

ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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Bleeding Following Wide-Field Endoscopic Resection in the Colon

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G&H Is bleeding a common complication of endoscopic mucosal resection?

MJB Significant post-endoscopic mucosal resection (EMR) bleeding (PEB) is defined as bleeding that requires medical attention (ie, presentation to the emergency room and/or hospital admission). PEB occurs in 5–7% of colonic EMR cases. The need for medical assessment usually leads to hospital admission and ancillary investigations, including repeat colonoscopy and, less frequently, blood transfusion. The risk of developing PEB diminishes the advantages of EMR as a safe, cost-effective, minimally invasive therapy for advanced mucosal neoplasia of the colon.

G&H What are the most common risk factors for developing colonic PEB?

MJB Few studies have specifically examined the risk factors for developing colonic PEB. Several heterogeneous reports with different study designs and definitions have focused on the risk of bleeding after conventional polypectomy; however, the focus has often been on immediate intraprocedural bleeding rather than true delayed bleeding. Risk factors that have been reported by most studies include large lesion size (>1 cm), presence of chronic renal disease, anticoagulant use, and, often, comorbidity or cardiovascular disease. Most reports do not identify an association between

PEB and aspirin or nonsteroidal anti-inflammatory drug (NSAID) use. There is a lack of consensus and standardization regarding the definition and treatment of postpolypectomy bleeding. Immediate intraprocedural bleeding can generally be managed during the initial procedure, without significant patient morbidity. As the size and complexity of endoscopically treated lesions increase, immediate intraprocedural bleeding is increasingly being seen as part of the procedure and should not be regarded as a complication unless it alters the clinical pathway.

G&H Could you discuss the study design and findings of your recent study that examined risk factors for colonic PEB?

MJB Data for this single-center study were derived from 2 large, prospective, observational, cohort studies that examined colonic EMR. The patient population consisted of patients who were referred to Westmead Hospital for the management of large colonic polyps and laterally spreading tumors larger than 20 mm. Data were recorded in comprehensive databases from August 2006 to April 2008 and then from July 2008 to May 2009. (This latter period comprised the early part of the ACE study.) As PEB occurs more commonly with antiplatelet therapy, our protocol in both studies was to cease aspirin use for 7 days prior to EMR and then to recommence aspirin use 5 days after the procedure. Therefore, “use of aspirin” was defined in this study as failing to comply with this advice by ingesting aspirin within 7 days of the procedure. Patients who failed to comply and those requiring continued aspirin

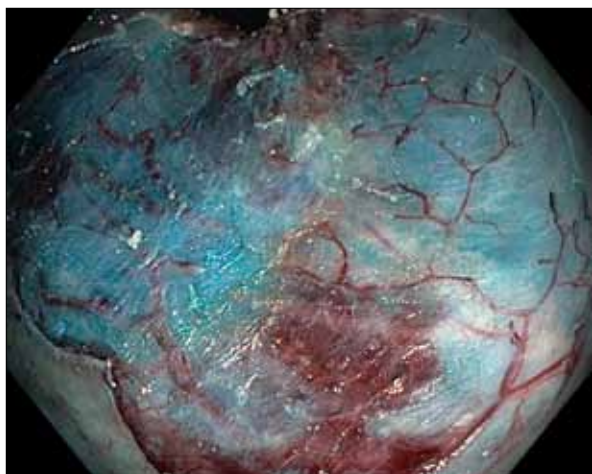


Figure 1. A large distal rectal postresection mucosal defect. Numerous vessels are visible ramifying within the submucosal plane. Despite the number of vessels, the postprocedural bleeding risk in this case is low, given the rectal location.

