

Management of anticoagulants and antiplatelet agents in elective endoscopy: Weighing the risks and benefits

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As the indications for endoscopic diagnosis and therapy continue to expand, an increasing number of patients receiving anticoagulants and antiplatelet agents will be encountered in gastroenterology practice. The management of these patients at the time of elective endoscopy can be challenging. Furthermore, this population has not been well studied, and thus, current guidelines are largely based on expert opinion. Ultimately, the risk of bleeding must be weighed against the risk of thromboembolic events when deciding whether to reverse anticoagulation or discontinue antiplatelet therapy before endoscopy. The present paper discusses three scenarios to highlight the authors' own clinical practice, and reviews the current published guidelines on this topic.

CASES TO CONSIDER

Case 1

A 58-year-old man is scheduled for a screening colonoscopy. He is asymptomatic, but his brother had colonic polyps and his father was diagnosed with colon cancer at 60 years of age. The patient has essential hypertension and is on lifelong warfarin therapy for chronic atrial fibrillation. He has no history of thromboembolic events.

Case 2

A 41-year-old woman has abdominal pain and elevated liver enzymes. A transabdominal ultrasound reveals cholelithiasis and a dilated biliary tree, but no obvious choledocholithiasis. She is on lifelong warfarin therapy for a mechanical mitral valve. You are planning to perform an endoscopic retrograde cholangiopancreatography plus sphincterotomy for her suspected common bile duct stone(s).

Case 3

A 52-year-old woman is referred for an upper endoscopy due to recurrent solid food dysphagia. She has a history of a peptic stricture and was dilated five years ago. She is diabetic and has

been on long-term acetylsalicylic acid (ASA) and clopidogrel since she suffered a transient ischemic attack while on ASA two years ago. You anticipate performing a dilation.



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PROCEDURE-RELATED BLEEDING RISKS

The potential to cause significant or uncontrolled bleeding varies, depending on the endoscopic procedure performed. Clinically significant bleeding has been defined as bleeding that requires hospitalization, transfusion, endoscopic intervention and/or surgery (1-3). In the absence of anticoagulants and antiplatelet agents, the American Society for Gastrointestinal Endoscopy (ASGE) has defined a low-risk procedure as one that carries a risk of clinically significant bleeding of less than 1% (1). This includes diagnostic upper and lower endoscopies, endoscopic retrograde cholangiopancreatography without sphincterotomy and endoscopic ultrasound without fine-needle aspiration (Table 1). High-risk procedures carry greater than 1% risk of clinically significant bleeding, such as colonic polypectomy (range 0.2% to 3% risk) (4,5), variceal band ligation (range 3% to 5% risk) (6,7) and endoscopic sphincterotomy (range 0.76% to 3.2% risk) (8,9). Also included in this group are interventions that have the potential to produce bleeding that is inaccessible or uncontrollable by endoscopic means, such as endoscopic ultrasound-guided fine-needle aspiration, pneumatic balloon dilation and percutaneous endoscopic gastrostomy tube placement (Table 1).

CONDITION-RELATED THROMBOEMBOLIC RISKS

Similarly, the indications for which anticoagulants are prescribed can be stratified into low- and high-risk thromboembolic conditions, based on the annual risk of stroke or risk of recurrent venous thromboembolism (Table 1) (10,11). For example, considering all patients with nonvalvular atrial fibrillation, the annual stroke rate without anticoagulation is 4% to 5% (11).

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TABLE 1
Procedure and condition risks during elective endoscopy

Procedure risks	
High-risk	Low-risk
Variceal band ligation	EGD ± biopsy
Biliary sphincterotomy	Colonoscopy ± biopsy
Gastric polypectomy	Diagnostic ERCP ± stent insertion
Colonic polypectomy	Diagnostic EUS
EUS with FNA	
PEG tube placement	
Esophageal dilation	
Condition risks	
High-risk	Low-risk
Atrial fibrillation with >1 clinical risk factor or prosthetic valve	Nonvalvular atrial fibrillation with ≤1 clinical risk factor
Within three months of DVT	More than three months after DVT
Mechanical valve in mitral position, or in mitral and aortic position; or old generation ball-cage valve	New-generation mechanical valve in aortic position
Previous cardiac embolism	

DVT Deep vein thrombosis; EGD Esophagogastroduodenoscopy; ERCP Endoscopic retrograde cholangiopancreatography; EUS Endoscopic ultrasound; FNA Fine-needle aspiration; PEG Percutaneous endoscopic gastrostomy

However, a patient with atrial fibrillation and no other high-risk conditions (ie, congestive heart failure, hypertension, diabetes, age older than 75 years or previous stroke) has an adjusted annual stroke risk of 1.9% (low-risk condition). In contrast, an individual with all five risk factors has an annual stroke risk of 18.5% (high-risk condition) (12). Twenty per cent of strokes are fatal, and 40% result in permanent disability (13). Overall, anticoagulation lowers the risk of arterial or venous thromboembolism by 66% to 80% (10,13). Therefore, the decision to reverse anticoagulation therapy is not always straightforward.

