Communication from the ASGE Standards of Practice Committee

GUIDELINE

Management of antithrombotic agents for endoscopic procedures

This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE) prepared this text. This guideline combines and updates 2 previously issued guidelines, "Guideline on the management of antithrombotic and antiplatelet therapy for endoscopic procedures"[1] and "ASGE guideline: the management of low-molecular-weight heparin and nonaspirin antiplatelet agents for endoscopic procedures."[2] To prepare this guideline, a search of the medical literature was performed using PubMed. Studies or reports that described fewer than 10 patients were excluded from analysis if multiple series with more than 10 patients addressing the same issue were available. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time the guidelines are drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations are based on reviewed studies and were graded on the strength of the supporting evidence (Table 1).[3] The strength of individual recommendations is based on both the aggregate evidence quality and an assessment of the anticipated benefits and harms. Weaker recommendations are indicated by phrases such as "we suggest," whereas stronger recommendations are typically stated as "we recommend."

This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from this guideline.

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Antithrombotic agents include anticoagulants (eg, warfarin, heparin, and low molecular weight heparin) and antiplatelet agents (eg, aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), thienopyridines (eg, clopidrogrel and ticlopidine), and glycoprotein IIb/IIIa receptor inhibitors). Antithrombotic therapy is used to reduce the risk of thromboembolic events in patients with certain cardiovascular conditions (eg, atrial fibrillation and acute coronary syndrome), deep venous thrombosis (DVT), hypercoagulable states, and endoprostheses. The most common site of significant bleeding in patients receiving oral anticoagulation therapy is the GI tract.[4] The antithrombotic drug classes with duration of action and routes for reversal are described in Table 2.

Before performing endoscopic procedures on patients taking antithrombotic medications, one should consider the urgency of the procedure and the risks of (1) bleeding related solely to antithrombotic therapy, (2) bleeding related to an endoscopic intervention performed in the setting of antithrombotic medication use, and (3) a thromboembolic event related to interruption of antithrombotic therapy. Alternative diagnostic studies for patient evaluation (eg, video capsule endoscopy or radiologic studies) should also be considered as well as the use of resources for hospitalization, parenteral antithrombotic therapy, and laboratory tests used to monitor antithrombotic therapy. Furthermore, potential thromboembolic events that may occur with withdrawal of medication can be devastating, whereas bleeding after high-risk procedures, although increased in frequency, is rarely associated with any significant morbidity or mortality. Discussion with the patient and his or her prescribing physician before the procedure is invaluable to help determine whether antithrombotic agents should be stopped or adjusted in any particular patient. This guideline is an update of two previous ASGE guidelines[1,2] and addresses the management of patients undergoing endoscopic procedures who are receiving antithrombotic therapy, providing recommendations and management algorithms.

DEFINITIONS

Procedure risks

Endoscopic procedures vary in their potential to produce significant or uncontrolled bleeding (Table 3). Low-risk procedures include all diagnostic procedures including those with mucosal biopsy[5,6] and ERCP without

TABLE 1. GRADE system for rating the quality of evidence for guidelines

Quality of evidence	Definition	Symbol
High quality	Further research is very unlikely to change our confidence in the estimate of effect	⊕⊕⊕⊕
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	⊕⊕⊕◯
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	⊕⊕◯◯
Very low quality	Any estimate of effect is very uncertain	⊕◯◯◯

Weaker recommendations are indicated by phrases such as "we suggest," whereas stronger recommendations are typically stated as "we recommend."
Adapted from Guyatt et al.[3]

sphincterotomy,[7,8] diagnostic balloon-assisted enteroscopy,[9] and EUS without FNA or Tru-Cut needle biopsy.[10] Higher-risk procedures include those associated with an increased risk of bleeding, such as endoscopic polypectomy,[11,12] therapeutic balloon-assisted enteroscopy,[9,13] endoscopic sphincterotomy,[14] and those procedures with the potential to produce bleeding that is inaccessible or uncontrollable by endoscopic means such as dilation of benign or malignant strictures,[15-17] percutaneous endoscopic gastrostomy,[18] and EUS-guided FNA.[19] Finally, patients requiring hemostasis should be considered at higher risk of rebleeding regardless of whether their initial procedure was low risk.

