Trust guideline for the management of *adult patients on therapeutic anticoagulation who require elective surgery or an invasive procedure*

Contents

Introduction

Anticoagulants are widely used in the management of Venous Thromboembolic disease (VTE), Atrial Fibrillation (AF), other vascular occlusive disorders and for patients who have diseased or prosthetic cardiac valves.

Warfarin has been the oral anticoagulant of choice in the United Kingdom for many years; management of anticoagulation with Warfarin in the peri-operative period is well established. The introduction of newer oral anticoagulants (specific inhibitors of factor IIa - Dabigatran, and factor Xa - Rivaroxaban, Apixaban, Edoxaban) has made the field more complex, particularly in respect of anticoagulant reversal.

Optimal perioperative management of patients taking therapeutic anticoagulants must balance the risk of a thrombotic event associated with interruption of anticoagulation and the risk of haemorrhage associated with the procedure. This balance of risks will vary between individual patients and according to the nature of the procedure. Large, prospective trials do not exist to guide management of perioperative anticoagulation. This guideline incorporates the current published evidence to provide a simple, hospital-wide protocol for the management of perioperative anticoagulation.

This guideline addresses the management of adult patients (> 16 years) on oral anticoagulants who are to undergo a planned (elective) surgical procedure. For the management of patients on oral anticoagulants or antiplatelet agents who are to undergo endoscopy, consult chart held in endoscopy.

Be aware that for the majority of procedures in certain specialties (eg: dental / oral surgery, ophthalmology, cardiology - insertion of cardiac pacemaker, coronary angiography) it is now considered acceptable to operate without stopping the oral anticoagulant. In these specialties it is recommended that if the patient is on Warfarin, the INR should be checked and confirmed as being in the therapeutic range during the week prior to surgery.

Warfarin - a widely used oral anticoagulant that works through the liver to inhibit the conversion of Factors II, VII, IX and X into their active forms (IIa, VIIa, IXa, Xa.) Warfarin has a long half-life and therefore requires a longer time period for its effect on coagulation to reduce. The effect of Warfarin is normally monitored by measuring the INR (International normalised ratio). Surgery can be safely carried out with an INR ≤1.5, checked on the day of surgery.

Non vitamin K antagonist Oral Anticoagulants (NOACs):
- Dabigatran (*Pradaxa)* acts as a direct inhibitor of Thrombin (factor IIa.)
- Rivaroxaban (*Xarelto),* Apixaban (*Eliquis),* Edoxaban (*Lixiana*) act as inhibitors of Factor Xa.

The NOACs have a relatively short half-life, this is increased in renal impairment. There are no readily available specific laboratory tests to measure or monitor the effect of the NOACs

Low Molecular Weight Heparin (LMWH) - a parenteral anticoagulant, given by subcutaneous injection. It is often used in the peri-operative period to provide on-going anticoagulation during interruption of oral anticoagulant therapy. This is sometimes referred to as “bridging anticoagulation”

Recommendations

All patients undergoing elective surgery should be evaluated *before the procedure* and those on oral anticoagulants identified. This guideline should enable an appropriate plan for management of anticoagulation in the peri-operative period, to be made for the individual patient. The details of the plan should be explained to the patient, copied to relevant clinicians (surgical team, General Practitioner) and recorded clearly in the case notes.

The assessment should include:

- reason for anticoagulation
- type of oral anticoagulant (Warfarin or NOAC)
- nature of planned surgical procedure and associated bleeding risk

This information is used to determine whether the patient is "High risk" or "Standard risk" and the appropriate guidance in this document can be followed in accordance with the risk group for the individual patient

Special situations

Recent VTE

Patients should only be considered for surgery within 3 months of a VTE if the procedure is urgent; in this situation consideration may need to be given to the use of an IVC filter to prevent pulmonary embolism. Otherwise wait until >3 months, when the risk of a further event following interruption of anticoagulation is much lower.

Atrial Fibrillation

The risk of a cardio-embolic stroke during perioperative interruption of anticoagulation for patients with AF is small. In the majority of patients who have AF and no history of stroke/TIA, anticoagulation can be safely interrupted to allow surgery to occur. Bridging therapy is not required. Patients who have had a previous stroke should be considered at higher risk of perioperative stroke. These patients should be offered bridging therapy with LMWH.

Mechanical Heart Valves

The thrombotic risk to patients with mechanical heart valves is significantly influenced by the site and type of valve. Mechanical aortic valves are associated with a very small risk of thrombotic events during perioperative interruption of anticoagulation. Bridging therapy with LMWH is not required. The risk is higher for mechanical mitral valves. As a general rule mechanical mitral valves should be considered a high thrombotic risk and receive bridging therapy with LMWH. Because of the individual nature of thrombotic risk, perioperative management of all patients with prosthetic cardiac valves should ideally be discussed with the patient's cardiologist prior to surgery.

