

Management of Anticoagulation in the Perioperative Period

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Abstract: *The most common indications for anti-coagulation therapy are atrial fibrillation, venous thromboembolism, and presence of a mechanical heart valve. The perioperative management of patients receiving oral anticoagulants is problematic because the medication must be discontinued to prevent excessive bleeding for many invasive and surgical procedures. The purpose of this article is to examine the associated risks, benefits and challenges of anticoagulation therapy management during surgery. A rational approach and strategies are discussed for specific situations.*

Introduction

Oral anticoagulants are commonly prescribed for patients at risk for arterial or venous thromboembolism. The most common indications for warfarin therapy are atrial fibrillation, venous thromboembolism, and presence of a mechanical heart valve.¹⁻² In the United States alone, it has been estimated that 2.3 million patients currently have atrial fibrillation, approximately 40% of whom receive anticoagulants.³

The perioperative management of patients receiving oral anticoagulants is problematic because the medication must be discontinued to prevent excessive bleeding for many invasive and surgical procedures. After warfarin therapy is discontinued, it takes several days for its antithrombotic effect to recede, and when it is resumed, several days are needed to re-establish therapeutic anticoagulation. Rebound hypercoagulability may occur following the abrupt cessation of anticoagulation. Substituting intravenous heparin or subcutaneous low-molecular-weight heparin (LMWH) while oral anti-coagulation is withheld, can decrease the risk of thromboembolism. But it may increase the risk of postoperative bleeding and, in the case of intravenous heparin, increase the hospitalization requirement. There is no general consensus on the appropriate perioperative management of anticoagulation for patients who have been on long term warfarin therapy. In this review, we discuss a rational perioperative approach in patients who require warfarin because of atrial fibrillation, mechanical heart valve, or a history of thromboembolism. The management of antiplatelet agents will also be discussed.

Risk of Thrombosis

A number of factors affect the risk of thrombosis following the discontinuation of anticoagulation. They include the type of condition requiring anticoagulation, the time period since the initial event, duration of anti-coagulation, and comorbidities of the patient.

Venous Thromboembolism – The risk of recurrent venous thromboembolism after an acute episode of venous thromboembolism in the first three months approaches 50% in the absence of anticoagulation.⁴ However, the risk of recurrence

declines rapidly over the following three months. Anticoagulation reduces the risk of recurrent venous thromboembolism by about 80%.⁵ Long term anticoagulation as prophylaxis against recurrent venous thromboembolism is generally necessary for patients with multiple or recurrent venous or pulmonary thromboembolism, hereditary hypercoagulable states, or active cancer. Discontinuation of warfarin in such patients is associated with a significant risk of thromboembolism of approximately 15% per year.⁶

Arterial Thromboembolism – Patients with nonvalvular atrial fibrillation have a risk of thromboembolism of 4.5% per year without anticoagulation.⁷ However, the risk may be as high as 20% in patients with risk factors such as valvular atrial fibrillation, left ventricular dysfunction and previous cerebral embolism. Anti-coagulation reduces the risk of embolism by about 66% in patients with nonvalvular atrial fibrillation.⁷ Embolic stroke is associated with severe neurological deficits in over 60% of the patients. Unequivocally, patients with risk factors such as severe LV dysfunction and left ventricular aneurysm derive the greatest benefit from anticoagulation and would be at a higher risk for embolic events when anticoagulation is withheld. Management should therefore be tailored to an individual patient's risk of thromboembolism, as compared to risk of bleeding during surgery.

Mechanical Heart Valves – With mechanical heart valves, the average risk of thromboembolism without anti-coagulation is approximately 4 percent per year. Anti-coagulation with warfarin reduces the risk by 75%.⁸

Risk of Bleeding With Surgery – The risk of bleeding in patients taking anticoagulant therapy and undergoing surgery is dependent upon patients' age, the presence of other disease states, the type of surgery being performed, the anticoagulant regimen and the intensity, duration, and stability of anti-coagulation therapy. Prolonged, complex surgical procedures are more likely to cause significant bleeding risk than short, simple and minor surgical procedures like arthrocentesis or cataract surgery. These subjective qualifiers are best determined by the operating surgeon based on the individual patients.

