

ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: Todd H. Baron, MD

Polypectomy and the Efficacy and Safety of Postpolypectomy Clipping



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G&H What are the indications for polypectomy?

HP In general, polyps should be resected if they have neoplastic potential (eg, tubular adenomas or sessile serrated lesions). Whether polyps should be removed by endoscopic means or by surgery is a little more complicated. Twenty to 30 years ago, patients with large (≥ 20 mm) colorectal polyps were typically referred to surgery, regardless of whether the polyps were cancerous or not. Over the past few decades, tools and techniques have been developed to remove large polyps from the colon endoscopically. The indications for surgery are primarily a clear sign of deep submucosal invasion of cancer in non-pedunculated lesions (defined pathologically as ≥ 1 mm of submucosal invasion) and polyps that cannot be resected by endoscopic means.

G&H How should lesions be selected for endoscopic resection?

HP Pedunculated lesions, including those with features of submucosal invasion, should be resected en bloc endoscopically regardless of size. The primary approach for all

nonpedunculated lesions without overt features of cancer is endoscopic resection.

Polyps that extend into the appendiceal orifice, the terminal ileum, or a diverticulum, or those located at the anal verge, may be challenging to remove and are often referred to surgery. However, advancements in endoscopic technique and skill allow for endoscopic resection of any of these lesions. For instance, polyps within the appendiceal orifice or a diverticulum may be resected using the endoscopic full-thickness resection device (FTRD, Ovesco). If in doubt, such lesions should be referred to an expert endoscopist. It is important to recognize overt signs of cancer (Kudo class V or Paris class III) to make the appropriate decision for surgical referral. Some features suggest a greater risk of cancer within the lesion, and endoscopic resection should aim for removing these lesions en bloc (by endoscopic mucosal resection, if not possible by endoscopic submucosal dissection) to aim for curative resection of early submucosal lesions without high-risk features. Such risk factors include larger size, rectal location, and nongranular morphology, all of which underline the importance of being able to “read” a polyp. Features that make resection of lesions challenging include large size; submucosal fibrosis and scarring, including from prior

biopsy or attempts at resection; and difficult location, and may constitute reasons to refer patients to specialty endoscopy centers for endoscopic resection of complex benign colorectal polyps. However, these factors can be overcome by standardized tools employed by interventional colonoscopists. Of note, making the right decision to refer a patient for surgical resection or not is important, as surgery has a morbidity between 15% and 25% and a mortality of 0.7% as compared to endoscopic resection of large lesions, which has a morbidity of approximately 10% and a mortality of 0.08%.

G&H What adverse events are associated with polypectomy, and how significant is the risk of bleeding following polypectomy?

HP Generally, the risk of any severe adverse event is approximately 1 in 100 to 1 in 200 for patients who have a polyp removed during a screening or surveillance colonoscopy. Perforation risk is extremely low, between 1 in 1000 to 1 in 2000 overall, with the risk increasing to a maximum of 1% for a large polyp. The risk of bleeding depends primarily on the size of the polyp as well as on the type of removal. Postpolypectomy syndrome, which is related to a focal inflammation as a result of electrocautery snare resection of a polyp and is associated with abdominal pain, leukocytosis, and fever, occurs in less than 1% of patients who have large polyps resected. A polyp that is 1 to 5 mm in size that is removed during an elective colonoscopy carries a very low chance of bleeding. For polyps that are 20 mm or larger and nonpedunculated that require the use of endoscopic mucosal resection, the risk of bleeding increases to 5% to 10%.

G&H What qualifies as a bleeding event?

HP It is important to note the differences in how a bleeding event is defined because it affects the rate of bleeding reported in studies. If a patient presents with light rectal oozing following a polyp resection and is concerned about blood coming from the rectum but has no other issues (for instance, requiring hospital transmission or blood transfusion and the blood count is stable), the patient has what could be considered a mild bleeding event. However, if the patient experiences a drop in hemoglobin and needs to be admitted to the hospital, that could be considered a clinically significant bleeding event. Importantly, the categorization of a severe bleeding event varies. The US Food and Drug Administration defines it as a threat to health or to disability requiring admission to the hospital. However, the lexicon for endoscopic adverse events, published by Dr Peter Cotton and colleagues in 2010 as a report of an American Society for

Gastrointestinal Endoscopy workshop, classifies a severe bleeding event as one in which a patient is admitted to a hospital for 10 days or to an intensive care unit (ICU) for at least 2 days. In general, such a severe bleeding event that requires ICU admission or a prolonged hospitalization is less common.

G&H What factors affect the risk of acute or delayed bleeding?

HP Patient-related risk factors include use of antithrombotic agents (antiplatelets or anticoagulants) in the peri-procedural period, advanced age, and comorbidities, although not all studies have found associations with the latter 2 factors.