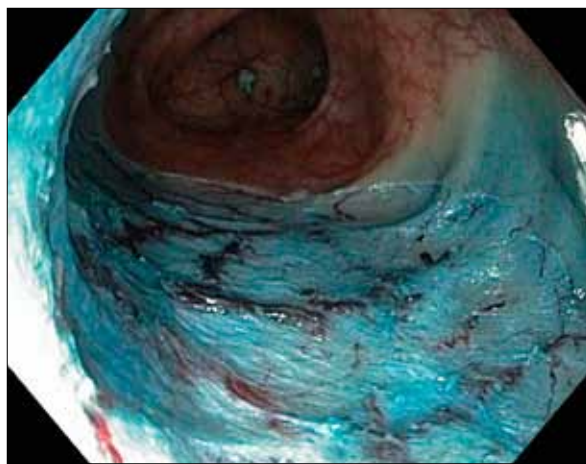


Figure 2. A large post-endoscopic mucosal resection defect in the ascending colon, with some herniating vessels.



Figure 3. A close-up of herniated vessels within a large endoscopic mucosal resection defect.

for medical reasons (eg, a drug-eluting coronary stent) were included in this group. Clopidogrel use was similarly defined. Management of anticoagulant therapy was standardized according to accepted guidelines; patients were advised to cease warfarin use for 4 doses prior to undergoing EMR. Intravenous heparin or subcutaneous enoxaparin was substituted in the event of mechanical heart valves. Warfarin use was recommenced the following day.

During the study period, 302 lesions were excised in 288 patients. Clinically significant bleeding that warranted presentation to the emergency room and hospital readmission for at least one night occurred in 21 patients (7%). In multiple logistic regression analysis

with backward stepwise variable selection (controlling for lesion size, morphology, and other factors), the risk of bleeding was related to 2 factors: location in the right colon (at the hepatic flexure or beyond; odds ratio, 4.4; $P=.014$) and any antiplatelet use within 7 days of the procedure (odds ratio, 6.3; $P=.005$). The risk of bleeding was 12% in the cecum, 10% at the ileocecal valve or in the proximal ascending colon, 7% at the hepatic flexure, and 2–3% in the left colon. My coauthors and I speculated that these findings may reflect a relative difference in the number, size, or fragility of submucosal vessels in the right colon, compared to the distal colon (Figures 1–3).

A recent smaller retrospective study from The Netherlands that examined risk factors for postprocedural bleeding after conventional polypectomy found similar results in respect to bleeding risk and location, with cecal lesions having a risk of 12–13%.

G&H How should PEB be managed?

MJB Currently, there are no accepted guidelines dictating how patients with PEB should be managed. My approach to managing these patients is based on findings from studies conducted by my colleagues and I, our significant experience managing PEB, and the following observations. Ninety percent of PEB occurs within 48 hours of the procedure, and 60% of these cases occur within the first 24 hours. Bleeding is usually self-limited and often ceases spontaneously. Patients may present to the hospital with serious symptoms, including hypotension, which usually responds to fluid resuscitation. There may be a decrease of 20–40 g/L in hemoglobin level, but blood transfusion is usually not required.

Patients with PEB can usually be managed without endoscopic hemostasis or repeat colonoscopy. Patients who fail to respond to fluid resuscitation with ongoing hypotension or a second episode of hypotension with rectal bleeding require colonoscopic intervention with endoscopic hemostasis.

Usually, the EMR defect has a significant amount of adherent clot, which can be readily cleared by irrigation or cold guillotining via a snare. One or two visible vessels may be exposed. In the thin-walled colon and, furthermore, within a significant cautery ulcer, these vessels are best treated via endoscopic clipping, rather than thermal hemostasis, which is associated with a significant risk of transmural injury and subsequent perforation.

If PEB occurs within the first 48 hours of the procedure, a complete bowel preparation is usually not necessary. Intraluminal blood acts as a cathartic. It is usually straightforward to identify and treat the bleeding site because its location is known. Angiographic embolization is rarely required in severe bleeding.

It is likely that the type of current used during EMR influences the timing of postprocedural bleeding. A microprocessor-controlled generator that alternates cycles of short cutting bursts with prolonged periods of coagulation usually results in early bleeding (within 48 hours of the procedure). Pure coagulating current results in a deeper thermal injury and may lead to a deep cautery ulcer. Early bleeding is infrequent; if delayed bleeding occurs (usually 5–7 days after the procedure), it may be more severe due to erosion of deeper vessels, including arteries.

