REVIEW ARTICLE

Systematic review comparing radiofrequency ablation and complete endoscopic resection in treating dysplastic Barrett's esophagus: a critical assessment of histologic outcomes and adverse events CME

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Background: With recent advances in endoscopy, endoscopic techniques have surpassed esophagectomy in the treatment of dysplastic Barrett's esophagus (BE).

Objective: To compare the efficacy and safety of complete EMR and radiofrequency ablation (RFA) in the treatment of dysplastic BE.

Design: Systematic review of literature.

Patients: Diagnosis of BE with high-grade dysplasia or intramucosal cancer.

Intervention: Complete EMR or RFA.

Main Outcome Measurements: Complete eradication of dysplasia and intestinal metaplasia at the end of treatment and after >12 months' follow-up. Adverse event rates associated with treatment.

Results: A total of 22 studies met the inclusion criteria. Only 1 trial directly compared the 2 techniques; most studies were observational case series. Dysplasia was effectively eradicated at the end of treatment in 95% of patients after complete EMR and 92% after RFA. After a median follow-up of 23 months for complete EMR and 21 months for RFA, eradication of dysplasia was maintained in 95% of patients treated with complete EMR and 94% treated with RFA. Short-term adverse events were seen in 12% of patients treated with complete EMR but in only 2.5% of those treated with RFA. Esophageal strictures were adverse events in 38% of patients treated with complete EMR, compared with 4% of those treated with RFA. Progression to cancer appeared to be rare after treatment, although follow-up was short.

Limitations: Small studies, heterogeneous in design, with variable outcome measures. Also follow-up durations were short, limiting evaluation of long-term durability of both treatments.

Conclusion: RFA and complete EMR are equally effective in the short-term treatment of dysplastic BE, but adverse event rates are higher with complete EMR. (Gastrointest Endosc 2014;79:718-31.)

Barrett's esophagus (BE) can progress through a dysplasia-carcinoma sequence to esophageal adenocarcinoma.[1,2] As it does, the risk of progression to cancer increases from 0.1% per year for nondysplastic BE[3] to 5.6% per year if high-grade dysplasia (HGD) is present.[4]

Abbreviations: APC, argon plasma coagulation; BE, Barrett's esophagus; CE-D, complete eradication of dysplasia; CE-IM, complete eradication of intestinal metaplasia; HGD, high-grade dysplasia; RFA, radiofrequency ablation.

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Traditionally, esophagectomy has been the recommended treatment for BE with either HGD or intramucosal cancer, but this is associated with significant morbidity and mortality.[5] As a result, endoscopic therapies for treatment of superficial neoplastic lesions have been developed, and these therapies minimize treatment-related morbidity.

Ideally, endoscopic treatments need to target the entire BE mucosa and reduce the risk of recurrence from metachronous lesions in the remaining segment.[6] To date, 2 distinct endoscopic approaches have been widely used to date for this purpose. The first is complete EMR of the BE mucosa, which has the advantage of providing a large histologic specimen and may result in removal of the genetic alterations associated with neoplasia.[7] The other approach is ablation of the BE mucosa by using a variety of

techniques including photodynamic therapy, argon plasma coagulation (APC), and more recently, radiofrequency ablation (RFA). In recent years, RFA has become the ablative treatment of choice in the management of dysplastic BE, with early studies suggesting good efficacy and low rates of adverse events.[8] As a result, RFA has superseded earlier ablative techniques, and newer techniques such as cryotherapy and multipolar electrocautery are not widely available.

RFA is administered by using the HALO system (BARRX Medical, Sunnyvale, Calif), which provides high frequency alternating current to the mucosa with the aim of ablating neoplastic mucosa to allow regrowth of normal squamous mucosa. Two types of HALO devices are available—HALO^{360}, which provides circumferential treatment, and HALO^{90}, which provides more focal treatment. Before ablation, any nodules should be resected, first to ensure that the disease does not extend into the submucosa (making endoscopic therapy unsuitable) and second to ensure that the mucosa is flat so that RFA can be applied effectively.

To date, only one trial has directly compared complete EMR and RFA in treating dysplastic BE.[9] The aim of this systematic review is to compare the efficacy and safety of these 2 techniques. This is important because RFA is substantially more expensive than complete EMR and may require multiple procedures over 6 months or more, making it less acceptable to patients. Therefore, in order to justify use of RFA in the future it must be convincingly proven to be superior to complete EMR, in terms of both efficacy and risk of adverse events.

METHODS

The reporting of this systematic review follows the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[10]

Selection criteria

Studies were selected for inclusion if they reported using complete EMR or RFA to treat BE with HGD or intramucosal cancer, and the treatment intention was complete eradication of the BE mucosa.

Studies in which participants had had previous endoscopic treatment for BE or previous reflux surgery were excluded. Studies were also excluded if the patient cohorts overlapped with other studies, to avoid dual reporting of the same patient cohort. In this situation, the study with the longest follow-up and most detailed results was included.

Search process and study selection

A systematic literature search was performed by 2 authors (G.C., S.M.) in January 2013. The following databases were searched: Pubmed (MEDLINE), EMBASE, and the Cochrane Library. Bibliographies of included articles and the abstracts from the previous 3 years of Digestive Disease Week also were reviewed for relevant reports. A subsequent literature search was performed in October 2013 to identify any additional articles published in the previous year.

Titles and abstracts were independently screened by the 2 authors for relevance. The full text of potentially relevant publications was reviewed to determine inclusion, and results from selected articles were independently extracted by the 2 authors.

Summary measures

The primary outcome was complete eradication of dysplasia (CE-D) and intestinal metaplasia (CE-IM) at the end of treatment, defined as absence of any dysplasia or intestinal metaplasia, respectively, on esophageal biopsy within 12 months of completing treatment. During the initial treatment stage, patients could receive additional endoscopic "escape" treatment. This was defined as any treatment deviation from the preplanned treatment regimen before completion of initial treatment, for example, use of RFA to ablate small areas of residual BE. The frequency with which escape treatment was needed and the approaches used are highlighted in Table 1.

Secondary endpoints

- CE-D/CE-IM at follow-up more than 12 months after completing treatment. Use of additional "touch up" treatment during follow-up to treat recurrence was recorded.
- Short-term adverse events, related to initial endoscopic treatment.
- Long-term adverse events, for example, esophageal stenosis and/or stricture, "buried BE" (the persistence of glandular epithelium beneath the new squamous epithelium), and cancer recurrence.

Results are presented on an intention-to-treat basis. Patients were excluded from analysis if initial endoscopy revealed that the lesion was not been amenable to endoscopic treatment (eg, submucosal invasion). Patients who did not complete treatment or who were lost to follow-up had success of treatment determined by most recent histology. If that was unknown, they were considered treatment failures. Some retrospective studies reported results only for patients successfully treated and followed up. These studies are highlighted in Tables 2 and 3.

Statistical methods

Summary estimates for effectiveness outcomes were generated by pooling results from the prospective studies to calculate an overall mean and 95% confidence intervals (CI). Overall means for all the studies were calculated for the risks of short-term and long-term adverse events.

Assessment of study quality

Quality of included studies was assessed by using the Newcastle-Ottawa Scale for Cohort Studies.[11]