Published in final edited form as:

Gastrointest Endosc. 2020 February ; 91(2): 257–265. doi:10.1016/j.gie.2019.09.033.

Antiplatelets, anticoagulants, and colonoscopic polypectomy

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Abstract

The management of antiplatelet and anticoagulant (ie, antithrombotic) agents is challenging in the perendoscopic setting. In this state-of-the-art update, we review current best practice recommendations focusing on the risk of immediate and delayed postpolypectomy bleeding in the context of drug discontinuation (ie, temporary interruption) and drug continuation. The data regarding polypectomy technique (cold snare vs conventional thermal-based) and prophylactic placement of hemostatic clips are evaluated to assess whether these endoscopic techniques are beneficial in reducing postpolypectomy bleeding. Finally, clinical takeaways are provided to facilitate safer polypectomy among patients on antiplatelet and anticoagulant agents.

After acute coronary syndrome, prescription of antiplatelet agents (thienopyridine drugs clopidogrel, prasugrel, and ticagrelor and acetylsalicylic acid [ASA]) for 6 to 12 months (class 1 recommendation) is standard, and in some patients the indefinite use of antiplatelet agents can be suitable (class IIB recommendation).¹ More than 115 million patients worldwide are currently on clopidogrel.² Patients with coronary artery disease are twice as likely to develop colonic polyps and colon cancer.³ Potential biologic mediators linking cardiovascular patients to an elevated risk of polyposis include increased insulin resistance, obesity, and chronic inflammation.⁴

In patients with nonvalvular atrial fibrillation, prescription of warfarin and direct oral anticoagulant agents (DOACs; dabigatran, rivaroxaban, apixaban, edoxaban, and betrixaban) for stroke prevention and treatment of deep venous thromboembolism is common. Additionally, warfarin is prescribed for valvular cardiac disease to ensure patency of mechanical and bioprosthetic valves. More than 33.5 million patients have atrial fibrillation worldwide,⁵ with most between the ages of 65 and 85 years.^{6,7}

Optimizing antithrombotic management is an essential first step in preventing postpolypectomy adverse events. Postpolypectomy bleeding (PPB; immediate or delayed) is rarely associated with surgery or death.⁸ Transfusions, hospitalization, repeat endoscopy for hemostasis, and angiography with embolization can be required to manage the adverse event. Surprisingly, there is a noticeable lack of literature regarding the natural history of PPB in patients with coronary artery disease, a population in whom acute GI bleeding has been shown to increase 4-fold annual all-cause and cardiovascular mortality.^{9,10} Medical

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literature regarding optimal polypectomy anticoagulant management in the growing atrial fibrillation population is also sparse.

What is the safest strategy? PPB can be challenging to locate and its occurrence difficult to anticipate. Are there recommended endoscopic and medication alternatives to minimize risk while ensuring timely and effective colonoscopy?

In this review, we highlight current best practice recommendations focusing on PPB (immediate and delayed) in the setting of drug discontinuation (ie, temporary interruption) and drug continuation. Guidelines for the temporary discontinuance of antithrombotic agents are reviewed as well as the risk of thromboembolic adverse events in the endoscopic setting. The choice of polypectomy technique (cold snare vs conventional thermal-based method) and prophylactic placement of hemostatic clips are reviewed to ascertain if these practices are beneficial in reducing PPB. This review does not replace existing clinical practice guidelines.¹¹ Instead, it supplements previous evidence-based recommendations¹¹ to extend knowledge by interpreting recently published literature that further shapes the discussion of the safest strategy.

QUANTIFYING PPB: DOES TECHNIQUE MATTER?

