How to treat diminutive polyps? Do we need more evidence?

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Bibliography
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The question of whether we manage polyps effectively has come to prominence because of the rates of interval or post-colonoscopy colorectal cancers, which range from 2.5% to 10.7% and which may in part be due to a failure to resect polyps completely (radically) [1,2]. This issue was highlighted in the recently reported CARE (Complete Adenoma REsection) study of polyps 5 to 20 mm in size, which reported an overall rate of incomplete resection of 10% [3]. However, the vast majority of polyps resected at colonoscopy (80%) are 5 mm or smaller in size [4]. Although the rate of advanced disease on a per-polyp basis is low, the fact that small polyps are so common means that the absolute number of small polyps harboring advanced disease is comparable with the number of larger (6 – to 9-mm) polyps [5]. It is therefore possible that a reasonable percentage of interval cancers arise in diminutive polyps that have been nonradically, partially resected [2].

These lesions have traditionally been considered low risk, and therefore low risk methods to resect them – that is, cold techniques – have increasingly been favored. Hot biopsy is more difficult to justify, given the risks for bleeding and late perforation and the supportive data against hot biopsy derived from animal models [6,7]. There is also a requirement to retrieve tissue for pathology to allow a determination of correct surveillance intervals; however, retrieving small polyps is a challenge, and the use of hot techniques can lead to tissue destruction, rendering pathologic assessment impossible.

Optical biopsy may help here because a diagnosis is potentially available for 100% of detected polyps, whereas 17% of small and diminutive lesions may be lost or destroyed [8,9]. Recent European Society of Gastrointestinal Endoscopy guidelines support the limited use of optical biopsy for diminutive polyps in controlled circumstances and in expert hands, but community-based data suggest that this approach is not yet suitable for widespread implementation [8, 10]. Therefore, one option in expert hands may be not to treat some of these lesions at all and to leave them in situ, avoiding issues of resection risk, retrieval, and pathologic assessment as well as reducing costs—the DISCARD (Detect InSpect ChAracterise Resect and Discard) strategy [9], endorsed in the American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) statement [11].

Nevertheless, the majority of lesions proximal to the rectosigmoid do require resection. If we reject hot biopsy as too dangerous, as many have done, then the remaining three methods are cold forceps polypectomy, cold snaring, and hot snaring. Gómez and colleagues present pilot data in this issue of *Endoscopy International Open*, looking at the effectiveness of a CARE type of study, in which the resection beds of diminutive lesions are analyzed for residual polyp [12]. The fact that such a pilot study has been performed and reported is a testament to the maturity developing in endoscopic research trial design, in which a controlled, stepwise approach is adopted to establish feasibility and highlight potential pitfalls before larger definitive trials are undertaken. The Mayo team members are to be congratulated on this. Specifically, they observe that for most endoscopists, cold endoscopic mucosal resection of the polyp base after polypectomy is not feasible, and that biopsy of the edge of the base is more feasible.

The trial team had two main aims. The first was to demonstrate the feasibility of recruiting patients into a polypectomy trial with an outcome measure of completeness of polypectomy, in which they would be randomized to one of three methods of polypectomy. With 60 patients included at baseline, 62 polyps were randomized and resected from 37 patients. The study team does not state how many patients had to be approached before 60 patients were recruited, which is an im-

portant consideration. No patients reported harm from the procedure at 30 days. Therefore, a larger trial with this methodology seems viable.

The second aim was to collect data on the rate of incomplete resection to support a power calculation for the main study. Here, the authors found that 5 of 60 polyps (8%; 95%CI 3%–19%) had residual tissue in the polyp base; however, this was not evenly distributed. None of 20 hyperplastic polyps showed residual tissue, whereas 3 of 31 adenomas (10%) and 2 of 4 sessile serrated adenomas (50%) had residual tissue. Of the polyps, 89% were classified as sessile and 11% as flat, presumably based on the Paris classification, although this is not explicitly stated. There has been recent concern about the validity of the Paris classification, with only "moderate" inter-observer agreement among experts ($\kappa = 0.42$) for all polyps; agreement is worse for diminutive polyps, with a κ value of 0.27 ("fair") [13]. This may be relevant for diminutive polyps, in which tissue grip may be better on the steeper sides of a sessile lesion.

There are a number of interesting findings in this small data set: that residual neoplastic tissue is as common as was seen in the CARE study, and that serrated lesions seem to be at greater risk for residual tissue than adenomas, although the numbers are very limited. It is also striking that none of the 20 hyperplastic polyps showed residual tissue. Again, this may reflect the small number but sits in stark contrast to the high rates for sessile serrated adenomas. The failure of cold forceps polypectomy with multiple bites in polyps up to 5 mm in size is unsurprising, and a salutary lesson is that resection with this technique generally should be limited to polyps that can be completely engulfed in the cups of the biopsy forceps in a single bite – that is, polyps less than 2.8 mm in size [7,14]. However, the failure of cold snaring despite optimal technique, with a small rim of normal tissue left, is more surprising and suggests that we may also need to review this technique as more data become available. This is in the context of endoscopists feeling that they could not see residual tissue in polyp bases when they used modern high resolution and high definition colonoscopes.

Does this pilot study lead to any conclusions regarding the question posed in the title of this editorial: do we need still more evidence? Undoubtedly, yes. Like the best research, this pilot study raises more questions than it was expected to answer, suggesting that residual tissue after the resection of diminutive polyps may be at least as important as it is in the larger, 5 – to 20-mm polyps described in the CARE study. A larger study involving multiple operators and ideally conducted at multiple centers is needed, and these data demonstrate that such a study is feasible. In an ideal world, such a study would also involve longer-term follow-up to discover what happens to incompletely resected lesion sites and to see if important dysplasia recurs in the colonic segments in which incomplete (nonradical) resection is proven. The safety of hot snaring techniques will also be a key issue, especially in the right side of the colon. In the era of heroic endoscopic mucosal resection and endoscopic submucosal dissection, the resection of diminutive polyps has become something of a Cinderella topic. This pilot study suggests that diminutive polyps must also come to the ball.

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