NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Management plan for patients on warfarin and direct oral anticoagulants (DOACs) in the peri-operative period

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The online version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Management plan for patients on warfarin and direct oral anticoagulants (DOACs) in the peri-operative period

Contents

1) Introduction

Scope of guideline

For the purpose of the guideline, the following clinical situations are not covered:

- neurosurgery
- vascular surgery
- orthopaedic trauma
- pregnancy and 6 weeks post-partum
- interventional radiology patients
- paediatrics

This guideline aims to balance the competing risks of thrombosis versus haemorrhage, which occurs in the peri-operative period for patients anticoagulated with warfarin or direct oral anticoagulants (DOACs). In doubtful cases it is usually safer to omit anticoagulant drugs rather than over treat, but each case needs individual assessment. Consult senior colleagues and/or seek Haematology advice promptly in unclear cases.

2) Haemorrhage and Emergency Invasive Procedures

Most anticoagulated patients admitted with trauma, major bleeding or for emergency surgery, have risks from haemorrhage that usually far outweigh the thrombotic risks (even in high thrombotic risk patients). Full and immediate anticoagulation reversal is required:

1. Check full coagulation screen, full blood count, INR (if on warfarin) and cross match blood.
2. Withhold warfarin or DOAC
3. Reverse anticoagulation fully and rapidly – guidance linked below.
    - Reversal of Antithrombotic Therapy
4. If any concerns or uncertainty, discuss with on-call haematologist.
5. Proceed to surgery as appropriate.
6. Only when you are sure the risk of bleeding has abated, re-anticoagulate as appropriate using the patient's thrombotic risk category (as per the recommendations below).

3) Elective Procedures

3a) Risk stratification

Invasive procedures can be classified according to their bleeding risk and patients can be classified according to the thrombosis risk of their underlying conditions. These two factors need to be considered to determine the most appropriate management throughout the peri-operative period. Tables 1-3 below should be used to categorise the bleeding and thrombosis risk for individual patients.

N.B. Some patients or procedures may not be easily classified into the following categories - if so, they should be discussed with the relevant senior clinician (e.g. haematologist, cardiologist, surgeon).

Table 1 – List of procedures categorised by bleeding risk

Low risk of bleeding:

- Standard dental procedures e.g. simple extractions <4 teeth
- Routine upper gastrointestinal (GI) endoscopy or colonoscopy including simple biopsy (unless part of the national bowel cancer screening programme - see below)
- Cataract extraction and lens implantation
- Bone marrow biopsy
- Joint injections (refer to separate guideline available here)

High risk of bleeding:

- Any colonoscopy performed as part of the national bowel cancer screening programme, polypectomy, endoscopic treatment of varices, or ERCP
- Most formal surgical procedures
- Anaesthesia involving spinal or epidural anaesthetic

Extremely high risk of bleeding:

- Neurosurgical interventions

Table 2 – List of conditions categorised by thrombosis risk

Low risk of thrombosis:

- Atrial fibrillation with CHA_2DS_2-VA score < 5 (with exceptions below)
- Venous thromboembolism >3 months previously (including patients with recurrent VTE)

High risk of thrombosis:

- Atrial fibrillation
    - within 3 months of a stroke, TIA or embolism
    - with CHA_2DS_2-VA score ≥ 5 (see table 3 below)
    - with moderate or severe mitral stenosis irrespective of CHA_2DS_2-VA score
- Venous thrombosis
    - within previous 3 months
    - with known high risk thrombophilia (e.g. deficiencies of Protein C, S, antithrombin; antiphospholipid syndrome)
- Prior recurrent venous thrombosis on warfarin with target INR 3.5

Extremely high risk of thrombosis:

- Mechanical heart valve in any position.

