Guideline Number & Full Title:	2854 - Guideline for Adult Patients taking Oral Vitamin K Antagonist Therapy Undergoing Planned, Non-cardiac, Non-neurosurgical Surgical Intervention
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Scope:	Anaesthetists, Surgeons, Haematologists, Physicians, pre-operative assessment nurses
Review date:	April 2025
Explicit definition of patient group to which it applies:	Adult patients taking oral vitamin K antagonist (VKA) therapy who require an planned surgical procedure or intervention which requires interruption of VKA treatment Exclusions: • Patients requiring emergency surgery • Patients taking any of the direct oral anticoagulant drugs, rivaroxaban (Xarelto®), dabigatran (Pradaxa®), apixaban (Eliquis®) or edoxaban (Lixiana®) • Patients taking oral anti-platelet agents • Children or pregnant patients • Patients undergoing neurosurgical intervention • Patients undergoing cardiac surgery or implantable cardiac devices • Patients in the critical care unit
Summary of evidence base this guideline has been created from:	See reference list in document
This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.	

Guideline for Adult Patients taking Oral Vitamin K antagonists undergoing planned, non-cardiac, non-neurosurgical surgical intervention

Scope

The purpose of this document is to provide recommendations for the management of peri-procedural anticoagulation for adult patients on warfarin therapy who require interruption of treatment to allow a surgical procedure or intervention. They are adapted from the guidelines by the American College of Chest Physicians (Douketis *et al*, 2012), the British Committee for Standards in Haematology (Keeling *et al*, 2016), review of the available literature (March 2022) and expert opinion.

This guideline may also be used for the management of patients who are on other vitamin K antagonists; acenocoumarol (Sinthrome®).

If regional analgesia/anaesthesia is planned, this guideline should be used in conjunction with NUH guidelines for the use of anticoagulants and antiplatelet medicines alongside epidural analgesia in adults http://nuhnet/nuh_documents/Guidelines/Specialist%20Support/Anaesthesia/2717.pdf

This document provides general guidance only and is not a substitute for clinical judgment of an individual patient. Patients in whom there are specific concerns regarding thrombosis or bleeding risk should always be discussed with a haematologist when making a preoperative anticoagulation plan

Exclusions

- Patients requiring emergency surgery
- Patients taking any of the direct oral anticoagulant drugs, rivaroxaban (Xarelto®), dabigatran (Pradaxa®), apixaban (Eliquis®) or edoxaban (Lixiana®) – see NUH Guidelines for the perioperative management of patients taking Direct Oral Anticoagulants (DOACs) http://nuhnet/nuh_documents/Guidelines/Cancer%20and%20Associated%20Specialties/Clinical%20Haematology/2782.pdf
- Patients taking oral anti-platelet agents
- Children <18 years of age or pregnant patients
- Patients undergoing neurosurgical intervention
- Patients undergoing cardiac surgery or implantable cardiac devices
- Patients in the critical care unit

Summary: Perioperative guideline for patients receiving vitamin K antagonists who require surgical intervention

Identify indication for anticoagulation

Pre-operatively; Risk stratify the patient

Discuss with a haematologist if:
- VTE within 3 months
- Antiphospholipid syndrome + VTE
- Antithrombin deficiency or multiple thrombophilic abnormalities
- Unable to receive LMWH or previous heparin induced thrombocytopenia

(QMC SpR on call via switchboard)

	Mechanical Heart Valves (MHV)	Atrial Fibrillation (AF)	Venous Thrombosis (VTE)
High Risk	• All mechanical mitral heart valves • All mechanical valves + previous valve thrombosis • All mechanical valves + stroke/TIA within 6 months • Modern bileaflet aortic valve prosthesis and another risk factor: – atrial fibrillation – prior stroke or TIA, hypertension – diabetes – congestive cardiac failure – Age >75 years	• Previous stroke/TIA within 3 months. • Previous stroke/TIA and three or more of the following risk factors: – Congestive cardiac failure – Hypertension (>140/90 mmHg or on medication) – Age >75 years – Diabetes mellitus	• VTE within 3 months • Antiphospholipid syndrome + VTE (See above re d/w Haematology) • Recurrent VTE • VTE with pulmonary hypertension • VTE + active cancer (treated within 6 months or palliative) • Target INR 3-4
Standard Risk	• Modern bileaflet aortic valve prosthesis without AF and no other risk factors for stroke • Mitral/aortic/tricuspid biological replacement valves or repair without AF	• Low risk AF with none of the above risk factors	• VTE > 3 months previously with no other risk factors