G&H Should patients be allowed to take aspirin during EMR?

MJB Aspirin, NSAIDs, and clopidogrel have not been shown to increase the risk of postprocedural bleeding following conventional polypectomy. These agents are not stopped for routine colonoscopy, particularly if antiplatelet agents are being used for secondary prevention in patients who have had prior cardiovascular events.

However, advanced endoscopic resection likely represents a very different clinical scenario than conventional polypectomy. EMR causes a wide mucosal defect of varying size (generally >20 mm but possibly up to 100 mm). This defect is a raw mucosal wound with a large area of exposed submucosa, where there are often numerous vessels, some of which may have been injured during the procedure and may lead to postprocedural bleeding. Antiplatelet agents appear to magnify the risk of bleeding. The results of our study suggest that specific guidelines should be developed regarding antiplatelet therapy and colonic EMR.

G&H How significant of a factor is endoscopist experience on the rate of bleeding?

MJB I do not believe that there are any data suggesting that the experience of the endoscopist influences the frequency of PEB; rather, the experience and skill (both technical and cognitive) of the endoscopist directly influence the technical outcomes of the procedure. An experienced and skilled endoscopist who makes good decisions may resect large lesions with good outcomes in terms of complete endoscopic excision, minimal recurrence, and negligible complications.

Early recognition of complications is important. My colleagues and I recently published a paper on the “target sign,” a means by which one can readily detect injury to the muscularis propria. Despite a high-volume case load of advanced endoscopic resections for large colonic lesions, we continued to have a 1–2% incidence rate of muscularis propria injury (either partial or full thickness). Inevitably, these patients would immediately develop or return with a clinical perforation soon after their procedure. Since we have identified this sign and taken to immediately closing the muscle layer with clips, clinical perforation in our colonic EMR practice has been virtually absent.

G&H What training is necessary to perform these procedures safely and effectively?

MJB Currently, most gastroenterology trainees complete a 3-year training program. Those who wish to perform more advanced procedures undertake an additional dedicated year of training either in endoscopic retrograde cholangiopancreatography (ERCP) or endoscopic ultrasound (EUS). The use of ERCP and EUS is specialized and requires dedicated training. Likewise, the skills needed to perform advanced endoscopic resection—whether involving the duodenum, esophagus, or colon—requires a special skill set and knowledge base that is readily learned by individuals with an aptitude for endoscopy. This aspect should be recognized by authoritative training and credentialing bodies such as the American and European Societies for Gastrointestinal Endoscopy. The days of learning on the job should be left behind.

On a yearly basis, our department offers 2 advanced fellowships that incorporate dedicated training and research experience in complex endoscopic resection. Each trainee performs 5 or more tertiary-level, advanced resections each week and participates in our research program. By the end of the year, their work is often indistinguishable from that of my own or my coworkers (and, on occasion, better). There is a gradual transition over the 12-month period. Many related nontechnical skills—such as lesion assessment or complication recognition and management—are acquired

during this time period; these skills directly enhance the outcome of the procedure, more so than the pure technical skills of lesion resection.

G&H What are your next steps in PEB research?

MJB PEB requires further study. Recently, a large Japanese observational study suggested that prophylactic endoscopic coagulation is effective in reducing the incidence of postprocedural bleeding following gastric endoscopic submucosal dissection. My colleagues and I are currently conducting an Australian multicenter randomized trial examining the role of prophylactic endoscopic coagulation. Our results should be released in late 2012.

Other novel approaches to PEB also merit consideration. It may be possible to incorporate a hemostatic agent in the submucosal injectate or apply an adherent hemostatic gel at the end of the procedure. It may also be possible to predict post-EMR outcomes and PEB risk based on the features of the post-EMR defect. We are conducting experimental and clinical research in these areas.

Suggested Reading

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