The assumed risk of PPB is quite low (1%) in patients who are *not* taking antithrombotic agents.¹¹ The size of the polyp is the most important feature distinguishing high or low risk of postprocedural bleeding.¹¹ Removing lesions ≥ 1 cm is associated with a 1% to 2% PPB rate related to inadequate cauterization of underlying small vessels (immediate bleeding)⁸ or thermal injuries causing ulceration and delayed bleeding.² Choice of electrocautery (pure-cut rather than blend-current), patient age (>65 years), polyp morphology, and antithrombotic agents also increase PPB.^{8,12}

Nonthermal polypectomy of small lesions (≤ 1 cm) is believed to be associated with a lesser risk ($<1\%$) given the absence of thermal injury related to cautery. However, the largest cohort studies of cold polypectomy (forceps biopsy sampling or cold snare) of lesions <1 cm suggest otherwise.¹³ Of 1015 cold polypectomies, 18 patients experienced immediate PPB (1.8%) successfully treated with hemostasis. There was no delayed bleeding at 30 days. The calculated per-patient bleeding rate was 2.2% (95% confidence interval [CI], 1.2%-3.2%) with a per-polyp bleeding rate of 1.8% (95% CI, 1.0%-2.6%).¹³ A 1.8% PPB rate was also observed in the Munich Polypectomy Study using a nonthermal polypectomy method.¹⁴ Both the Repici et al study¹³ and the Munich Polypectomy Study¹⁴ excluded patients on antiplatelets and anticoagulants or with known bleeding diathesis.

To date, only 1 randomized study has examined the risk of cold-snare polypectomy (CSP) of lesions <1 cm in patients on antithrombotic agents. Horiuchi et al¹⁵ performed a single-site study in which the authors randomized 70 continuously anticoagulated (warfarin) patients (159 polyps) to CSP ($n = 35$; 78 polyps) or conventional polypectomy ($n = 35$; 81 polyps; endo-cut mode). Delayed bleeding (within 14 days and requiring endoscopic intervention) was the primary outcome of interest. The endoscopic procedure for CSP was standardized to include cap-assist and dual-loop snare without tenting. The mean size of the polyps was 6.5

mm, and international normalized ratio was checked on the day of the procedure (mean international normalized ratio, 2.3). With immediate bleeding (defined as visible bleeding that persisted >30 seconds) a hemostatic clip is used, irrespective of the type of polypectomy.

Among persistently anticoagulated patients, immediate PPB occurred in 5.7% of patients randomized to CSP versus 23% for conventional polypectomy and delayed bleeding in 14% of conventional polypectomies and 0% of CSP. The overall rate of PPB was clinically different between CSP (11%) versus conventional polypectomy (46%). Immediate bleeding in the conventional group (23%) was higher than expected and may be related to the lack of precision in the definition of immediate bleeding or inadequate cauterization of underlying small vessels. This study¹⁵ demonstrated a much higher than anticipated risk of PPB associated with CSP of small lesions in patients who are continuously anticoagulated (11%). CSP may be safer than conventional polypectomy, but the risk is still much higher than the previously assumed 1% to 2% associated with conventional polypectomy of a lesion >1 cm in a patient not on antithrombotic agents.⁸

The safety of CSP of polyps >1 cm in patients on antithrombotic agents remains unclear. A systematic review of 9 case series that excluded patients on antithrombotic agents suggests an immediate PPB of .7% (95% CI, 0%-1.4%) and a delayed PPB rate of .5% (95% CI, .1%-1.2%) with CSP of polyps ranging from 1 to 2.3 cm.¹⁶ The attributable risk of bleeding associated with antithrombotic therapy remains unknown, limiting the ability to extrapolate the potential benefit of noncautery techniques when removing polyps >1 cm.

Cardiovascular patients prescribed antiplatelet or anticoagulant agents are a higher risk polypectomy population because of frequent coexistent chronic comorbidities (ie, hepatorenal),^{17,18} advancing age,¹⁹ and associated polypharmacy that increases the risk of altered metabolism and excretion of antithrombotic agents. These factors can result in clinically significant antithrombotic effects during polypectomy, even with the temporary interruption of prescribed antiplatelet or anticoagulant agents. Consequently, patients prescribed these drugs may not behave in the same fashion after polypectomy as those patients who are not on these agents. The latter is the population that informs the current estimates of CSP PPB risk.^{11,20}

PPB estimates of nonthermal polypectomy of lesions <1 cm vary tremendously in the literature from 1.8%¹³ to 7.0%²¹ with temporary interruption of the anticoagulant or antiplatelet agent to 11% with the continuation of the anticoagulant.¹⁵ Estimates of PPB range from 3.8% to 8.5% with the continuation of antiplatelet agents, with little difference between CSP versus conventional techniques.² The marked variation in estimates is not surprising given the absence of high-quality randomized controlled trials and the reliance on single-site case-series or small cohort studies. The definitions for immediate and delayed PPB are often ill-defined or inconsistently defined (within 14 days, within 30 days, etc). Furthermore, there is an absence of standardized endoscopic technique and the use of hemostatic clipping without defined criteria.