Therapeutic bridging required
Use high risk template 1

No bridging required
Use standard risk template 2

For all patients in addition to templates 1 - 2

- For patients with renal impairment see section 1.4 for bridging advice
- If regional anaesthesia has been used refer to NUH guidelines http://nuhnet/nuh_documents/Guidelines/Specialist%20Support/Anaesthesia/2717.pdf
- If the patient is NBM or expected to have reduced oral absorption, continue with Enoxaparin until oral treatment can be resumed
- Platelet count should be monitored every 3 days to check for the development of HIT
- If renal function has deteriorated, the Enoxaparin dose should be adjusted appropriately
- Ensure that the patient has not been started on any drug which could interact with a Vitamin K antagonist
- Ensure referral to anticoagulation clinic or primary care at discharge for ongoing INR monitoring

Perioperative treatment template 1: Bridging anticoagulation for elective surgery for patients who are considered to be HIGH risk for thromboembolism

This template is intended to be used for (non-pregnant) adult patients taking warfarin who are considered HIGH risk for thromboembolism who require elective surgery or invasive procedures. Bridging anticoagulation with enoxaparin is required.

Pre-operatively

- Take last dose of warfarin 5 days pre-op (leave 5 clear days)
  If taking acenocoumarol (Sinthrome) this should be stopped 4 days pre-op
- Commence **treatment dose*** subcutaneous enoxaparin 3 days pre-operatively (See dosing guidance below)
- The last dose of enoxaparin should be taken >24 hours before the operation
- Check INR on the morning of the procedure and review before proceeding

Postoperatively

Postoperative anticoagulation should not be re-started until the patient has been assessed by a doctor, haemostasis is secure and it is safe to restart

- If low risk of post-operative bleeding
  - Consider giving enoxaparin at a weight appropriate prophylactic dose, 6 hours post operatively **provided that haemostasis is secure**
  - Increase to therapeutic enoxaparin the following morning
- If post-operative bleeding risk is high
  - Consider starting prophylactic enoxaparin as soon as haemostasis is secure
  - Do not recommence therapeutic enoxaparin until at least 48 hours post op
  - If there is ongoing bleeding risk, therapeutic enoxaparin should not be recommenced
- Restart warfarin (or acenocoumarol) at the **usual maintenance dose (no loading dose)** the day after therapeutic enoxaparin has been commenced
  - If there is a risk of re-bleeding or return to theatre, do not commence warfarin until this risk is no longer present
- Continue Enoxaparin with warfarin (or acenocoumarol) until the INR is within range.
- Prior to discharge, contact the anticoagulation team and ensure arrangements have been made for ongoing INR monitoring.
- Ensure attention to hydration, mobilisation and use of antiembolic stockings (if indicated) as for routine thromboprophylaxis.

***Dosing of Therapeutic Enoxaparin for therapeutic bridging**

Indication for bridging	Dose of therapeutic bridging anticoagulation
Mechanical Heart Valves Antiphospholipid syndrome + VTE Antithrombin deficiency + VTE	Enoxaparin 1mg/kg twice daily
All other indications	Enoxaparin 1.5mg/kg once daily (weight <150kg) Enoxaparin 1mg/kg BD (weight ≥150kg)

The above plan assumes that the patient has normal renal function and platelet count. See section 1.4 for advice on bridging anticoagulation in patients with renal impairment

Perioperative Treatment Template 2: Elective surgery for patients who are considered to be STANDARD risk for thromboembolism

This template is intended to be used for patients taking warfarin who are considered <u>STANDARD</u> risk for thromboembolism. Bridging with therapeutic enoxaparin is not required; enoxaparin is given for thromboprophylaxis only.