Condition risks

The probability of a thromboembolic complication related to the temporary interruption of antithrombotic therapy for an endoscopic procedure depends on the preexisting condition that resulted in the use of antithrombotic therapy. These conditions may be divided into low- and higher risk groups based on their associated risk of thromboembolic events (Table 4). Low-risk conditions include DVT, chronic or paroxysmal atrial fibrillation not associated with valvular disease, bioprosthetic valves, and mechanical valves in the aortic position. Higher-risk conditions include atrial fibrillation associated with valvular heart disease (whether surgically corrected or not), mechanical valves in the mitral position, and mechanical valves in patients who have had a previous thromboembolic event. Patients with coronary stents (especially those with a drug-eluting stent [DES]) are at higher risk of stent thrombosis, particularly when dual antiplatelet therapy (DAT) is discontinued before minimum duration recommendations. Current guidelines from the American Heart Association (AHA) recommend that DAT should ideally be continued for 12 months beyond the date of placement in patients with a DES.[20]

The risk of major embolism (causing death, residual neurologic deficit, or peripheral ischemia requiring surgery) in the absence of antithrombotic therapy in patients with mechanical valves is 4 per 100 patient-years.[21] With antiplatelet therapy, this risk is reduced to 2.2 per 100 patient-years and with warfarin to 1 per 100 patient-years.[22] In a pooled analysis of 5 randomized controlled trials, nonanticoagulated patients with sustained atrial fibrillation had an annual stroke rate of 4.5%.[23] In patients with atrial fibrillation and concomitant dilated cardiomyopathy, valvular heart disease, or recent thromboembolic events, the risk of thromboembolism is greater.[24] Anticoagulation therapy for DVT is typically performed for 1 to 6 months.[25] Short-term discontinuation of anticoagulation therapy does not seem to significantly increase the risk of pulmonary embolism.

ELECTIVE ENDOSCOPIC PROCEDURES IN PATIENTS RECEIVING ANTITHROMBOTIC THERAPY

Risk of bleeding from specific procedures while taking antithrombotic agents

Diagnostic endoscopy. Although aspirin has been shown to prolong bleeding times as long as 48 hours after ingestion,[26,27] there are no clinical trials demonstrating an increased incidence of bleeding in patients who have undergone upper or lower endoscopy with and without biopsy while taking aspirin or clopidogrel. Moreover, there is evidence that continuing therapeutic anticoagulation with warfarin during the periendoscopic period has a low risk of bleeding in such low-risk procedures. A retrospective study by Gerson et al[28] of 104 patients who underwent 171 endoscopic procedures while maintaining therapeutic warfarin dosing found that in low-risk procedures (upper endoscopy and colonoscopy including the use of mucosal biopsy), no clinically evident bleeding occurred.[28]

Colonoscopic polypectomy. Several studies examined the risk of antithrombotic therapy in postpolypectomy bleeding. Although 1 prospective study of 694 patients found a small (<1%) increased risk of trace postpolypectomy bleeding in patients taking aspirin or NSAIDs,[29] other larger retrospective studies did not find this association.[30,31] Because the absolute risk of postpolypectomy bleeding seems to be low, even in the setting of aspirin or NSAID use, very large studies would be required to demonstrate a significantly elevated risk (if the risk was actually increased). For example, to have an 80% power to detect a 50% increase in absolute risk of bleeding with aspirin or NSAIDs from 2% to 3%, more than 4000 patients would

TABLE 2. Antithrombotic drugs: duration of action and routes for reversal

Drug class	Specific agent(s)	Duration of action	Routes for reversal	
			Elective	Urgent
Antiplatelet agents	Aspirin	10 days	NA	Transfuse platelets
	NSAIDs	Varies	NA	Transfuse platelets
	Dipyridamole	2-3 days	Hold	Transfuse platelets
	Thienopyridines (clopidrogrel, ticlopidine)	3-7 days	Hold	Transfuse platelets ± desmopressin if overdose
	GP IIb/IIIa inhibitors (tirofiban, abciximab, eptifibatide)	Varies	NA	Transfuse platelets; in case of overdose, some agents can be removed with dialysis
Anticoagulants	Warfarin	3-5 days	Hold	FFP ± vitamin K, consider protamine sulfate*
	Unfractionated heparin	4-6 h	Hold	Hold or consider protamine sulfate*
	LMWH	12-24 h	Hold	Hold or consider protamine sulfate*

NA, Not applicable; *NSAID*, nonsteroidal anti-inflammatory drug; *GP*, glycoprotein; *FFP*, fresh frozen plasma; *LMWH*, low molecular weight heparin.
*Caution: Can cause severe hypotension and anaphylaxis.

need to be included in each group. Thus far, there has not been a prospective study of this magnitude conducted. Although the data are limited, postpolypectomy bleeding risk seems to be increased for patients taking warfarin[31,32] or resuming warfarin or heparin within 1 week after polypectomy.[31] Case series of prophylactic clip application after polypectomy of small polyps (<1 cm) in patients taking antithrombotic agents demonstrate low rates of bleeding (0%-3.3%).[32-35] However, no randomized controlled trials in patients actively using antithrombotic agents have been performed. Because of the lack of definitive clinical data and associated costs, routine application of prophylactic mechanical clips or detachable snares in these patients cannot be recommended at this time.

