Prevention of clinically significant post-EMR bleeding: To clip or not to clip?

Endoscopic mucosal resection (EMR) is the existing standard of care for the management of large nonpedunculated colon polyps (LNPCPs), having a high safety and cost profile compared with other resection techniques such as endoscopic submucosal dissection and surgery. Adverse events (AEs) related to EMR include post-EMR bleeding, perforation, and postpolypectomy syndrome. Clinically significant post-EMR bleeding (CSPEB) occurs in 5% to 7.2% of cases and is more common in the right side of the colon. Significant risk factors for post-EMR bleeding include polyp size ≥10 mm, right-sided colonic lesions, laterally spreading tumors, use of anticoagulants, pedunculated lesions with thick stalks, and patient comorbidities such as cardiovascular or chronic renal disease. Despite these identified risk factors, the optimal therapy to prevent bleeding after colorectal EMR has not been determined. Moreover, the specific patient or lesion criteria by which to apply prophylactic therapy has not been defined. Several risk scoring systems have been validated in an attempt to help individualize management. Additionally, several advances, including prophylactic clipping, suturing, and coagulation have been studied to reduce the rates of these AEs, with variable results.

Prophylactic clipping has been extensively used as a simple way to prevent bleeding after EMR of large colon polyps, although only selective application in high-risk patients has been shown to be cost effective. Furthermore, owing to uncertainty regarding applicability, recommendations regarding the benefits of prophylactic clipping for bleeding prevention remain nonspecific, with moderate-quality evidence in consensus recommendations. The United States Multi-Society Task Force recommends prophylactic clipping of defects ≥20 mm in the right side of the colon when feasible. By contrast, the 2017 European Society of Gastrointestinal Endoscopy does not recommend routine endoscopic clip closure or other methods of prophylaxis to prevent delayed bleeding for sessile polyps. However, that organization does suggest that there may be a role for mechanical prophylaxis such as clip closure in certain high-risk cases after EMR and recommend that the decision be individualized based on the patient’s risk factors.

With regard to cost-effectiveness, a prospective multicenter study analyzed the cost-effectiveness of prophylactic clip closure after EMR of LNPCPs for both Spanish and U.S. economic contexts. A total of 2263 EMRs in 2130 patients were included. The Spanish Endoscopic Resection Group (GSEED-RE2) delayed bleeding risk score was used to risk stratify those at high risk (GSEED-RE2 score >6), which comprised 12% of the total cohort. The authors found that selective clipping in the high-risk of DB GSEED-RE2 subgroup was cost-effective and cost-saving, but that universal clipping was not. This study sheds further light on the utility of selective clipping in high-risk patients.

In this issue of Gastrointestinal Endoscopy, Forbes et al analyze the efficacy of clipping as a method to prevent AEs after EMR of proximal LNPCPs measuring ≥20 mm. Their systematic review and meta-analysis included a total of 4 homogenous randomized control trials, representing 1248 patients who had proximal LNPCPs. Of these patients, 623 underwent prophylactic clip closure after resection, and 625 did not undergo clipping. The authors used both individual patient data (available for 1150 patients from 3 studies) and traditional meta-analysis approaches during data analysis. The primary outcome was CSPEB, defined as hematochezia or melena resulting in any of these factors: hospitalization; repeated endoscopic, surgical, or radiologic intervention; or a drop in hemoglobin of ≥2 g, occurring within 14 days of EMR.

The overall rate of CSPEB was 6.3%, with a rate of 3.5% in the clipped group and 9.0% in the unclipped group. Prophylactic clip closure was efficacious in preventing CSPEB, with a relative risk of 0.39 (95% CI, 0.24-0.64) from meta-analysis of 4 studies representing 1248 proximal LNPCPs and an odds ratio of 0.31 (95% CI, 0.17-0.54) from individualized patient data. In terms of absolute effects, this
estimate suggests that prophylactic clip closure would result in 55 fewer cases of CSPEB per 1000 patients treated (corresponding to a number needed to treat of 18), which is a clinically noteworthy result.

Interestingly, there was a much lower baseline risk of CSPEB after EMR of transverse colonic lesions, which was 1.0% (compared with 6.1% in the ascending colon and 9.1% in the cecum, \( P = .001 \)) despite the presence of similar mean lesion sizes of 32.6 mm, 32.9 mm, and 32.2 mm in the cecum, ascending colon or hepatic flexure, and transverse colon, respectively (\( P = .80 \)) on subanalyses. This is reflected by the results, in that prophylactically clipping lesions in the transverse colon is much less efficacious in the prevention of CSPEB compared with lesions in the ascending colon or cecum. This warrants further studies, inasmuch as prior published reports suggest that proximal colon lesions (which by definition include the transverse colon) would benefit from prophylactic clipping. Because the distinction between the transverse colon and the ascending colon is not always obvious, one may argue that it is reasonable to consider universal clipping of all proximal lesions.

The results also demonstrated no difference in efficacy of clipping to prevent CSPEB between any clinically relevant subgroup, including patient age, gender, antiplatelet or anticoagulation use, American Society of Anesthesiologists score, or lesion size. This supports the ongoing challenge of individualizing prophylactic clipping to specific patients. It is also relevant to note that analyses showed clipping was not associated with perforation or abdominal pain, though these analyses were limited by low event rates, supporting the role of clipping as a safe prophylactic measure.

Another important aspect analyzed by the authors was that of partial and full clip closure of proximal LNPCPs. They found that full clip closure resulted in significantly lower bleeding rates compared with no attempted closure (2.6% vs 9.0%, \( P < .001 \)); similarly, partial clip closure also resulted in significantly lower bleeding compared with no attempted clip closure (1.7% vs 9.0%, \( P = .001 \)). Although there is no clear definition as to what extent of partial clip closure is effective in preventing post-EMR bleeding, this is still a good alternative, and it is preferable to no closure. Further studies are required to further elucidate this point.

We commend the authors for their effort to help achieve clarity on this important topic. Their analysis was thorough, and the clinical benefits of the results appear to be clinically applicable. Although this has been assessed in other meta-analyses, the use of original trial data provides data granularity not seen in other studies.\(^\text{10-12}\) One limitation of this analysis is the small number of studies included, which was in part due to the strict inclusion criteria provided. The included studies also did not report on the cost effectiveness of this method. Although this is an important aspect to consider, the wide availability of clips of various price ranges has made them more affordable. The use of scoring systems or consideration of other individual patient and polyp factors, including specific EMR location within the right side of the colon, are areas that could be better delineated to more accurately assess their applicability. This will allow us to better address this question: not whether we should clip proximal lesions, but rather under which circumstances it would be safe and justifiable not to clip.

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Sarah S. Al Ghamdi, MBBS, FRCPC
Division of Gastroenterology and Hepatology
Department of Medicine
King Abdulaziz University
Saudi Arabia
Saowanee Ngamruengphong, MD
Division of Gastroenterology and Hepatology
Johns Hopkins Hospital
Baltimore, Maryland, USA

Abbreviations: AEs, adverse events; CSPEB, clinically significant post-EMR bleeding; LNPCPs, large nonpedunculated colorectal polyps.

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