Thrombophilia

Patients on warfarin with a high risk thrombophilia (anti-phospholipid syndrome, anti-thrombin deficiency) should be discussed with a haematologist prior to surgery.

Assess Thrombotic risk

Higher Thrombotic risk Need bridging while Warfarin/NOAC stopped	Standard thrombotic risk Can stop Warfarin/NOAC do not need bridging
• VTE within 3 months • VTE or recurrence while anticoagulated at any time in the past • Atrial fibrillation **and** past history of stroke, TIA or systemic embolism of cardiac origin, or CHADS-VASc ≥ 4 • Mechanical prosthetic mitral heart valve • Mitral valve repair within last 3 months • Venous stent within one year • Antiphospholipid syndrome; anti-thrombin deficiency	• VTE > 3 months previously • Single or recurrent VTE while not on anticoagulation • Atrial fibrillation **with no** previous stroke or TIA or systemic embolism of cardiac origin • Venous stent > one year
• Follow high risk chart - appendix 1 or 4 • Counsel patient regarding risks of interrupting anticoagulant	• Follow standard risk chart - (appendix 2 or 3) • Counsel patient regarding risks of interrupting anticoagulant

If indication for anticoagulation not in table above, discuss with relevant clinician

References:

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2. Douketis JD et al. (2012) The perioperative management of antithrombotic therapy: American College of Chest Physicians Evidence-Based Clinical practice Guidelines (9th Edition) Chest 2012; 141 e326S-350S

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Apixaban, Dabigatran, Rivaroxaban, Edoxaban

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Appendix 1: Perioperative management of patients undergoing elective surgery who are taking Warfarin

High Thrombotic Risk Patients

	Day -5	Day -4	Day -3	Day –2	Day-1	Day 0 Surgery	Day +1	Day +2	Day +3	Day +4	Day +5
Check INR					✓				✓		✓
Enoxaparin 1.5 mg (150 units)/kg 18.00 hrs	OMIT	OMIT	OMIT	GIVE	OMIT	OMIT	GIVE (After assessing bleeding risk)**	Give daily until INR in therapeutic range** then stop			
Warfarin 18.00hrs (REFER PATIENT TO ANTICOAGULATION TEAM FOR DOSING)	GIVE USUAL DOSE	OMIT	OMIT	OMIT	OMIT	OMIT	Give patients USUAL daily dose* if : 1. Not likely to return to theatre 2. Patient is not actively bleeding/high risk of bleeding 3. Epidural catheter not present Otherwise OMIT until safe to restart				
Enoxaparin 4000 u (40mg) s/c 18.00 hrs	OMIT	OMIT	OMIT	OMIT	GIVE	GIVE	(Give daily if both Warfarin and Enoxaparin full dose -150 units/kg - are being withheld)				
Mechanical thromboprophylaxis measures (stockings, pneumatic compression) should be used as per departmental thromboprophylaxis policy during hospital admission											

INR should be <1.5 for major surgery or <2.0 for minor surgery to proceed.

* Give patient the dose of warfarin they were on, prior to admission (DO NOT give a loading dose).

If actively bleeding or needs to return to theatre imminently **OMIT dose until bleeding risk falls.

If the procedure has a significant postoperative bleeding risk the therapeutic Enoxaparin dose 1.5 mg/kg (≡150 Units/kg) should be given as 2 divided doses (75 U/kg @ 18.00 & 06.00hrs) starting no earlier than 18.00hrs on Day +1 (If epidural catheter present, once daily dosing is preferable).

Refer all patients to VTE nurses for advice re Warfarin dosing once Warfarin restarted (ext 2098; bleep 307)

Appendix 2: Perioperative management of patients undergoing elective surgery who are taking Warfarin

Standard Thrombotic Risk Patients

	Day -5	Day -4	Day -3	Day –2	Day-1	Day 0 Surgery	Day +1	Day +2	Day + 3	Day +4	Day +5
Check INR					✓				✓		✓
Enoxaparin 40mg (4000units) s/c 18.00 hrs**	OMIT	OMIT	OMIT	GIVE (if patient in hospital)	GIVE (if patient in hospital)	GIVE	GIVE (if patient in hospital)	GIVE (if patient in hospital)	GIVE (if patient in hospital)	GIVE (if patient in hospital)	GIVE (if patient in hospital)
Warfarin 18.00hrs (REFER PATIENT TO ANTICOAGULATION TEAM FOR DOSING Bleep 307)	GIVE USUAL DOSE	OMIT	OMIT	OMIT	OMIT	OMIT	Give patients USUAL daily dose* if : 1. No return to theatre likely 2. Patient is not actively bleeding 3. Epidural catheter not present Otherwise OMIT until safe to restart				
Mechanical thromboprophylaxis measures (stockings, pneumatic compression) should be used as per departmental thromboprophylaxis policy during hospital admission											

INR should be ≤1.5 for major surgery or ≤2.0 for minor surgery to proceed.