<u>Pre-operatively</u>

- Take last dose of warfarin 5 days pre-op (leave 5 clear days)
  If taking acenocoumarol (Sinthrome) this should be stopped 4 days pre-op
- No enoxaparin needed pre-operatively
- Check INR on the morning of the procedure and review before proceeding

<u>Postoperatively</u>

Postoperative thromboprophylaxis should not be re-started until the patient has been assessed by a doctor, haemostasis is secure and it is safe to restart

- If low risk of post-operative bleeding commence enoxaparin at a weight appropriate prophylactic dose 6 hours post operatively
- If post-operative bleeding risk is high, enoxaparin prophylaxis should not be started until haemostasis is secure.
- Once haemostasis is secure, and there are no plans to return to theatre recommence warfarin (or acenocoumarol) at the **usual maintenance dose (no loading dose)**
- For patients with previous VTE, enoxaparin thromboprophylaxis should be continued until the INR is in the therapeutic range
- For patients with standard risk AF, enoxaparin can be stopped at discharge, unless the surgical procedure necessitates extended thromboprophylaxis
- Prior to discharge, contact the anticoagulation team and ensure arrangements have been made for ongoing INR monitoring.
- Ensure attention to hydration, mobilisation and use of anti-embolic stockings (if indicated) as for routine thromboprophylaxis.

The above plan assumes that the patient has normal renal function. See section 1.4 for advice on bridging anticoagulation in patients with renal impairment

Please Note;
It is the responsibility of the treating team to implement these plans; this includes counselling and informing the patient of the plan, prescribing any necessary medication and referral of the patient back to the anticoagulation clinic/GP when discharged from hospital for ongoing.

If an epidural catheter or spinal anaesthetic will be used, please also see NUH Guidelines for the use of anticoagulants and antiplatelet medicines alongside epidural analgesia in adults

Perioperative treatment template 3: To be used if IV UFH is required for perioperative bridging anticoagulation

This template is intended to be used for patients taking warfarin who require IV unfractionated heparin bridging. This is predominantly patients with renal impairment (see section 1.4)

Pre-operatively

- Take last dose of warfarin 5 days pre-op (leave 4 clear days)
  If taking acenocoumarol (Sinthrome) this should be stopped 4 days pre-op
- Admit to hospital d-3 and check INR
- When INR falls below target range commence IV unfractionated heparin infusion
  - Check APTTr 4 hours after starting infusion and adjust rate as per as per infusion chart
- Check the INR the day before operation
  - If remains significantly elevated discuss with cardiac surgery team for consideration of IV vitamin K
- Stop IV UFH infusion 6 hours pre operatively
- Check INR on the morning of the procedure to ensure this has normalised before proceeding

Postoperatively

Postoperative anticoagulation should not be re-started until the patient has been assessed by a doctor, haemostasis is secure and it is safe to restart

- Commence IV UFH as soon as the surgical team are happy it is safe to do so and when haemostasis is secure
  - Do **not** give the loading bolus dose
  - Check APTTr 4 hours after starting infusion and adjust rate as per as per infusion chart
- Restart warfarin (or acenocoumarol) at the **usual maintenance dose (no loading dose)** the day after the operation
  - If there is a risk of re-bleeding or return to theatre, do not commence warfarin until this risk is no longer present
- Continue IV UFH with warfarin (or acenocoumarol) until the INR is within range.
- Prior to discharge, contact the anticoagulation team and ensure arrangements have been made for ongoing INR monitoring.
- Ensure attention to hydration, mobilisation and use of antiembolic stockings (if indicated) as for routine thromboprophylaxis.

