Comparison of endoscopic treatment modalities for Barrett's neoplasia

Waseem J. David, MD,[1] Bashar J. Qumseya, MD,[1,2] Yazen Qumsiyeh, MD,[1,3] Michael G. Heckman, MS,[4] Nancy N. Diehl, BS,[4] Michael B. Wallace, MD, MPH,[1] Massimo Raimondo, MD,[1] Timothy A. Woodward, MD,[1] Herbert C. Wolfsen, MD[1]

Jacksonville, Florida; Thomasville, Georgia; Burlington, Vermont, USA

Background: There are few data comparing endoscopic treatment outcomes for Barrett's esophagus (BE).

Objective: To compare treatment outcomes in BE patients treated with radiofrequency ablation (RFA), RFA after EMR, and porfimer sodium photodynamic therapy (Ps-PDT).

Design: Retrospective, observational study.

Setting: Single tertiary center between 2001 and 2013.

Patients: A total of 342 BE patients treated with RFA (n = 119), EMR+RFA (n = 98), and Ps-PDT (n = 125).

Main Outcome Measurements: Rates of complete remission of intestinal metaplasia (CRIM), BE recurrence, and adverse events.

Results: Baseline BE high-grade dysplasia (HGD) and adenocarcinoma were more common in the Ps-PDT group (89%) compared with the EMR-RFA (70%) and RFA (37%) groups. At a median follow-up of 14.2 months, 173 patients (50.6%) achieved CRIM. CRIM was significantly more common in Ps-PDT patients compared with RFA ($P < .001$) and EMR-RFA ($P < .001$) patients on multivariable analysis. In patients who achieved CRIM, the rates of subsequent BE recurrence were relatively similar among the 3 groups. Although the rates of bleeding were similar, strictures were less common in RFA patients (2.4%) compared with EMR-RFA (13.3%, $P = .001$) and Ps-PDT (10.4%, $P = .043$) patients.

Conclusion: This study of endoscopic treatment for Barrett's dysplasia and neoplasia found that complete remission was achieved more often and more rapidly after Ps-PDT with similar disease recurrence rates compared with EMR or RFA. Adverse events were more common after EMR and Ps-PDT. Further studies are required to determine which ablation and resection techniques are ideally suited for each BE patient. (Gastrointest Endosc 2015;82:793-803.)

(footnotes appear on last page of article)

Barrett's esophagus (BE) is a premalignant condition associated with long-standing GERD and the replacement of squamous epithelium with intestinal columnar mucosa.[1,2] Recent medical literature suggests that the rate of progression of cancer or dysplasia from intestinal metaplasia is low.[3] The risk of cancer development increases in dysplastic mucosa with unregulated cell proliferation, tumor-suppressor gene inactivation, and activation of oncogenes. In a recent prospective trial, progression of low-grade dysplasia to carcinoma was found in 8.8% of patients after 3 years.[4] Patients with BE high-grade dysplasia (HGD) have an even greater risk of cancer, with estimates ranging from 6% to 19% to 28%.[5] Therefore, the goal of endoscopic treatment of dysplastic BE and early-stage adenocarcinoma is to prevent progression to advanced-stage disease.[6]

Endoscopic therapy has advanced from palliative treatments for those who have obstructing tumors to alternative treatments for those who have HGD or early cancer but were unfit fit for surgical resection. Ultimately, prospective, randomized, and controlled trials demonstrated the efficacy of porfimer sodium photodynamic therapy (Ps-PDT) and radiofrequency ablation (RFA), often used

Use your mobile device to scan this QR code and watch the author interview. Download a free QR code scanner by searching "QR Scanner" in your mobile device's app store.

after EMR, for the ablation of BE dysplasia with decreased rates of progression to adenocarcinoma. These techniques ablate or resect the tissue, producing damage to varying depths of the esophagus wall. Depending on the dosimetry selected for drug and light, Ps-PDT features tissue penetration at least to the submucosa. These characteristics make Ps-PDT an effective form of ablation, but Ps-PDT can increase the risk of stricture formation.[5,7-15] EMR also extends to the superficial submucosa layers and, depending on the lateral extent of the resection performed, is also associated with the risk of bleeding, perforation, and stricture formation.[16] To limit the risk of stricture and bleeding, RFA was designed to ablate only the Barrett's glandular mucosa without damage to the deeper esophageal wall. Although EMR for nodular lesions followed by RFA for the remainder of the flat BE is now considered the first-line endoscopic treatment for BE at most centers, complete disease eradication is not always achieved.[17-21] This study compares the clinical outcome and adverse events associated with endoscopic therapy in BE patients treated with EMR and RFA, RFA alone, and Ps-PDT.