Regardless of the discrepancy in the definitions of immediate and delayed PPB, these estimates suggest that in a cardiac patient prescribed an antithrombotic agent, overall PPB is higher than 1% to 2%, and the use of nonthermal polypectomy techniques may not be the panacea for postpolypectomy adverse events. Further high-quality studies in this unique population are necessary to inform the choice of polypectomy method. These studies also suggest that immediate PPB rates are higher in the setting of antithrombotic drug continuation when compared with patients in whom the antithrombotic drug has been temporarily interrupted. All patients are at risk of delayed PPB with the resumption of the drug (3%-11%). Until we know how to minimize mucosal and vascular trauma at polypectomy sites, the reintroduction of an antithrombotic drug will always place the patient at risk of delayed PPB. Advising patients of the risk and educating them about PPB symptoms and how to seek emergency attention are imperative for patient safety.

TEMPORARY INTERRUPTION AND RESUMPTION OF ANTIPLATELET AGENTS

Cardioprotective ASA does not require discontinuation before endoscopic procedures, and it is reasonable and safe to perform all endoscopic procedures while on low-dose ASA.^{11,22} Avoid discontinuing dual antiplatelet therapy (ie, ASA plus a thienopyridine agent) during high-risk periods of thromboembolism such as within 30 days after bare-metal stent placement, within 1 year of drug-eluting stent placement, and 90 days after acute coronary syndrome.¹¹ The most prudent strategy is to defer elective polypectomy until after the high-risk period so the antiplatelet agent can be safely interrupted.

The length of temporary interruption depends on the drugs' half-life (Table 1). Short-term discontinuation of a thienopyridine agent is safe if the patient remains on ASA monotherapy (ie, ASA 81 mg/day) during the antiplatelet interruption. ASA irreversibly acetylates platelets, inactivating them for 7 to 10 days. Continuation of cardiac ASA before polypectomy protects cardiac patients from acute coronary syndrome, late stent thrombosis, and premature death.²³⁻²⁵ The time to a thrombotic event can be as short as 7 days if ASA and thienopyridines are discontinued simultaneously or sequentially in patients after implantation of a drug-eluting stent.²⁵ Furthermore, in the setting of acute upper or lower GI bleeding, discontinuation of cardiac ASA is associated with an increased risk of mortality and cardiac sequelae.^{26,27}

Surprisingly, some providers choose to discontinue low-dose ASA in cardiac patients. The most commonly cited reasons include concern about bleeding (60%) and the erroneous belief that there is "no downside to stopping aspirin" (35%).²⁸ The choice to discontinue cardiac ASA is an example of perceived risk versus actual risk. An individual's history of adverse events and subjective fear of medical liability influences risk perception. The fear of medical liability can motivate physician behavior.^{28,29} However, that which physicians fear is often poorly correlated to actual liability risk.²⁹ An inaccurate perceived risk may result in a cognitive error by emphasizing rare events while minimizing an event that may cause harm.²⁹

All antiplatelet agents should be resumed once immediate hemostasis (after polypectomy) is achieved, ideally within 24 hours,³⁰ to ensure a safe balance between platelets previously exposed to irreversible acetylation (ie, from ASA) and P2Y₁₂ receptor antagonism (ie, from thienopyridine agents), and new platelets entering the circulating platelet pool unexposed to antiplatelet drug activity. The risk of significant adverse cardiac events increases within 1 to 2 weeks after antiplatelet discontinuation. In this postendoscopic period, the thrombotic effect of circulating new platelets offsets the antiplatelet effect of the previously exposed platelets, predisposing the patient to a thrombotic adverse event.³¹

