Management of Polypectomy Complications

Selvi Thirumurthi, MD, MS, Gottumukkala S. Raju, MD*

KEYWORDS

• Colonoscopy • Polypectomy • Complications • Postpolypectomy bleeding
• Perforation • Prevention • Management

KEY POINTS

- The major complications of colonoscopy with polypectomy are postpolypectomy bleeding and colon perforation.
- Risk factors for postpolypectomy bleeding can be categorized as polyp-related, patient-related, and technique/device-related factors.
- Postpolypectomy bleeding can be controlled with injectable solutions and thermal and mechanical hemostatic devices.
- Risk factors for colon perforation can be polyp-related or technique/device-related.
- Methods of closure of colon perforation include endoclip placement, suturing, and others; appropriate management of patients with perforation is essential.

INTRODUCTION

Approximately 1.27 million colonoscopies are performed annually for colorectal cancer sreening. The risk of complications increases in patients who undergo colonoscopy with polypectomy (**Figs. 1** and **2**). The rate of serious complications (ie, requiring hospitalization within 30 days of colonoscopy) is 10-fold higher (7.0 per 1000 examinations) if biopsy or polypectomy is performed compared with colonoscopy without these interventions.[1] The 2 most significant complications include postpolypectomy bleeding (PPB) and colon perforation. The goal of this article is to review these complications in detail, assess risk factors for bleeding and perforation, and make recommendations regarding prevention and management.

No financial disclosures.
Department of Gastroenterology, Hepatology and Nutrition, University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Unit 1466, Houston, TX 77030, USA
* Corresponding author.
E-mail address: gsraju@mdanderson.org

Gastrointest Endoscopy Clin N Am ■ (2015) ■–■
http://dx.doi.org/10.1016/j.giec.2014.11.006 **giendo.theclinics.com**

POSTPOLYPECTOMY BLEEDING

The expected incidence of PPB ranges from 0.1% to 0.6%.[2] A rate greater than 1% in a practice should prompt a review of endoscopist technique.[3] PPB can be classified as immediate (intraprocedural or within 24 hours of the examination) or delayed (between 1 day to 14 days after the examination) and the severity of bleeding can be graded as follows: grade 1 (spontaneous hemostasis within 1 minute); grade 2 (continuous oozing but decreases over 1 minute); grade 3 (continuous oozing over 1 minute that requires endoscopic treatment); or grade 4 (active spurting) (**Box 1**).[4]

Most bleeding episodes are clinically trivial, whereas those episodes that require hospitalization, blood transfusion, repeat endoscopic intervention, or surgery are considered true complications.

Risk Factors for Postpolypectomy Bleeding

Polyp-related factors

Risk factors include polyp size, location, and morphology. Polyp size is the main factor and is consistently linked to higher bleeding rates. Polyps that are 1 cm or larger in size have a 2.0-fold to 4.5-fold increased risk of PPB[5,6]; this risk grows by 9% to 13% per millimeter increase in polyp size greater than 1 cm.[7,8] Polyps located in the right hemicolon are associated with a 2.6-fold to 4.6-fold increased risk of PPB.[5,7,9,10] Polyp morphology (pedunculated with a thick stalk or laterally spreading lesions) and histology (adenoma, villous features, and presence of adenocarcinoma) are associated with an increase in PPB.[4,5,11–13] In a prospective Australian Colonic Endoscopic Resection Study of patients undergoing wide field endoscopic mucosal resection (EMR) of large sessile colonic polyps, intraprocedural bleeding was associated with larger lesions, lesion histology, and Paris endoscopic classification of type 0–IIa + Is.[14]

Patient-related factors

Patient-related factors, such as age greater than 65, hypertension, cardiac disease, and renal disease, have been associated with a higher risk for PPB.[4,6,11] Older patients and those with cardiovascular disease are often on antithrombotic therapy when they present for colonoscopy. The use of anticoagulants before polypectomy and resumption of therapy afterward have been associated with a 3.7-fold and 5.2-fold increased risk for PPB, respectively.[4,8] Risks for PPB vary based on the type of antithrombotic agent, whether an anti-platelet agent (aspirin, nonsteroidal anti-inflammatory drugs [NSAIDs], clopidogrel, ticlopidine) or an anticoagulant (warfarin, heparin), and these are reviewed later in this article (**Table 1**).

Box 1
Grading scale of immediate postpolypectomy bleeding

Grade 1: Spontaneous hemostasis within 1 minute of observation

Grade 2: Continuous oozing but decreases over 1 minute of observation

Grade 3: Continuous oozing over 1 minute of observation and requires endoscopic therapy

Grade 4: Active spurting, requires endoscopic therapy, possible hospital admission, and transfusion

Adapted from Kim HS, Kim TI, Kim WH, et al. Risk factors for immediate postpolypectomy bleeding of the colon: a multicenter study. Am J Gastroenterol 2006;101:1333–41; with permission.

Table 1
Management of antithrombotic agents and risk of postpolypectomy bleeding

Antithrombotic Agent	Effect on Postpolypectomy Bleeding	Current Guidelines for Periprocedural Management[a]	Suggested Endoscopic Intervention
Aspirin/NSAIDs (antiplatelet)	No compelling data	Continue	Consider holding if large EMR planned
Clopidogrel (antiplatelet)	Mixed data: suggestion of increased delayed PPB Increases risk of PPB in combination with aspirin	Hold for 7–10 d preprocedure and restart the next day postprocedure (depending on intervention performed)	Consider prophylactic clip placement over polypectomy site(s)
Warfarin (anticoagulation)	Increases risk of PPB	Hold for 3–5 d preprocedure and 1 d postprocedure	
Heparin (anticoagulation)	Increases risk of PPB	Hold for 4–6 h (unfractionated heparin) 12–24 h (low molecular weight heparin)	
SSRIs (antiplatelet)	Increased risk of *upper* GI bleeding; no studies with colonoscopy or polypectomy Risk is further increased with simultaneous aspirin and NSAID use	N/A	Consider holding aspirin ± NSAIDs
Novel oral anticoagulants	Likely increased risk although no data available	No data available	Discontinue agents based on half-life and with input from cardiologist

[a] ASGE guidelines: Management of antithrombotic agents for endoscopic procedures. NB: The decision to discontinue antithrombotic therapy for endoscopy should be individualized to balance the risk of the planned endoscopic intervention and with the risk of the underlying condition for which the patient is on therapy.[20]

Aspirin and nonsteroidal anti-inflammatory drugs Although aspirin exposure results in a prolonged bleeding time of normal colonic mucosa, studies evaluating the impact of aspirin use on PPB reveal mixed results.[15] An increased risk for PPB with aspirin use before colonoscopy has been described in one small study (odds ratio [OR] 6.7). Another group reported increased risk of bleeding after EMR of lesions 2 cm or larger in patients with aspirin use within 7 days of the procedure (OR 6.3).[10,16] However, most data show that aspirin use, alone or in combination with other NSAIDs, does not increase the risk of PPB.[17–19] Variation in the aspirin dosage (81 mg vs 325 mg) may be a confounding factor.

Clopidogrel Current guidelines recommend holding thienopyridines (clopidogrel and ticlopidine) for at least 7 days before polypectomy based on the indication for antithrombotic therapy and the risk to the patient.[20] In a recent meta-analysis of PPB in patients on continued clopidogrel therapy, the overall pooled relative risk (RR) for PPB was 2.5 ($P<.05$).[21] The RR for delayed bleeding was 4.6 ($P<.05$) with the RR for immediate PPB 1.76 (however, $P>.05$).[21] Other studies have also reported higher rates of delayed PPB with uninterrupted clopidogrel therapy compared with controls, but the rates of PPB were low (less than 1%) and applied mainly to large polyps (greater than 1 cm in size).[22–24] Interestingly, clopidogrel monotherapy was not identified as an independent risk factor for PPB, but only increased the risk of PPB when used in combination with aspirin.[24] The risk of delayed PPB can be mitigated during colonoscopy by the application of through-the-scope clips (TTSC; endoclips) to the polypectomy site in patients who are on clopidogrel therapy during colonoscopy or are expected to resume it after the procedure.

