American Society For Gastrointestinal Endoscopy

Guideline on the management of anticoagulation and antiplatelet therapy for endoscopic procedures

This is one of a series of statements discussing the practice of gastrointestinal endoscopy in common clinical situations. It is intended to aid endoscopists in determining the appropriate use of endoscopic procedures in conjunction with anticoagulation and/or antiplatelet therapy. Guidelines for the appropriate practice of endoscopy are based on critical review of the available data and expert consensus. Controlled clinical studies would be beneficial to clarify some aspects of this statement and revision might be necessary as new data appear. Clinical consideration may justify a course of action at variance from these specific recommendations.

INTRODUCTION

Anticoagulation therapy with warfarin is used to reduce the risk of thromboembolic events in patients with certain cardiovascular conditions, deep vein thrombosis (DVT), and hypercoagulable states. Anticoagulation therapy complicates the management of gastrointestinal bleeding. Interruption of anticoagulation therapy may be desirable for some patients undergoing endoscopic procedures. When preparing for an endoscopic procedure on an anticoagulated patient considerations include (1) the risk of complications of the underlying gastrointestinal disorder related directly to anticoagulation therapy; (2) bleeding related to an endoscopic intervention carried out in the setting of anticoagulation; and (3) a thromboembolic event related to interruption of anticoagulation therapy. Additional considerations include the utilization of resources for hospitalization, parenteral anticoagulation therapy, and laboratory tests used to monitor and document adjustment of anticoagulation therapy.

This guideline addresses the management of patients undergoing endoscopic procedures who are on either anticoagulation therapy or aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDS). First, the endoscopic management of acute gastrointestinal bleeding in therapeutically anticoagulated patients is discussed. Second, the risk of bleeding related to endoscopic interventions is considered. Third, the risk of thromboembolic events associated with interrupting anticoagulation therapy is discussed. Management schemes for patients on long-term anticoagulation therapy are proposed. Last, the risk of bleeding related to the use of aspirin or other NSAIDS in the periendoscopic period is reviewed and recommendations for management are provided.

ACUTE GASTROINTESTINAL HEMORRHAGE IN THE ANTICOAGULATED PATIENT

The most common site of significant bleeding in patients receiving oral anticoagulation therapy is the gastrointestinal tract.[1] A history of prior gastrointestinal bleeding, but not a history of peptic ulcer disease alone, is associated with an increased risk of major gastrointestinal hemorrhage during warfarin therapy (30% at 3 years versus 5% in those with no prior bleeding history).[2] The risk of gastrointestinal bleeding is also increased when the international normalized ratio (INR) is above the therapeutic range (see: "Condition Risks") and by concomitant aspirin use. Gastrointestinal hemorrhage is likely to originate from an endoscopically identifiable bleeding site, most commonly a duodenal or gastric ulcer.[3]

RECOMMENDATIONS

The decision to reverse anticoagulation, risking thromboembolic consequences, must be weighed against the risk of continued bleeding by maintaining the anticoagulated state. The degree of reversal of anticoagulation should be individualized. A supratherapeutic INR may be treated with fresh frozen plasma. In one series, 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.[3] In contrast to the use of fresh frozen plasma, the administration of vitamin K has a delayed onset of action, and prolongs the time required to re-establish therapeutic anticoagulation.[4]

After appropriate endoscopic management, it is generally safe to reinstitute warfarin therapy within a few days. In a series of 27 patients who developed gastrointestinal bleeding while on warfarin, there was one episode of thromboembolism after withdrawal of anticoagulation for a median of 4 days and no subsequent bleeding after reinstitution of antico-

agulation.[5] When rapid resumption of anticoagulation is desired, intravenous heparin should be used.

ELECTIVE ENDOSCOPIC PROCEDURES IN THE ANTICOAGULATED PATIENT

Procedure risks

Endoscopic procedures vary in their potential to produce significant or uncontrolled bleeding. Low-risk procedures include diagnostic esophagogastroduodenoscopy (EGD), flexible sigmoidoscopy and colonoscopy with or without biopsy, diagnostic endoscopic retrograde cholangiopancreatography (ERCP), and biliary stent insertion without endoscopic sphincterotomy, endosonography (EUS), and push enteroscopy. High-risk procedures include those associated with an increased risk of bleeding such as colonoscopic polypectomy (1%-2.5%),[6] gastric polypectomy (4%),[7] laser ablation and coagulation (less than 6%),[8,9] endoscopic sphincterotomy (2.5%-5%),[10] and those procedures with the potential to produce bleeding that is inaccessible or uncontrollable by endoscopic means such as pneumatic or bougie dilation of benign or malignant strictures, percutaneous endoscopic gastrostomy, and EUS-guided fine needle aspiration.

