The perioperative management of anticoagulation

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SYNOPSIS

The perioperative management of patients on long-term warfarin therapy poses particular problems. This situation is exacerbated by the absence of randomised trials. The strategy used is based on the assessment of each patient's thromboembolic and bleeding risks. These determine the need for withholding warfarin and switching to heparin. Most patients having minor procedures can continue to take warfarin, provided that they are closely monitored and local measures are used to ensure adequate haemostasis.

Index words: thromboembolism, heparin, warfarin, haemostasis.

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Introduction

The most common indications for long-term oral anticoagulation with warfarin are venous thromboembolism, mechanical cardiac valves and atrial fibrillation. When patients with these conditions need surgery, the perioperative management of their warfarin therapy poses a major problem. Withholding warfarin increases the risk of thromboembolism, particularly in the context of surgery which itself increases the thrombotic risk. To minimise the risk of perioperative thrombosis, alternate anticoagulation with heparin is often used. Perioperative anticoagulation is accompanied by an increased risk of postoperative bleeding. There is no consensus on the optimal approach to anticoagulation in the perioperative period. In each individual patient, rational decisions must be made after weighing up the haemorrhagic and thrombotic risks.

Risks of temporarily withholding warfarin

The risks are difficult to quantify due to the lack of randomised trials examining this issue. They vary according to the indication for the warfarin therapy.

Patients with cardiac valve replacement

In patients with mechanical heart valves, the thromboembolic risk increases 3.7 fold when anticoagulation is stopped.[1] The incidence of thrombotic complications is higher in patients with the following risk factors:

- patient related:
  - advanced age
  - left atrial enlargement
  - history of thromboembolism
  - increased fibrinogen
  - atrial fibrillation and/or cardiomyopathy
  - congestive cardiac failure
- valve related:
  - mechanical versus tissue valves
  - first generation valves (Starr-Edwards, Bjork Shiley) versus later generation valves (St. Jude, ATS, Carbomedics)
  - mitral position

The rates of thromboembolic events differ with valve position and type. In a study of 1608 patients with mechanical valves, the lowest event rate was seen in patients with a prosthetic aortic valve.[2] Bileaflet valves (e.g. St. Jude) had the lowest thromboembolic event rate followed by the tilting-disc (Bjork Shiley) and caged-ball (Starr-Edwards) valves.

Do the benefits of anticoagulation outweigh the risks?

The approach to the management of anticoagulation in patients with prosthetic valves undergoing non-cardiac surgery remains controversial. The need for perioperative anticoagulation in patients with mechanical heart valves has been questioned in a recent review. The authors argue that for every 10 000 patients with mechanical heart valves who are given perioperative intravenous heparin, three thromboembolic events are prevented at the cost of 300 major postoperative bleeding episodes.[3] These figures are calculated by assuming an average thromboembolic rate of 8% per year in patients with mechanical heart valves, an anticoagulation-free period of four days and a 3% risk of major postoperative bleeding with intravenous heparin. In light of these calculations, a risk-benefit analysis would preclude the use of *full dose* anticoagulation during the perioperative period in patients with mechanical valves, except in patients with very recent arterial embolism who have a high risk of recurrence in the absence of anticoagulation. In the absence of recent embolism, the authors recommend, for hospitalised patients, the use of subcutaneous low dose unfractionated or low molecular weight heparin at doses used for *prophylaxis* against venous thromboembolism, with no prophylaxis for outpatients.

There are limited prospective data to support or contradict these recommendations. The available literature consists mainly of small, non-randomised trials from which no definitive conclusions can be drawn. In one of the few prospective studies, 45 patients with mechanical heart valves underwent

non-cardiac surgical procedures.[4] No thromboembolic events were seen in 26 patients with *aortic* prostheses in whom warfarin was withheld for a total of 6–10 days perioperatively. In 19 patients with *mitral* prostheses, the warfarin effect was reversed with vitamin K on the day of surgery. A heparin infusion was started 12 hours after the operation and warfarin was resumed on the third postoperative day. No thromboembolic events were observed in this group.

Besides being a small non-randomised trial, the other drawback of this study was the lack of long-term follow-up. Valve thrombosis, especially with the tilting-disc (Bjork Shiley) valves, develops slowly and insidiously and may not be evident for 1–2 months. Hence, an uneventful early postoperative period may provide false reassurance that the perioperative anticoagulation has been safe and successful.

A recent review evaluated retrospectively the risk of perioperative bleeding during non-cardiac surgery in 235 patients with mechanical prosthetic heart valves.[5] A variety of perioperative anticoagulation strategies was used. On multivariate analysis, only a tilting-disc valve in the mitral position and surgery for tumour were found to be predictive factors for a thromboembolic event. Discontinuation of warfarin less than 48 hours before surgery and reinstitution of intravenous heparin within four hours following surgery significantly increased the risk of bleeding. No embolic or haemorrhagic events were detected in 22 patients treated with perioperative low molecular weight heparin.

