A Hittelet, J Devière. Management of anticoagulants before and after endoscopy. Can J Gastroenterol 2003;17(5):329-332.

The risk of procedure-related bleeding while taking anticoagulants needs to be weighed against the risk of thromboembolism from discontinuing these drugs. It is not necessary to adjust anticoagulation for low-risk procedures, such as upper endoscopy with biopsy, colonoscopy with biopsy or endoscopic retrograde cholangiopancreatography with stent insertion (but without sphincterotomy). Procedures that incur a high risk of bleeding include polypectomy, endoscopic sphincterotomy, laser therapy, mucosal ablation and treatment of varices. For these procedures, warfarin should be discontinued four to five days beforehand. Depending on the risk of thromboembolism, that is based on the nature of the underlying condition, the patient may require vitamin K and/or fresh frozen plasma (to ensure that coagulation parameters are within the normal range) or heparin infusions (to ensure that some degree of anticoagulation is maintained). Low molecular weight heparin is an alternative to unfractionated heparin for select cases with a high risk of thromboembolism. Warfarin therapy may generally be resumed on the night of the procedure and may be supplemented by heparin in patients with a high risk of thromboembolism. It is not necessary to discontinue acetylsalicylic acid or nonsteroidal anti-inflammatory drugs, when used in standard doses, for endoscopic procedures. There are insufficient data to make recommendations regarding newer antiplatelet drugs, such as ticlopidine or clopidogrel, but it is prudent to discontinue these medications seven to 10 days before a high-risk procedure.

**Key Words:** Anticoagulant; Bleeding; Endoscopy; NSAID; Thromboembolism

**PROCEDURE RISKS**

Endoscopic techniques can be classified into those with high and low risks for bleeding (Table 1). Low-risk procedures include diagnostic esophagogastroduodenoscopy (EGD), colonoscopy (even with biopsy), endoscopic retrograde cholangiopancreatography (with stent insertion but without sphincterotomy), endosonography (EUS), and push enteroscopy. For example, the risk of bleeding during EGD has been estimated at 0.03% (2).

High-risk procedures include gastric polypectomy (which has a 4% risk of bleeding), colonoscopic polypectomy (0.2% to 3%), mucosectomy from the esophagus, stomach or colon, endoscopic sphincterotomy (2.5% to 5%), amputectomy, tak-
Arterial thromboembolism

The most frequent causes of arterial thromboembolism are atrial fibrillation (AF) and valvular heart disease (native or prosthetic). Patients with AF without valvular heart disease have an average incidence of systemic embolism of 4.5% per year in the absence of antithrombotic therapy (8). The risk is approximately 1% per year for patients without any other risk factor, 12% per year for patients with recent cerebral embolism, and as great as 17% per year in patients older than 75 years of age who have more than one of the following: hypertension, congestive heart failure, past history of thromboembolism, history of cerebrovascular accident or diabetes mellitus (8,9). Other data suggest that the risk of recurrent embolism from any cardiac source is approximately 0.5% per day during the first month after a stroke (10). Anticoagulation reduces the likelihood of embolism by 66% in patients with AF without valvular heart disease (8,9). Approximately 20% of arterial thromboemboli are fatal and 40% result in permanent disability (8-12).

The average rate of major thromboembolism in patients with mechanical heart valves is 8% per year without treatment, and is reduced by 75% by anticoagulant therapy (13,14). The complication rate is less in patients with the newer generation of aortic valve prostheses. In patients with these prostheses, even if the international normalized ratio (INR) is subtherapeutic for four to seven days, the risk of thrombosis is only one to two per 1000 patients (15). Therefore, heparin is not necessary in such cases unless the INR is expected to be less than 2.0 for at least five days.

Mechanical heart valves that are associated with a high risk of thrombosis include those that are in the mitral position or in both the mitral and aortic positions, and caged-ball or disk valves of the old generation (14,16). Patients with concomitant AF, prior embolic events or severe left ventricular dysfunction are also at high risk for thrombosis. In these situations, the INR should be monitored daily, and intravenous heparin should be initiated when the INR falls below 2.0 (16,17).