CONTINUED NON-ASA ANTIPLATELETS AND PPB RISK

A meta-analysis of small retrospective and case-control studies of continued clopidogrel during polypectomy (574 PPB events; 6169 control events) revealed a 5-fold increased risk of delayed PPB (relative risk ratio, 4.66; 95% CI, 2.37-9.17), up to 30 days postprocedure.³² There was no increase in immediate PPB (1.76; 95% CI, .90-3.46). However, the heterogeneity of pooled studies is noted ($I^2 = 30$).³²

Chan et al² examined the hypothesis that uninterrupted clopidogrel therapy increases delayed PPB in the CUP (Clopidogrel Uninterrupted Postpolypectomy Bleeding) trial. Patients prescribed clopidogrel alone or in combination with other antiplatelet agents, scheduled for screening or surveillance colonoscopy, or with symptoms requiring a colonoscopy were eligible to participate. Excluded patients included cardiac patients within 30 days of coronary stent implantation, within 6 months of drug-eluting stent placement, with a history of cardiovascular event within 3 months, who were prescribed concomitant anticoagulants, and with a history of bleeding diathesis, pregnancy, or terminal illness. All eligible patients discontinued clopidogrel 7 days before colonoscopy and were randomized in a 1:1 fashion to 7 days of treatment drug (ie, continuous clopidogrel) or placebo (ie, temporary interruption of clopidogrel for 7 days) until the morning of the colonoscopy. Clopidogrel was resumed once oral intake was allowed, and delayed PPB was measured on days 2, 7, and 30.

The CUP trial revealed a numerical trend toward increased immediate PPB with uninterrupted clopidogrel (8.5% vs placebo 5.5%; $P = .380$). There was no difference in delayed PPB between the 2 study arms (clopidogrel 3.8% [95% CI, 1.4-9.7] vs placebo 3.6% [95% CI, 1.4-9.7]; $P = .945$) or any meaningful difference in serious cardiac events (clopidogrel 1.5% [95% CI, .5-4.7] vs placebo 2.0% [95% CI, .8-5.4]; $P = .713$). Delayed PPB with the continuation of clopidogrel was similar to previous reports; however, PPB after interruption of clopidogrel (placebo) was higher than anticipated (3.6%) and attributed to cauterization-related thermal injuries at the site of the mucosal defect that bled after the reinitiation of clopidogrel. In the CUP trial, 60% of polyps were removed using electrocautery and 40% using CSP.

The studies above suggest continued clopidogrel before polypectomy is associated with an increased risk of immediate and delayed PPB. Appropriate temporary interruption of non-ASA antiplatelet agents is not associated with severe cardiac sequelae. The question of best

polypectomy technique (conventional vs CSP) remains unclear because the lack of standardized methods prevents meaningful interpretation of the published data in this regard.

INTERRUPTION, BRIDGING, AND RESUMPTION OF ANTICOAGULATION

The timing of discontinuation of a DOAC depends on the creatinine clearance of the patient and the specific agent (Table 2).¹¹ In general, the higher the impairment of kidney function (ie, the lower the creatinine clearance), the more significant the residual anticoagulant effect; thus, a more prolonged interruption is required.³³ The DOAC should be restarted once immediate hemostasis is achieved, anticipating maximal drug effect within 2 to 4 hours with normal renal function.

Because of the short half-life of these drugs, it is imprudent to prolong postprocedural DOAC interruption.¹¹ In most cases, rivaroxaban and edoxaban can be resumed at the full dose the next day after polypectomy. Apixaban can be restarted with the evening dose if immediate hemostasis is ensured and then with the regular dose the next day.³⁴ Dabigatran should be dosed at 75 mg in the evening postprocedure and resumed at the prescribed dose the day after the procedure.³⁵ With significant mucosal defects (ie, EMR or endoscopic submucosal dissection) it may be reasonable to wait 48 to 72 hours before resuming the DOAC. Properly dosed DOACs (pre- and postprocedure) should not need bridging.³⁶ A substudy of the RE-LY (Randomized Evaluation of Long Term Anticoagulant Therapy [RE-LY] With Dabigatran Etxilate) trial revealed an increased risk of bleeding with bridge therapy and no associated cardiac benefit.³⁷