Sphincterotomy and PEG. The overall risk of postsphincterotomy bleeding is 0.3% to 2.0%.[36-38] Withholding aspirin or NSAIDs, even as long as 7 days before sphincterotomy, does not seem to reduce the risk of bleeding.[39] However, anticoagulation with oral warfarin or intravenous heparin within 3 days after has been shown to increase the risk of postsphincterotomy bleeding.[40] PEG placement has an overall bleeding complication rate of approximately 2.5%.[41,42] The risk of bleeding for PEG placement in the patient receiving antithrombotic therapy is unknown.

Risk of stopping antithrombotic therapy before elective endoscopy

When antithrombotic therapy is temporary, such as for DVT, elective procedures should be delayed, if possible, until anticoagulation is no longer indicated. This is particularly true in patients with a recently placed coronary stent (see detailed discussion below) who have significant risks of spontaneous stent occlusion with subsequent acute coronary syndrome and death.[43-45] If a decision is made to perform endoscopy in patients receiving antithrombotic therapy, the need to stop or reverse these agents should be individualized. The administration of vitamin K to reverse anticoagulation for elective procedures should be avoided because it delays therapeutic anticoagulation once anticoagulants are resumed.[46] The 2006 AHA/American College of Cardiology (ACC) guidelines recommend that in patients at low risk of thrombosis (Table 4) warfarin simply be held before the procedure and that bridge therapy with heparin is usually unnecessary. The absolute risk of an embolic event for patients in whom anticoagulation is interrupted for 4 to 7 days is approximately 1%.[47,48] In 1 large prospective multicenter observational study, almost 1300 cases (in 1024 patients) of warfarin interruption were examined.[47] The most common indications for anticoagulation were atrial fibrillation (43%), venous thrombosis (11%), and mechanical heart valves (10%). Only 73 patients were considered at higher risk of thromboembolism, with 93% of the patients deemed at low risk. Only 7 (0.7%) patients had a postprocedure thromboembolic event within 30 days of the procedure, although more than 80% of the total study population had anticoagulation held for less than 5 days. None of the 7 patients who experienced a thromboembolic event received bridging therapy (ie, short-acting anticoagulation medication use), despite the fact that 2 of these patients were technically high risk because of active malignancy and recent DVT, respectively. A high percentage (61%) of the 23 patients who had periprocedural bleeding events received bridging therapy with heparin.

TABLE 3. Procedure risk for bleeding

Higher-risk procedures	Low-risk procedures
Polypectomy	Diagnostic (EGD, colonoscopy, flexible sigmoidoscopy) including biopsy
Biliary or pancreatic sphincterotomy	ERCP without sphincterotomy
Pneumatic or bougie dilation	EUS without FNA
PEG placement	Enteroscopy and diagnostic balloon-assisted enteroscopy
Therapeutic balloon-assisted enteroscopy	Capsule endoscopy
EUS with FNA	Enteral stent deployment (without dilation)
Endoscopic hemostasis	
Tumor ablation by any technique	
Cystogastrostomy	
Treatment of varices	

TABLE 4. Condition risk for thromboembolic event

Higher-risk condition	Low-risk condition
Atrial fibrillation associated with valvular heart disease, prosthetic valves, active congestive heart failure, left ventricular ejection fraction <35%, a history of a thromboembolic event, hypertension, diabetes mellitus, or age >75 y	Uncomplicated or paroxysmal nonvalvular atrial fibrillation
Mechanical valve in the mitral position	Bioprosthetic valve
Mechanical valve in any position and previous thromboembolic event	Mechanical valve in the aortic position
Recently (<1 y) placed coronary stent	Deep vein thrombosis
Acute coronary syndrome	
Nonstented percutaneous coronary intervention after myocardial infarction	

The role of bridge therapy in endoscopy

To reduce the risk of thromboembolic events, patients on warfarin may be switched to a shorter-acting (ie, bridge) therapy in the periendoscopic period. Evidence of the use of unfractionated heparin (UFH) and low molecular weight heparin (LMWH) as bridging therapy for endoscopic procedures in patients taking warfarin is limited. One study of 98 patients undergoing endoscopy with bridging therapy with bemiparin (a second-generation LMWH not yet approved in the United States) found no thromboembolic events and only 2 major bleeding episodes that were unrelated to the endoscopy or the therapy.[49] Current guidelines from the AHA and the ACC regarding the management of anticoagulation in patients with atrial fibrillation and/or valvular heart disease undergoing elective invasive procedures are summarized in Table 5.[50-52] Data on the use of LMWH for prophylaxis of thromboembolism in patients with mechanical valves come primarily from observational studies,[53] although short-term use of LMWH seems to be safe. Despite this, controversy over its use in patients with mechanical valves continues.[52] Fatal thrombosis of mechanical valves in both men and women (pregnant and nonpregnant) receiving LMWH for thromboprophylaxis has been reported.