Polyp-related factors include larger polyp size, morphology (specifically, pedunculated polyps with a thick stalk), and location. Polyps located in the proximal colon, particularly in the cecum, carry a higher risk of bleeding.

Some procedural technique factors may also affect the risk of bleeding; for instance, the use of injection with epinephrine may reduce the bleeding risk, although there have been no comparative trials. Using a microprocessor-controlled electrosurgical unit that adjusts applied energy based on tissue resistance carries a lower risk of bleeding than the traditional units that deliver the same amount of energy throughout the cut. We are now recognizing that hot resection (with cautery) in general seems to have a higher risk of bleeding than cold resection, when no cautery is used. Cold snare resection has a risk of bleeding that approaches 0%, even with large polyps. It is not yet known whether cold snare resection is as effective as hot snare resection in terms of recurrence rates.

G&H What have studies shown regarding the efficacy of endoscopic clipping for reducing the risk of postpolypectomy bleeding?

HP In 2013, Dr Douglas Rex published a retrospective study showing that the risk of bleeding in patients with clipping was 2% compared to 10% in historical controls. This finding sparked interest in performing randomized trials; 3 were published last year in *Gastroenterology*. My colleagues and I participated in the largest trial that enrolled more than 900 patients. This trial showed a 50% reduction in the risk of bleeding overall, from 7.1% to 3.5%, when using clips. However, this reduction was only seen in polyps located in the proximal colon (from 9.6% to 3.3%, an approximately one-third reduction); clipping had no effect on bleeding for polyps in the distal colon. A study from Spain evaluated the use of clips in 200 patients with high-risk lesions (≥ 4 cm, among other criteria) and found that clipping reduced

the risk of bleeding from 12% to approximately 5%. The third study, which was a Veterans Affairs study, included all polyps that were 10 mm or larger, with the majority being less than 20 mm; the authors did not find a reduction of bleeding with clipping.

A recent meta-analysis summarized these and other smaller studies and reported a risk reduction when using clips from 10% to 4%, but only for polyps 20 mm or larger, and only for polyps located in the proximal colon, which is proximal to the splenic flexure. Thus, any patient who had a 20 mm or larger nonpedunculated polyp located in the transverse colon, ascending colon, or cecum that was removed by hot snare resection should have the mucosal defect closed with clips to reduce the risk of bleeding. No benefit was found for smaller lesions or distal polyps.

G&H Were there any other key findings from this meta-analysis?

HP One interesting aspect of the meta-analysis is that while there was no significant difference in bleeding risk for smaller lesions (10-20 mm), there was a numerical difference for proximal lesions, from 4% to 2% for those that were clipped. Although there was a 50% risk reduction, the numbers are so low that the difference is not seen as significant. Thus, thousands of patients would be needed to show a difference as being significant. Even if the difference were significant, approximately 50 patients with such polyps would need to be clipped to benefit 1 patient. This raises the question of cost-effectiveness and if it is really worthwhile to clip any lesion. Studies have shown that only clipping polyps with a greater risk of bleeding would be cost-effective, yet the price for clips also needs to be reduced to be cost-saving.

The downsides of clipping are time and cost. It takes 1 to 2 minutes for a single clip to be placed, and clips vary in price, between \$150 and \$250. However, companies have recognized the benefit of clipping and the reluctance to use expensive clips, and less costly clips are being developed and marketed.

G&H Are there any other benefits or risks associated with placing clips following polypectomy?

HP There have been some concerns about distorting the mucosa with clip placement that might challenge the assessment of the resection site at surveillance colonoscopy. However, even if the site looks a little more irregular, the pit pattern is not actually changed, and it is still possible to distinguish recurrent neoplastic tissue from the distorted but nonneoplastic tissue. Some sites are more difficult to clip than others; if a large lesion is behind a

fold, or if it is very large, it is more challenging to clip. For instance, my colleagues and I observed in our study on clipping that only two-thirds of defects could be completely closed with clips, and of lesions 4 cm or larger, only approximately 40% could be completely closed, yet clipping still benefited the entire group of such large polyps in an intention-to-treat analysis. Overall, placing clips requires skill and time, and most risks arise when either of those factors is not met.

G&H When is routine use of prophylactic clipping recommended?

HP In general, routine clipping is not uniformly recommended. Earlier this year, the US Preventive Services Task Force updated its polypectomy guidelines to suggest clipping mucosal defects for large (≥ 20 mm) nonpedunculated proximal polyps.

G&H What are the priorities of research in this field?