1. Specialist advice for perioperative planning

1.1 Haematology

Patients who are particularly complicated or high risk for thrombosis or bleeding can be discussed with the haematology team in advance of the procedure. Patients for whom additional advice may be required include:

- Patients at high risk of bleeding or thrombosis
- Patients with high risk thrombophilia (antithrombin deficiency or multiple thrombophilic defects) or antiphospholipid syndrome
- VTE which has occurred within 3 months of elective surgery
- Patients with heparin allergy or previous heparin induced thrombocytopenia
- Patients with active malignancy and recent thrombosis
- Patients with significant thrombocytopenia
    - Whether bridging with enoxaparin is appropriate requires review in patients with a platelet count less than 75. This can usually continue whilst platelet count remains above 50, unless the operation has a high risk of post operative bleeding. Advice can be sought from haematology as needed.
    - If the platelet count falls below 50, enoxaparin bridging may no longer be appropriate; discussion with haematology is advised.
- Patient with severe renal impairment of undergoing renal replacement therapy; please discuss with the renal team before contacting haematology

It may not be possible to offer advice for patients referred from other trusts due to lack of clinical information; peri-operative anticoagulation advice in these instances must be sought from the patient's local treating team.

The haematology team should be contacted by bleeping the Haematology StR on call based at QMC. In rare cases, it may be necessary to formally review the patient in clinic in order to make a safe anticoagulation plan; there can be several weeks delay in arranging a haematology clinic appointment and therefore early referral is advised in these cases.

1.2 Patients with Mechanical Heart Valves

Patients with mechanical heart valves who require additional advice for perioperative planning should be discussed with the cardiac surgery team in advance of the operation

In this instance the cardiac surgery StR on call should be contacted for advice on 07812275357

For patients with prosthetic heart valves, it is essential that accurate information is available to assess the thrombotic risk for an individual patient in the event that anticoagulation needs to be interrupted for a surgical procedure.

Information required will be:

- Type and site of prosthetic valve – check NoTis letter from cardiac surgery team as this is usually documented
- Any other cardiac and non-cardiac co-morbidities eg previous stroke or embolization
- Target INR/range – this information is available on NoTis (documented below the INR results from anticoagulation clinic)

Patients with modern bileaflet aortic valves are low risk for thrombosis and do not require bridging anticoagulation unless they have additional risk factors. All patients who have had an aortic valve sited in Nottingham since 2010 will have a modern valve

Ideally the ***team planning the surgery*** should obtain relevant information from the patient's cardiac surgeon at the time the patient is listed for surgery.

Patients with prosthetic heart valve surgery performed in childhood

Patients who have had their surgery performed outside Nottingham frequently do not have information regarding their valves available in their local record to assess thrombotic risk accurately. Many patients in the East Midlands will have had their surgery performed at Glenfield Hospital, Leicester. A paediatric cardio-thoracic surgeon is available 24 hours a day for advice on these patients

In the situation where there is no information available on the type of valve in situ, the patient should be bridged according to the high risk template with therapeutic enoxaparin.

1.3 Stroke Medicine

Patients who are particularly complex should be discussed with the stroke physician on call (contact via stroke Unit). Examples include:

- The patient needs anticoagulation but has recently suffered a cerebral haemorrhage
- The patient is taking anticoagulants for cerebral venous sinus thrombosis.
- Recent stroke (within the previous 3 months)

It is advisable to discuss these patients as soon as the patient is listed for surgery so as to avoid delay to the surgical procedure.

1.4 Dosing of Enoxaparin in Patients with Renal Impairment

Low molecular weight heparins are excreted renally and therefore dosing of any bridging Enoxaparin requires further consideration in patients with renal impairment.

All patients should have a Cockroft Gault creatinine clearance calculated. If bridging anticoagulation is required, Enoxaparin should be dosed as shown in table 1 and 2

Creatinine clearance (ml/min)	**PRE operative management**
<15 or renal dialysis	Discuss with renal team preoperatively for specific perioperative plan
15-30 (non mechanical valve patients)	Do not give any pre operative LMWH bridging
15 – 30 (Patients with mechanical valve)	Bridge with Enoxaparin using doses as per NUH guideline*
>30	Bridge with Enoxaparin using doses as per NUH guideline*

Table 1: Pre operative management of Enoxaparin in patients with renal impairment