Condition risks

The probability of a thromboembolic complication depends on the pre-existing condition prompting anticoagulation therapy. 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 valve heart prostheses is 4 per 100 patient-years.[11] With antiplatelet therapy this risk is reduced to 2.2 per 100 patient-years, and with warfarin to 1 per 100 patient-years.[11,12] The risk varies with the type and location of the valve. Mechanical valves in the mitral positron or mitral and aortic positions, carry the greatest risk.[11] Caged-ball or disk valves carry a greater risk than bileaflet or tilting dish valves.[13] Concomitant atrial fibrillation and prior embolic events further increase the risk. The target INR for patients with mechanical prosthetic heart valves is 3.0 to 4 0.[13]

In nonanticoagulated patients with sustained atrial fibrillation unassociated with valvular disease, the risk of thromboembolic events is 5% to 7% annually.[14] In patients with atrial fibrillation and concomitant dilated cardiomyopathy, valvular heart disease, or recent thromboembolic events, the risk is greater. In such patients the target INR is 3.0. No therapeutic benefit is apparent with anticoagulation below an INR of 1.5.[15]

Anticoagulation therapy for DVT is typically carried out for 1 to 6 months.[16] Early cessation of anticoagulation therapy for short time periods does not appear to increase significantly the risk of pulmonary embolus. Anticoagulation profiles for hypercoagulable states and some vascular grafts have not been well standardized. Conditions prompting anticoagulation therapy may be divided into low- and high-risk groups based on their associated risk of thromboembolic events. Low-risk conditions may include DVT, chronic or paroxysmal atrial fibrillation not associated with valvular disease, bioprosthetic valves, and mechanical valves in the aortic position. High-risk conditions may include atrial fibrillation associated with valvular heart disease, including the presence of a mechanical valve, mechanical valves in the mitral position, and mechanical valves in patients who have suffered a prior thromboembolic event. The absolute risk of an embolic event (major, minor, valve thrombosis) for patients with a low risk condition in whom anticoagulation is interrupted for 4 to 7 days may be estimated at 1 to 2 per 1000 patients.

General considerations

When anticoagulation therapy is temporary, such as for DVT, elective procedures should be delayed, if possible, until anticoagulation is no longer indicated. The administration of vitamin K to reverse anticoagulation for elective procedures should be avoided because it delays therapeutic anticoagulation once anticoagulants are resumed.

Recommendations

1. Low-risk procedures: No adjustments in anticoagulation need be made irrespective of the underlying condition. However, elective procedures should be avoided when the level of anticoagulation is above the therapeutic range.
2. High-risk procedures in patients with low-risk conditions: Warfarin therapy should be discontinued 3 to 5 days before the scheduled procedure. The decision to obtain a preprocedure prothrombin time should be individualized.
3. High risk procedures in patients with high risk conditions: Warfarin therapy should be discontinued 3 to 5 days before the procedure. The decision to administer intravenous heparin once the INR falls below the therapeutic level should be individualized. Preliminary experience suggests there may be a role for monitored reduction in the INR without the use of heparin. Heparin, if used, should be discontinued 4 to 6 hours before the scheduled procedure and may be resumed 2 to 6 hours after the procedure. Warfarin therapy may generally be resumed the night of the procedure.

Table 1. Acute gastrointestinal hemorrhage in the anticoagulated patient.

The decision to reverse anticoagulation and the extent of anticoagulation reversal should be individualized, weighing the risk of thromboembolism against the risk of continued bleeding.

A supratherapeutic INR may be corrected with infusion of fresh frozen plasma. Correction of the INR to 1.5 - 2.5 permits effective endoscopic diagnosis and therapy.

Reinstitution of anticoagulation should be individualized.

Recommendations for the management of anticoagulation, aspirin and NSAID use in patients undergoing endoscopic procedures based on the relative risks of the procedure and underlying condition.

	Condition risk for thromboembolism	
Procedure risk	High	Low
High	Discontinue warfarin 3-5 days before procedure. Consider herapin while INR is below therapeutic level.	Discontinue warfarin 3-5 days before procedure. Reinstitute warfarin after procedure.
Low	No change in anticoagulation. Elective procedures should be delayed while INR is in supratherapeutic range.	