Venous thromboembolism

The risk of recurrent proximal venous thromboembolism (VTE) after an acute episode is greatest during the first month, and approaches 50% without anticoagulant therapy (18). The administration of warfarin during this month reduces the risk to roughly 10%, and three months of therapy reduces the risk to 5% (19-21). A vena cava filter should be considered if a high risk endoscopic procedure is required during the first two weeks after VTE. In patients with a hereditary hypercoagulable state or active cancer, discontinuation of warfarin is reported to be associated with a risk of thromboembolism of 15% per year (22).

The consequences of VTE are significant. The risk of pulmonary embolism is 6.4% within the first two weeks after surgery in patients with a history of VTE (23). It has been estimated that 6% of these episodes are fatal and 2% result in permanent disability (19,20,24).

Overall, anticoagulation reduces the risk of recurrent VTE by about 80% (18,20,24). Prophylactic measures that are less likely to cause bleeding than intravenous heparin should be promoted. These include low molecular weight heparin (LMWH), graduated compression stockings, and intermittent pneumatic compression.

Some factors associated with endoscopic procedures may be important but have not been specifically evaluated. Colonoscopy preparation, particularly when administered to

---

**TABLE 1**

| Procedure                                      | Low (less than 1%) | High (greater than 1%) |
|------------------------------------------------|--------------------|------------------------|
| Polypectomy, gastric                                  | EGD                | Colonoscopy (± biopsy)  |
| Polypectomy, colonic                                    | Sigmoidoscopy (± biopsy) | Colonoscopy (± biopsy) |
| Mucosectomy, (2% to 5%)                                 | ERCP without dilation or sphincterotomy | sphincterotomy |
| Endoscopic sphincterotomy, (2% to 3%)                 | Diagnostic EUS      | Enteroscopy            |
| Treatment of varices                                    | EUS-guided therapy* | Fine needle aspiration (by EUS)* |
| PEG*                                                   | Polyectomy with use of a detachable snare† | Pneumatic dilation* |
| EUS-guided therapy*                                    | Esophageal stentling | PEG Percutaneous endoscopic gastrostomy; † With or without polypectomy when the polyp is pedunculated. | EGD: Esophagogastroduodenoscopy; ERCP: Endoscopic retrograde cholangiopancreatography; EUS: Endoscopic ultrasound; PEG: Percutaneous endoscopic gastrostomy. |
elderly subjects, can cause intravascular volume depletion (25,26), which may increase the risk of VTE. One should consider intravenous hydration before and during colonoscopy in such patients.

BLEEDING RISKS

Most bleeding that occurs after an endoscopic procedure is immediate, and results from inadequate hemostasis (27). In more than 80% of cases of bleeding, the diagnosis is made within 48 h of the procedure (28,29). Most of the remainder of bleeding episodes occur within the next 10 days.

Some studies have found that severe acute bleeding from peptic ulcer disease can safely be managed endoscopically even in patients who take antiplatelets (30,31). Nevertheless, surgical studies have shown that the restoration of intravenous heparin therapy immediately after surgery increases the absolute rate of major hemorrhage by approximately 3%, and that 3% of these episodes are fatal or lead to long term disability (21,32,33).

WARFARIN

After warfarin is discontinued, the INR can be expected to fall to 1.5 in almost all patients within roughly four days if the INR starts at 2.0 to 3.0, or within five days if the INR starts at 2.5 to 3.5 (34). Once the INR reaches 1.5, surgical or endoscopic procedures can be performed without an increased risk of bleeding (34,35).

The INR should be measured on the day before endoscopy. If the INR is higher than 1.7, a small dose of vitamin K (1 mg subcutaneously) should be administered. If the INR is between 1.7 and 2.0 immediately before endoscopy, fresh frozen plasma may be given (21).

After warfarin therapy is resumed, approximately three days are required for the INR to reach 2.0 (36). Therefore, warfarin therapy may be restarted on the night of the procedure provided that there is no obvious bleeding. Although there is biochemical evidence of a hypercoagulable state after cessation of oral anticoagulants (37), the existence of this phenomenon has not yet been confirmed clinically (38).

HEPARIN

In high-risk patients who undergo high-risk procedures, bridging anticoagulant therapy is required when the INR is less than 2.0. LMWHs are being increasing used, even though there has been no prospective controlled study of their safety and effectiveness for gastrointestinal procedures. They are associated with lower risks of bleeding than that with conventional (unfractionated) heparin, at doses that provide equivalent antithrombotic effects (39). Because their dose-response relationships are more predictable, LMWHs are given in fixed doses without laboratory monitoring, which reduces the perioperative hospitalization and related costs (40,41). They should not be used, however, in cases of renal insufficiency.

