## **EDITORIAL**

# Ablation of the Post Endoscopic Mucosal Resection Margin: The New Standard?

See "Thermal ablation of mucosal defect margins reduces adenoma recurrence after colonic endoscopic mucosal resection," by Klein A, Tate DJ, Jayasekeran V, et al, on page 000.

**E** ndoscopic mucosal resection (EMR) has become the primary approach to remove large, nonpedunculated colorectal polyps. However, a high risk of recurrence, ranging from 10% to 30%, has remained a major challenge.<sup>1-7</sup> The main risk factors for recurrence include piecemeal resection, larger size, and intraprocedural bleeding.<sup>8</sup> So far, systematic attempts to reduce recurrence and assure complete resection, for instance by extending the resection margin, have not been successful.<sup>1</sup> The search for a method to reduce recurrence after EMR and improve its efficacy was therefore ongoing.

Perhaps no longer. In the current issue of Gastroenterology, Klein et al<sup>4</sup> from the Australian Colonic Endoscopic resection study group report the results of a randomized trial that included 390 patients with 416 large ( $\geq 20$  mm) nonpedunculated colorectal polyps. After visibly complete polyp removal by EMR, polyps were randomized to ablation or no ablation of the resection margin. In the ablation group, the entire resection margin was ablated with soft coagulation using the tip of the resection snare (snare tip soft coagulation [STSC]). Recurrence was observed far less frequently in the ablation group (5%) than in the control group (21%). Ablation was most beneficial for polyps that were >40 mm (36% vs 3% recurrence), and less so for polyps that were <40 mm (12 vs 6%; P = .1). Importantly, a reduction in risk was only seen for polyps that were removed with piecemeal and not with en bloc resection.

The findings corroborate a small prior randomized, controlled trial, in which margin ablation with argon plasma coagulation decreased adenoma recurrence.<sup>9</sup> However, the small sample size (n = 22) and the use of older generation endoscopes without high-definition white light to properly visualize the margins question the generalizability of the findings. An unusually high recurrence rate of 64% in the control group further raises questions about the quality of the resection technique used in the study.

The results of the study by Klein et al<sup>4</sup> are potentially practice changing because of the magnitude of the observed effect and the quality of the underlying trial methodology. The randomized design, a large sample size, adequate power, and participation of multiple endoscopists at several centers are factors that strengthen the validity and generalizability of the findings. The main limitations include that endoscopists could not be blinded to the intervention (which is in the nature of such studies) and the definition of recurrence. Recurrence was based on visible assessment of the resection site at follow-up, not on histology, because biopsies were missing for 24% of cases. However, in additional analysis, the authors also show that visible assessment of recurrence achieved a negative predictive value of 99%, ensuring the reader that the obtained results are valid.

Are there any concerns that might give us pause in adopting margin ablation as a new standard? Three considerations come to mind. First, the results are in contrast with a prior study by the same group, in which extending the resection to include a 5-mm healthy tissue margin had no effect on recurrence.<sup>1</sup> If residual tissue is the nidus for regrowth, an extended margin must lower recurrence, unless (a) the recurrence originates from islands at the resection base-but this should have been an issue in both studies, or (b) an intended 5-mm margin was not truly achieved in that study. The latter seems a more plausible explanation, because one might easily lose sight of the extent of the lesion when removing it piece by piece and when cautery artifacts may further obscure visibility. The discordant results also caution us to change practice based on a single study, no matter what quality.

Second, the recurrence rate of 21% in the control group was greater than reported in a systematic review  $(15\%)^{10}$ and in previous reports by the same group (16%).<sup>6</sup> Such recurrence was observed despite the exclusion of more difficult lesions that failed previous resection attempts into the study. Furthermore, there was a broad variation of recurrence rates among individual endoscopists, ranging from 0% to 42% in the control arm and 0% to 21% in the treatment arm. These observations raise the question of endoscopist bias. However, even when excluding the endoscopists with high recurrence rates in the control group, the benefit of ablation remained apparent. Potentially, some endoscopists obtain a wider margin and additional ablation may be less useful. It seems, therefore, important to better understand what specific technical details make ablation more or less effective.

Third, complete ablation of the margin with STSC may seem easy in expert hands. In this study, the primary investigator trained all participating endoscopists. It is unclear if this technique will be as effective in the broader community of endoscopists.

It is important to note that a visibly clean resection base is required to minimize recurrence. Although polyps with previous incomplete resection were excluded from the study, one can imply that margin treatment may lower recurrence in these lesions too; however, ensuring a clean base is particularly important for these lesions with a higher risk of submucosal fibrosis.

So, how should we approach our next large polyp? Perhaps the most important take home message is: It is all 116

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about the margin! The study is convincing that the margin 120 harbors the seed for neoplastic regrowth and bears extra 121 attention. Ablating the resection margin with STSC after 122 piecemeal resection should be strongly considered. Other 123 techniques might work too and should be investigated. For 124 instance, extending the resection to reliably obtain a healthy 125 margin-that is, after marking the extent of the lesion as 126 done with ESD-should yield a similar decrease in recur-127 rence. Argon plasma coagulation may also be effective; 128 however, whether it has the same ablation effect on tissue 129 as STSC is unclear. 130

Directed marginal ablation will likely become the new 131 addition to the armamentarium of EMR skills, which already 132 includes recognizing pit patterns and morphology, applying 133 the right electrocautery setting, controlling of bleeding, 134 treating perforation, and mastering clipping.<sup>11–13</sup> Such skills 135 will ensure that EMR of large colorectal polyps will be as 136 effective and safe as possible, emphasizing the need for 137 complex polyp resections to be done by adequately trained 138 endoscopists. 139

Future studies should be encouraged that examine how 140 STSC performs in general practice and how STSC compares 141 to other margin treatments. Furthermore, long-term data on 142 delayed recurrence and need for surgery would be helpful 143 to understand the cost effectiveness of STSC. Overall, the 144 presented study solidifies EMR as the primary choice for 145 removal of large colorectal nonpedunculated polyps. With 146 the right technique almost all polyps can be removed safely 147 and completely. 148

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The authors disclose no conflicts.	Q2
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