Hypercoagulability/Discontinuation of Warfarin – Surgery itself increases the risk of thromboembolism due to changes in hemostasis, acute phase response and wound healing processes. This can be compounded by a rebound hypercoagulable state after withdrawal of warfarin before surgery.

Management of Anticoagulation & Elective Surgery

After the cessation of oral warfarin, it usually takes a few days for the International Normalized Ratio (INR) to fall to below 2.0. For patients taking oral anticoagulants as thromboprophylaxis, the INR can be maintained around 1.5 before surgery. However, for patients with mechanical

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prosthetic valves, the preoperative INR should be maintained around 2.0.

Once the INR is 2.0 or below, surgery can be performed with relative safety. Following surgery and after warfarin is restarted, it takes three to four days for the INR to rise above 2.0. It is therefore estimated that if warfarin is withheld for four days before surgery and treatment is started as soon as possible afterwards, patients would have a sub therapeutic INR for approximately two days before surgery and two days after surgery.⁷

The risk of this short period of sub therapeutic anticoagulation is uncertain. A slight elevation of the INR to about 1.5 should theoretically provide partial protection against thromboembolism. However, a small increase in the risk of thromboembolism is probably unavoidable.⁹

Venous Thromboembolism – In the first month after an acute episode of venous thromboembolism, each day without anticoagulation is associated with a 1.0 percent absolute increase in the risk of recurrence. Despite doubling the rate of bleeding, postoperative intravenous heparin therapy results in a net reduction in serious morbidity in these patients because the risk of postoperative venous thromboembolism is extremely high. Preoperative intravenous heparin is also warranted while the INR is sub therapeutic. If acute venous thromboembolism has occurred within two weeks or if the risk of bleeding during intravenous heparin is high, a vena caval filter should be considered.⁷

In the second and third months after an acute episode of venous thromboembolism, the risk of recurrence has dropped sufficiently that preoperative intravenous heparin therapy is not justified unless the patient has other risk factors for thromboembolism (e.g., hospitalization or malignancy). However, because of the expected 100-fold increase in the risk of venous thromboembolism after surgery, postoperative therapy with intravenous heparin is indicated.⁷

More than three months after an acute episode of venous thromboembolism, preoperative anticoagulation is not warranted. In these circumstances, the argument for postoperative intravenous heparin is also weak because of the marked decline over time in the absolute risk of venous thromboembolism. In this setting, postoperative intravenous heparin can be expected to cause as many episodes of significant bleeding as it will prevent major thromboembolic events. However, prophylactic measures that are associated with a lower risk of bleeding than intravenous heparin (for instance, subcutaneous low-molecular-weight heparin, given with or without the use of graduated-compression stockings or intermittent pneumatic compression devices) are likely to be a safer alternative for such patients.⁷

Recommendations

The following approach to the perioperative management of anticoagulation in patients with a history of venous thromboembolism undergoing surgery is recommended:

- Elective surgery should be avoided in the first month after an acute episode of venous thromboembolism.
- If avoidance of elective surgery is not possible, warfarin should be withheld for three to four days and intravenous heparin or low molecular weight heparin should be given before and after the procedure while the INR is below 2.0.
- The activated partial-thromboplastin time (aPTT) should be monitored during intravenous heparin use. Heparin should be continued until six hours before surgery.
- Heparin or low-molecular-weight heparin should not be restarted postoperatively until at least 12 hours after surgery and delayed longer if there is any evidence of bleeding.
- If the patient has been receiving warfarin for more than one month but less than three months, preoperative intravenous heparin is probably not needed unless there are additional risk factors for recurrence. However, postoperative intravenous heparin is recommended until warfarin therapy is resumed and the INR is above 2.0.
- If it has been three months or more since the last episode of acute venous thromboembolism and the patient has been taking warfarin, preoperative heparin is not necessary, but postoperative prophylaxis with subcutaneous heparin or low molecular weight heparin is recommended until oral anticoagulation is reestablished.¹⁰

Arterial Thromboembolism – With patients at risk for arterial thromboembolism, there is a stronger argument in favor of preoperative intravenous heparin than there is for postoperative therapy. The risk of thromboembolism is similar before and after surgery, but the relative risk of post operative bleeding is much higher.

