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Endoscopic therapy for flat dysplastic Barrett esophagus

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Abstract

Both stepwise radical resection (SRER) and radiofrequency ablation (RFA) are effective endoscopic strategies for the treatment of patients with flat dysplastic Barrett esophagus. Findings from a recent randomized, controlled trial indicate that the two treatments have similar efficacy, but considerably more complications are associated with SRER compared to RFA.

For patients with non-nodular Barrett esophagus and high-grade dysplasia, some form of intervention is recommended as this is associated with an up to 19% per patient-year risk of developing esophageal adenocarcinoma.^{1,2} Endoscopic treatment of patients who have Barrett esophagus with high-grade dysplasia has been demonstrated to markedly decrease this risk, and results in reversion to neosquamous epithelium in the majority of patients.^{1,2} For patients with visible mucosal abnormalities in Barrett esophagus, focal resection by endoscopic mucosal resection enables increased accuracy of histological grading of the lesion, as well as potentially curative resection of superficial esophageal adenocarcinoma. However, identifying the most appropriate treatment for patients with non-nodular high-grade dysplasia has generated debate. In a recent paper, van Vilsteren and colleagues attempt to address this issue.¹

To date, endoscopic techniques have focused on either cutting or burning (or freezing) high-risk tissue in patients with Barrett esophagus. Stepwise radical endoscopic resection (SRER) removes all Barrett esophagus with consecutive sessions of endoscopic mucosal resection. By contrast, ablation techniques focus on burning or freezing dysplastic tissues by a variety of methods. Because both methods can result in the complete removal of the neoplastic lesion, their relative merits are fiercely contested. Proponents of SRER point to the large resection specimen achieved with this method, which enables superior histological grading of the lesion. Compared to mucosal ablation, SRER also enables an increased depth of tissue destruction, which presumably results in a decreased incidence of residual buried glandular epithelium. Investigators who favor ablative modalities reference the proven effectiveness of these strategies in inducing reversion to neosquamous epithelium and in decreasing the rate of progression to cancer. They further cite the ease of use of ablative modalities and the relatively low risk of complications, especially strictures, compared to SRER. Therefore, a randomized comparison of SRER and mucosal ablation in the setting of non-nodular high-grade dysplasia is desirable and logical.

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Competing interests

N. J. Shaheen declares associations with the following companies: AstraZeneca, BÂRRX Medical, CSA Medical, NeoGenomics Labs, Oncoscope and Takeda. See the article online for full details of the relationships. A. F. Peery declares no competing interests.

Against this backdrop, a recent multicenter, randomized, controlled trial by van Vilsteren and colleagues assessed the safety of SRER compared to RFA with focal endoscopic resection.³ The trial included patients who had Barrett esophagus <5 cm in length. Participants underwent a maximum of four endoscopic treatments and were then eligible for salvage treatment with an alternative modality. Patients randomized to RFA received salvage therapy with either endoscopic resection or ablation with hot biopsy forceps. Patients randomized to SRER received salvage therapy with either RFA, argon plasma coagulation or ablation with hot biopsy forceps. Patients who underwent RFA therapy were treated with the BÂRRX HALO³⁶⁰ and HALO⁹⁰ devices at 40 W/cm² and 12 J/cm². Those undergoing SRER were treated in a hemicircumferential pattern with the endoscopic resection-cap, multiband mucosectomy or simple snare techniques.

In keeping with prior studies, there were high rates of complete eradication of neoplastic tissue (96% versus 100% for RFA and SRER, respectively) and intestinal metaplasia (96% versus 92% for RFA and SRER, respectively) among the 47 randomized patients, regardless of the endoscopic therapy received.^{1,4-11} However, the incidence of complications was markedly different between the two arms. Of patients who underwent SRER, 88% developed a symptomatic esophageal stricture and one-quarter (6/25) had scarring and strictures that prevented further SRER and required salvage treatment with endoscopic ablation (RFA or argon plasma coagulation) to obtain complete eradication of disease. One patient in the SRER arm of the study had an esophageal perforation. By comparison, only 14% of patients who received RFA developed symptomatic strictures and none had perforations.

The implications of stricture formation in patients who undergo endoscopic therapy go beyond dysphagia and patient dissatisfaction. Such patients are more difficult to monitor for recurrent disease than patients without stricture formation because of the difficulty in visualizing a strictured and scarred lumen. Strictures often necessitate additional endoscopic procedures for evaluation and treatment, which increases the risks and costs associated with endoscopic therapy. Not surprisingly, the patients who underwent SRER in this trial required twice the number of endoscopic procedures compared with patients in the RFA arm.

The increased risk of strictures associated with using SRER to treat patients with non-nodular dysplastic Barrett esophagus might be tolerable if resection provided an additional benefit. For example, if the use of SRER enabled diagnosis of previously undetected invasive adenocarcinoma, such a finding could clearly change treatment plans. However, patients with non-nodular dysplasia very rarely have invasive cancer. Treatment with ablation might delay the diagnosis of invasive cancer, but is unlikely to change the poor prognosis of nodal disease. The current paper by van Vilsteren *et al.* adds to growing sentiment that it is unwise to subject our patients to a substantial likelihood of stricture by performing SRER for flat dysplasia for the unproven benefit of better outcomes.

Endoscopic mucosal resection and ablation are complimentary methods. When used judiciously, they reduce the risk of esophageal cancer with a tolerable adverse effect profile. The paper by van Vilsteren and colleagues further confirms that resection of visible mucosal abnormalities and ablation of the remaining Barrett esophagus provides excellent overall results for the appropriately chosen patient, such as subjects with nodular high-grade dysplasia. Endoscopic ablation with focal resection of nodular disease offers the benefit of tissue acquisition of the most worrisome endoscopic lesion with a reduced risk of complications when compared to SRER. Although it would be desirable to have the entire pre-cancerous lesion for histological assessment, the additional morbidity associated with SRER makes it an inferior choice for those with non-nodular dysplastic Barrett esophagus.

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