Procedure risk	
High-risk procedures	Low-risk procedures
• Polypectomy • Biliary sphincterotomy • Pneumatic or bougie dilation • PEG placement • Endosonographic guided fine needle aspiration • Laser ablation and coagulation • Treatment of varices	• Diagnostic EGD ± biopsy Flex sig ± biopsy Colonoscopy ± biopsy • ERCP without sphincterotomy • Biliary/pancreatic stent without endoscopic sphincterotomy • Endosonography without fine needle aspiration • Enteroscopy

Condition risk	
High-risk conditions	Low-risk conditions
• Atrial fibrillation associated with valvular heart disease • Mechanical valve in the mitral position • Mechanical valve and prior thromboembolic event	• Deep vein thrombosis • Uncomplicated or paroxysmal nonvalvular arterial fibrillation • Bioprosthetic valve • Mechanical valve in the aortic position

Aspirin and other NSAID use

In the absence of a pre-existing bleeding disorder, endoscopic procedures may be performed in patients taking aspirin or other NSAIDs.

Heparin infusion and Warfarin should overlap for a period of 4 to 5 days or until the INR has achieved the target therapeutic range for 2 to 3 days.[17] However, the risk of major hemorrhage after sphincterotomy is between 10% and 15% if anticoagulation is reinstituted within 3 days of the sphincterotomy.[18] Therefore, the benefits of immediate anticoagulation should be carefully weighed against the risks and would be advisable only in a situation where the risk of thromboembolic events significantly exceeds the risk of hemorrhage from sphincterotomy.

There has been an evolving literature supporting the use of low molecular weight heparin (LMWH) "bridging therapy" for patients on chronic anticoagulation who need various non-GI procedures.[18-20] The concept of bridging therapy has been based on the assumption that LMWH can provide equal efficacy as the traditional use of unfractionated heparin in the prevention of thromboembolic events during a perioperative time period and by cost considerations associated with its use in ambulatory care setting and a reduction in pre- and postprocedure hospital LOS and resource consumption. Although use in colonoscopy has been modeled based on economic considerations,[21] there have been no prospective studies evaluating efficacy or safety. Small trials have been conducted for nonendoscopic procedures suggesting an economic benefit without heightened risks for thromboembolic events.[18-20] However, these studies were not powered to evaluate equivalency for the prevention of thromboembolic events compared with traditional approaches. Despite the

absence of objective evidence of efficacy or safety, the ACCP (American College of Chest Physicians) has offered low molecular weight heparin bridge therapy as an alternative therapy during the perioperative period.[22,23]

Two new classes of anti-platelet agents include antagonists of the platelet cell-surface adenosine diphosphate receptor (P2T receptor), which result in inhibition of platelet aggregation, and therapies directed against the glycoprotein IIb/IIIa receptor, which normally promotes adherence of platelets to fibrinogen and thrombus formation.

P2T receptor antagonists include ticlopidine and the newer agent clopidogrel, which is associated with fewer side-effects than ticlopidine (neutropenia and thrombotic thrombocytopenia purpura).[24] These agents are generally used in combination with aspirin to reduce the incidence of serious coronary events after stent placement, and are associated with an increased risk of bleeding complications, particularly the combination of Ticlopidine and aspirin.[25,26]

Antiplatelet therapies directed against the IIb/IIIa receptor include eptifibatide, abciximab, and tirofiban. These drugs are designed to reduce the risk of acute ischemic complications in high-risk patients after coronary angioplasty. In phase III trials, treated patients had an approximately 2-fold increased risk of major bleeding, but no increase in cerebral hemorrhage or lethal bleeding.[27]

Data regarding gastrointestinal bleeding in patients treated with these newer antiplatelet agents are inadequate to make firm recommendations. Any decision regarding discontinuation of therapy before endoscopy has to be weighed against the patient's risk for an adverse coronary event related to cessation of the medication (reocclusion of coronary stents, etc.). For elective high-risk procedures, temporary discontinuation of these medications, particularly if the patient is on concomitant aspirin, is desirable.

Aspirin and other NSAIDs in patients undergoing elective endoscopic procedures

Aspirin and most NSAIDs inhibit platelet cyclooxygenase resulting in suppression of thromboxane A2-dependent platelet aggregation. Limited published data, however, suggest that aspirin and other NSAIDs in standard doses do not increase the risk of significant bleeding after EGD with biopsy, colonoscopy with biopsy, polypectomy or biliary sphincterotomy.[10,28,29]

Recommendations

In the absence of a pre-existing bleeding disorder, endoscopic procedures may be performed on patients taking aspirin and other NSAIDS in standard doses.

The data on other drugs affecting platelet function such as ticlodipine and dipyridimol are inadequate to make recommendations.

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Prepared by:
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