* Give patients the dose of warfarin they were on prior to admission (**DO NOT** give a loading dose).
If actively bleeding or needs to return to theatre imminently **OMIT dose until bleeding risk falls.
Enoxaparin can be stopped postoperatively when INR therapeutic.
Refer all patients to VTE nurses for warfarin dosing once warfarin restarted (ext 2098; bleep 307)
Discharge does not need to be delayed for anticoagulation – discuss with VTE nurses.

Appendix 3:

Perioperative management of patients undergoing elective surgery who are taking one of the non Warfarin oral anticoagulants (NOACs) i.e. Apixaban, Dabigatran, Rivaroxaban, Edoxaban

Standard thrombotic risk

	Day -4	Day -3	Day –2	Day-1	Day 0 Surgery	Day +1	Day +2	Day + 3
Patient takes NOAC usual dose at usual time	Give	Give (Omit if on Dabigatran and eGFR <50 ml/min/1.73m^2)	Omit	Omit	Omit	Omit	Omit	Restart NOAC at usual dose/time providing: • Haemostasis achieved • Can take oral drugs • Return to theatre unlikely • No epidural in situ • Stable renal function Otherwise continue with Enoxaparin prophylaxis
Enoxaparin 40 mg s/c (4000 u) 18.00 hrs	Omit	Omit	Give (if patient in hospital)	Give (if patient in hospital)	Give (if patient in hospital)	Give (if patient in hospital)	Give (if patient in hospital)	
Mechanical thromboprophylaxis (stockings, pneumatic compression) should be used as per departmental thromboprophylaxis policy during hospital admission								

- This protocol does not replace the need for thrombosis risk assessment (TRA). All patients should have a TRA on admission
- Patients prescribed extended thromboprophylaxis on discharge should discontinue this, as soon as usual NOAC dose restarted
- NOAC can be restarted before Day +3 in procedures with low risk of post op bleeding, at surgeon's discretion
- Check renal function preoperatively. These drugs are renally excreted. If eGFR <30 ml/min/1.73m^2, seek advice.
- Spinal anaesthesia is acceptable if >48 hours since last dose of Dabigatran and eGFR >50 ml/min/1.73m^2.
- Spinal anaesthesia is acceptable if >48 hours since last dose of Apixaban or Rivaroxaban, Edoxaban and eGFR >30 ml/min/1.73m^2. For other situations seek advice

Appendix 4:

Perioperative management of patients undergoing elective surgery who are taking one of the non Warfarin oral anticoagulants (NOAC's) i.e. Apixaban, Dabigatran, Rivaroxaban, Edoxaban

High thrombotic risk

	Day -4	Day -3	Day –2	Day-1	Day 0 Surgery	Day +1	Day +2	Day + 3
Give NOAC at patients usual dose at usual time	Give	Give (Omit if on Dabigatran and eGFR <50 ml/min/1.73m^2)	Omit	Omit	Omit	Omit	Omit	Restart NOAC at usual dose/time providing : • Haemostasis achieved • Can take oral drugs • Return to theatre unlikely • No epidural in situ • Stable renal function Otherwise continue with Enoxaparin 1.5 mg/kg (150 units/kg) s.c. OD
Enoxaparin 1.5 mg/kg (150 units/kg) s/c 18.00 hrs*	Omit	Omit	Give	Omit	Omit	Give	Give	
Enoxaparin 40mg (4000 units) s/c 18.00 hrs	Omit	Omit	Omit	Give	Give	Omit	Omit	
Mechanical thromboprophylaxis (stockings, pneumatic compression) should be used as per departmental thromboprophylaxis policy								

* assess risk of bleeding. If high risk of post op bleeding omit Enoxaparin, or give as 2 divided doses (75 U/kg @ 18.00 & 06.00hrs) starting no earlier than 18.00hrs on Day +1 (If epidural catheter present, once daily dosing is preferable).

- This protocol does not replace the need for thrombosis risk assessment (TRA). All patients should have a TRA on admission
- NOAC can be restarted before Day +3, in procedures with low risk of post op bleeding, at surgeon's discretion (instead of Enoxaparin 150 units/kg OD)
- Check renal function preoperatively. These drugs are renally excreted. If eGFR <30 ml/min, seek advice.
- Spinal anaesthesia is acceptable if >48hours since last dose of Dabigatran and eGFR >50 ml/min/1.73m$^{2.}$
  Spinal anaesthesia is acceptable if >48 hours since last dose of Apixaban, Rivaroxaban, Edoxaban and eGFR >30 ml/min/1.73m^2.
  For other situations seek advice