Creatinine clearance (ml/min)	**POST operative management**
<15 or renal dialysis	Discuss with renal team preoperatively for specific perioperative plan
15-30 Low post operative bleeding risk	Bridge with Enoxaparin using doses as per NUH guideline*
15 – 30 High post operative bleeding risk	Consider bridging with IV unfractionated heparin (template 3) if post op bleeding risk is high.
>30	Bridge with Enoxaparin using doses as per NUH guideline*

Table 2: Post operative management of Enoxaparin in patients with renal impairment

*Weight and renal function appropriate guidance for dosing of Enoxaparin in patients with renal impairment can be found at http://nuhnet/nuh_documents/Guidelines/Cancer%20and%20Associated%20Specialties/Clinical%20Haematology/2248.pdf

There is a risk of accumulation of Enoxaparin in patients with renal impairment which may increase risks of bleeding. It is therefore important that these patients are converted back onto warfarin as soon as it is safe to do so.

Anti Xa levels are not routinely required for most patients as they will be receiving Enoxaparin for a short time. Anti Xa levels should be monitored in patients with renal impairment if

- Unexpected bleeding occurs
- The patient remains on Enoxaparin at 7 days post operatively
- Levels of Anti Xa to aim for are;
    - Prophylaxis 0.2 – 0.4
    - Treatment 0.6 – 1.2

The table and information above provides general guidance only and is not a substitute for clinical judgment. If the patient has borderline renal function, particularly if they are planned for an operation or procedure which has an associated high bleeding risk then further advice should be sought from the renal team.

2. Bridging anticoagulation in patients with mechanical heart valves

Guidelines for the perioperative management of patients with mechanical heart valves (MHV) differ in their advice with regards to the bridging anticoagulation used.

The European Society of Cardiology Guidelines for valvular disease (2021) state;
In patients with mechanical heart valves, preoperative bridging with UFH or LMWH before surgery imposes a risk of perioperative bleeding while interrupting anticoagulation results in an increased risk of thromboembolism. Therefore, anticoagulation in patients with MHVs undergoing elective NCS requires careful management by multidisciplinary consensus. For minor surgical procedures (e.g. dental, cataract, skin incision) in which blood loss is usually small and easily controlled, it is recommended that oral anticoagulation is not interrupted. Major surgeries require temporary interruption and therapeutic bridging with either UFH or LMWH, aiming for an INR <1.5. Fondaparinux should not be routinely used for bridging, but may have a role in patients with history of heparin-induced thrombocytopenia

The British Society of Haematology (BSH) Guidelines (2011) recommend; *If bridging therapy is given it is now usually with LMWH. This is effective in VTE prevention but there are fewer data for using LMWH in patients with AF or a MHV and it appears to be less effective than warfarin in MHV patients*
The updated guideline in 2016 did not make any changes to this recommendation and added advice with regards to stopping LMWH pre operatively.

The American College of Chest Physicians (ACCP) Guidelines (2012) gives recommendations on bridging anticoagulation vs no bridging anticoagulation and discussed both LMWH and IV UFH but does not give specific recommendations regarding one regimen in preference to another. The updated guidance in 2019 did not alter this recommendation.

Recent publications in the literature have sought to address the question as to whether IV UFH or LMWH is preferable for patients with MHV. A meta analysis by Caldeira (2014) considered 10 studies of 1042 patients with MHV. They concluded that LMWH was effective and safe for temporary use in patients with MHV in terms of thromboembolic risk. Spyropoulos (2008) looked at perioperative bridging anticoagulation in 901 patients, 246 of whom had MHV. 83% of patients were bridged with enoxaparin and there was no significant different in thromboembolic risk between patients treated with LMWH and IV UFH with a trend to less bleeding in the LMWH treated patients.

PERIOP-2 was a randomised control trial published in 2018 explored the efficacy and safety of postoperative LMWH bridging of patients with atrial fibrillation or a mechanical heart valve who required interruption of warfarin for a planned procedure. All patients received pre op bridging therapy. There was however no benefit from post-procedure LMWH bridging in terms of thrombotic outcome.