WEIGHING THE RISKS

Based on the above classifications of bleeding and thromboembolic risks, the ASGE has put forth guidelines for the management of warfarin and low molecular weight heparin (LMWH) around the time of endoscopy (1,14). The guidelines state that for low-risk procedures, no adjustment needs to be made to anticoagulation therapy. For high-risk procedures, delaying the procedure should always be considered in cases in which a finite period of anticoagulation has been prescribed. Otherwise, for a high-risk procedure in a patient with a low-risk condition, warfarin should be discontinued three to five days before the procedure. The decision regarding when to restart anticoagulation should be individualized. When both the procedure and the condition are high risk in nature, warfarin should again be discontinued three to five days before the procedure. However, simultaneous bridging anticoagulation therapy with LMWH should be initiated, then held for at least 8 h before the procedure. Whether to obtain a preprocedure international normalized ratio (INR) and the timing of restarting LMWH and/or warfarin should be individualized based on the nature and success of the intervention. LMWH should be continued until the INR is therapeutic for two to three days, generally three to five days after the procedure (15).

With respect to antiplatelet agents (eg, ASA, nonsteroidal anti-inflammatory drugs and clopidogrel), the available literature (16-18) suggests a theoretically increased risk of bleeding but no difference in clinically significant bleeding when performing any endoscopic procedure, irrespective of the baseline bleeding risk. Thus, the ASGE recommends that, in the absence of a pre-existing bleeding disorder, antiplatelet agents do not need to be discontinued when performing any endoscopic procedure (1,14). However, for high-risk interventions, one can consider discontinuing clopidogrel seven to 10 days before the procedure (14).

CASE ANALYSES

Case 1

In this commonly encountered clinical situation, the patient's condition carries a low risk for thromboembolic complications (nonvalvular atrial fibrillation with one risk factor – hypertension). His bleeding risk is either low or high, depending on whether a polypectomy is performed. One strategy would be to perform a diagnostic colonoscopy (low-risk procedure) while the patient is on full anticoagulation and bring the patient back following reversal of anticoagulation for a polypectomy if indicated. Alternatively, his warfarin could be discontinued for three to five days, allowing polypectomy to be performed safely at the time of the initial procedure. In this man's case, the likelihood of encountering polyps is high, given the patient's age and strong family history. We would discontinue his warfarin for five days before colonoscopy and perform a polypectomy during the same procedure if needed. A recent decision analysis supports this strategy as safe and cost effective (19). In addition, we routinely order a preprocedure INR when there is a high likelihood of performing a high-risk procedure. Even if the INR has not completely normalized, one can at least be aware of the factors potentially contributing to bleeding, should it occur. Obtaining an INR is inexpensive, and we see few disadvantages to this approach. Finally, we would instruct the patient to restart warfarin the evening of the procedure in the absence of known complications.

Case 2

The second case describes a woman with a high-risk condition undergoing a high-risk procedure. A thorough discussion with the patient, outlining both the risks of bleeding and of holding anticoagulation, is critical and should ideally be done in the office setting. She requires discontinuation of warfarin therapy with bridging anticoagulation, using LMWH around the time of her procedure, while her INR is subtherapeutic. LMWH has been shown to be as safe as unfractionated heparin for short-term thromboprophylaxis of prosthetic valves (20). If available, this is best managed through the expertise of an anticoagulation clinic. We differ from the ASGE guidelines as to when to hold the LMWH before the procedure. The ASGE guidelines state that LMWH should be discontinued at least 8 h before the procedure, citing that although the duration of action of LMWHs varies, the anticoagulant effect generally does not persist beyond 12 h (21). There are no published studies on the use of LMWH in the setting of endoscopy, but there is evidence of significant differences between the LMWHs, particularly the duration of action (22). Our approach takes into account this variable therapeutic effect: LMWHs are held either 12 h or 24 h before the procedure, depending on whether it is dosed every 12 h or 24 h, respectively.

We prefer to schedule these procedures earlier in the day to minimize the risk of patients presenting with early bleeding complications in the middle of the night. Given that endoscopic sphincterotomy carries one of the highest bleeding risks, our policy is to check the patient's INR the morning of the procedure. We either delay the case or administer fresh frozen plasma if the INR is greater than 1.5. In this case, LMWH and warfarin should be restarted expeditiously. However, we prefer to wait at least 24 h after the procedure to restart anticoagulation, to minimize bleeding while respecting the higher risk of thrombosis.

Case 3

The third case describes a woman with a low-risk condition who is undergoing a high-risk procedure. Following the ASGE recommendations, one could continue the ASA and consider holding the clopidogrel, given the high likelihood of performing a dilation. There is a theoretical risk of prolonged bleeding with antiplatelet agents and a lack of evidence for equivocal

bleeding risk in patients on dual antiplatelet therapy. Furthermore, a bleeding complication in this situation would be difficult to control endoscopically. Therefore, our practice is to discontinue both ASA and clopidogrel for seven days before an anticipated therapeutic procedure. We generally restart these medications the day following the procedure.

CONCLUSIONS

To safely manage patients on anticoagulants and/or antiplatelet agents undergoing elective endoscopy, one must consider both the underlying condition for which anticoagulation has been prescribed and the inherent bleeding risk of the scheduled procedure. Although guidelines are available, each clinical scenario demands a careful and individualized approach, including a thorough discussion of the risks and benefits with the patient. In this increasingly common and relatively understudied population, we believe that it is always best to 'err on the side of caution'.

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