A simplified version of DOAC temporary interruption, without a heparin bridge, is studied in the PAUSE (Perioperative Anticoagulation Use for Surgery Evaluation) cohort study.³⁸ This study involved 23 clinical centers in Canada, the United States, and Europe, enrolling 3007 atrial fibrillation patients on apixaban, dabigatran, or rivaroxaban.³⁸ Surgical procedures were classified based on the criteria used by the BRIDGE (Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation) trial investigators.³⁹ Under these criteria, all endoscopic procedures are “low-risk procedures,” including colonoscopy with polypectomy. By protocol, DOAC was held 1 day before the endoscopic procedure and restarted the day after endoscopy. This standardized approach is associated with a <2% rate of periprocedural major bleeding and <1% risk of arterial thromboembolism. Furthermore, >90% of patients had a minimal or no residual anticoagulant effect at the time of the procedure. Most importantly, there was no requirement for heparin bridge or preprocedure coagulation function testing.³⁸

Holding warfarin for 5 days before the procedure is associated with <1% to 3% risk of thromboembolism.^{40,41} If the patient’s only indication for chronic anticoagulation is nonvalvular atrial fibrillation (of low to moderate severity; mean congestive heart failure, hypertension, age [65 = 1 point, 75 = 2 points], diabetes, and stroke/transient ischemic attack [2 points] (ie, CHADS2 score) score of 2.5 or mean congestive heart failure, hypertension, age [65 = 1 point, 75 = 2 points], diabetes, and stroke/transient ischemic attack [2 points], vascular disease [peripheral arterial disease, previous myocardial infarction, aortic atheroma], and sex category [female gender] (ie, CHA2DS2-VASC) score

of 4.25), it is unnecessary to provide an anticoagulant bridge. The BRIDGE trial and the ORBIT-AF (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation) trial demonstrate increased bleeding (7.8% with bridging vs 1.5% no bridge) with no thromboembolic benefit.^{39,42} Patients at high risk of stroke (CHA2DS2-VASC score of 5 and CHADS2 score of 3) were under-represented in these trials, so future studies are expected to provide additional guidance. Heparin bridge therapy is an independent risk factor for PPB,⁴³ with an incidence of 20% in the bridged patient compared with 1.4% in the nonbridged patient.⁴⁰

Takeuchi et al⁴⁴ published an open-label trial simultaneously assessing 2 crucial factors related to PPB, anticoagulation approach and polypectomy technique. In this nonblinded, parallel-arm study of 182 patients comparing continuous anticoagulation with CSP (n = 90) with heparin bridge with hot-snare polypectomy (n = 92), the authors suggested the experimental arm (continuous anticoagulation with CSP) was not inferior to heparin bridge with hot-snare polypectomy with regard to delayed PPB requiring endoscopic hemostasis (risk difference, 7.3%; 95% CI, -1.0% to 15.75%). However, this study had substantial design issues that undermine the internal validity of results. Both the endoscopist and participant remained unblinded to the allocation group, and the unregulated recruitment procedure likely introduced selection bias. It is also questionable whether the control arm regimen (ie, heparin bridge given to DOAC and non-DOAC patients) is appropriate in the post-BRIDGE-trial, ORBIT-AF trial, or RE-LY trial era.^{37,39,42} Given these methodologic limitations the data are less relevant to the evolving practice paradigm.