What to do

The lack of adequate data makes it difficult to give firm recommendations. Patients on warfarin for *tissue* valves (usually mitral) are usually managed preoperatively by cessation of their warfarin without heparin replacement. In contrast, common practice in Australia has been to admit patients with *mechanical* valves prior to surgery for full dose anticoagulation with intravenous heparin. There are preliminary data to suggest that subcutaneous low molecular weight heparin may be substituted safely for intravenous unfractionated heparin. The evidence suggests that anticoagulation with either heparin may not be required for all patients. The final decision should take into account individual patient factors such as the surgical procedure, the type and location of the prosthetic valve and whether or not there are other indications for anticoagulation.

Patients with prior venous thromboembolism

The risk of withholding warfarin therapy in patients with venous thromboembolism depends on the timing of the thrombosis and the patient's history.

Time interval following the thromboembolic event

The risk of recurrence in the absence of anticoagulation is highest in the first month following a deep vein thrombosis (DVT) and declines sharply over a three month period. Although the risk of withholding warfarin in the immediate post-thrombotic period has not been quantified, it is estimated to be 40% over a one month interval i.e. greater than 1% for each day without anticoagulation.[3] This suggests that, if possible, surgery should be avoided in the first month following an acute DVT and, if surgery is imperative, full dose intravenous heparin should be used.

History of recurrent DVT

Discontinuation of warfarin is associated with a risk of thromboembolism of approximately 15% per year. These patients should receive perioperative heparin, especially if they are having urological or orthopaedic surgery.

Patients with atrial fibrillation

In patients with non-valvular atrial fibrillation, the average risk of systemic embolism in the absence of anticoagulation is approximately 4.5% per year.[6] The risk is higher in individuals with a history of systemic embolism in the past 12 months. The risk appears to be higher in the first month following an arterial thromboembolic event. However, the overall risk of thrombosis is so low that the risk of bleeding following major surgery probably outweighs the benefits of postoperative heparin even in prophylactic doses.

Strategy for perioperative anticoagulation

The anticoagulation strategy selected depends upon an evaluation of the thromboembolic risk and the haemorrhagic risk of the surgical procedure.

Minor procedures

Oral anticoagulants may be continued at a lower therapeutic level (INR 1.5–1.8) for minor procedures with a low risk of bleeding.[7] These include excision of skin lesions, bone marrow biopsies, cataract surgery and procedures in which the bleeding can be controlled readily by local measures. This approach is not recommended for laparoscopic surgery and ultrasound or CT-guided biopsies.

Major procedures

The strategy for perioperative anticoagulation in patients undergoing major surgery is based more on the assessment of the risk of thromboembolism than the risk of haemorrhage. Patients can be divided into two risk groups (Table 1). In the low-risk group warfarin is withheld for five days before surgery, but no alternate anticoagulation is given (Table 2). High-risk patients should receive aggressive alternate anticoagulation with unfractionated or low molecular weight heparin (Table 2).

Low molecular weight heparins are commonly used as prophylaxis against venous thromboembolism prior to and after major surgery. They are more effective than low dose heparin in orthopaedic patients who are at high risk for venous thromboembolism. Low molecular weight heparins do not increase the risk of bleeding any more than low dose heparin and are more convenient to use as laboratory monitoring is generally not required.

There is considerable variability amongst individual surgeons as to an acceptable upper limit of the INR on the day of surgery. In particular, neurosurgeons generally prefer a near normal INR, while vascular surgeons may accept an INR of 1.5–2.0.

Table 1

Risk of thromboembolism if anticoagulation is withdrawn

	Low	*High*
Atrial fibrillation and/or cardiomyopathy	Without stroke or systemic embolisation in the last 12 months	With stroke or systemic embolisation within the last 12 months
Biological heart valves	Except during first three months	During first three months
Prosthesis	Vascular grafts	Cardiac mechanical valves (mitral>aortic)
Venous thrombosis	Not within the last three months and without a confirmed hypercoagulable state	*Within the last three months, or recurrent venous thrombosis
Systemic arterial emboli	Non-recurrent	Recurrent

Note: two low-risk factors = high risk

* The risk in patients with a confirmed hypercoagulable state but no venous thrombosis within the previous three months, and no recurrent thrombosis, has not been established.

The acceptable INR will also depend on the individual surgical characteristics of each patient.

Insertion of a vena caval filter should be considered if (a) the patient has had a pulmonary embolism or proximal DVT within a month or (b) the risk of bleeding from anticoagulation is unacceptable in a high-risk patient.

Anaesthetic considerations

There are concerns about the possibility of extradural haematoma formation in patients receiving heparin and undergoing epidural/spinal anaesthesia. Unfractionated heparin should be ceased at least six hours prior to such an anaesthetic and low molecular weight heparin ceased a minimum of 12 hours (and preferably 16–18 hours) beforehand, at which time anti-Xa values (the best laboratory test for activity of such heparins) fall to low levels. A longer delay is advisable in patients with renal insufficiency in whom excretion of low molecular weight heparin is reduced. If a low molecular weight heparin is used the night prior to epidural/spinal anaesthesia planned for the next morning, the dose preferably should be the thromboprophylactic dose rather than the full anticoagulation dose.