Audit data within Nottingham (2018) shows that the management of IV UFH is poor; the time in treatment range for patients locally who have been treated with IV UFH is only 50%. The remainder of patients are being under and over anticoagulated which presents either a thrombotic or bleeding risk respectively. Having reviewed local audit data along with the best available data in the literature, we have agreed that the use of LMWH is a safe approach for most patients. Although this involves the 'off label' use of LMWH we believe this is the best option. The highest risk patients will be discussed with the cardiac surgery team and an individualised management plan made which may include the use of IV UFH.

3. Further information for the interested reader

The peri-procedural management of patients receiving oral anticoagulant therapy is based upon an individual assessment of each patient for the risk of a thromboembolic event when anticoagulation is interrupted balanced against the perioperative bleeding risk when anticoagulation is continued. Consideration of these risks will determine whether anticoagulation needs to be stopped peri-procedurally, and if so, whether bridging therapy is required.

- If the risk of procedure related bleeding whilst continuing oral anticoagulation is thought to be small, anticoagulation may be continued

- If the risk of procedure related bleeding is thought to outweigh the risk of thromboembolic events, anticoagulation should be stopped and bridging anticoagulation considered depending on the thrombotic risk.

Bridging anticoagulation therapy is administered to cover the period of time off oral anticoagulation with an alternative, short acting anticoagulant; usually low molecular weight heparin (LMWH). For the purposes of this guideline, 'bridging anticoagulation' refers to treatment with therapeutic doses of LMWH. Enoxaparin is the drug of choice within NUH. Bridging aims to minimise the risk of arterial thromboembolism such as stroke or systemic embolism in patients with mechanical heart valves or atrial fibrillation (AF) and to minimise the risk of recurrent thrombosis in patients with previous venous thrombo-embolism (VTE).

There is little evidence in the literature and few large trials to guide optimum management of perioperative anticoagulation; much advice is based on expert opinion. The lack of evidence needs to be borne in mind when making treatment decisions for this group of patients.

Some patients are taking antiplatelet agents in combination with a vitamin K antagonist; either single or dual antiplatelet therapy. Risk of thromboembolism is based on the clinical indication for the drug. It is important that there is a clear assessment regarding whether these agents should be continued peri-operatively or temporarily interrupted.

3.1 Assessing thrombotic risk

Patients with venous thrombosis (VTE)

It takes approximately 3 months to treat an acute venous thrombotic event and the risk of recurrent thrombosis is higher if anticoagulation treatment is discontinued during this time (Kearon 2014). Risk of recurrence is also higher in patients in whom the initial VTE event was unprovoked, patients with recurrent events or persistent risk factors for thrombosis and in patients with antiphospholipid syndrome. The severity of the initial event also needs to be borne in mind; for example patients with a severe PE associated with pulmonary hypertension (even if >12 months ago) are at higher risk.

Patients with atrial fibrillation (AF)

Patients with arterial indications for anticoagulation such as AF are at increased risk of stroke in the absence of anticoagulation. In patients with non-valvular AF the $CHADS_2$ and CHADSVasc scoring systems have been validated to give an estimation of stroke rate per 100 patient years in a non-surgical setting (see appendix 1, tables 3 and 4). Preliminary data suggests that the $CHADS_2$ score can be used to predict stroke risk postoperatively (Spyropoulos 2012). If the annual risk of stroke in untreated AF is 4% per annum, this will translate to approximately 0.5 events per 1000 patients who have 5 days without anticoagulation. For AF with previous stroke, the figures are approximately 12% per annum or approximately 1.6 cases per 1000 patients for 5 days without anticoagulation. However, typical rates of peri-operative arterial thromboembolism that have been reported are much higher than these calculated figures (Keeling 2011). Patients at highest risk for stroke are those with a previous stroke/TIA or rheumatic valvular heart disease

Patients with mechanical heart valves (MHV)

Patients with MHV are at increased risk of systemic embolisation or valve thrombosis if anticoagulation is interrupted. Older, caged-ball valves (ie, Starr-Edwards) are the most thrombogenic, followed by tilting disc valves (ie, Bjork-Shiley), and with bileaflet valves (ie, St Jude) being the least thrombogenic. In addition, valves in the mital position have a higher thrombotic risk than those in the aortic position. Patients with prosthetic valves with other risk factors for embolization (such as prior embolic event, severe left ventricular dysfunction, AF and an underlying hypercoagulable state) are also considered at high risk for thrombosis.