Patients with a mechanical valve, rheumatic valvular disease, or history of venous thromboembolism or cerebrovascular accident/transient ischemic attack within the last 3 months will require a bridge with unfractionated heparin or low-molecular-weight heparin.^{37,45} Occasionally, delaying colonoscopy with polypectomy until after the window for bridge therapy is necessary is desirable.⁴⁵ If it is not feasible to postpone endoscopy, unfractionated heparin is administered when the international normalized ratio is less than 2 and held 4 to 6 hours before the colonoscopy. If using low-molecular-weight heparin, the last dose should be delivered 24 hours before the procedure. It remains unclear whether other prothrombotic patients (ie, cancer, thrombophilia, etc) require bridge therapy. In these situations, individualize treatment as the benefit may outweigh bleeding risk.⁴⁶

PROPHYLACTIC HEMOSTATIC CLIP USE

It is tempting to use a hemostatic clip after polypectomy in patients who require reinitiation of antithrombotic drugs within 24 hours. Data regarding the effectiveness of prophylactic clipping of large lesions (>1 cm) to reduce PPB have been mixed in the literature, highlighting the importance of technique and the possibility of postclipping injury.⁴⁷⁻⁴⁹ Prophylactic clipping may be favorable if the PPB rate is 3.4% (anticoagulant bleeding risk) or 2.5% (antiplatelet bleeding risk).⁵⁰ This cost-effectiveness model was sensitive to the probability of PPB and 5 independent factors, including clip effectiveness in reducing bleeding rate, cost of GI bleed hospitalization, cost of clip, number of clips administered, and theoretical risk of harm from clip placement. As the number of clips placed increases, clip placement becomes less economically favorable.⁵⁰

A recently published, multicenter, randomized controlled, equivalence study of prophylactic hemoclips versus none (n = 1098) to prevent delayed PPB after removal of polyps >1 cm demonstrated no benefit.⁵¹ Within 30 days of colonoscopy, 2.3% of patients in the hemoclip group and 2.9% of patients without hemoclip experienced delayed PPB. Study design issues undermined the usefulness of this study and are worth noting. Because of the termination of funding and underestimated PPB rate during power calculation, the study was underpowered. A limited number of enrolled patients were on antithrombotic drugs (5.7% on thienopyridine agents, 6.8% on warfarin, 1.7% on DOACs, 2.6% on heparin). Finally, the study protocol failed to standardize the polypectomy technique (95% hot snare with or without lift technique), number of hemoclips placed, bridging strategy, and strategy for temporary interruption of thienopyridine agents among recruiting sites. These shortcomings limit the usefulness of these data to inform an endoscopist's decision to use a hemoclip after polypectomy in the antithrombotic population.

Pohl et al⁵² randomized 918 patients to clip closure or no closure after EMR of large, pedunculated polyps of at least 2 cm. They measured postprocedural bleeding, defined as a clinically significant bleeding event requiring hospitalization; blood transfusion; colonoscopy; surgery; or other invasive intervention within 30 days of polypectomy. The trial design took the additional step of randomizing current setting (a blended or pure coagulation current) to minimize potential for electrocautery to confound results. In a subgroup analysis they measured delayed PPB considering the use of antithrombotic medications. However, randomization failed to balance antithrombotic drug use between exposure arms. The proportion of patients on an antithrombotic agent was higher in the control group (34.2%) versus the clip group (26.6%). The approach to antithrombotic management followed American Society for Gastrointestinal Endoscopy guidelines for temporary interruption and resumption.¹¹

Unlike the Feagins et al study,⁵¹ delayed bleeding after EMR of large proximal polyps was reduced after clip closure (3.3% PPB with clip vs 9.6% without).⁵² On average, 4 clips were used to close mucosal defects. The absolute risk difference of 6.3% (95% CI, 2.5%-10.1%) translates to a number needed to treat of 16 patients. Thus, only 16 patients undergoing EMR for polyps >2 cm would need to be treated with clip closure to prevent 1 additional significant delayed PPB. A less-favorable number needed to treat of 71 patients exists with clip closure of distal lesions.⁵²

The subgroup analysis of antithrombotic drug users suggested a lower rate of delayed PPB in the clip group versus the control group; however, there was a higher proportion of antithrombotic use in the control arm. Accordingly, the clip group was favored to perform better with outcome measurement because there were fewer patients on antithrombotic agents in the clip arm. The authors attempted to address this imbalance by adjusting for antithrombotic drug status during outcome assessment. However, unmeasured confounding variables introduced by the failure of randomization to balance antithrombotic drug use cannot be excluded.