The optimal management of antithrombotic agents in pregnant patients with mechanical heart valves needing endoscopic procedures has not been studied.[54] It is recommended that elective procedures be delayed until after delivery whenever possible. When delay is not possible, bridge therapy with UFH or LMWH should be considered. Consultation with the patient's cardiologist and obstetrician should be obtained because there have been reports of bleeding complications with these agents,[55] mechanical prosthetic valvular thromboses in pregnant women treated with enoxaparin,[56] and fatal thromboembolic events with UFH.[55] Moreover, dosing of UFH and LMWH may change during pregnancy, thus requiring close monitoring of activated partial thromboplastin time levels and often serum antifactor Xa levels.[57]

Reinitiation of antithrombotic agents after elective endoscopy

There is no consensus as to the optimal timing for resumption of antithrombotic therapy after endoscopic interventions. The benefits of immediate reinitiation of antithrombotic therapy in preventing thromboembolic events should be weighed against the risk of hemorrhage, and the decision is likely to depend on procedure-specific circumstances (eg, risk of bleeding after sphincterotomy, polypectomy, or endoscopic mucosal resection). In 1 study involving 94 patients who had undergone 109 colonoscopies (including hot biopsy or snare polypectomy in 47% of patients), patients were instructed to restart warfarin therapy on the day after the examination.[58] There was only 1 (0.92%) case of procedure-related bleeding that occurred after 7 days of warfarin therapy and required hospitalization and transfusion. None of the patients undergoing diagnostic colonoscopy experienced bleeding. Conversely, a second study involving 173 patients found that resuming warfarin or heparin within 1 week after polypectomy was associated with increased risk of bleeding (odds ratio 5.2; 95% CI, 2.2-12.5).[31] Because of the ongoing risk of thromboembolic events, the AHA/ACC guidelines recommend that in patients with valvular heart disease and a low risk of thromboembolism, warfarin be restarted within 24 hours of the procedure and in patients with high risk of thromboembolism that UFH or LMWH be

TABLE 5. Periprocedural management of warfarin for patients with atrial fibrillation or valvular heart disease undergoing elective endoscopy

Condition	Associated diagnosis	Management
Atrial fibrillation	None	Hold warfarin 3-5 days before procedure. Restart warfarin within 24 h.*
	Mechanical valve(s) and/or history of cerebrovascular accident, transient ischemic attack, or systemic embolism	Hold warfarin and start UFH when INR $\leq$2.0. Stop UFH 4-6 h before procedure and restart after procedure. Resume warfarin on the evening of the procedure and continue both agents until INR is therapeutic.* Therapeutic doses of SQ UFH or LMWH may be considered in lieu of IV UFH.
Valvular heart disease	Mechanical bileaflet, aortic valve	Hold warfarin 48-72 h before procedure for a target INR $<$1.5. Restart warfarin within 24 h.*
	Mechanical mitral valve or mechanical aortic valve plus any of the following: atrial fibrillation, previous thromboembolic event, left ventricular dysfunction, hypercoagulable condition, mechanical tricuspid valve or $>$1 mechanical valve	Hold warfarin and start UFH when INR $\leq$2.0. Stop UFH 4-6 h before procedure and restart after procedure. Resume warfarin on the evening of the procedure and continue both agents until INR is therapeutic.* Therapeutic doses of SQ UFH or LMWH may be considered in lieu of IV UFH.

UFH, Unfractionated heparin; *INR*, international normalized ratio; *SQ*, subcutaneous; *LMWH*, low molecular weight heparin.
*Continuation or reinitiation of anticoagulation should be adjusted according to the stability of the patient and estimated risks surrounding the specific intervention/procedure performed. This table was adapted from the following guidelines: 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines[50] and American College of Cardiology/American Heart Association 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.[52]

restarted as soon as ''bleeding stability allows'' and continued until the international normalized ratio (INR) reaches an appropriate therapeutic level.[51] After a therapeutic procedure, UFH may be restarted 2 to 6 hours later. The optimal time to restart LMWH after endoscopy has not been determined.

ENDOSCOPIC PROCEDURES IN THE ACUTELY BLEEDING PATIENT RECEIVING ANTITHROMBOTIC THERAPY

Stopping or reversing antithrombotic agents in the acutely bleeding patient

The decision to stop, reduce, and/or reverse antithrombotic therapy, risking thromboembolic consequences, must be weighed against the risk of continued bleeding by maintaining antithrombotic agents, and this should be individualized. According to guidelines from the American College of Chest Physicians, it is recommended that warfarin be held and vitamin K be given (10 mg by slow intravenous administration) in all cases of serious or life-threatening bleeding and that fresh frozen plasma (FFP), prothrombin complex concentrate, or recombinant factor VIIa be given (for life-threatening bleeding) or considered (for serious bleeding).[59] Guidelines from the AHA/ACC recommend that high-dose (10 mg) vitamin K not be given routinely to patients with mechanical valves because this may create a hypercoagulable condition.[51] Furthermore, they state that FFP is preferable to high-dose vitamin K. Alternatively, low-dose vitamin K (eg, 1-2 mg) with or without FFP may be appropriate.