Warfarin It is recommended that patients anticoagulated with warfarin should hold therapy for 3 to 5 days before colonoscopy.[20] Although there is no clearly established target international normalized ratio (INR) that is safe for polypectomy, an INR of 1.6 or less is generally considered acceptable. However, preprocedure INR is not routinely obtained in clinical practice. Some studies showed that patients on warfarin therapy had a higher risk of PPB (OR 11.6–13.3), whereas those on aspirin, NSAIDs, thienopyridines, and low-molecular-weight heparin did not.[25,26] Other predictors of PPB were the number of polyps removed (OR 1.2) and male gender (OR 9.2).[26]

Bridging therapy with heparin When evaluating the risk of warfarin therapy on PPB, it is important to consider the risk of thromboembolic events after temporary discontinuation of the drug. Patients at high risk for thromboembolic events are bridged with heparin while anticoagulation is suspended. In a CORI database study, the use of periprocedural heparin was not a risk factor for PPB.[27] In another study, patients on warfarin or antiplatelet agents were either bridged with heparin or simply discontinued antithrombotic therapy.[28] In patients on heparin bridge therapy, the risk of PPB was not only higher but also delayed in onset and recurrent, resulting in prolonged hospitalization. Warfarin use, bridging with heparin, and pedunculated polyps were independent predictors of PPB.[28] Endoscopists should consider empiric placement of endoclips at polypectomy sites in patients on warfarin therapy. Patients with an average INR of 2.3 and polyps ranging from 3 mm to 10 mm in size were successfully clipped and experienced no PPB when warfarin was held for only 36 hours preprocedure.[29]

Thrombocytopenia and selective serotonin reuptake inhibitors Endoscopists often hesitate to perform polypectomy on patients with cancer with thrombocytopenia or cirrhosis of the liver because of a perceived increased risk of PPB. In a study of

patients with cancer with platelet counts of 75 $\times$ 10^3 or less, the risk of bleeding was 1.5% after biopsy and 4% after polypectomy for lesions 1 cm in size or smaller.[30] In addition, hemostasis was successfully achieved in 95% of actively bleeding patients, resulting in a decreased need for transfusion of blood products.[30]

Patients with early-stage liver cirrhosis (Child-Pugh score A or B) with an INR of 1.5 or less and platelet counts ranging between 30 $\times$ 10^3 and 242 $\times$ 10^3 had immediate PPB in 3% of patients; immediate hemostasis was achieved with clips, and there was no delayed bleeding.[31] Biopsy and polypectomy may be safe in patients with thrombocytopenia or early-stage cirrhosis with appropriate precautions. Patients with more advanced cirrhosis (Child-Pugh score B or C) were at increased risk for PPB (hazard ratio [HR] 3.5) along with polyp size (HR 3.6) and pedunculated type polyps (HR 2.4).[32]

The use of selective serotonin reuptake inhibitors (SSRIs) has been associated with an increased risk of both organ hemorrhage and adverse outcomes of surgery. SSRIs are thought to inhibit platelet adhesion by up to 50%, an effect that varies by agent and dosage.[33] Multiple studies have demonstrated an increased risk of *upper* gastrointestinal (GI) bleeding in patients using SSRIs (OR 1.6).[34–36] This effect is compounded by the concomitant use of NSAIDs (OR 4.2–8.0) and even more so when aspirin is added to the mix (OR 28.0).[34,35] There are little data evaluating the effect of SSRIs on lower GI bleeding to make recommendations at this time.

Technique/Device-Related Factors

There is wide variation in endoscopic resection techniques among gastroenterologists, specifically with the type of cut (cold vs hot snare resection) and type of current (pure cut vs pure coagulation vs blended current).

Polyps less than 1 cm in size are often removed with a biopsy forceps or a cold snare. Although "cold" snare resection of polyps increases risk of intraprocedural bleeding, it is easily controlled; it is not associated with delayed PPB as observed in a prospective multicenter trial of more than 1000 polypectomies.[37] There is no difference in PPB between cold-snare and hot-snare resection of polyps less than 1 cm.[38,39] However, rates of PPB were higher in hot-snare polypectomy in patients on warfarin.[40]

Cautery is generally used to resect polyps greater than 1 cm in size. There is variability among gastroenterologists in the electrosurgical settings used for snare resection in the United States: 46% use pure coagulation, 46% use blended current, and 3% use pure cut for polypectomy.[41] Pure cutting current increases the risk of bleeding, while pure coagulation current increases the risk of perforation. Hence, a blended cutting and coagulation current is used to minimize both of these complications.[2] Although there was no difference in the rate of PPB, immediate bleeding was more common after blended current use, whereas delayed bleeding was frequent in anticoagulated patients.[42] This area needs further investigation to help standardize endoscopic practice.

Prevention of Postpolypectomy Bleeding

Several studies report outcomes of the different techniques available to prevent PPB. These techniques include injectable solutions, placement of endoclips, deployment of a detachable loop, and application of thermal energy (with coagulation forceps or argon plasma coagulation) as well as a combination of these techniques (**Box 2**).

Solutions—epinephrine injection

Submucosal injection of fluid underneath a polyp elevates the lesion, separates it from the deeper layers, prevents transmural thermal injury, and thus improves the safety of

Box 2
Evidence for prophylaxis of postpolypectomy bleeding

Early bleeding

- Epinephrine injection superior to control (OR 0.37)
- Combination therapy superior to monotherapy (OR 0.12)
- Detachable loop superior to epinephrine or control (OR 0.25)

Delayed bleeding

- Epinephrine versus control: no difference in bleeding rates
- Combination therapy versus monotherapy: no difference in bleeding rates
- Neither detachable loops nor endoclips versus other techniques: no difference in bleeding rates

polypectomy. Dilute epinephrine offers the additional advantage of shrinking polyp size and reducing the risk of bleeding. This principle has been used to remove large pedunculated polyps with the injection of dilute epinephrine into the head and into the stalk of the polyp for volume reduction (epinephrine volume reduction).[43] Compared with saline injection or no preinjection, epinephrine injection results in lower PPB.[44,45] Saline tends to dissipate quickly from the submucosal cushion in highly vascularized areas like the rectum. Although this could be minimized by hypertonic saline (3.0%–4.7%) in combination with epinephrine or 50% dextrose, these solutions can result in local inflammation and delayed tissue damage. A 0.5% hyaluronic acid solution provides the most durable cushion but is also associated with an inflammatory reaction. A combination of saline and methylene blue or indigo carmine dye stains the submucosal space and provides visual confirmation of the depth of resection. Use of other solutions have been reported (fibrinogen, albumin, glycerol), but these are expensive and there are little data to support their use.[41]

Endoclips

Endoclips are frequently used to prevent PPB. Although clips have not been shown to be useful in the prevention of PPB after resection of smaller lesions, a recent study demonstrated that clips prevent delayed bleeding after EMR of lesions greater than 2 cm.[46,47] When endoclips were placed before polypectomy in patients on uninterrupted antithrombotic therapy, there was no PPB in either the endoclip or the control groups.[48] It is cost-effective in patients planning to resume antithrombotic therapy after the procedure, as shown in a decision analysis.[49] Clip application may be ineffective if the clip is unable to span across a thick stalk and occlude all the feeding blood vessels and may cause counterburn during snare resection if applied to a short stalk.[50]

Detachable loops

Detachable loops applied to the stalk of a pedunculated polyp result in vasoconstriction of feeding blood vessels and reduce the risk of PPB. The efficacy of endoloops in the prevention of PPB is similar to other mechanical hemostatic devices such as clips.[51] Endoloop ligation is particularly useful in the prevention of PPB from large polyps (>2 cm).[52]

Cautery

Cautery can be applied to treat and prevent PPB. However, neither argon plasma coagulation nor coagulation forceps treatment of nonbleeding vessels has been effective in the prevention of PPB.[53,54]

Combination therapy

Combination hemostatic therapy with epinephrine injection and application of mechanical devices (detachable loop or endoclip or both) reduces rates of PPB as well as severity of PPB in large polyps (>2 cm) compared with epinephrine injection alone.[55,56]

A meta-analysis and systematic review summarizes the data from available quality studies.[57] Both monotherapy (epinephrine injection or mechanical hemostasis) and a combination of epinephrine injection and mechanical hemostasis reduce early PPB; combination therapy is superior to monotherapy in the prevention of early PPB. Epinephrine injection alone is ineffective in the prevention of delayed PPB, whereas monotherapy with mechanical devices and a combination of epinephrine and mechanical devices are effective in the prevention of delayed PPB.[57]

Management of Postpolypectomy Bleeding

Three options are currently available to manage PPB depending on the timing and severity of bleeding: injectable solutions, thermal devices, and mechanical devices. A decision of whether to treat bleeding during or immediately after resection can be made and implemented promptly (**Box 3**).