Table 2

Recommendations for perioperative anticoagulation of patients undergoing major elective surgery

Day	*Low-risk patients*	*High-risk patients*
– 5 (pre-op)	Cease warfarin	
– 4	No anticoagulation	Cease warfarin Measure INR Start full dose UFH as inpatient ***OR*** LMWH* as outpatient. Continue daily until day –1.
– 1		Stop LMWH a minimum of 12 hours and UFH six hours before surgery.
0 (surgery day)	Measure INR and if >2.0 on the morning of surgery, options include: postponement of surgery, fresh frozen plasma. Consult haematologist.	
+ 1	Start warfarin as soon as oral fluids tolerated using the preoperative maintenance dose. A lower dose may be required if INR >1.2 or if other drugs are being used.	Once haemostasis secured, and generally after at least six hours post surgery: • recommence LMWH (preferred) or UFH (do not commence with bolus dose) • start warfarin as soon as oral fluids tolerated using the preoperative maintenance dose. A lower dose may be required if INR >1.2 or if other drugs are being used. • cease UFH/LMWH when INR >2.0 on at least two consecutive days • if patient discharged before INR >2.0, use LMWH as an outpatient

UFH = standard unfractionated heparin
LMWH = low molecular weight heparin

* Alternatives include enoxaparin 1.5 mg/kg once daily, dalteparin 100 IU/kg twice daily or nadroparin (weight adjusted). At present, these drugs have Pharmaceutical Benefits Scheme listing for treatment of deep venous thrombosis and for prophylaxis of hip surgery. These doses are those approved, as at February 2000, for full-dose anticoagulation for venous thromboembolism.

Notes:

- Insertion of a vena caval filter should be considered if (a) the patient has had a pulmonary embolism or proximal DVT within a month or (b) the risk of bleeding from anticoagulation is unacceptable in a high-risk patient.
- These guidelines may not necessarily be applicable to neurosurgical procedures or for patients with mechanical valves undergoing cardiac surgery. Generally, each department has established their own individual guidelines.

Dental surgery in the anticoagulated patient

Non-surgical dental procedures (professional cleanings, fillings, crowns, etc.) are not associated with a significant bleeding risk and can be performed safely while the INR is in the therapeutic range.

Traditionally, many dentists have withdrawn warfarin before some dental surgical procedures. Recent evidence, however, suggests that the recommended approach is not to discontinue warfarin. In the English language literature, there are reports of approximately 2014 dental surgical procedures including multiple and full mouth extractions, alveoectomies and surgical extractions in 774 patients taking warfarin.[8] Less than 2% of these patients had serious bleeding problems, defined as bleeding uncontrolled by local measures. Another study compared postoperative bleeding following dental extractions in 106 patients on warfarin and 106 normal patients. It found no difference in the incidence or severity of bleeding.

In contrast, in 542 dental procedures in 493 patients in whom warfarin was withheld for the procedure, five (1.0% of patients; 0.9% of procedures) had serious embolic complications (including four deaths). Although suggestive, a direct cause and effect relationship between withholding warfarin and a thromboembolic event is unproven.

Approach to dental surgery

1. Check INR the day before the procedure to ensure it is within the therapeutic range for the patient. If above this, delay surgery until the INR is within the therapeutic range.
2. In the majority of cases, continue warfarin therapy throughout the dental procedure and postoperative period. This may need to be reassessed for multiple and complex dental extractions, particularly if infection is a concern, in which case an INR of under 1.6 may be desirable. Table 3 is an example of a patient information sheet for use in this situation.
3. Daily or alternate day monitoring of the INR may be required, especially if the patient is receiving antibiotics.
4. Judicious use of local measures to ensure adequate haemostasis e.g. packs soaked in 5% tranexamic acid placed over the extraction site.
5. In patients with excessive oozing, tranexamic acid mouthwash (10 mL of 5% solution) held in the mouth for two minutes is helpful when used six hourly for 3–5 days. Practically, this preparation may be difficult to obtain other than from major teaching hospital pharmacies.

Table 3

Instructions for patients on warfarin for multiple and complicated surgical tooth extraction *

1. Cease your warfarin two nights before procedure and do not take it again until the evening of the day on which you have the extraction.
2. Have an INR test performed on the morning of the extraction before the procedure. This result will be telephoned to your dentist.
3. If the INR is >1.6 (normal <1.3), it is suggested that, if possible, the extraction be deferred for another occasion.
4. Start taking warfarin tablets again the night after the procedure, with the same dosage you had been taking previously before the extraction, and continue each day until the next INR test.
5. If you are prescribed antibiotics for the procedure, have an INR test 3-4 days afterwards to check warfarin dose. Do this earlier if excessive bleeding occurs.

Dental procedures of a less traumatic nature, provided infection is not present, generally do not require alterations in warfarin dosage.

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Self-test questions

The following statements are either true or false (answers on page 23)

5. Patients taking warfarin should stop their treatment two days before any routine dental procedure.
6. The risks of bleeding probably outweigh the benefits of anticoagulation with heparin when patients with non-valvular atrial fibrillation have major surgery.

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