For patients taking antiplatelet agents with life-threatening or serious bleeding, options include stopping these agents and/or administration of platelets. Cessation of antithrombotic agents in patients with a DES who experience acute GI bleeding (GIB) is discussed below in a separate section.

Efficacy of endoscopic therapy in patients actively taking antithrombotic agents

Endoscopic evaluation and therapy in patients who have GIB while using antithrombotic agents is both warranted and safe.[60] The most common causes of upper GI blood loss in these patients are peptic ulcer disease and erosive disease of the esophagus, stomach, and duodenum,[61] whereas diverticular bleeding seems to be the most common cause of lower GIB.[62,63] In 1 retrospective series of 52 patients, correction of the INR to 1.5 to 2.5 allowed successful endoscopic diagnosis and therapy at rates comparable with those achieved in nonanticoagulated patients.[4] In a recently reported large series in which 95% of patients had INRs between 1.3 and 2.7, endoscopic therapy achieved initial success in 94.7% (233/246) of patients by using a variety of hemostatic techniques including injection therapy, heater probe, and hemoclips.[64] Although the rebleeding rate in this series was 23%, the preprocedure INR was not a predictor of rebleeding. In another retrospective study, rates of rebleeding in patients

with a supratherapeutic INR ($\geq$ 4.0) were not significantly different from those with INRs in the therapeutic range (2.0-3.9).[63] There are no prospective data available to determine what INR level is necessary for endoscopic therapy to be safe and effective. Mechanical hemostasis (eg, hemoclips) may provide therapeutic advantages in patients who must resume anticoagulated states after endoscopy, although this has not been rigorously studied.

Restarting antithrombotic agents after endoscopic hemostasis

Most patients will require resumption of antithrombotic therapy after control of acute bleeding. However, there are very limited data to guide the timing of reinstitution of antithrombotic therapy. For patients in whom aspirin-related peptic ulcer disease with GIB develops, it has been shown that resumption of aspirin with concurrent proton pump inhibitor therapy is superior to switching to clopidogrel alone for the prevention of recurrent GIB.[65,66] Furthermore, although withholding aspirin for 30 days versus resumption at 3 to 5 days after bleeding was associated with a numerically lower rate of rebleeding (11% vs 19%, $P = .25$), mortality at 2 months was more common (14.5% vs 1.7%, $P = .012$) in patients who did not resume taking aspirin after endoscopic hemostasis.[67] There are no data regarding the appropriate time to resume other antiplatelet agents. The risk of thromboembolic events was shown to be low in 2 small studies that withheld warfarin for 4 to 15 days (1/27 patients[68] and 0/28 patients,[69] respectively). When rapid resumption of anticoagulation therapy is desired, intravenous UFH should be used because of its relatively short half-life.

ENDOSCOPY IN THE PATIENT WITH A VASCULAR STENT OR ACS TAKING ANTITHROMBOTIC DRUGS

Elective endoscopy in the patient with a vascular stent

The use of DAT, such as aspirin and clopidogrel, in the care of patients with a vascular stent, acute coronary syndrome (ACS), and cerebrovascular disease has become increasingly commonplace in clinical practice today. According to current guidelines from the ACC and the AHA, DAT is recommended for a minimum of 1 month after placement of a bare metal stent and ideally for 12 months after placement of a DES or in patients who have undergone percutaneous coronary intervention who are not at high risk of bleeding.[20,44] Use of DAT may confer a 3-fold increase in the risk of upper GIB over single-agent antithrombotic therapy.[70] Despite this increased risk, the high rate of stent thrombosis associated with premature discontinuation of DAT, particularly in patients with a DES, is a compelling reason to avoid cessation of these agents whenever possible.[44] Given the current evidence, all elective and semielective (eg, removal of polyps) high-risk endoscopic procedures in patients receiving DAT should be delayed until the patient has received the minimum length of therapy as recommended by the ACC/AHA guidelines.[20] Once this minimum period has elapsed, the decision to proceed with such procedures should be made after discussion with the patient and the relevant consultants and after weighing the associated risks and benefits. Endoscopy is often performed after withdrawing 1 of the 2 antithrombotic agents, although there are no trials specifically comparing endoscopic bleeding risks associated with discontinuation of one particular agent rather than another (eg, stopping clopidogrel but continuing aspirin). There are limited data comparing clopidrogrel with aspirin as a single agent to reduce the risk of thromboembolic events. A single-blind, prospective study randomized patients to clopidigrel or aspirin and found that clopidrogrel was more effective than aspirin in reducing the risk of ischemic stroke, myocardial infarction (MI), and vascular death.[71] Despite this, there are far more data on the safety of polypectomy while taking aspirin than while taking clopidogrel at the current time.[29-31]