Table 3 – CHA_2DS_2-VA Score

Condition	**Points**
Congestive Heart Failure	1
Hypertension	1
Age ≥ 75	2
Age 65-74	1
Diabetes Mellitus	1
Stroke/TIA/Thromboembolism history	2
Vascular disease (prior MI, peripheral arterial disease, aortic plaque)	1

3b) Elective procedures with high risk of bleeding

N.B. For elective procedures with a very high risk of bleeding (e.g. neurosurgery), consult the appropriate senior colleague (do not apply recommendations below)

WARFARIN

- For pre-operative management, see Table 4 on page 8

- For post-operative management, see Table 5 on page 9

DOACs

- For time frame between last dose of DOAC and procedure with high bleeding risk, see Table 6 on page 10

- For peri-operative management, see Table 7 on page 11

********For prophylactic and therapeutic dose Low Molecular Weight Heparin dosing advice, please see Appendix 1 *********

Table 4 Management of patients undergoing procedure with high risk of bleeding in the pre-operative period on **warfarin**		
5 Days before procedure		
Low risk of thrombosis	**High risk of thrombosis**	**Extremely high risk of thrombosis**
Stop warfarin (i.e. omit 5 doses prior to procedure). No pre-op LMWH is required.	Stop warfarin (i.e. omit 5 doses prior to procedure). Organise the prescription and administration of **therapeutic dose LMWH** for days -3, -2 and -1 in the morning. [1] (The final dose to be administered in the morning the day before surgery)	Stop warfarin (i.e. omit 5 doses prior to procedure). Organise the prescription and administration of **therapeutic enoxaparin 1mg/kg TWICE DAILY** for days -3, -2 and -1 for 5 doses[1] Do not exceed single dose of 150mg. (The final dose to be administered in the morning the day before surgery).
Pre-operative anticoagulation Day -3, & -2		
No pre-op LMWH is required. In the unplanned/acute setting, warfarin may be withheld pending a procedure. In this case, prophylactic dose LMWH would be appropriate when INR <2.0	**Therapeutic dose LMWH** in the morning between 8am and 10am	**Therapeutic dose enoxaparin 1mg/kg TWICE DAILY**.
Pre-operative day -1		
No pre-op LMWH is required. Check INR. In the unplanned/acute setting, warfarin may be withheld pending a procedure. In this case, prophylactic dose LMWH would be appropriate when INR <2.0	**Therapeutic dose LMWH in the morning between 8am and 10am.** If dose cannot be administered before 10am it should be omitted. Check INR.	**Therapeutic dose enoxaparin 1mg/kg to be taken in the morning** between 8am and 10am. If dose cannot be administered before 10am it should be omitted. Check INR
Day of Procedure		
Ideally, patient should **not be 1st on the** operating list - this allows time for a day zero INR to be obtained prior to surgery if required. Recheck INR at 8am if not already ≤1.4 on day -1. Target INR for procedure is ≤1.4. If INR > 1.4 administer vitamin K (phytomenadione) IV 1mg as a single dose [2] and repeat INR		

1. LMWH should be prescribed and issued from secondary care, and the patient instructed on self-administration. [Ideally organised through Same Day Admission Unit]. The aim is for patients, or carers, to self-administer LMWH at home, however liaison with district nurse services may be required. Please ensure patients are given a sharps bin to safely dispose of LMWH syringes.
2. Use an insulin syringe to draw up 0.1 ml of phytomenadione 10mg/1ml before adding to 100ml glucose 5% bag and administering over 15-30 minutes.

Table 5 Management of patients undergoing procedures with high bleeding risk in the post-operative period in patients on **warfarin**		
Low risk of thrombosis	**High risk of thrombosis**	**Extremely high risk of thrombosis**
Day of Surgery: If adequate haemostasis, consider **prophylactic dose LMWH at 6pm** (or 4 hours post-op, whichever is later)		
Post-operative anticoagulation Day +1 and subsequent days: If bleeding risk remains high, consider **prophylactic dose LMWH at 6pm.** When bleeding risk is low (generally day 2 onwards), proceed as below. (If bleeding risk remains high in patients at extremely high risk of thrombosis on day 2, the case should be discussed with a cardiologist to allow the approach to bridging to be individualised)		
• Give **prophylactic dose LMWH at 6pm**. • Only after any epidural has been removed, restart warfarin as soon as safe and practicable (i.e. adequate gut function) with the patient's usual daily dose and monitor INR daily • Continue prophylactic dose LMWH until INR is ≥2, or patient ready for discharge if sooner	• **Give therapeutic dose LMWH at 6pm** ensuring 6h has elapsed from removal of an epidural if applicable before starting. • Only after any epidural has been removed, restart warfarin as soon as safe and practical (i.e. adequate gut function) with the patient's usual daily dose and monitor INR daily • Continue LMWH until INR is ≥2	• **Give therapeutic dose enoxaparin 1mg/kg TWICE DAILY** ensuring 6h has elapsed from removal of an epidural if applicable. Do not exceed single dose of 150mg. • Only after any epidural has been removed, restart warfarin as soon as safe and practical (i.e. adequate gut function) with the patient's usual daily dose and monitor INR daily • Continue enoxaparin until INR is ≥2
Post Discharge		
Stop prophylactic dose LMWH on discharge if INR not within therapeutic range. Arrange INR monitoring as appropriate.	Continue **therapeutic dose** LMWH on discharge until INR is ≥2. Arrange INR monitoring as appropriate.	Continue **therapeutic dose enoxaparin 1mg/kg TWICE DAILY** on discharge until INR is ≥2. Arrange INR monitoring as appropriate.