HP In this field, the priorities concern safety and efficacy. In terms of bleeding, even a 3% to 5% bleeding risk with clipping is still fairly extensive. Is there a way to reduce the bleeding risk further? One promising possibility is to avoid electrocautery snare resection and to resect the lesions cold, which seems to carry a bleeding risk close to 0%. Findings from a meta-analysis as well as from several recent studies support this approach. However, not every polyp can be resected cold. For those lesions that do require cautery, the question is how to achieve closure of the defect. Clipping can be difficult and needs improvement, but there are stitching devices and other technical methods. Spraying the surface with a component that reduces the risk of bleeding, for example, with Hemospray (Cook Medical), may be beneficial.

With respect to efficacy, the priorities are ensuring that polyps are removed completely at the time of colonoscopy and having the lowest recurrence rate possible. There is debate surrounding the use of endoscopic mucosal resection vs endoscopic submucosal dissection. The latter has a lower recurrence rate but a higher risk of complications, and the procedure time is longer and requires a greater skill level. Alternatively, full-thickness resection devices are available to remove fibrosed polyps in 1 piece, but these are limited by their size. Hybrid versions also exist. Research is needed to understand how to advance our current tools and techniques to improve the efficacy of resection, which would allow for a lower risk of recurrence. An Australian study published in 2018 found that ablating the resection margin after removing a polyp leads to a much lower risk of recurrence, from

21% to 5%. Randomized studies are needed to confirm this finding.

G&H Is there anything you would like to add?

HP Several questions should be asked before removing large lesions: Is the removal of a polyp within my skill level? Do I have adequate time to complete the procedure? Do I have a support team? Can I manage any bleeding? Do I have the knowledge to “read” a polyp and recognize invasive cancer? It is important for the endoscopist to feel comfortable to remove larger lesions. If there is any doubt, the patient should be referred to an expert who is more experienced with large polyp resection. Additionally, once a polyp resection is started, the appropriate time should be dedicated to completing it; it is not a procedure that can be rushed or squeezed into a timeslot. An experienced assistant should be available who understands snare options and cautery setting. It is important to stop any bleeding that may occur. The endoscopist should be familiar with various electrocautery settings and their appropriate application; if not, the patient should be referred to a colleague. In addition, at the end of the resection, the current recommendation is that the resection margin is ablated, either with snare tip soft coagulation or another mode such as argon plasma coagulation. Ablating, as well as closing the defect as best as possible, requires skill. Knowledge of the Paris classification, Kudo pit pattern, and lateral spreading tumor morphology is essential. Following resection, it is crucial to examine the resection base for any possible risk of deep mural injury to recognize the risk for delayed perforation and, if present, to close such a defect or injury.

Disclosures

Dr Pohl has received research grants from Steris and Cosmo. The views expressed in this column are those of the author and do not necessarily represent the views of the Department of Veterans Affairs or the United States government.

Suggested Reading

Albéniz E, Álvarez MA, Espinós JC, et al. Clip closure after resection of large colorectal lesions with substantial risk of bleeding. *Gastroenterology*. 2019;157(5):1213-1221.e4.

Albéniz E, Gimeno-García AZ, Fraile M, et al. Clinical validation of risk scoring systems to predict risk of delayed bleeding after EMR of large colorectal lesions. *Gastrointest Endosc*. 2020;91(4):868-878.e3.

Burgess NG, Hourigan LF, Zanati SA, et al. Risk stratification for covert invasive cancer among patients referred for colonic endoscopic mucosal resection: a large multicenter cohort. *Gastroenterology*. 2017;153(3):732-742.e1.

de Neree Tot Babberich MPM, Bronzwaer MES, Andriessen JO, et al. Outcomes of surgical resections for benign colon polyps: a systematic review. *Endoscopy*. 2019;51(10):961-972.

Feagins LA, Smith AD, Kim D, et al. Efficacy of prophylactic hemoclips in prevention of delayed post-polypectomy bleeding in patients with large colonic polyps. *Gastroenterology*. 2019;157(4):967-976.e1.

Hassan C, Antonelli G, Dumonceau J-M, et al. Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) guideline—update 2020. *Endoscopy*. 2020;52(8):687-700.

Kaltenbach T, Anderson JC, Burke CA, et al. Endoscopic removal of colorectal lesions—recommendations by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology*. 2020;158(4):1095-1129.

Mangira D, Cameron K, Simons K, et al. Cold snare piecemeal EMR of large sessile colonic polyps ≥ 20 mm (with video). *Gastrointest Endosc*. 2020;91(16):1343-1352.

Pohl H, Grimm IS, Moyer MT, et al. Clip closure prevents bleeding after endoscopic resection of large colon polyps in a randomized trial. *Gastroenterology*. 2019;157(4):977-984.e3.

Spadaccini M, Albéniz E, Pohl H, et al. Prophylactic clipping after colorectal endoscopic resection prevents bleeding of large, proximal polyps: meta-analysis of randomized trial. *Gastroenterology*. 2020;159(1):148-158.e11.