dysplasia BE, what risk factors predict the progression to EAC?
- In adult patients diagnosed with low grade dysplasia BE, does earlier treatment with RFA, compared to standard intermittent endoscopic surveillance, reduce the progression to EAC?
- In adult patients with complete eradication of Barrett's esophagus, what influences the recurrence of dysplastic progression after successful RFA?

Literature Review

Review of the updated recommendations with consideration of identified risk factors is essential to ensure adequate diagnosis and treatment of BE considering the devastation of progression to EAC.

• Pathophysiology of Barrett's Esophagus

Main precursor for development of BE is a chronic reflux of stomach acids into the lower esophagus, inducing a premalignant condition in which normal squamous epithelial lining of the esophagus is replaced with columnar epithelium and goblet cells, known as intestinal metaplasia. Degrees of neoplastic change occur during the sequence of epithelial transition predisposing to the development of EAC.

• Risk factors for the dysplastic transitions in BE and EAC

- Wani, et al. (2011), the Barrett's Esophagus Study (BEST), identified risk factors for progression of LGD to EAC to include BE length, age > 60, presence of hiatal hernia, and Caucasian male. Pohl, et al. (2013), reported combinations of certain risk factors influence disease progression at different times. Singh, et al. (2014), found the grade of dysplasia, the length of the BE segment, and the use of expert pathologists determined progression of BE to EAC.
- **Early RFA treatment in BE-LGD to reduce the progression to EAC**
- Shaheen et al. (2011), in the AIM Dysplasia Trial, found early dysplastic BE can be successfully treated with RFA with a durability of up to three years. The SURF study (Surveillance vs Radiofrequency Ablation) by Phoa, et al. (2014) reported the ablation group risk for progression to HGD/EAC was reduced by 25.0 % (95% CI, 14.1%-35.9 %; P, .001) and the risk of neoplastic progression to EAC by 7.4% (95%CI, 0%-14.7%; P=.03). Bulsiewicz et al. (2013) found 77% of the patients, achieved complete eradication of intestinal metaplasia after RFA despite the degree of dysplasia. Success of RFA depended on healing time between RFA treatments and the length of the BE segment.
- **Determine effective follow-up endoscopic surveillance intervals after RFA.**
- Gupta, et al. (2013) analyzed data regarding return of intestinal metaplasia after successful RFA. The median time to CRIM was 22 months with 56% in complete remission by 24 months. The findings suggest the importance of longer term endoscopic surveillance follow up after successful RFA in subjects with varying degrees of BE dysplasia.

- Pasricha, et.al (2014) utilized the RFA registry to determine how treatments with RFA and pretreatment data affected outcomes for biopsies 12 months after the receiving RFA. CEIM was achieved in 85% of these patients and 15% had persistent dysplasia. During the average follow up of 2.4 years after CRIM, IM recurred in 334 (20%) patients. Compared to patients without recurrence, patients with recurrence after successful CRIM, were found to be non-Caucasian, older age, have longer BE segments, and require higher numbers of RFA treatment sessions.

Discussion

- Several risk factors identified in the literature review influence progression of neoplastic transition in BE. These include male gender, advanced age, hiatal hernia, GERD, ethnicity, smoking, poor dietary intake of fruits and vegetables, the type of dysplasia and length of the BE segment. Accurate description and confirmation of biopsies by a second expert pathologist, is highly recommended.
- RFA is proven to be a successful intervention to eradicate IM. Implementation of early treatment of BE demonstrates lower progression rates of LGD-BE to EAC.
- There is not a confirmed number of RFA treatments that can determine long term remission rates of BE or definitive stop time for endoscopic surveillance.
- More studies are needed to determine long term (>5yrs) success of early eradication of LGD.
- There is controversy between studies regarding whether the extent and length of LGD is a predictor of progression to EAC. Being male doubled the risk for GERD patients to develop BE which further doubled the risk of BE patients to develop EAC.
- Evidence supports the efficacy and durability of RFA. Predictors for success for achieving CRIM are related to younger age and shorter initial BE segment length. Advanced age was associated with a higher grade of BE and advancement to EAC.
- The progression of cellular changes in BE is inconsistent, but the risk factors associated with disease progression are clear. Guidelines provided by various gastroenterology societies can assist practitioners to determine patient care management for endoscopic screening, therapy and disease surveillance.

Applicability to Clinical Practice

- Primary care providers need to consistently identify risk factors such as age, race, diet, tobacco, obesity and duration of GERD symptoms when determining candidates for early endoscopic screening for BE.
- Factors that predict the progression of non-dysplastic BE to EAC include the initial dysplasia histology and the length of the BE segment.
- Counsel and teach patients regarding control of modifiable risk factors with emphasis of tobacco cessation and management of co-morbidities.
- A diagnosis of EAC has poor survival rates. Risk stratification can help patients make and maintain good decisions for a better overall health outcome.
- Establish a trusting provider to patient relationship so facts regarding BE and the risks of progression to EAC can be clearly shared and communicated.
- Endoscopic therapy with radiofrequency ablation is now the standard of care for treatment of dysplastic BE. It has high rates of success and durability when used alone or in combination with other gastric therapy.
- Follow-up should be individualized, and treatment decisions should reflect consideration of current guidelines. Lifestyle modification should be exhausted before ablative therapy is decided.

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Gastroenterology societal guidelines for screening and surveillance in Barrett's Esophagus

Gastroenterology Society	Screening	Surveillance NDBE	Surveillance LGD	Surveillance HGD
American Gastroenterology Association	Screen for patients with multiple risk factors: >50 yr. old, male, white race, chronic GERD, Hiatal hernia, elevated body mass index, intra-abdominal distribution of body fat. No screening for general population	No dysplasia, surveillance every 3-5 years	Low grade dysplasia: every 6-12 months	High grade dysplasia unable to eradicate: every 3 months
American Society for Gastrointestinal Endoscopy	Consider endoscopic screening in patients with multiple risk factors for BE and EAC, inform patients this is not a cancer prevention	Consider no surveillance, or every 3-5 yrs. with 4-quadrant biopsies, ablation in select cases	Confirm with GI expert; repeat EGD in 6 mo. to confirm LDG; Yearly surveillance; Endoscopic resection or ablation if warranted	Confirm with GI expert; Consider surveillance EGD 3 mo. in select patients; Endoscopic resection, RFA, or surgical consultation
American College of Physicians	Upper endoscopy in men >50 yr. old with chronic GERD and additional risk factors	Surveillance evaluation for men and women with history of BE; BE without dysplasia, surveillance frequency 3-5 yr. more frequent in patients with BE and dysplasia		