Intraprocedural bleeding is associated with clinically significant delayed PPB after wide field EMR, and it should be treated aggressively and immediately.[58] One could consider injection of epinephrine or application of clips, loops, or cautery to control bleeding immediately depending on the source of bleeding.

Delayed PPB requires careful assessment of the patient and the severity of bleeding. The best course of action should be determined based on clinical features, such as hemodynamic instability, frequency of bloody bowel movements, comorbid conditions, patient age, resumption of antithrombotic agents, and so on. If resuscitation measures fail, patients should undergo urgent intervention: colonoscopy with hemostasis, angioembolization, or surgery. If resuscitation measures are successful, patients should be admitted to hospital for observation and monitoring of hemoglobin, platelets,

Box 3
Hemostatic devices

Thermal (contact)

- Heater probe
- Gold probe
- Snare tip cautery
- Hemostatic forceps

Thermal (noncontact)

- Argon plasma coagulation

Mechanical

- TTSC or endoclips
- Detachable loop
- OTSC
- Grasp bleeding stalk with snare device and constrict
- Band ligation
- Endoscopic suturing device

and coagulation profile. More than half of all bleeding subsides spontaneously and does not need any further intervention. Risk factors for ongoing bleeding or recurrence of bleeding that requires intervention include hematochezia hourly or every few minutes, hemodynamic instability, low hemoglobin on admission (<12 g/dL), transfusion requirement, and American Society of Anesthesiologists class of II or higher. If bleeding resolves spontaneously, the patients should be observed for 24 hours before discharge. If it continues or recurs, urgent intervention with colonoscopy is required.[14]

Injectable solutions for hemostasis

In the setting of active bleeding, injection of a 1:10,000 epinephrine-saline solution into the site will help achieve temporary hemostasis by a tamponade effect as well as vasoconstriction of the bleeding vessel.

Thermal hemostatic devices

Thermal devices generate heat and cause edema, coagulation, and vessel constriction through direct contact with the tissue (heater probe, gold probe, snare tip, hemostatic forceps) or indirectly (argon plasma coagulation). Bipolar devices, such as the heater probe and gold probe, complete the circuit within the device and no grounding pad is needed. Although tissue contact is necessary, pressure should not be applied in the colon, unlike when these devices are used in the stomach, because the colon wall is thinner and the settings should also be reduced accordingly (15 J heater probe, 10–15 W gold probe).[59]

When bleeding occurs after polypectomy, the snare is often readily available and the tip of snare can be applied to the bleeding site and soft coagulation applied. The snare is extended out of the sheath by 1 to 2 mm and the wire tip is applied to the bleeding point. Soft coagulation is applied until hemostasis occurs. The coagulation setting allows for desiccation of the tissue, which creates resistance to further current flow, thus limiting injury. This method alone (80 W, effect 4) was successful in 91% of cases when immediate PPB was seen.[60] Studies have also demonstrated the use of hemostatic forceps or graspers in pinching and retracting bleeding points to stop postpolypectomy and diverticular bleeding.[61]

Noncontact thermal energy can be applied with argon plasma coagulation where electron flow through ionized argon gas results in tissue desiccation. Again, desiccated tissue limits further energy flow, and the argon stream will shift to adjacent conductive tissue, allowing for hemostasis of the bleeding vessel.[62]

Mechanical hemostatic devices

The most popular method for endoscopic hemostasis is the application of endoclips or TTSC. In a survey of United States Department of Veteran Affairs gastroenterologists, placement of an endoclip was the preferred method to achieve hemostasis in cases of PPB in 76% of respondents (as well as for bleeding prophylaxis in patients on anticoagulation). For persistent bleeding after cold forceps biopsy, 55% of gastroenterologists would not apply any therapy.[63] Multiple studies have demonstrated that application of TTSC to the bleeding vessel achieves successful hemostasis. A novel technique of endoscopic clip tamponade has been described for bleeding in the midst of an EMR. The endoclip is closed over the lesion for 3 minutes to control bleeding; then the clip is opened so that resection may continue.[64] TTSC placement has also been used in combination with a detachable loop, which is placed to lasso the deployed endoclips together and provide an additional level of mechanical force.[65]

Other devices for mechanical hemostasis include the detachable loop, which is placed more easily over protuberant lesions like a bleeding polypectomy stalk. Endoscopic band ligation can be used in these situations.[66] Although over-the-scope clips

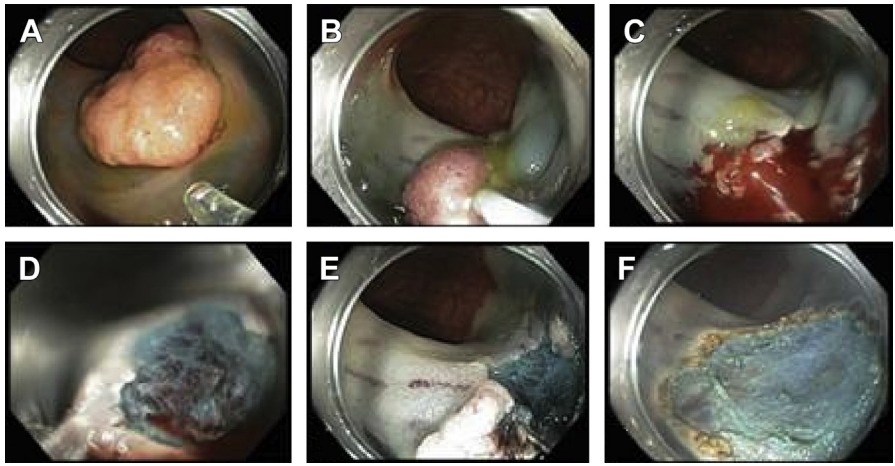

Fig. 1. Endoscopic hemostasis. (*A*) A large sessile polyp in the rectum. (*B*) Endoscopic mucosal resection. (*C*) Brisk arterial bleeding. (*D, E*) Hemostasis achieved with coagulation grasping forceps. (*F*) Clean resection base after APC with complete hemostasis. APC, argon plasma coagulation.

(OTSC) play a greater role in closing perforations, they been effective in PPB in small studies.[67,68] The precise placement of an OTSC may be challenging in the face of an active arterial bleed and would also require the scope to be withdrawn from the patient after localizing the site to retrofit the clip on to the scope. There have been no comparative studies of TTSC with OTSC for hemostasis in humans. The endoscopist should use the device that they are most familiar with and that is readily available in the setting of an acute arterial PPB.

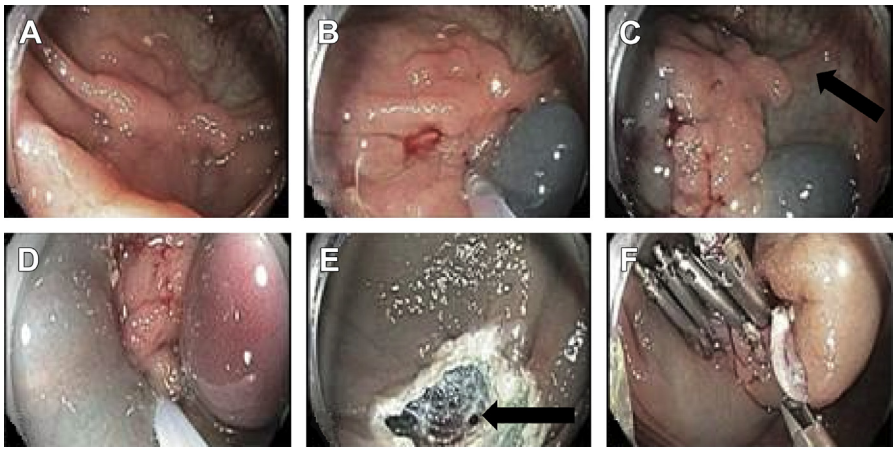

Fig. 2. Endoscopic clip closure of perforation and red flags suggestive of impending perforation. (*A*) Large flat lesion in the cecum with converging folds and central depression suggests submucosal fibrosis. (*B*) Mucosal bleb after injection of dilute indigo carmine solution without a submucosal lift indicates submucosal fibrosis. (*C*) A separate injection lifts the lesion, but the converging fold in the right upper corner (*arrow*) suggests submucosal fibrosis. (*D*) Inability to lift the lesion entrapped by snare is another sign of submucosal fibrosis ("sunken snare sign"). (*E*) Perforation in the middle of submucosal fibrosis (*arrow*). (*F*) Clip closure successful.