Biological tissue valve replacements or repair are associated with a low risk of thrombosis and therefore bridging with enoxaparin is not required.

3.2 Stratifying the risk

A higher thromboembolic risk increases the importance of minimising the interval without anticoagulation. A suggested strategy for assessing baseline thrombotic risk was published by the American College of chest Physicians in 2012 (Douketis and Spyropolous, 2012) and is shown in table 3. This stratified patients into high, moderate or low based on the indication for anticoagulant therapy although this remains unvalidated. In this suggested risk classification, patients classified as high risk have a 10% annual risk for thromboembolism, moderate risk have a 5-10% annual risk for thromboembolism and low risk have <5% annual risk for thromboembolism whilst off anticoagulation.

Table 3: Risk stratification based on indication for anticoagulation

Risk	Prosthetic Valves	AF	VTE
High	• Any mitral valve prosthesis • Any caged ball or tilting disc aortic valve prosthesis • Stroke/TIA within 6 months	• $CHADS_2$ score of 5 or 6 • Recent (within 3 months) stroke or TIA • Rheumatic valvular heart disease	• Recent (within 3 months) VTE • High risk thrombophilia (eg, deficiency of protein C, protein S, or antithrombin, antiphospholipid antibodies or multiple abnormalities (eg homozygous factor V leiden, compound heterozygosity)
Moderate	• Bileaflet aortic valve prosthesis and one or more of following risk factors: – AF – prior stroke or TIA, – hypertension – diabetes – congestive cardiac failure – age >75 years	$CHADS_2$ score of 3 or 4	• VTE within the past 3-12 months • Other thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 months or palliative)
Low	• Bileaflet aortic valve prosthesis without AF and no other risk factors for stroke	• $CHADS_2$ score of 0 to 4 (assuming no prior stroke or TIA)	• VTE > 12 months previous and no other risk factors

It is also important to consider general risk factors for thrombosis which may increase thrombotic risk. These include:

- Active cancer or cancer treatment
- Age > 60 years
- Critical care admission
- Dehydration
- Known thrombophilia or antiphospholipid syndrome
- Obesity (body mass index [BMI] over 30 kg/m^2)
- One or more significant medical comorbidities (for example: heart disease; metabolic, endocrine or respiratory pathologies; acute infectious diseases; inflammatory conditions, nephrotic syndrome, myeloproliferative disorders)
- Personal history or first-degree relative with a history of VTE
- Use of hormone replacement therapy or oestrogen-containing contraceptive therapy
- Varicose veins with phlebitis or leg ulcers
- Immobilisation (>48 hours pre-op, >24 hours post op)
- Non-weight bearing lower limb procedure or plaster cast
- Pregnancy or within 2 months of delivery

A limitation of the risk stratification described above is that individual patient factors may increase thrombotic risk, for example some patients will have multiple risks within each category. The type of surgery which a patient is to undergo also needs to be considered as variability exists in the risks of stroke and thrombosis with different surgical procedure.

Assessment of peri-operative thromboembolic risk therefore needs to be individualised, taking into consideration both the estimated baseline risk, the individual factors related to the patient and the surgery or procedure type.

3.3 Assessing bleeding risk

Surgery with a low risk bleeding includes procedures for which bleeding, if it occurs, will be minor, non-critical in its location and/or easily controlled by simple mechanical haemostasis.Conversely, high risk bleeding surgery includes all procedures for which the probability of clinically significant bleeding cannot be excluded, any surgery that is usually haemorrhagic or for which the consequences of bleeding would be unacceptable.

A higher bleeding risk confers a greater need for perioperative haemostasis and hence a longer period of anticoagulation interruption. Stratification of bleeding risk in the context of perioperative anticoagulation and bridging therapy is difficult because the available evidence is based mainly on case series involving selected types of surgery. All patients should be assessed by the surgical team with regards to the bleeding risk of the planned procedure. Further consideration should be given if the patient is also taking an antiplatelet agent regarding whether this needs to be continued or stopped; see section on antiplatelet agents.