PUTTING IT ALL TOGETHER

Estimates of immediate and delayed PPB associated with antithrombotic agents vary widely in the literature. With temporary interruption and prompt resumption of the drug, overall PPB is 1.8% to 7.0%. Without brief interruption of the drug, delayed PPB can be as high as 11%, with a trend toward higher immediate PPB (Table 3). When it comes to counseling patients, there is no tug-of-war between the heart and GI tract: The heart always wins. Appropriate temporary interruption of the antithrombotic agent is associated with a 30-day thromboembolic risk of less than 1%. Timely resumption of antithrombotic agents once achieving immediate hemostasis is critical to reducing thromboembolic risk. Patient education regarding the symptoms of PPB and after-hours emergency contact information is vital to include during consent procedures and postdischarge documentation.

The quality of published evidence limits our knowledge of PPB in this unique population. Existing studies underrepresent the antithrombotic community, fail to standardize polypectomy technique, do not clearly define a measurable outcome, or use hemostatic clips without defined criteria. In the future, well-designed randomized trials are essential to quantify PPB risk better and clarify incremental drug-related risk. The optimal duration of antithrombotic interruption and reduction of bleeding risk from temporary discontinuation of antithrombotic therapy merits a more-rigorous investigation. Finally, an examination of the potential benefit of noncautery, standardized polypectomy techniques and the strategic use of hemostatic clipping would help inform our future approach to polypectomy in this patient population.

Acknowledgments

DISCLOSURE: *The following author received research support for this study from the Agency for Healthcare Research and Quality (grant R01HS025402): N. S. Abraham. The content is solely the responsibility of the author and does not necessarily represent the official views of the Agency for Healthcare Research and Quality. The collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication were solely the responsibility of the author listed. The author disclosed no other financial relationships relevant to this publication.*

Abbreviations:

ASA	acetylsalicylic acid
BRIDGE	Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation [trial]
CSP	cold-snare polypectomy
CUP	Clopidogrel Uninterrupted Postpolypectomy Bleeding [trial]
DOAC	direct oral anticoagulant agent
ORBIT-AF	Outcomes Registry for Better Informed Treatment of Atrial Fibrillation [trial]
PPB	postpolypectomy bleeding

RE-LY

Randomized Evaluation of Long Term Anticoagulant Therapy (RE-LY) With Dabigatran Etxilate [trial].

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Table 1.

Temporary interruption of antiplatelet drugs

Drug	Timing of discontinuation (days)
Acetylsalicylic acid	N/A
Nonsteroidal anti-inflammatory drug	N/A
Ticlopidine	10-14
Clopidogrel	5-7
Prasugrel	5-7
Ticagrelor	3-5
Vorapaxar	5-13

N/A, Not applicable.

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Table 2.

Temporary interruption of direct oral anticoagulant agent

Rivaroxaban		Apixaban		Edoxaban		Dabigatran	
CrCl (mL/min)	Last dose* (days)	CrCl (mL/min)	Last dose (days)	CrCl (mL/min)	Last dose (days)	CrCl (mL/min)	Last dose (days)
>90	1					>80	1-3
60-90	2	>60	1-2	>60	1	50-80	1-3
30-59	3	30-59	3	30-60	>1	30-49	1.5-4
15-29	4	15-29	4	15-30	>1	29	2-6

CrCl, Creatinine clearance.

* Last dose refers to the timing of the previous dose of direct oral anticoagulant agent before the planned endoscopic procedure.

Table 3.