Table 6: Time frame between last dose of DOAC and procedure with high bleeding risk

CrCl (ml/min)	Apixaban, Edoxaban & Rivaroxaban	Dabigatran
≥ 80ml/min	Take the last dose three days before the procedure (e.g. Procedure on Wednesday take the last dose on Sunday)	Take the last dose three days before the procedure (e.g. Procedure on Wednesday take the last dose on Sunday)
50-80ml/min	Take the last dose three days before the procedure (e.g. Procedure on Wednesday take the last dose on Sunday)	Take the last dose four days before the procedure (e.g. Procedure on Wednesday take the last dose on Saturday)
30-50ml/min	Take the last dose three days before the procedure (e.g. Procedure on Wednesday take the last dose on Sunday)	Take the last dose five days before the procedure (e.g. Procedure on Wednesday take the last dose on Friday)
15-30ml/min	Take the last dose four days before the procedure (e.g. Procedure on Wednesday take the last dose on Saturday)	Contraindicated
< 15ml/min	Contraindicated	Contraindicated

Notes:

1. Factor Xa inhibitor drugs (apixaban, edoxaban and rivaroxaban) should be omitted for the timeframes above aiming for a normal prothrombin time (PT). NOTE: A normal PT does not exclude the possibility of therapeutic anticoagulant levels.
2. **Patients undergoing elective colonoscopy under bowel screening programme:**
    1. For patients on apixaban, edoxaban or rivaroxaban, there is no requirement to check renal function in line with table 6 above. Taking the last dose 3 days prior to the endoscopy is sufficient and in line with British Society of Gastroenterology Guidelines.
    2. Patients on dabigatran require an up to date calculation of renal function and the recommendations in table 6 followed as dabigatran is more affected by changes in renal function.

Table 7: Management of patients on **DOACs** in the perioperative period undergoing procedures with a high bleed risk	
Prior to Procedure	
Low risk of thrombosis	**High risk of thrombosis**
Stop DOAC prior to procedure in line with times in table 6 There is no need to give any LMWH pre-operatively in the elective setting. In the unplanned/acute setting, the DOAC may be withheld pending a procedure. In this case, prophylactic dose LMWH would be appropriate while the DOAC is withheld. LMWH should be started at 6pm, at least 24h after the last dose of DOAC.	Stop DOAC prior to procedure in line with times in table 6 There is no need to give any LMWH pre-operatively in the elective setting. In the unplanned/emergency setting, the DOAC may be withheld pending a procedure. In this case, the surgical team should consider whether to treat with **therapeutic dose LMWH** while the DOAC is withheld. LMWH should be started at 8am **at least** 24 hours after the last dose of DOAC. It should be discontinued at least 24 hours prior to the procedure.
Day of Procedure No monitoring is required prior to the procedure unless the timescales in table 6 have not been met[1].	
Post Procedure	
If adequate haemostasis, consider **prophylactic dose LMWH at 6pm** (or 4 hours post-op, whichever is later). This should continue the day following the procedure also. The DOAC can be considered for restarting 2 days following the procedure. If the team do not want to start the DOAC at this stage, prophylactic dose LMWH should continue until the patient is deemed suitable to restart the DOAC.	If adequate haemostasis, consider **prophylactic dose LMWH at 6pm** (or 4 hours post-op, whichever is later). This should continue the day following the procedure also. The DOAC can be considered for restarting 2 days following the procedure. If the team do not want to start the DOAC at this stage, prophylactic dose LMWH should be continued, or therapeutic dose LMWH can be considered, until the patient is deemed suitable to restart the DOAC.[2]
Restarting the DOAC	
The DOAC can be restarted after a minimum of 12h after the last dose of prophylactic LMWH and be based on the patient's usual dosing time. At least 6 h must have elapsed from removal of an epidural catheter before restarting the DOAC	The DOAC can be restarted no earlier than 12h after the last dose of prophylactic LMWH, with consideration given to the patient's usual dosing time. At least 6 h must have elapsed from removal of an epidural before restarting the DOAC If on treatment dose LMWH, the DOAC should be started no earlier than when the next dose of the LMWH is due.
*****DOAC and LMWH should not be prescribed concurrently*****	