Urgent endoscopy in the patient with ACS or a recently placed vascular stent

Antithrombotic agents are commonly used in the management of ACS and in patients with a recently placed vascular stent, with many patients receiving multiple agents simultaneously including the potent platelet glycoprotein IIb/IIIa receptor antagonists. It is estimated that in 1% to 3% of patients with an ACS, GIB will be present or develop during their index hospitalization.[72-75] Furthermore, patients in whom GIB develops in the setting of ACS have an almost 4- to 7-fold increased risk of in-hospital mortality over patients with ACS and no GIB.[73,74] In this context, clinicians are faced with the dilemma of proceeding with endoscopic evaluation in a patient who is at an increased risk of procedural complications.[76,77] Although the rate of procedural complications may be as high as 12% in patients who undergo endoscopy on the same day as their acute cardiac event,[78] the overall rate of complications in this setting associated with upper endoscopy is approximately 1% to 2%,[76,78] whereas that for colonoscopy is 1%.[77] Despite the clinical significance of GIB during ACS, the data on endoscopic findings and the management of patients with GIB in the setting of ACS remain sparse. In 1 retrospective case-control study, 200 patients underwent endoscopy within 30 days (mean 9.1 $\pm$ 8.9 days, median 7 days) of an acute MI.[76] Serious complications (fatal ventricular tachycardia and near respiratory arrest) occurred in 2 patients. Common endoscopic diagnoses included gastritis (n = 32), duodenal ulcer (n = 29), gastric ulcer (n = 28), and Mallory-Weiss tear (n = 7). Patients may present with acute MI after acute GIB, and these patients are likely to benefit from endoscopic evaluation. A recent retrospective study showed that patients who presented with upper GIB leading to acute MI were more likely to

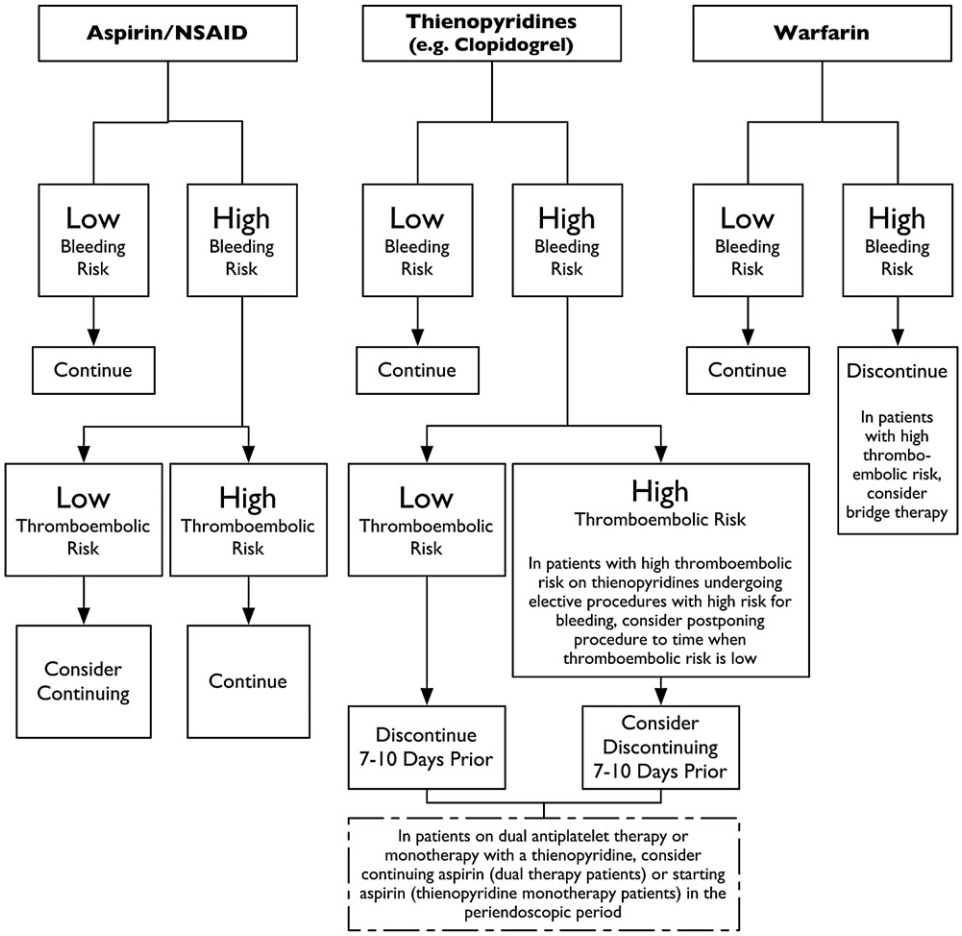

Figure 1. Management of antithrombotic agents in the elective endoscopic setting.