Clinical summary

Conclusion	Recommendations
Limited quality of published evidence limits our existing knowledge regarding risk.	Future studies focused on the antithrombotic population are required that include methodologic attention to standardized polypectomy techniques, clearly defined outcomes, and approach to temporary interruption and hemostatic clipping.
Estimates of immediate and delayed PPB vary widely in the literature. Variation in the definition of immediate and delayed PPB and lack of standardization in polypectomy technique (hot vs cold snare) limit accurate assessment of overall, immediate, and delayed PPB at this time.	With the temporary interruption of antithrombotic agents and prompt resumption of the drug, overall PPB is 1.8% to 7.0% (anticoagulant or antiplatelet agent). Nonthermal polypectomy of lesions <1 cm may be favorable when combined with temporary interruption; future studies are required to test this hypothesis. Without temporary interruption of antithrombotic agents, delayed PPB is slightly higher than with brief interruption (ie, up to 11%) with a trend toward higher immediate PPB (5.7% with continuous anticoagulant and 3.8%-8.5% with continuous antiplatelet use).
Cold- vs hot-snare polypectomy.	At this time, there is insufficient high-quality evidence in the antithrombotic population to unequivocally endorse cold-snare polypectomy as a technique to reduce PPB; however, the literature is promising in this regard. Future studies should focus on the polypectomy technique using an appropriate definition of PPB while considering a standardized approach to antithrombotic temporary interruption and resumption.
The risk of adverse cardiac events associated with temporary interruption of antithrombotic agents is low.	In endoscopic studies, the risk of adverse cardiac thromboembolic is <1%-3% at 30 days postprocedure, with appropriate temporary interruption of antiplatelet or anticoagulant drugs.
The timing of temporary interruption of antiplatelet agents is related to the drug's half-life.	See Table 1.
Do not discontinue cardiac ASA (81 mg/day) among patients with a prior heart attack or stroke (ie, ASA for secondary prophylaxis).	Discontinuation of cardiac ASA is associated with an increased risk of postprocedural major adverse cardiac events (including myocardial infarction and drug-eluting stent occlusion) and all-cause mortality.
Temporary interruption of warfarin before polypectomy.	Hold 5 days before the procedure with the resumption of the drug after achieving immediate hemostasis. Patients prescribed warfarin for nonvalvular atrial fibrillation (only) do not require pre- or postbridge therapy.
Bridge therapy.	Heparin bridge therapy is an independent risk factor for PPB with an attributable rate as high as 20%. Preprocedural and postprocedural bridge therapy is necessary with warfarin discontinuation in all patients with mechanical heart valves. You can consider using bridge therapy in patients with atrial fibrillation and a CHA ₂ DS ₂ -VASC score 5, venous thromboembolism, or stroke within 3 months of a planned colonoscopy if prescribed warfarin; however, risk-benefit of this approach is unknown. Future studies in these particular populations will inform future recommendations.
DOAC temporary interruption.	Current best practice recommendations recommend brief interruption based on the patient's creatinine clearance, risk of postendoscopic procedure bleeding, and specific DOAC agent (see Table 2). A simplified regimen that discontinues the DOAC 1 day before the endoscopy and resumes the DOAC the day after endoscopy has been shown to have favorable bleeding and cardiac outcomes. In the simplified regimen, no DOAC patients underwent a heparin bridge, and all endoscopic procedures (including polypectomy) are considered low risk. It is unknown whether similar favorable outcomes are associated with endoscopic surgeries causing significant mucosal defects (EMR or endoscopic submucosal dissection).
Prophylactic hemostatic clip use.	Data are mixed with regard to efficacy of prophylactic mechanical hemostasis after polypectomy in antithrombotic patients. Prophylactic clipping may be favorable if the PPB rate is 3.4% (anticoagulant bleeding risk) or 2.5% (antiplatelet bleeding risk). However, cost-effectiveness declines when more than 1 clip is placed. Clip closure of large, proximal EMR defects >2 cm (4 clips used per defect) may decrease delayed PPB (number needed to treat, 16). However, failure of randomization to balance antithrombotic drug use between control and clip groups may have introduced unmeasured confounding variables and favored the clip group outcome.
Documentation and procedural consent considerations.	Advise patients of the risk of antithrombotic-related PPB bleeding, document this risk, and educate them about PPB symptoms and how to seek emergency attention.

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PPB, Postpolypectomy bleeding; *ASA*, acetylsalicylic acid; *CHA₂DS₂-VASc*, Congestive heart failure, Hypertension, Age ($65 = 1$ point, $75 = 2$ points), Diabetes, and Stroke/transient ischemic attack (2 points), Vascular disease (peripheral arterial disease, previous myocardial infarction, aortic atheroma), and Sex Category (female gender); *DOAC*, direct oral anticoagulant agent.