COLON PERFORATION

Colon perforation, a dreaded complication of polypectomy, is rare with routine polyp removal. The incidence of colonoscopic perforation varies from 0.7% to 0.9%.[1,69,70] However, the incidence of perforation has certainly increased with the introduction of endoscopic submucosal dissection (ESD) in the colon. The rates of perforation with ESD are 4% to 10%.[71]

The colon wall is approximately 3 mm thick. The submucosa is the strongest layer in the GI tract. Full-thickness resection of the submucosa leaving the muscularis propria intact results in postpolypectomy syndrome and delayed perforation[72]; this could be avoided by prophylactic clip closure of deep resections where the muscularis propria is exposed.

Once a perforation occurs, air escapes into the peritoneum. A massive air leak could result in tension pneumoperitoneum and cardiovascular arrest[73]; this could be prevented by the routine use of carbon dioxide instead of room air for colon insufflation, because carbon dioxide gets reabsorbed into the body faster than room air. In addition, periodic decompression of the colon by removing the biopsy cap and allowing the gas in the colon to vent out reduces this risk. Tension pneumoperitoneum presents with pulseless electrical activity. Once recognized, this requires immediate treatment. It involves insertion of a wide-bore needle or angiocath into the peritoneal cavity after confirming the presence of pneumoperitoneum by insertion of a smaller-gauge needle attached to a syringe filled with saline and observing air bubbles come up the syringe.[74] One could leave the endoscope in the colon as abdominal decompression is performed, so that the perforation could be closed once the patient is stabilized.

Within minutes of perforation, fluid leaks out of the colon and peritonitis sets in. If stool escapes, fecal peritonitis sets in. Hence, it is important to have a clean colon and aim for an excellent colon preparation.[75] In addition, making an effort to suction and dry up the colon segment where a resection is performed as well segments proximal and distal to the site of resection avoids the risk of flooding the site of resection if colon perforation were to occur. Placing the lesion in a nondependent position minimizes the risk of flooding of fluid and avoids fluid escape in case of perforation.

Once a perforation occurs, one should be ready to close it immediately if needed. Small perforations without peritoneal leakage of gas or fluid can be closed after extending and completing the resection; hurried closure and entrapment of polyp in the clip closed defect may result in a refractory recurrence that may be difficult to eradicate. Closure can be undertaken with TTSC or OTSC.

Microperforation and Macroperforation

Colonic perforations can be categorized based on the size of perforation and the timing of detection. Microperforations occur because of colonic wall thinning after the application of cautery and dissection of the submucosal layer that is not detected during endoscopy. These microperforations are detected when free air is seen on imaging studies done routinely after ESD in some centers.[76] Macroperforations occur because of deep and full-thickness resection of the colon wall and are obvious to the endoscopist in real time. These macroperforations result from inadequate injection of submucosal solution that fails to lift the lesion adequately, resection of the lesion into deep submucosa, or submucosal fibrosis from prior manipulation of the lesion (ie, attempted polypectomy).

Although immediate perforation detected during colonoscopy may be addressed endoscopically, delayed perforation often requires surgery. Patients presenting within 24 hours after the procedure are likely to have minimal peritoneal contamination and

can successfully undergo surgical repair compared to patients with delayed presentation where fecal peritonitis has occurred and require a diversion procedure.[75,77] Risk factors for postoperative morbidity include blunt injury, poor bowel preparation, corticosteroid use, and age less than 67.[75,77]

Risk Factors for Perforation

Polyp-related factors

Polyp-related risk factors include location, size, and morphology of the lesion. Cecal location is an important risk factor for perforation. A nonpedunculated polyp in the cecum is associated with a 12-fold increased risk of perforation over a similar sized polyp in the distal colon.[78] Nonpolypoid or laterally spreading lesions are at risk for perforation (OR 4.1).[79] Lesions that may involve deeper tissue layers (Vienna classification 4: noninvasive high-grade dysplasia and Vienna classification 5: invasive neoplasia) were an independent risk factor for perforation.[70] Submucosal fibrosis from prior polypectomy attempts will impair successful lifting of the lesion with submucosal injection and increase the risk of perforation (OR 4.5).[80] Submucosal injection of hyaluronic acid solution is protective against perforation because of its ability to prolong the submucosal cushion effect for several minutes (OR 0.3).[79] It is critical to evaluate the morphology of the lesion in terms of their risk for perforation when contemplating resection so that adequate precautions can be taken (**Box 4**).

Technique/device-related factors

Colon perforation can result from mechanical injury (blunt force or torque-related) (55%), polypectomy (27%), or thermal injury (18%).[75,77]

Mechanical injury may occur while negotiating the colonoscope through a sigmoid colon that may be fixed by adhesions or extremely redundant.[77] It can also occur with retroflexion of the colonoscope in a small rectum, which is frequently observed in patients with severe proctitis or after pelvic radiation therapy. Blunt trauma results in large perforations (mean size 2 cm) of the rectosigmoid colon and may not be amenable to endoscopic closure.[81]

Box 4
Risk factors for colonic perforation

Polyp-related

- Morphology (laterally spreading, nonpedunculated)
- Location (cecum)
- Nonlifting with submucosal fluid injection (deeper layer involvement, prior attempted polypectomy)

Technique-related

- Mechanical injury (retroflexion in a small rectum, redundant sigmoid, or fixed angulation)
- Polypectomy injury
  - Resection of polyps greater than 1 cm in the right colon
  - Resection of polyps greater than 2 cm in the left colon
  - Multiple polyps
  - Thermal injury (argon plasma coagulation, electrocautery)
- Barotrauma (routinely decompress the colon, use carbon dioxide for insufflation)

Perforation related to polypectomy is due to unintentional deep thermal injury, full-thickness resection of the submucosa, or dissection through the muscularis propria. The incidence of perforation varies with type of resection: 0.01% with hot biopsy, 0.17% with polypectomy, 0.91% with EMR, and 3.3% with ESD.[69] Right hemicolon polyps larger than 1 cm, left hemicolon polyps larger than 2 cm, and multiple polyps all increase the risk for perforation.[9] Polypectomy perforations, EMR perforations, and ESD perforations tend to be smaller than those from blunt injury and are usually amenable to endoscopic closure.

Thermal injury from electrocautery or argon plasma coagulation used to ablate tissue or control bleeding may cause perforation. Unlike the perforations resulting from mechanical injury and polypectomy, perforations from thermal injuries tend to be small (1 cm) and are often located in the cecum.[81]

Skilled gastroenterologists with high procedural volume have a lower rate of perforation compared with non-GI endoscopists (surgeons, family physicians, and others). Additional risk factors include procedures performed at ambulatory surgery centers, older patients, female patients, and those with multiple comorbidities. Use of propofol for sedation does not increase the risk of perforation (see **Box 4**).[81–85]

Prevention of Colon Perforation

Several precautions can be taken by an endoscopist to minimize the risk of perforation and its consequences during polypectomy (**Box 5**).

Preprocedure counseling

Patients should be adequately counseled about the risks of EMR, especially if a large or complicated polypectomy is planned. Although this can be accomplished in patients referred for EMR by a preprocedure clinic visit, this may not be possible when one incidentally encounters a large flat lesion during a screening colonoscopy. This lesion could be managed by opting for one of these 3 approaches: (1) reschedule the patient on a separate day, which gives an opportunity to counsel the patient about the risks and benefits of EMR; (2) refer the patient to an EMR expert, who will counsel the patient and perform the procedure; or (3) resect during the same session. Take the opportunity to counsel the patient during the informed consent process that you may be removing a large polyp if encountered during a screening examination to avoid the need for a second procedure. As long as the patient understands the differences in risks between screening colonoscopy and colonoscopy with EMR, it is appropriate to proceed. This approach may avoid sampling the lesion, which increases the risk of turning the lesion into a defiant polyp, and make resection safer.[86]

Box 5
Prevention of colonic perforation

- Polyp is accessible and scope position can be maintained
- Lesion is positioned in a nondependent location
- Bowel preparation is excellent; residual feces and liquid are removed from the entire colon
- Appropriate volume of solution is injected into the submucosal space
- Adequate submucosal lift is achieved (especially if polypectomy has previously been attempted)
- Carbon dioxide used for insufflation

Bowel preparation

Colonoscopy should be deferred in patients with a poor bowel preparation because escape of feces and luminal contents into the peritoneal cavity results in fecal peritonitis. In those cases, colostomy with fecal diversion will be required and simple closure may not suffice.[75] Colon explosion can occur in patients undergoing polypectomy in the presence of poor colon preparation and accumulation of methane gas when combined with cautery.