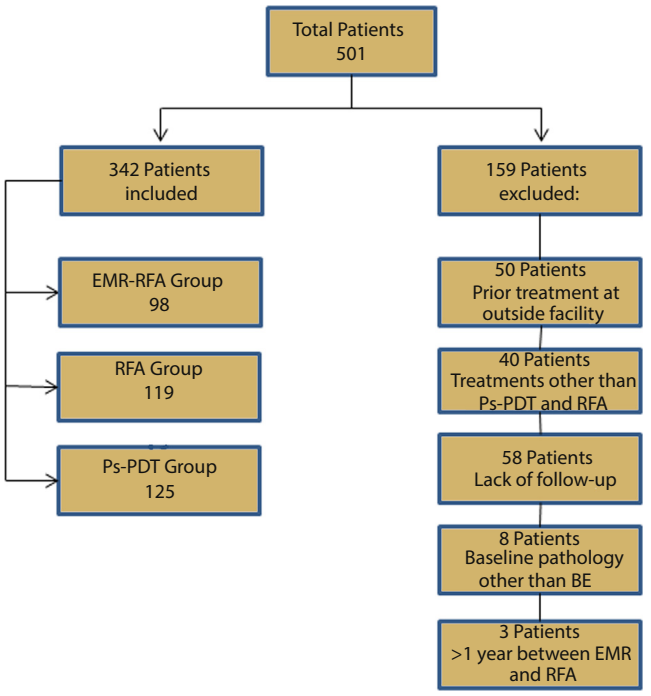

Figure 1. Schematic illustration of the total patients included in the study and the patients excluded from the study. *BE*, Barrett's esophagus; *Ps-PDT*, porfimer sodium photodynamic therapy; *RFA*, radiofrequency ablation.

METHODS

Study patients

This retrospective, observational, cohort study was approved by the Mayo Clinic Institutional Review Board and describes the experience of 501 patients who were referred for evaluation and management of BE between August 2001 and June 2013. Demographic information was collected, including patient age, sex, race, and body mass index. Other recorded information included previous tobacco smoking, chest radiation, coronary artery disease, esophageal cancer, diabetes, and a history of esophagus surgery. Use of aspirin, nonsteroidal anti-inflammatory agents, clopidogrel, warfarin, proton pump inhibitors, and statin cholesterol-lowering agents was also recorded. We also collected Barrett's disease characteristics, including baseline histology, segment length, and the presence of hiatal hernia. Of the 501 total patients, we included 342 who underwent endoscopic therapy (n = 98 EMR-RFA, n = 119 RFA, n = 125 PDT). The use of Ps-PDT occurred more frequently early in the study period. Of the 125 PDT patients, 120 began treatment between 2001 and 2007, whereas 95 of 98 EMR-RFA patients and 82 of 119 RFA patients began treatment between 2008 and 2013. Figure 1 details our selection and exclusion criteria. Most commonly, patients were excluded because they were treated with an alternative form of endoscopic treatment such as cryotherapy, had previously undergone endoscopic treatment elsewhere, or were lost to follow-up. We specifically divided our groups in an attempt to determine the effect of EMR in patients who are subsequently treated with RFA. However, in a secondary analysis, we grouped the EMR-RFA and RFA-alone patients together and compared outcomes between this combined RFA group with those of Ps-PDT patients. In addition, we excluded patients who have undergone EMR before Ps-PDT because the sample size was small and would not allow for meaningful conclusions. There were 30 EMR-PDT patients, but most of them would have been excluded due to a lack of any follow-up and baseline histology of invasive or in situ squamous cell carcinoma or severe squamous dysplasia.

Endpoints

The primary study endpoint was complete remission of intestinal metaplasia (CRIM), defined as a lack of visible columnar-lined esophagus at endoscopy and at least 2 consecutive normal biopsy specimens from the previous BE segment after the start of treatment. The start of treatment was the date of the first endoscopic treatment. For patients who achieved CRIM, a secondary endpoint was BE recurrence, which was defined as the subsequent detection of specialized columnar mucosa in biopsy samples from the target mucosa in the distal esophagus. Finally, we collected data on adverse events that occurred within 48 hours after treatment; these included bleeding, perforation, nausea, vomiting, chest pain, and dysphagia. Bleeding that was self-limited or endoscopically controlled was not considered an adverse event. However, bleeding that required hospitalization or medical intervention such as transfusion were considered adverse events. Stricture was defined as symptomatic dysphagia with esophageal