Commentary

Efficacy and safety of a single staged endoscopic approach to Barrett's esophagus and early esophageal adenocarcinoma

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Over the past decade, endoscopic eradication therapy (EET) has replaced esophagectomy as the preferred treatment approach for patients with high-grade dysplasia (HGD) and low-risk, early stage esophageal cancer, largely owing to the significant morbidity and mortality associated with this procedure. Further, esophagectomy carries a significant negative impact on patient quality of life for those achieving long-term survival. Currently, endoscopic mucosal resection (EMR) followed several weeks later by radiofrequency ablation (RFA) of the adjacent esophageal mucosa is the most commonly employed strategy with successful eradication of disease in most patients. However, this approach requires serial endoscopies for treatment and surveillance, and comparative quality of life data to support the assertion that EET is associated with improved quality of life compared to esophagectomy is lacking. In their study "*Single-session endoscopic resection and focal radiofrequency ablation for short-segment Barrett's esophagus with early neoplasia*", Barret *et al.* examine the safety and efficacy of concomitant EMR and RFA for management of HGD and early adenocarcinoma to reduce the number of endoscopies required for successful disease eradication (1).

In summary, this retrospective review evaluates the safety and efficacy of combining EMR with RFA in a one-step procedure for patients with biopsy proven Barrett's esophagus (BE) and early adenocarcinoma. EMR was accomplished in a piece-meal fashion and utilized either the MBM or endoscopic resection-cap technique. Focal RFA was administered circumferentially to the gastro-esophageal junction using the Barrx^{90} ablation device (Covidien, Sunnyvale, CA, USA), with care taken to avoid ablation of the exposed submucosa at the EMR site. The majority of patients (90%) received 15 J/cm^2 as their ablative regimen, and the primary outcome was biopsy proven resolution of BE after initial treatment. Secondary outcomes included long-term endoscopic and histologic resolution, with a median follow up period of 19 months and complications of endoscopic therapy. In the intention to treat analysis, complete histologic remission of intestinal metaplasia and dysplasia was achieved after one treatment in 43% of patients, and at the completion of the EET protocol in 95%, with sustained remission in 83% of patients at 19 months follow up. One patient developed a post-treatment esophageal perforation, and 33% of patients developed clinically significant esophageal stenosis requiring a median of two endoscopic dilations.

The treatment algorithm for early EAC and BE/HGD has evolved over the last decade and remains somewhat controversial. Traditionally, esophagectomy has been the treatment choice for these pathologies owing to very high 5-year survival rates. However, despite the proliferation of minimally invasive esophagectomy, morbidity rates remain as high as 40% (2-4). Endoscopic management of low-risk esophageal adenocarcinoma (defined as T1a lesions without evidence of submucosal extension, de-differentiation, or lymphovascular invasion) has emerged as a successful alternative to invasive surgical procedures (2,5-7).

The paradigm shift from esophagectomy to EET in these patients has been driven by the success of local resection due to the low lymph node metastasis rate of 0–2.5% (5,8).

Currently, options for endoscopic management include EMR, stepwise radical endoscopic resection, RFA and a combination of these modalities. While EMR has proven to be very effective in margin assessment and managing nodular disease (4-7), the addition of RFA has effectively reduced the rate of metachronous lesions in comparison to EMR alone (9-11). In contrast, stepwise radical EMR with or without the addition of RFA has been associated with prohibitively high rates of post-operative stenosis (5). Review of our institutional data supports this algorithm; a recent retrospective review at the Ohio State Wexner Medical Center reported complete eradication of T1a EAC in 93% of patients with a median follow up of 15.5 months (3,4). The main concern regarding this treatment is disease recurrence and malignant progression, which, in patients with either positive deep or radial margins, can be significant within the first 6 months of treatment and highlights the importance of appropriate patient selection and strict surveillance schedules (4,12).

The results of the present study add to the increasing body of data suggesting that combination EMR/RFA therapy produces excellent short and medium-term eradication of EAC and represents an effective alternative to aggressive surgical management. More specifically, this review attempts to address how best to deliver this combination therapy. Based on current guidelines, EMR is performed initially and ablative therapy is scheduled 6–12 weeks later and repeated as needed to achieve complete eradication of disease. The delay between EMR and RFA not only allows for the resection bed to heal but also provides time for definitive pathologic evaluation and appropriate decision-making. While this time course is generally well tolerated, there have been reports of esophageal stenosis after aggressive endoscopic resection, which can impede the success of future RFA sessions. Furthermore, separating each therapy requires at least three separate endoscopic procedures. Given these concerns, the authors attempted to provide preliminary evidence to support combining EMR and RFA into a single session to limit the number of procedures while optimizing the environment for RFA.

On review of our institutional data, approximately 40.7% of patients undergoing EMR of esophageal nodules with curative intent were found to have high-risk features that required referral for esophagectomy (4). In this study, 10% of patients demonstrated high-risk pathologic features following the initial combined session. Although only one of these patients was a surgical candidate, this highlights the potential for unnecessary ablative therapies prior to surgical management. On the other hand, the remaining patients did show complete disease eradication after an average 1 or 2 procedures, with 43% requiring only one therapeutic endoscopy. Although this suggests that concomitant EMR/RFA may reduce the need for additional endoscopic procedures, it would be interesting to know if any trends exist to suggest that precursor lesions (BE/LGD or HGD) respond differently to the single-stage approach than those with invasive cancers in terms of treatment success or complications.

When considering the single-stage approach as a method for reducing the number of required endoscopies, complication rate becomes important. In the present study, concomitant EMR/RFA was associated with a 33% esophageal stenosis rate, significantly higher than that reported in series of stepwise EMR followed by RFA (2-4,11,13,14). While these strictures were successfully managed endoscopically, these patients required an average of two additional endoscopies for management of the stricture, negating this advantage of the single stage approach in these patients. One explanation for the relatively high stenosis rate observed in this study is the use of the 15 J/cm^2 approach used in most patients, rather than the more commonly utilized 12 J/cm (3). However, one previous preclinical study of concomitant EMR/RFA in a porcine model also found very high esophageal stricture rates associated with this approach (15).

Overall, the authors should be commended for driving the evolution of EET and continuing to publish on this important topic. As the search for the optimal method of EET continues, it is important to consider both oncologic outcomes and patient quality of life during and after treatment. Clearly, EET has emerged as the preferred approach in low-risk, early-stage esophageal adenocarcinoma given the high rates of disease eradication with these techniques in this and other studies. Further studies of the efficacy, morbidity, and psychological burden of serial endoscopic surveillance associated with concomitant or sequential EMR and RFA are required to determine the optimal approach for EET.

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