Excellent bowel preparation reduces the risk of serious complications if a perforation were to occur. A split dose preparation with 2 L of PEG (polyethylene glycol) solution consumed over a period of 2 hours both the day before the procedure and the morning of the procedure, with the preparation completed 4 hours before procedure start time to ensure excellent colon preparation, is critical. One should aim for a Boston Bowel Preparation Scale score of 7 or greater.[87] The bowel preparation should be individualized based on the patient's need to travel to the facility, comorbid conditions (ie, diabetes, renal insufficiency), quality of previous bowel preparations, and tolerance of preparation solution.

Management of antithrombotic agents

The American Society of Gastrointestinal Endoscopy guidelines offer recommendations for the appropriate interval for discontinuing these agents and resuming them postprocedure. The decision to modify antithrombotic therapy should be individualized and optimally made in conjunction with the patient's primary care physician or cardiologist (see **Table 1**).[20]

Room setup and checklist

The endoscopy room should be set up to ensure patient safety and procedural efficiency and to minimize injury to the gastroenterologist. This setting is especially important when performing prolonged or complicated polypectomy or EMR.[88] Procedural efficiency lessens the strain on the endoscopist and can be critical in rescuing therapeutic misadventures when they occur. Therefore, all necessary equipment, supplies, and personnel should be readily available in the endoscopy room to minimize and manage complications of polypectomy. It is important to review the case with the team and ensure all equipment, including the ones required for rescue from complications, is available in the room. Recommendations to optimize the ergonomics of endoscopy are outlined in **Box 6**.

Patient positioning

It is important to position the patient such that it allows the lesion to be kept in a nondependent position. This position avoids escape of fluid into the peritoneum if a perforation were to occur. All residual fluid in the upstream and downstream segments of the colon should be suctioned before polypectomy to minimize the risk of peritoneal soiling.[81]

Endoscope setup—distal cap attachment, carbon dioxide

Although studies have not demonstrated the benefit of a cap-fitted colonoscope, the authors use it routinely for all polyp resections. The cap helps in accessing the lesion hidden under folds. In addition, the cap could be used to achieve tamponade if bleeding were to occur and helps to optimize endoclip placement. Carbon dioxide insufflation is preferable to room air especially with prolonged and high-risk procedures. It gets reabsorbed into the body faster than air if it escapes through a perforation and minimizes the risk of tension pneumoperitoneum that may otherwise require needle puncture of the abdomen and decompression. In addition, it reduces

Box 6
Room setup for colonoscopy with polypectomy

- Monitor positioned directly in front of endoscopist and just below eye level
- Monitors must be adjustable to accommodate endoscopists of varying heights (optimal viewing angle of 15°–25° below the horizon, viewing distance 52–182 cm)
- Examination table at or 0–10 cm below elbow level of endoscopist
- Adequate recovery time between procedures to rest endoscopist muscle groups
- Availability of both pediatric and adult colonoscopes and distal cap attachment
- Polypectomy devices (different shapes and sizes of snares, cold snares, injection needles, polyp retrieval nets)
- Agents to mix solutions for safe polypectomy (saline, indigo carmine, epinephrine)
- Hemostatic and closure devices (clips, hemostatic forceps, argon plasma coagulation (APC) machine, endoloop, and so on)
- Functioning argon plasma coagulation machine, probes, and grounding pads
- Capability to use carbon dioxide insufflation
- Technician/assistant with competency in using all necessary devices

Adapted from Shergill AK, McQuaid KR, Rempel D. Ergonomics and GI endoscopy. Gastrointest Endosc 2009;70:145–53; with permission.

postprocedure abdominal pain and hospitalizations.[89] The authors decompress the colon by removing the biopsy valve to allow passive venting of the colon, which may reduce the risk of a massive gas leak out of an otherwise distended colon through a perforation if it were to occur.

Management of Colon Perforations

During the last couple of decades, knowledge in assessing the depth of resection and identification of perforation during endoscopy has allowed management of these complications with prompt endoscopic closure, thus avoiding the need for surgery (**Box 7**).

Assessing the depth of resection

It is important to assess the depth of resection right after the cut is made. If a dye solution (like methylene blue or indigo carmine) is used to form a cushion underneath the polyp before resection, the submucosal space is tinted blue and confirms an appropriate depth. What if there are areas that are unstained in the polypectomy defect site? The technique of topical submucosal chromoendoscopy will help in these situations.[90] The injection catheter is positioned over the unstained area and irrigated with dye solution with the needle withdrawn. If this area absorbs the stain, submucosal

Box 7
Assessing depth of resection and defect closure devices

- Topical submucosal chromoendoscopy, target sign, stain resistance
- TTSC or endoclips
- OTSC
- Endoscopic suturing device, T-tags

depth is confirmed. Persistent nonstaining represents deep injury (white cautery ring indicating disruption of the muscularis propria layer), exposed muscle (uninterrupted concentric muscular rings), or submucosal fibrosis (dense white to yellow tissue).[90] The white cautery ring indicating disruption of the muscularis layer resembles a target sign surrounded by blue-stained submucosa. A corresponding target sign will also be present on the underside of the resected specimen.[72] These advances allow early detection of perforation during the procedure and well before the patient develops clinical signs of perforation or free air is seen on radiographic imaging and stresses the importance of methodically examining the polypectomy defect. Full-thickness resections and deep resection with exposure of the muscle should be closed with clips.

Through-the-scope clips

Binmoeller and colleagues[91] reported successful closure of a gastric perforation with endoscopic clips in the 1990s. Compared with the original clip, current versions allow one to rotate the clip to a desired angle for accurate placement and reopen the clip if the application is not satisfactory.[92] These clips are widely used for endoscopic closure of perforations and large defects.[46,93] Although TTSC are an effective method in closing polypectomy defects, they are limited by a smaller wingspan and lower closure force that can compromise tissue apposition and often necessitate the placement of multiple clips that adds to procedural cost and time.[94]

Over-the-scope clips

OTSC (Ovesco Endoscopy AG, Tubingen Germany) were first introduced in 2007. These clips are made of nitinol (nickel titanium alloy) and are housed on a metal applicator cap that fits over the distal tip of the endoscope, much like a band ligator. OTSC with rounded teeth are used for hemostasis, while those with pointed teeth are useful in closure of perforations. Compared with TTSC, OTSC grasp more tissue and offer a durable closure because of its higher grip force. The main disadvantage of OTSC is that they need to be loaded on to the scope before it can be deployed.[95–97]

Endoscopic suturing

Several endoscopic plicating devices have been introduced but are only used in a few specialized centers. Examples include the Eagle Claw VIII (Olympus Corporation, Tokyo, Japan), purse-string suturing device (LSI Solutions, Victor NY, USA), Flexible Endostitch (Covidien, North Haven, CT, USA), and Plicator (NDO Surgical Inc, Mansfield, MA, USA). Much of the experience with suturing devices comes from experimental models with only a few in vivo studies.[98] Other suture closure devices include T-tags, where a needle loaded with a metal T-tag and thread is inserted into the endoscope channel. Tissue is punctured, and the T-tag is ejected. This process is repeated on the opposite side of the defect, and the threads are cinched together.[99] More clinical work needs to be done using these devices, but they may offer a role in endoscopic closure of perforations in the future.

Endoscopic clip closure techniques

TTSC is the most popular device and can be used to safely close defects smaller than 2 cm in diameter by most endoscopists. These endoclips can successfully approximate the mucosal and submucosal layers in a partial thickness closure.[100] Endoscopists and their technicians should be familiar with the operation of the endoclips available in their endoscopy suite. When applying TTSC to a perforation site, it is important to keep the endoclip close to the tip of the scope for maximal control. The open wings of the endoclips should be positioned perpendicular to the defect and the lower edge of a transverse perforation captured with the lower wing. Gentle

suction is applied to collapse the lumen to the endoclip to engage the opposite edge of the defect and capture maximal tissue. Once the endoclip is closed, optimal placement must be confirmed before deployment. An improperly positioned endoclip will hinder further endoclip placement. This process should begin at one end of the defect and be repeated until complete closure has been achieved.[81]

Proficiency with endoclip placement can be achieved with real-time experience in clinical practice. There are also hands-on courses held by major gastroenterology organizations worldwide where the technique can be perfected. In addition, DVDs are available from gastroenterology societies wherein this technique and others can be observed as performed by experts in the field.