require endoscopic therapy than patients in whom GIB developed after being treated for acute MI (odds ratio 3.9; 95% CI, 1.8-8.5).[75] Other factors associated with the need for endoscopic therapy included hemodynamic instability and hematemesis on presentation. The benefit of endoscopy in the patient with significant GIB in the setting of acute MI was recently supported by a decision analysis that showed that upper endoscopy before cardiac catheterization was beneficial in patients who presented with overt GIB in the setting of ACS, reducing overall deaths from 600 to 97 per 10,000 patients, but was not beneficial in patients who presented with occult GIB and acute MI.[79]

In summary, our understanding of the safety of endoscopy in patients with ACS and/or a recently placed vascular stent taking antithrombotic medications, including DAT and glycoprotein IIb/IIIa inhibitors, is rapidly evolving and is likely to change as knowledge and experience are accumulated. For this reason, strong recommendations regarding the management of particular agents in the periendoscopic period cannot be made at this time and clinicians are encouraged to seek the input of relevant consultants (eg, cardiology and neurology) before discontinuing any antithrombotic agent.

I. Recommendations (summarized in Figures 1 and 2)

A Elective procedures

1. For patients on temporary anticoagulation therapy (eg, warfarin for DVT), we suggest that elective endoscopic procedures be deferred until antithrombotic therapy is completed. ⊕⊕◯◯
2. We recommend that aspirin and/or NSAIDs may be continued for all endoscopic procedures. ⊕⊕◯◯

   When high-risk procedures (Table 3) are planned, clinicians may elect to discontinue aspirin and/or NSAIDs for 5 to 7 days before the procedure, depending on the underlying indication for antiplatelet therapy.
3. We recommend that elective procedures be deferred in patients with a recently placed vascular stent or ACS until the patient has received antithrombotic therapy for the minimum recommended duration per current guidelines from relevant professional societies. Once this minimum period has elapsed, we suggest that clopidogrel or ticlopidine be withheld for approximately 7 to 10 days before endoscopy and that aspirin be continued. For those patients not taking aspirin, the addition of

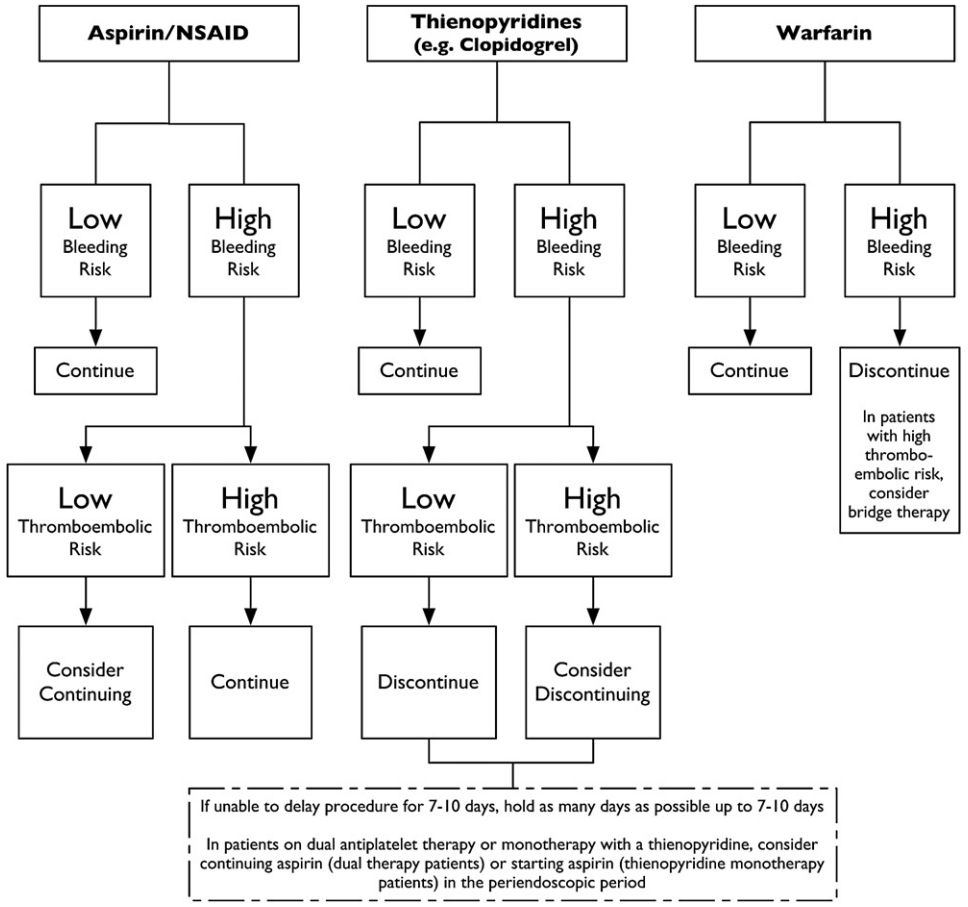

Figure 2. Management of antithrombotic agents in the urgent endoscopic setting.

