Eliminating a Need for Esophagectomy: Endoscopic Treatment of Barrett Esophagus With Early Esophageal Neoplasia

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Over the past several years, endoscopic ablation and resection have become a new standard of care in the management of Barrett esophagus (BE) with high-grade dysplasia (HGD) or intramucosal adenocarcinoma (IMC). Risk factors for failure of endoscopic therapy and the need for subsequent esophagectomy have not been well elucidated. The aims of this study were to determine the efficacy of radiofrequency ablation (RFA) with or without endoscopic mucosal resection (EMR) in the management of BE with HGD or IMC, to discern factors predictive of endoscopic treatment failure, and to assess the effect of endoscopic therapies on esophagectomy volume at our institution. Data were obtained retrospectively for all patients who underwent endoscopic therapies or esophagectomy for a diagnosis of BE with HGD or IMC in our department between January 1, 2004, and December 31, 2012. Complete remission (CR) of BE or HGD or IMC was defined as 2 consecutive biopsy sessions without BE or HGD or IMC and no subsequent recurrence. Recurrence was defined by the return of BE or HGD or IMC after initial remission. Progression was defined as worsening of HGD to IMC or worsening of IMC to submucosal neoplasia or beyond. Overall, 57 patients underwent RFA with or without EMR for BE with HGD ($n = 45$) or IMC ($n = 12$) between 2007 and 2012, with a median follow-up duration of 35.4 months (range: 18.5-52.0 months). The 57 patients underwent 181 ablation sessions and more than half (61%) of patients underwent EMR as a component of treatment. There were no major procedural complications or deaths, with only 2 minor complications including 1 symptomatic stricture requiring dilation. Multifocal HGD or IMC was present in 43% (25/57) of patients. CR of IMC was achieved in 100% (12/12) at a median of 6.1 months, CR of dysplasia was achieved in 79% (45/57) at a median of 11.5 months, and CR of BE was achieved in 49% (28/57) at a median of 18.4 months. Following initial remission, 28% of patients (16/57) had recurrence of dysplasia ($n = 12$) or BE ($n = 4$). Progression to IMC occurred in 7% (4/57). All patients without CR continue endoscopic treatment. No patient required esophagectomy or developed metastatic disease. Overall, 6 patients died during the follow-up interval, none from esophageal cancer. Factors associated with failure to achieve CR of BE included increasing length of BE (6.0 $\pm$ 0.6 vs 4.0 $\pm$ 0.6 cm, $P = 0.03$) and shorter duration of follow-up (28.5 $\pm$ 3.8 months vs 49.0 $\pm$ 5.8 months, $P = 0.004$). Shorter surveillance duration (17.8 $\pm$ 7.6 months vs 63.9 $\pm$ 14.4 months, $P = 0.009$) and shorter follow-up (21.1 $\pm$ 6.1 months vs 43.2 $\pm$ 4.1 months) were the only significant factors associated with failure to eradicate dysplasia. Our use of esophagectomy as primary therapy for BE with HGD or IMC has diminished since we began using endoscopic therapies in 2007. From a maximum of 16 esophagectomies per year for early Barrett neoplasia in 2006, we performed only 3 esophageal

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Dr. Watson has been a paid consultant to Covidien, Inc for projects unrelated to the current study. Dr Peters reports receiving consulting fees from Torax Medical and Given Imaging. Drs Lada, Shakoor, Nieman, Han, Tschoner, Peyre, and Jones have no commercial interests to disclose.

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http://dx.doi.org/10.1053/j.semtcvs.2014.12.004

resections for such early disease in 2012, all for IMC, and we have not performed an esophagectomy for HGD since 2008. Although recurrence of BE or dysplasia/IMC was not uncommon, RFA with or without EMR ultimately resulted in CR of IMC in all patients, CR of HGD in the majority (79%), and CR of BE in nearly half (49%). No patient treated endoscopically for HGD or IMC subsequently required esophagectomy. In patients with BE with HGD or IMC, RFA and EMR are safe and highly effective. The use of endoscopic therapies appears justified as the new standard of care in most cases of BE with early esophageal neoplasia.

Semin Thoracic Surg 26:274–284

Keywords: Barrett Esophagus, dysplasia, adenocarcinoma, ablation, esophagectomy

INTRODUCTION

The link between gastroesophageal reflux disease (GERD), Barrett esophagus (BE), esophageal dysplasia, and esophageal adenocarcinoma (EAC) has been well established. The prevalence of BE has been estimated to be between 1.6% and 6.8% of the general population, which translates into approximately 5-20 million people within the United States alone.[1,2] The 0.12%-0.4% annual risk of progression of nondysplastic BE to EAC has fueled surveillance of known BE.[3] Along with the increasing rates of obesity and GERD, the incidence of EAC in the United States has been rising over the past several decades. Data from the American Cancer Society for 2014 predict 18,100 esophageal cancer diagnoses with 15,450 deaths and an overall 5-year survival of 17%.[4-6]

Although patients commonly present with the manifestations of advanced, incurable esophageal malignancy, early-stage esophageal neoplasia can be treated with the expectation of cure. Esophagectomy has been the standard of care for BE with high-grade dysplasia (HGD) or intramucosal adenocarcinoma (IMC) for decades. Multiple surgical series have shown that esophagectomy, when performed by expert surgeons in specialty centers for early neoplasia, is associated with low perioperative mortality and acceptable morbidity.[7] More recently, endoscopic ablative and resective technologies and techniques have been introduced into clinical practice, altering the landscape of therapies available for eradication of early esophageal neoplasia in the setting of BE.

Current guidelines proposed by specialty medical societies in the United States, as well as the National Comprehensive Cancer Network, recommend endoscopic therapies as the preferred treatment for BE with HGD, relegating esophagectomy to the minority of cases not suitable for endoscopic approaches.[8-11] These same societies, however, have yet to take a stance on the optimal management of IMC. In addition, the risk factors for failure of endoscopic therapy and the need for subsequent esophagectomy in the setting of early neoplasia have not been well elucidated. The aims of this study were to determine the efficacy of radiofrequency ablation (RFA) with or without endoscopic mucosal resection (EMR) in the management of BE with HGD or IMC, to discern factors predictive of endoscopic treatment failure, and to assess the effect of endoscopic therapies on esophagectomy volume at our institution when undertaken for early esophageal neoplasia.

METHODS

Study Design

Data were obtained from a prospectively maintained clinical database and medical record review of all patients who underwent endoscopic treatment or esophagectomy for a diagnosis of BE with HGD or IMC in the Division of Thoracic and Foregut Surgery, Department of Surgery, at the University of Rochester Medical Center between January 1, 2004, and December 31, 2012. Endoscopic therapies were initiated in 2007. The clinical records of 102 consecutive patients undergoing endoscopic therapies were available for review. After exclusion of 42 patients with only low-grade dysplasia and 3 patients who underwent EMR alone with detection of submucosal disease, 57 patients treated with RFA with or without EMR for HGD or IMC remained in the final study population. Patient demographics and treatment characteristics, including age, sex, body mass index, comorbidities, clinical factors, treatment efficacy, complications, and survival were collected and compared. The data were recorded in a Microsoft Excel database file (Microsoft Corp, Redmond, WA).

Complete remission (CR) of BE or HGD of IMC was the primary end point. The secondary end point was survival from the time of initial treatment. Survival was assessed via medical record review and the Social Security Death Index (accessed on October 2, 2013) with patient status classified as