OTSC is helpful in larger defects and in full-thickness resection of the colon but requires removal of the colonoscope to retrofit the device. In these circumstances, the patient should be positioned so the defect is in a nondependent location and the colon is fully decompressed before scope withdrawal to attach the OTSC. Over-the-scope suturing devices have been successful in the closure of 8 colonic perforations after ESD (Apollo Endosurgery, Austin, TX, USA) without any adverse events.[101]

Patient management after perforation

Patients should be admitted with strict nothing per mouth and given broad spectrum intravenous antibiotics and fluids. Blood counts should be monitored every 6 to 8 hours. Baseline imaging can be helpful in patients that deteriorate clinically. The surgical service should be involved at the outset in cases even when endoscopic closure has been achieved. Tension pneumoperitoneum should be decompressed with an 18-gauge or 20-gauge needle to prevent cardiopulmonary compromise.[74] Patients should be closely monitored and oral intake can be resumed once pain and fever subside, appetite and bowel function return, and leukocytosis has resolved.

Surgery is indicated for large perforations, for generalized peritonitis or ongoing sepsis, and in those who clinically deteriorate after apparently successful endoscopic clip closure of the defect. In one series, the technical success rate of TTSC closure was 91% (29/32) with 7 patients requiring surgery. TTSC was clinically unsuccessful in 5 patients who went on to require surgical intervention. Risk factors associated with the need for early surgical treatment (within 24 hours of endoscopic closure) were perforations greater than 1 cm, persistent leukocytosis, fever, severe abdominal pain, and a large amount of free intraperitoneal air (extending more than 3 cm below the diaphragm).[102] Laparoscopic approach may be possible based on local expertise and for patients that present early in their clinical course.[100] Greater delay to time of surgery resulted in an open surgical approach and need for diversion colostomy,[102] stressing the need for close clinical observation in the postendoscopic closure period.

How do outcomes for endoscopic clipping compare to surgical outcomes? One study compared the outcomes of patients with endoscopic closure for perforation versus surgery for those presenting with delayed perforation. Patients with failed clipping (either technical failure or clinical failure) that went on to surgery were excluded from analysis. Although the defects were significantly smaller in the clipping group, patient outcomes in terms of duration of fasting, treatment with antibiotics, and length of hospital stay were comparable to the surgical group.[103]

Postpolypectomy Syndrome

Postpolypectomy syndrome is due to transmural thermal injury resulting in localized peritonitis without perforation.[104,105] The incidence varies from 1.0 in 1000 to 3.0 per 100,000 examinations.[105] Risk factors for postpolypectomy syndrome include lesions larger than 1 cm (OR 2.8), nonpolypoid morphology (OR 3.3), and hypertension

(OR 3.0).[106] Large flat lesions require higher prolonged thermal energy, which increases the risk of transmural injury. Patients present with fever, localized abdominal pain and tenderness, and leukocytosis 1 to 5 days after polypectomy.[105] Management includes hospitalization, close monitoring, nothing by mouth, intravenous fluids, and antibiotics until clinical recovery is achieved. Typically, patients require fasting for 3 days, hospitalization for 5 days, and antibiotics for 7 days.[106] Postpolypectomy syndrome can be prevented by careful selection of appropriate endoscopic technique.

SUMMARY

Advances in the understanding of the risk factors for bleeding and perforation after endoscopic resection of polyps as well as the technology and techniques to prevent and manage these complications help shift the pendulum away from the need for surgical repair and toward endoscopic solutions.

REFERENCES

1. Levin TR, Zhao W, Conell C, et al. Complications of colonoscopy in an integrated health care delivery system. Ann Intern Med 2006;145:880–6.
2. Ko CW, Dominitz JA. Complications of colonoscopy: magnitude and management. Gastrointest Endosc Clin N Am 2010;20:659–71.
3. Rex DK, Petrini JL, Baron TH, et al. Quality indicators for colonoscopy. Gastrointest Endosc 2006;63:S16–28.
4. Kim HS, Kim TI, Kim WH, et al. Risk factors for immediate postpolypectomy bleeding of the colon: a multicenter study. Am J Gastroenterol 2006;101:1333–41.
5. Kim JH, Lee HJ, Ahn JW, et al. Risk factors for delayed post-polypectomy hemorrhage: a case-control study. J Gastroenterol Hepatol 2013;28:645–9.
6. Watabe H, Yamaji Y, Okamoto M, et al. Risk assessment for delayed hemorrhagic complication of colonic polypectomy: polyp-related factors and patient-related factors. Gastrointest Endosc 2006;64:73–8.
7. Buddingh KT, Herngreen T, Haringsma J, et al. Location in the right hemi-colon is an independent risk factor for delayed post-polypectomy hemorrhage: a multi-center case-control study. Am J Gastroenterol 2011;106:1119–24.
8. Sawhney MS, Salfiti N, Nelson DB, et al. Risk factors for severe delayed postpolypectomy bleeding. Endoscopy 2008;40:115–9.
9. Heldwein W, Dollhopf M, Rosch T, et al. The Munich Polypectomy Study (MUPS): prospective analysis of complications and risk factors in 4000 colonic snare polypectomies. Endoscopy 2005;37:1116–22.
10. Metz AJ, Bourke MJ, Moss A, et al. Factors that predict bleeding following endoscopic mucosal resection of large colonic lesions. Endoscopy 2011;43:506–11.
11. Consolo P, Luigiano C, Strangio G, et al. Efficacy, risk factors and complications of endoscopic polypectomy: ten year experience at a single center. World J Gastroenterol 2008;14:2364–9.
12. Dobrowolski S, Dobosz M, Babicki A, et al. Blood supply of colorectal polyps correlates with risk of bleeding after colonoscopic polypectomy. Gastrointest Endosc 2006;63:1004–9.
13. Gimeno-Garcia AZ, de Ganzo ZA, Sosa AJ, et al. Incidence and predictors of postpolypectomy bleeding in colorectal polyps larger than 10 mm. Eur J Gastroenterol Hepatol 2012;24:520–6.

14. Burgess NG, Williams SJ, Hourigan LF, et al. A management algorithm based on delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. Clin Gastroenterol Hepatol 2014;12(9):1525–33.
15. Nakajima H, Takami H, Yamagata K, et al. Aspirin effects on colonic mucosal bleeding: implications for colonic biopsy and polypectomy. Dis Colon Rectum 1997;40:1484–8.
16. Pan A, Schlup M, Lubcke R, et al. The role of aspirin in post-polypectomy bleeding–a retrospective survey. BMC Gastroenterol 2012;12:138.
17. Manocha D, Singh M, Mehta N, et al. Bleeding risk after invasive procedures in aspirin/NSAID users: polypectomy study in veterans. Am J Med 2012;125: 1222–7.
18. Shiffman ML, Farrel MT, Yee YS. Risk of bleeding after endoscopic biopsy or polypectomy in patients taking aspirin or other NSAIDS. Gastrointest Endosc 1994; 40:458–62.
19. Yousfi M, Gostout CJ, Baron TH, et al. Postpolypectomy lower gastrointestinal bleeding: potential role of aspirin. Am J Gastroenterol 2004;99:1785–9.
20. ASGE Standards of Practice Committee, Anderson MA, Ben-Menachem T, et al. Management of antithrombotic agents for endoscopic procedures. Gastrointest Endosc 2009;70:1060–70.
21. Gandhi S, Narula N, Mosleh W, et al. Meta-analysis: colonoscopic post-polypectomy bleeding in patients on continued clopidogrel therapy. Aliment Pharmacol Ther 2013;37:947–52.
22. Feagins LA, Iqbal R, Harford WV, et al. Low rate of postpolypectomy bleeding among patients who continue thienopyridine therapy during colonoscopy. Clin Gastroenterol Hepatol 2013;11:1325–32.
23. Feagins LA, Uddin FS, Davila RE, et al. The rate of post-polypectomy bleeding for patients on uninterrupted clopidogrel therapy during elective colonoscopy is acceptably low. Dig Dis Sci 2011;56:2631–8.
24. Singh M, Mehta N, Murthy UK, et al. Postpolypectomy bleeding in patients undergoing colonoscopy on uninterrupted clopidogrel therapy. Gastrointest Endosc 2010;71:998–1005.
25. Hui AJ, Wong RM, Ching JY, et al. Risk of colonoscopic polypectomy bleeding with anticoagulants and antiplatelet agents: analysis of 1657 cases. Gastrointest Endosc 2004;59:44–8.
26. Witt DM, Delate T, McCool KH, et al. Incidence and predictors of bleeding or thrombosis after polypectomy in patients receiving and not receiving anticoagulation therapy. J Thromb Haemost 2009;7:1982–9.
27. Gerson LB, Michaels L, Ullah N, et al. Adverse events associated with anticoagulation therapy in the periendoscopic period. Gastrointest Endosc 2010;71: 1211–7.e2.
28. Inoue T, Nishida T, Maekawa A, et al. Clinical features of post-polypectomy bleeding associated with heparin bridge therapy. Dig Endosc 2014;26:243–9.
29. Friedland S, Soetikno R. Colonoscopy with polypectomy in anticoagulated patients. Gastrointest Endosc 2006;64:98–100.
30. Krishna SG, Rao BB, Thirumurthi S, et al. Safety of endoscopic interventions in patients with thrombocytopenia. Gastrointest Endosc 2014;80:425–34.
31. Jeon JW, Shin HP, Lee JI, et al. The risk of postpolypectomy bleeding during colonoscopy in patients with early liver cirrhosis. Surg Endosc 2012;26:3258–63.
32. Lee S, Park SJ, Cheon JH, et al. Child-Pugh score is an independent risk factor for immediate bleeding after colonoscopic polypectomy in liver cirrhosis. Yonsei Med J 2014;55:1281–8.