aspirin during the periendoscopic period may reduce the risk of thromboembolic events. Clopidogrel or ticlopidine may be reinitiated as soon as deemed safe with consideration of the patient's condition and any therapy performed at the time of endoscopy. Consultation with the patient's cardiologist or other relevant provider may help determine the optimal management of these patients. ⊕⊕⊕◯

4. When clopidogrel and ticlopidine are used for other indications, we suggest that these medications may be continued for low-risk procedures (Table 3), but should be discontinued for approximately 7 to 10 days before higher-risk procedures. For those patients not taking aspirin, the addition of aspirin during the periendoscopic period may reduce the risk of thromboembolic events. Clopidogrel or ticlopidine may be reinitiated as soon as deemed safe with consideration of the patient's condition and any therapy performed at the time of endoscopy. ⊕⊕◯◯
5. We suggest discontinuing anticoagulation (ie, warfarin) in patients with a low risk of thromboembolic events (Table 4) in whom it is safe to do so in the periendoscopic period. We suggest continuing the anticoagulation in patients at higher risk of thromboembolic complications (Table 4), switching to LMWH or UFH (ie, bridging therapy) in the periendoscopic period when indicated for known or expected therapeutic indications. ⊕⊕◯◯
6. There is insufficient evidence to recommend for or against the prophylactic use of mechanical clips after polypectomy in patients on anticoagulation. ⊕⊕◯◯
7. There is no consensus as to the optimal timing of reinitiation of anticoagulant therapy after endoscopic interventions, and decisions are likely to depend on procedure-specific circumstances as well as the indications for anticoagulation. We suggest that the benefits of immediate anticoagulant therapy in preventing thromboembolic events be weighed against the risk of hemorrhage and determined in a case-by-case basis. In patients at high risk of thromboembolic events, we suggest that UFH or LMWH (ie, bridging therapy) be restarted as soon as safely possible and that warfarin be restarted on the day of the procedure unless there

is significant concern for bleeding. UFH may be restarted 2 to 6 hours after a therapeutic procedure. The optimal time to restart LMWH after endoscopy has not been determined. In patients with a low risk of thromboembolic events, we suggest that warfarin be restarted on the evening after the endoscopy unless procedural circumstances suggest a high risk of postprocedure bleeding. Bridging therapy in patients with a low thromboembolic risk is not necessary (Table 4). ⊕⊕◯◯

8. In pregnant patients with mechanical heart valves needing endoscopic procedures, it is recommended that elective procedures be delayed until after delivery whenever possible, and when delay is not possible, that bridge therapy with LMWH or UFH be considered. Consultation with the patient's cardiologist and/or obstetrician should be obtained. ⊕⊕◯◯

B Urgent and emergent procedures

1. We suggest that patients with acute GIB taking antiplatelet agents should have these medications withheld until hemostasis is achieved. ⊕⊕

   Administration of platelets may be appropriate for patients with life-threatening or serious bleeding. In situations of significant bleeding occurring in patients with a recently (<1 year) placed vascular stent and/or ACS, we suggest that cardiology consultation be obtained before stopping antiplatelet agents. ⊕⊕◯◯
2. We recommend that patients with acute bleeding receiving anticoagulation therapy have these agents withheld until hemostasis is achieved. ⊕⊕◯◯

   The decision to use FFP, prothrombin complex concentrate, and/or vitamin K should be individualized. We suggest that protamine be reserved for patients with life-threatening bleeding on heparin because of the potential risks of anaphylaxis and severe hypotension. ⊕⊕◯◯

   In situations of significant bleeding occurring in patients with a recently (<1 year) placed vascular stent and/or ACS, we recommend that consultation with the prescribing service be obtained before stopping anticoagulants. ⊕⊕◯◯
3. We recommend that patients with acute GIB taking warfarin with a supratherapeutic INR undergo correction of anticoagulation, although the target level INR required for endoscopic therapy to be effective has not been determined. ⊕⊕⊕◯
4. The absolute risk of rebleeding after endoscopic hemostasis in patients who must resume anticoagulation is unknown, and the timing for resumption of anticoagulation should be individualized. We suggest that in patients with high-risk stigmata for rebleeding (eg, a visible vessel) intravenously administered UFH be used initially because of its relatively short half-life. ⊕⊕◯◯

Abbreviations: ACC, American College of Cardiology; ACS, acute coronary syndrome; AHA, American Heart Association; DAT, dual antiplatelet therapy; DES, drug-eluting stent; DVT, deep venous thrombosis; FFP, fresh frozen plasma; GIB, GI bleeding; INR, international normalized ratio; LMWH, low molecular weight heparin; MI, myocardial infarction; NSAID, nonsteroidal anti-inflammatory drug; UFH, unfractionated heparin.

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