3.4 Bridging anticoagulation therapy

If bridging therapy is given it is now usually with LMWH. This is effective in VTE prevention but there are fewer data for using LMWH in patients with AF or a mechanical heart valve and it appears to be less effective than warfarin in mechanical heart valve patients (Chan 2000, Keeling 2012). Despite its widespread use, there is little evidence in the literature on which to base guidance for perioperative bridging therapy.

Pre-operative bridging therapy carries a low risk of perioperative bleeding assuming an appropriate delay between the last dose of anticoagulant and the timing of surgery. Post-operative bridging however needs careful consideration as it increases the risk of bleeding, particularly in surgeries with a high risk of bleeding (Dunn 2007, Steinberg 2012, Seigal 2012).

A recent large randomised control trial assessed the impact of bridging therapy in patients with AF (Douketis 2015). The incidence of arterial thromboembolism was 0.4% in the no-bridging group and 0.3% in the bridging group. However the incidence of major bleeding was 1.3% in the no-bridging group and 3.2% in the bridging group suggesting that bridging therapy had no overall benefit in this group of patients. A limitation of the study was that few patients had a $CHADS_2$ score or 5 or 6 hence the highest risk patients were under-represented in their data. A further clinical trial (PERIOP 2) A Double Blind Randomized Control Trial of Post-Operative Low Molecular Weight Heparin Bridging Therapy Versus Placebo Bridging Therapy for Patients Who Are at High Risk for Arterial Thromboembolism is currently in progress and due to report in 2020. This may further guide management.

Until further trial data is available, recommendations for perioperative bridging are based on the available evidence and expert opinion.

In deciding whether a patient requires bridging anticoagulation, patients should be stratified into high, moderate or standard risk based on the summary flowchart

For emergency surgery where it is not possible to stop anticoagulation in advance of the procedure – see guidelines on Management of excessive anticoagulation in adults
http://nuhnet/nuh_documents/Guidelines/Cancer%20and%20Associated%20Specialties/Clinical%20Haematology/2401.pdf
For patients requiring surgical intervention within 4 weeks of acute VTE, consideration should be given to delaying any elective surgical procedures. If surgery is urgent, an IVC filter may be necessary; this should be discussed with a haematologist.

3.5 Postoperatively

- Post operative anticoagulation should only be started once the patient has been assessed by a Doctor and it is deemed safe to restart.
- Always ensure attention to hydration, mobilisation and use of anti-embolic stockings (if indicated) as for routine thromboprophylaxis
- If the patient is nil by mouth or expected to have reduced oral absorption, enoxaparin should be continued until oral treatment can be resumed
- Low molecular weight heparin is renally excreted and therefore dose adjustment may be required in patients who have developed renal impairment. (see appendix 2 regarding dosing of enoxaparin in renal impairment)
- Patients who weigh >100kg require increased doses of enoxaparin prophylaxis; see NUH guideline http://nuhnet/nuh_documents/Guidelines/Cancer%20and%20Associated%20Specialties/Clinical%20Haematology/2248.pdf
- Spinal/neuroaxial anaesthesia/analgesia carries additional risk in terms of development of spinal haematoma – see Guideline for the use of anticoagulants and antiplatelet medicines alongside epidural analgesia in adults http://nuhnet/nuh_documents/Guidelines/Specialist%20Support/Anaesthesia/2717.pdf
- The baseline platelet count should be checked prior to starting enoxaparin and repeated post operatively every 3 days (if therapy is continued) for the development of heparin induced thrombocytopenia (HIT). If the platelet counts falls, see NUH guidelines for the diagnosis and management of HIT for further advice and discuss with a haematologist
- Ensure that the patient has not been started on any drug which could interact with a Vitamin K antagonist
- Patients being discharged on warfarin should be referred to the NUH anticoagulation team for discharge dosing and arrangement of ongoing anticoagulant monitoring; this can be done via nervecentre.

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