33. Hallback I, Hagg S, Eriksson AC, et al. In vitro effects of serotonin and noradrenaline reuptake inhibitors on human platelet adhesion and coagulation. Pharmacol Rep 2012;64:979–83.
34. Anglin R, Yuan Y, Moayyedi P, et al. Risk of upper gastrointestinal bleeding with selective serotonin reuptake inhibitors with or without concurrent nonsteroidal anti-inflammatory use: a systematic review and meta-analysis. Am J Gastroenterol 2014;109:811–9.
35. Dall M, Schaffalitzky de Muckadell OB, Lassen AT, et al. An association between selective serotonin reuptake inhibitor use and serious upper gastrointestinal bleeding. Clin Gastroenterol Hepatol 2009;7:1314–21.
36. Jiang HY, Chen HZ, Hu XJ, et al. Use of selective serotonin reuptake inhibitors and risk of upper gastrointestinal bleeding: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2015;13(1):42–50.e3.
37. Repici A, Hassan C, Vitetta E, et al. Safety of cold polypectomy for <10mm polyps at colonoscopy: a prospective multicenter study. Endoscopy 2012;44:27–31.
38. Aslan F, Camci M, Alper E, et al. Cold snare polypectomy versus hot snare polypectomy in endoscopic treatment of small polyps. Turk J Gastroenterol 2014;25:279–83.
39. Paspatis GA, Tribonias G, Konstantinidis K, et al. A prospective randomized comparison of cold vs hot snare polypectomy in the occurrence of postpolypectomy bleeding in small colonic polyps. Colorectal Dis 2011;13:e345–8.
40. Horiuchi A, Nakayama Y, Kajiyama M, et al. Removal of small colorectal polyps in anticoagulated patients: a prospective randomized comparison of cold snare and conventional polypectomy. Gastrointest Endosc 2014;79:417–23.
41. Monkemuller K, Neumann H, Malfertheiner P, et al. Advanced colon polypectomy. Clin Gastroenterol Hepatol 2009;7:641–52.
42. Van Gossum A, Cozzoli A, Adler M, et al. Colonoscopic snare polypectomy: analysis of 1485 resections comparing two types of current. Gastrointest Endosc 1992;38:472–5.
43. Hogan RB, Hogan RB 3rd. Epinephrine volume reduction of giant colon polyps facilitates endoscopic assessment and removal. Gastrointest Endosc 2007;66:1018–22.
44. Lee SH, Chung IK, Kim SJ, et al. Comparison of postpolypectomy bleeding between epinephrine and saline submucosal injection for large colon polyps by conventional polypectomy: a prospective randomized, multicenter study. World J Gastroenterol 2007;13:2973–7.
45. Dobrowolski S, Dobosz M, Babicki A, et al. Prophylactic submucosal saline-adrenaline injection in colonoscopic polypectomy: prospective randomized study. Surg Endosc 2004;18:990–3.
46. Liaquat H, Rohn E, Rex DK. Prophylactic clip closure reduced the risk of delayed postpolypectomy hemorrhage: experience in 277 clipped large sessile or flat colorectal lesions and 247 control lesions. Gastrointest Endosc 2013;77:401–7.
47. Feagins LA, Nguyen AD, Iqbal R, et al. The prophylactic placement of hemoclips to prevent delayed post-polypectomy bleeding: an unnecessary practice? A case control study. Dig Dis Sci 2014;59:823–8.
48. Katsinelos P, Fasoulas K, Chatzimavroudis G, et al. Prophylactic clip application before endoscopic resection of large pedunculated colorectal polyps in patients receiving anticoagulation or antiplatelet medications. Surg Laparosc Endosc Percutan Tech 2012;22:e254–8.

49. Parikh ND, Zanocco K, Keswani RN, et al. A cost-efficacy decision analysis of prophylactic clip placement after endoscopic removal of large polyps. Clin Gastroenterol Hepatol 2013;11:1319–24.
50. Quintanilla E, Castro JL, Rabago LR, et al. Is the use of prophylactic hemoclips in the endoscopic resection of large pedunculated polyps useful? A prospective and randomized study. J Interv Gastroenterol 2012;2:183–8.
51. Ji JS, Lee SW, Kim TH, et al. Comparison of prophylactic clip and endoloop application for the prevention of postpolypectomy bleeding in pedunculated colonic polyps: a prospective, randomized, multicenter study. Endoscopy 2014;46:598–604.
52. Di Giorgio P, De Luca L, Calcagno G, et al. Detachable snare versus epinephrine injection in the prevention of postpolypectomy bleeding: a randomized and controlled study. Endoscopy 2004;36:860–3.
53. Lee CK, Lee SH, Park JY, et al. Prophylactic argon plasma coagulation ablation does not decrease delayed postpolypectomy bleeding. Gastrointest Endosc 2009;70:353–61.
54. Bahin FF, Naidoo M, Williams SJ, et al. Prophylactic endoscopic coagulation to prevent bleeding after wide-field endoscopic mucosal resection of large sessile colon polyps. Clin Gastroenterol Hepatol 2014. [Epub ahead of print].
55. Paspatis GA, Paraskeva K, Theodoropoulou A, et al. A prospective, randomized comparison of adrenaline injection in combination with detachable snare versus adrenaline injection alone in the prevention of postpolypectomy bleeding in large colonic polyps. Am J Gastroenterol 2006;101:2805 [quiz: 2913].
56. Kouklakis G, Mpoumponaris A, Gatopoulou A, et al. Endoscopic resection of large pedunculated colonic polyps and risk of postpolypectomy bleeding with adrenaline injection versus endoloop and hemoclip: a prospective, randomized study. Surg Endosc 2009;23:2732–7.
57. Li LY, Liu QS, Li L, et al. A meta-analysis and systematic review of prophylactic endoscopic treatments for postpolypectomy bleeding. Int J Colorectal Dis 2011;26:709–19.
58. Burgess NG, Metz AJ, Williams SJ, et al. Risk factors for intraprocedural and clinically significant delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. Clin Gastroenterol Hepatol 2014;12:651–61.e1–3.
59. Hong SP. How do I manage post-polypectomy bleeding? Clin Endosc 2012;45:282–4.
60. Fahrtash-Bahin F, Holt BA, Jayasekeran V, et al. Snare tip soft coagulation achieves effective and safe endoscopic hemostasis during wide-field endoscopic resection of large colonic lesions (with videos). Gastrointest Endosc 2013;78:158–63.e1.
61. Coumaros D, Tsesmeli N. Active gastrointestinal bleeding: use of hemostatic forceps beyond endoscopic submucosal dissection. World J Gastroenterol 2010;16:2061–4.
62. Asge Technology C, Conway JD, Adler DG, et al. Endoscopic hemostatic devices. Gastrointest Endosc 2009;69:987–96.
63. Feagins LA, Spechler SJ. Use of hemoclips and other measures to prevent bleeding during colonoscopy by gastroenterologists in Veterans Affairs hospitals. Am J Gastroenterol 2014;109:288–90.
64. Chen WC, Maru DM, Abraham SC, et al. Endoscopic clip tamponade of bleeding: a novel adjunct technique for endoscopic mucosal resection. Endoscopy 2013;45(Suppl 2 UCTN):E104–5.

