

large non-pedunculated colorectal polyps: meta-analysis of individual patient data from randomized controlled trials.” By representing 1248 patients with proximal large nonpedunculated colorectal polyps (LNPCPs) from 4 randomized controlled trials, the authors concluded that preventive clipping could effectively prevent the bleeding after EMR of proximal LNPCPs. We would like to share our reservations about the results of this study.

In addition to the above result, the author further discovered nonbleeding adverse events and concluded that clipping did not affect perforation because traditional meta-analyses showed that the relative risk of perforation was 0.76 (95% CI, 0.17-3.38), and by analyzing individual data on 1150 patients, the odds ratio of perforation was 0.78 (95% CI, 0.17-3.54).

However, there is a problem that cannot be ignored: the incidence of perforation after colonic EMR of lesions >2 cm was only 1.5%,² and the event rate of perforation in this overall cohort was only 0.6%. The low event rate may result in a type II statistical concern and makes it difficult to accurately assess. Thus, caution should be taken in concluding that preventive clipping is not associated with perforation. Additionally, whether clipping affects perforation should be discussed with other previous studies in the discussion section to enable a more rigorous conclusion to be drawn.

Overall, we think that whether preventive clipping is associated with perforation should be interpreted with caution.

DISCLOSURE

All authors disclosed no financial relationships.

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Response



We thank Deng et al¹ for their interest in our meta-analysis² and for their letter to the editor. In their letter, the authors raise concerns regarding our observed result that prophylactic clip closure was not associated with the incidence of delayed perforation after EMR of proximal large nonpedunculated colorectal polyps (LNPCPs). Deng et al correctly point out that a type II error could potentially be responsible for the lack of association between clipping and perforation, given the low event rate of 0.6%. Whereas this is technically true, we would like to point out 2 important points.

First, we would like to restate that the odds ratio of perforation with clip closure (vs no clip closure) from individual patient data in our study was 0.78 (95% confidence interval, .17-3.54). Although a lack of adequate power could theoretically be blamed for the failure to show a statistically significant association when in fact there is a true association (type II error), the modest odds ratio point estimate we observed would argue against this possibility. To illustrate this, if we were to imagine that the point estimate from our results was statistically significant, we would arrive at a number needed to treat of 631 patients to avoid 1 perforation. Even with a higher theoretical rate of perforation of 1.5%,³ as Deng et al¹ cite, using our cohort size, which represents all patients from randomized trials to date examining this population, the number needed to treat would still be 232 to prevent perforation, which is of doubtful clinical benefit. Although several meta-analyses have examined both the ideal efficacy and the real-world effectiveness of prophylactic clipping,⁴⁻⁶ ours was the first to report the risk of perforation specifically for proximal LNPCPs, but is still underpowered despite including data on >1200 patients. Given the difficulties with designing adequately powered trials to address this clinical question, future large-scale observational studies are likely required to further elucidate the real-world incidences of non-bleeding adverse events following prophylactic clipping.⁷

Second, as we noted in our article, our data provide conclusive support for contemporary guidelines recommending that prophylactic clip closure should be the standard of care after EMR of proximal LNPCPs because of the established benefit on the prevention of delayed bleeding.⁸ Thus, given the established benefits of prophylactic clipping in this clinical context, the small theoretical added benefits on mitigating the risk of delayed perforation, while possible, could arguably be considered a

moot point, because clip closure of these lesions should be attempted in any event. After EMR of nonproximal LNCPs or other lesions for which the guidelines do not recommend routine prophylactic clip closure, we maintain that the decision on whether or not to clip to prevent perforation should be based on the extent of deep mural injury observed at the time of resection,⁹ rather than performed routinely.

DISCLOSURE

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