In the first month after an acute episode of arterial thromboembolism, preoperative intravenous heparin is indicated. However, the reduction in the rate of long-term disability achieved by intravenous heparin therapy after major surgery is small and is gained at the expense of a greater number of episodes of less serious bleeding. Consequently, it is reasonable in this population at higher risk for forming arterial thromboemboli, to recommend postoperative therapy with intravenous heparin only for patients undergoing relatively minor surgery during which the risk of bleeding is low.

In conditions associated with a lesser risk of arterial thromboembolism (e.g., atrial fibrillation or the presence of a mechanical heart valve in patients with no recent embolism), postoperative intravenous heparin therapy increases rather than decreases serious morbidity. This is because the risks associated with postoperative thromboembolism are lower than the risks associated with heparin-induced bleeding. Although preoperative heparin therapy should reduce morbidity due to thromboembolism, the achieved benefit is small because the risk of embolism during the short period of sub therapeutic anticoagulation is extremely low.

Recommendations

The following is a recommended approach to the perioperative management of anticoagulation in patients at risk for arterial thromboembolism who are undergoing surgery.⁷ Unfractionated heparin should be stopped six hours before surgery with the expectation that the anticoagulation effect will have worn off by the time of surgery.¹¹ If LMW heparin has been used, it should be stopped at least 12 hours, and preferably 24 hours before surgery.¹²

- Elective surgery should be avoided in the first month after arterial thromboembolism. If surgery is essential, preoperative and postoperative heparin therapy is recommended as described above for venous thromboembolism prophylaxis, but only if the risk of postoperative bleeding is low.
- In patients receiving warfarin as prophylaxis against arterial embolization, such as low risk patients with a prosthetic heart valve or nonvalvular atrial fibrillation, the risk of thromboembolism is not high enough to warrant routine preoperative or postoperative therapy with intravenous heparin, especially in view of the bleeding risk.¹³⁻¹⁴ Subcutaneous low-dose heparin or low-molecular-weight heparin, in doses used for prophylaxis against venous thromboembolism, is recommended.¹¹

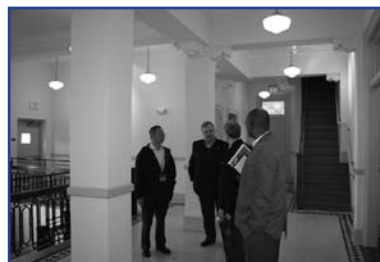
The approach is different in high-risk patients with atrial fibrillation (e.g., associated with prior thromboembolism, rheumatic heart disease, left ventricular dysfunction) or those with older generation mechanical heart valves, in whom there is a fragile balance between the risks of bleeding and thromboembolism. The approach in this setting is to administer intravenous heparin until six hours before the procedure and to restart heparin as soon as possible after surgery.¹¹ The dose is adjusted to achieve an activated PTT that is 2.0 times control. Warfarin is then reinstated prior to discharge from the hospital; the prothrombin time should be in the therapeutic range for at least 48 hours before heparin is discontinued.

Management of Anti-platelet Agents

The most common anti-platelet agents used are aspirin, clopidogrel and dipyridamole. Anti-platelet agents may increase intraoperative blood loss and hemorrhagic complications. However, the same effect can help decrease the risk of acute coronary syndrome or stroke. Patients believed to be at high risk for perioperative vascular complications, in whom perioperative hemorrhage would result in minimum morbidity, should continue aspirin. On the other hand, anti-platelet agents should be withheld prior to surgical procedures in which perioperative hemorrhage could be catastrophic (e.g. Central nervous system surgery) or could adversely impact the surgical outcome. Antiplatelet agents can be safely continued in most patients undergoing cataract surgery. If the decision is made to stop these medications, 7 days should elapse before surgery is undertaken and they should be resumed as early as possible in the postoperative period.

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***What is
happening
April 7
and where?***

See p. 46