65. Parra-Blanco A, Kaminaga N, Kojima T, et al. Hemoclipping for postpolypectomy and postbiopsy colonic bleeding. Gastrointest Endosc 2000;51:37–41.
66. Akahoshi K, Yoshinaga S, Fujimaru T, et al. Endoscopic resection with hypertonic saline-solution-epinephrine injection plus band ligation for large pedunculated or semipedunculated gastric polyp. Gastrointest Endosc 2006;63:312–6.
67. Alcaide N, Penas-Herrero I, Sancho-del-Val L, et al. Ovesco system for treatment of postpolypectomy bleeding after failure of conventional treatment. Rev Esp Enferm Dig 2014;106:55–8.
68. Singhal S, Changela K, Papafragkakis H, et al. Over the scope clip: technique and expanding clinical applications. J Clin Gastroenterol 2013;47:749–56.
69. Oka S, Tanaka S, Kanao H, et al. Current status in the occurrence of postoperative bleeding, perforation and residual/local recurrence during colonoscopic treatment in Japan. Dig Endosc 2010;22:376–80.
70. Wada Y, Kudo SE, Tanaka S, et al. Predictive factors for complications in endoscopic resection of large colorectal lesions: a multicenter prospective study. Surg Endosc 2014. [Epub ahead of print].
71. Asge Technology Committee, Kantsevoy SV, Adler DG, et al. Endoscopic mucosal resection and endoscopic submucosal dissection. Gastrointest Endosc 2008;68:11–8.
72. Swan MP, Bourke MJ, Moss A, et al. The target sign: an endoscopic marker for the resection of the muscularis propria and potential perforation during colonic endoscopic mucosal resection. Gastrointest Endosc 2011;73:79–85.
73. Kipple JC. Bilateral tension pneumothoraces and subcutaneous emphysema following colonoscopic polypectomy: a case report and discussion of anesthesia considerations. AANA J 2010;78:462–7.
74. Broeders E, Al-Taher M, Peeters K, et al. Verres needle desufflation as an effective treatment option for colonic perforation after colonoscopy. Surg Laparosc Endosc Percutan Tech 2014. [Epub ahead of print].
75. Iqbal CW, Cullinane DC, Schiller HJ, et al. Surgical management and outcomes of 165 colonoscopic perforations from a single institution. Arch Surg 2008;143:701–6 [discussion: 706–7].
76. Lee DW, Jeon SW. Management of complications during gastric endoscopic submucosal dissection. Diagn Ther Endosc 2012;2012:624835.
77. Raju GS. Gastrointestinal perforations: role of endoscopic closure. Curr Opin Gastroenterol 2011;27:418–22.
78. Rutter MD, Nickerson C, Rees CJ, et al. Risk factors for adverse events related to polypectomy in the English Bowel Cancer Screening Programme. Endoscopy 2014;46:90–7.
79. Lee EJ, Lee JB, Choi YS, et al. Clinical risk factors for perforation during endoscopic submucosal dissection (ESD) for large-sized, nonpedunculated colorectal tumors. Surg Endosc 2012;26:1587–94.
80. Kim ES, Cho KB, Park KS, et al. Factors predictive of perforation during endoscopic submucosal dissection for the treatment of colorectal tumors. Endoscopy 2011;43:573–8.
81. Raju GS, Saito Y, Matsuda T, et al. Endoscopic management of colonoscopic perforations (with videos). Gastrointest Endosc 2011;74:1380–8.
82. Chukmaitov A, Bradley CJ, Dahman B, et al. Association of polypectomy techniques, endoscopist volume, and facility type with colonoscopy complications. Gastrointest Endosc 2013;77:436–46.
83. Lohsiriwat V, Sujarittanakarn S, Akaraviputh T, et al. What are the risk factors of colonoscopic perforation? BMC Gastroenterol 2009;9:71.

84. Lorenzo-Zuniga V, Moreno de Vega V, Domenech E, et al. Endoscopist experience as a risk factor for colonoscopic complications. Colorectal Dis 2010;12:e273–7.
85. Bielawska B, Day AG, Lieberman DA, et al. Risk factors for early colonoscopic perforation include non-gastroenterologist endoscopists: a multivariable analysis. Clin Gastroenterol Hepatol 2014;12:85–92.
86. Buchner AM, Guarner-Argente C, Ginsberg GG. Outcomes of EMR of defiant colorectal lesions directed to an endoscopy referral center. Gastrointest Endosc 2012;76:255–63.
87. Lai EJ, Calderwood AH, Doros G, et al. The Boston bowel preparation scale: a valid and reliable instrument for colonoscopy-oriented research. Gastrointest Endosc 2009;69:620–5.
88. Shergill AK, McQuaid KR, Rempel D. Ergonomics and GI endoscopy. Gastrointest Endosc 2009;70:145–53.
89. Bassan MS, Holt B, Moss A, et al. Carbon dioxide insufflation reduces number of postprocedure admissions after endoscopic resection of large colonic lesions: a prospective cohort study. Gastrointest Endosc 2013;77:90–5.
90. Holt BA, Jayasekeran V, Sonson R, et al. Topical submucosal chromoendoscopy defines the level of resection in colonic EMR and may improve procedural safety (with video). Gastrointest Endosc 2013;77:949–53.
91. Binmoeller KF, Grimm H, Soehendra N. Endoscopic closure of a perforation using metallic clips after snare excision of a gastric leiomyoma. Gastrointest Endosc 1993;39:172–4.
92. Raju GS, Gajula L. Endoclips for GI endoscopy. Gastrointest Endosc 2004;59:267–79.
93. Raju GS. Endoscopic management of gastrointestinal leaks. Gastrointest Endosc Clin N Am 2007;17:487–503, vi.
94. Jayaraman V, Hammerle C, Lo SK, et al. Clinical application and outcomes of over the scope clip device: initial US experience in humans. Diagn Ther Endosc 2013;2013:381873.
95. Baron TH, Song LM, Ross A, et al. Use of an over-the-scope clipping device: multicenter retrospective results of the first U.S. experience (with videos). Gastrointest Endosc 2012;76:202–8.
96. Seebach L, Bauerfeind P, Gubler C. "Sparing the surgeon": clinical experience with over-the-scope clips for gastrointestinal perforation. Endoscopy 2010;42:1108–11.
97. Weiland T, Fehlker M, Gottwald T, et al. Performance of the OTSC system in the endoscopic closure of iatrogenic gastrointestinal perforations: a systematic review. Surg Endosc 2013;27:2258–74.
98. Pham BV, Raju GS, Ahmed I, et al. Immediate endoscopic closure of colon perforation by using a prototype endoscopic suturing device: feasibility and outcome in a porcine model (with video). Gastrointest Endosc 2006;64:113–9.
99. Raju GS. Endoscopic closure of gastrointestinal leaks. Am J Gastroenterol 2009;104:1315–20.
100. Paraskeva KD, Paspatis GA. Management of bleeding and perforation after colonoscopy. Expert Rev Gastroenterol Hepatol 2014;8(8):963–72.
101. Kantsevoy SV, Bitner M, Mitrakov AA, et al. Endoscopic suturing closure of large mucosal defects after endoscopic submucosal dissection is technically feasible, fast, and eliminates the need for hospitalization (with videos). Gastrointest Endosc 2014;79:503–7.
102. Cho SB, Lee WS, Joo YE, et al. Therapeutic options for iatrogenic colon perforation: feasibility of endoscopic clip closure and predictors of the need for early surgery. Surg Endosc 2012;26:473–9.

103. Kim JS, Kim BW, Kim JI, et al. Endoscopic clip closure versus surgery for the treatment of iatrogenic colon perforations developed during diagnostic colonoscopy: a review of 115,285 patients. Surg Endosc 2013;27:501–4.
104. Kim HW. What is different between postpolypectomy fever and postpolypectomy coagulation syndrome? Clin Endosc 2014;47:205–6.
105. ASGE Standards of Practice Committee, Fisher DA, Maple JT, et al. Complications of colonoscopy. Gastrointest Endosc 2011;74:745–52.
106. Cha JM, Lim KS, Lee SH, et al. Clinical outcomes and risk factors of postpolypectomy coagulation syndrome: a multicenter, retrospective, case-control study. Endoscopy 2013;45:202–7.