ANTIPLATELET DRUGS

Although published data are limited, it has been stated that, when used in standard doses, acetylsalicylic acid and non-steroidal anti-inflammatory drugs do not increase the risk of significant bleeding after EGD with biopsy, colonoscopy with biopsy, polypectomy or biliary sphincterotomy (5,42).

The thienopyridine, platelet adenosine diphosphate-receptor blocker, such as ticlopidine and clopidogrel, are less likely than acetylsalicylic acid to cause gastrointestinal and other bleeding, although the risk is not zero (43-45). Seven days are required for the total pool of functioning platelets to be restored when these drugs are used, which is an important consideration when treating patients who are at a high risk of bleeding.

Some authorities recommend that antiplatelet drugs be withdrawn for seven to 10 days before liver biopsy (46). This recommendation may be extrapolated to endoscopic procedures that could induce bleeding that is endoscopically intractable, such as pneumatic dilation of benign or malignant strictures, EUS-guided fine-needle aspiration and percutaneous endoscopic gastrostomy.

RECOMMENDATIONS

Low-risk procedures

No adjustment in anticoagulation is required for low-risk procedures, regardless of the underlying condition. Elective procedures should be avoided, however, when the INR is above the therapeutic range.

High-risk procedures in patients with low-risk conditions

In these situations, warfarin should be discontinued four to five days before the scheduled procedure, and the INR should be measured on the day before the procedure. If the INR is greater than 1.5, 1 mg of vitamin K should be given subcutaneously. Fresh frozen plasma can be given immediately before the procedure, if necessary, to reduce the INR to 1.5. A prophylactic dose of LWMH could be used as an alternative treatment in select cases.

High-risk procedures in patients with high-risk conditions

In these situations, warfarin should be discontinued four to five days before the procedure. The decision to administer intravenous heparin, once the INR falls below the therapeutic range (ie, INR less than 2.0), should be made on an individual basis. Therapeutic doses of LMWH could be used as an alternative to heparin in selected cases.

High-risk procedures in patients with very high-risk conditions

If the procedure cannot be delayed, warfarin therapy should be discontinued four to five days before the procedure, and a heparin infusion should be administered as soon as the INR falls below 2.0. Heparin should be stopped 6 h before the procedure and restarted within 2 to 12 h after the procedure, in the absence of clinical bleeding. Warfarin therapy can generally be resumed on the night of the procedure. Heparin and warfarin should be given together until the INR has reached the target therapeutic range, usually within two or three days.

Drugs affecting platelet function

In the absence of a pre-existing bleeding disorder, endoscopic procedures may be performed on patients who take acetylsalicylic acid or nonsteroidal anti-inflammatory drugs in standard doses. The data on other drugs that affect platelet function, such as ticlopidine or clopidogrel, are inadequate to make a recommendation. Nevertheless, for a high-risk procedure, the medication probably should be discontinued seven to 10 days beforehand.
REFERENCES

1. Kadakia SC, Angueira CE, Ward JA, Moore M. Gastrointestinal endoscopy in patients taking antithrombotic agents and anticoagulants: Survey of ASGE members. American Society for Gastrointestinal Endoscopy. Gastrointest Endosc 1996;44:309-16.

2. Newcomer MK, Brazer SR. Complications of upper gastrointestinal endoscopy and their management. Gastrointest Endosc Clin North Am 1994;4:551-72.

3. ReMine SG, Hughes RW Jr, Weiland LH. Endoscopic gastric polypectomy. Mayo Clin Proc 1981;56:371-5.

4. Vemara AM, Jrd, Longo WE. Complications of endoscopic polypectomy. Surg Oncol Clin N Amer 1996;5:663-73.

5. Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications and their management: An attempt at consensus. Gastrointest Endosc 1991;37:383-93.

6. Mathus-Vliegen EM, Tytgat GN. Nd:YAG laser photocoagulation in colorectal adenoma. Evaluation of its safety, usefulness, and efficacy. Gastroenterology 1986;90:1865-73.

7. Rutgeerts P, Vantrappen G, Broeckaert L, et al. Palliative Nd:YAG laser therapy for cancer of the esophagus and gastrointestinal junction: impact on the quality of remaining life. Gastrointest Endosc 1988;34:87-90.

8. Risk factors for stroke and efficacy of antiplatelet therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. Arch Intern Med 1996;156:1440-57.

9. EAFT (European Atrial Fibrillation Trial) Study Group. Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. Lancet 1993;342:1255-62.

10. Cerebral Embolism Task Force. Cardiogenic brain embolism. Arch Neurol 1983;40:75-7.

11. Caplan LR, Hier DB, D'Cruz I. Cerebral embolism in the Michael Reese Stroke Registry. Stroke 1983;14:530-6.

12. Anderson CS, Jamrozik KD, Broadhurst RJ, Stewart-Wynne EG. Predicting survival for 1 year among different subtypes of stroke. Results from the Perth Community Stroke Study. Stroke 1994;25:1935-44.

13. Mok CK, Boey P, Wang R, et al. Warfarin versus dipridamole-aspirin and pentoxyfylline-aspirin for the prevention of prosthetic heart valve thromboembolism: a prospective randomized clinical trial. Circulation 1985;74:1059-63.

14. Cannegieter SC, Rosendaal FR, Briet E. Thromboembolic and bleeding complications in patients with mechanical heart valve prostheses. Circulation 1994;89:635-41.

15. American Society for Gastrointestinal Endoscopy. Guidelines on the management of anticoagulation and antithrombotic therapy for endoscopic procedures. Gastrointest Endosc 1998;48:672-5.

16. Tiede DJ, Nishimura RA, Gastroineau DA, Mullany CJ, Orsaluk TA, Schaff HV. Modern management of prosthetic valve anticoagulation. Mayo Clin Proc 1998;73:665-80.

17. Katholi RE, Nolan SP, McGuire LB. Living with prosthetic heart valves. Subsequent noncardiac operations and the risk of thromboembolism or hemorrhage. Ann Intern Med 1994;120:162-2.

18. Hall R, Delmore T, Genton E, et al. Warfarin sodium versus low-dose heparin in the long-term treatment of venous thrombosis. N Engl J Med 1997;332:1266-73.

19. Palareti G, Legnani C, Guazzaloca, et al. Activation of blood coagulation after abrupt or stepwise withdrawal of oral anticoagulants a prospective study. Thromb Res 1994;72:222-6.

20. Palareti G, Legnani C. Warfarin withdrawal. Pharmacokinetic-pharmacodynamic considerations. Clin Pharmacokinet 1994;26:347-55.

21. Harrison L, Johnston M, Massicotte MP, Crowther M, Mofat K, Hirsh J. Comparison of 5-mg and 10-mg loading doses in initiation of warfarin therapy. Ann Intern Med 1995;122:40-2.

22. Francis CW, Marder VJ, Evarts CM, Yaukoolbodi S. Two-step warfarin therapy. Prevention of postoperative venous thrombosis without excessive bleeding. JAMA 1983;249:374-8.

23. Harrison L, Johnston M, Massicotte MP, Crowther M, Mofat K, Hirsh J. Comparison of 5-mg and 10-mg loading doses in initiation of warfarin therapy. Ann Intern Med 1997;126:133-6.

24. Palareti G, Legnani C. Warfarin withdrawal. Pharmacokinetic-pharmacodynamic considerations. Clin Pharmacokinet 1994;26:347-55.

25. Ginsberg JS. Management of venous thromboembolism. N Engl J Med 1996;335:1816-28.

26. Goldstein JL, Larson LR, Yamashita BD, Fain JM, Schumock GT. Low molecular weight heparin versus unfractionated heparin in the prevention of postoperative venous thromboembolism. Circulation 1994;90:313-7.

27. Fries 1996;10:401-6.

28. Palareti G, Legnani C. Warfarin withdrawal. Pharmacokinetic-pharmacodynamic considerations. Clin Pharmacokinet 1994;26:347-55.

29. Boysen G. Bleeding complications in secondary stroke prevention by antithrombotic therapy: a benefit-risk analysis. J Intern Med 1999;246:239-45.

30. Jarvis B, Simpson K. Clopidogrel: a review of its use in the prevention of atherothrombosis. Drugs 2002;60:347-72.

31. Bravo AA, Sheth SG, Chopra S. Liver biopsy. N Engl J Med 2001;344:495-500.