1. If monitoring is required for apixaban, edoxaban or rivaroxaban, a desired level ≤ 25ng/ml measured by specific anti-Xa assay is required to proceed. A level above this should be discussed with haematology. For dabigatran, pre-operative assessment of routine coagulation screen may not accurately reflect the level of anti-coagulation, although a normal Thrombin Clotting Time (TCT) would imply negligible Dabigatran levels. If the time scales in table 6 below have not been met, discuss with haematology.

2. There might be instances, where the surgical team prefer to use LMWH post operatively at treatment doses rather than restarting the DOAC. This would be advantageous due to the shorter half-life of LMWH, allowing a shorter time period between the last dose and an unexpected surgical intervention being required. Examples where this may be desirable include: Increased bleed risk; potential need to return to theatre; oral route unavailable and acute kidney injury.

3c) Elective procedures with low risk of bleeding

Warfarin:

In general, standard dental procedures, routine endoscopy +/- simple biopsy, joint injections and cataract surgery can be undertaken without interrupting WARFARIN therapy. These patients should have their INR checked within 48 hours prior to surgery or intervention to ensure levels are not supra-therapeutic and are ideally <3.5.

DOACs:

Minor dental work

Dental procedures with low or no bleeding risk can usually be undertaken without interrupting DOAC therapy.

For procedures with a higher risk of bleeding the morning DOAC dose should be omitted.

The dental procedure should be undertaken early in the day, limiting the initial treatment area and assessing bleeding before continuing. Actively consider suturing or packing.

Post procedure:

For patients taking DABIGATRAN, EDOXABAN or RIVAROXABAN **once daily** in the evening, the evening dose should be taken at the usual time, but at least 4 hours after dental haemostasis has been achieved.

For patients taking APIXABAN or RIVAROXABAN **twice daily**, the deferred morning dose can either be omitted entirely or taken at least 4 hours after dental haemostasis has been achieved, providing the dose would not be taken within 6 hours of the next scheduled dose.

For patients taking DABIGATRAN **twice daily,** the deferred morning dose should be omitted and the evening dose should be taken at the usual time, but at least 4 hours after dental haemostasis has been achieved.

Joint injections

Refer to a Rheumatology specific guidance relating to joint injections available here.

Cataract Surgery and Endoscopy (excluding polypectomy or sphincterotomy)

The majority of patients taking DOACs should omit the DOAC on the morning of the procedure. Table 8 below shows the level of renal function that requires a longer period of omission. The next dose should be deferred until 4-6 hours post procedure (or longer if haemostasis has not been achieved)

Table 8: Time frame between last dose of DOAC and minor invasive procedure with low bleeding risk.

CrCl (ml/min)	Apixaban, Edoxaban, Rivaroxaban	Dabigatran
> 30ml/min	Take the last dose the day before the procedure (no later than 8pm)	Take the last dose in the morning the day before the procedure
≤ 30ml/min	Take the last dose two days before the procedure. E.g. For an endoscopy on Wednesday, the last dose should be taken on Monday.	Contraindicated

4) Special Considerations

4a) Neuro-axial anaesthesia (including spinal & epidural catheters)

Neuro-axial and deep local anaesthetic blocks should be considered as major invasive procedures for the purpose of this guidance. Catheter directed local anaesthetic techniques should not be used in patients anti-coagulated with LMWHs, WARFARIN or a DOACs unless the following conditions or timeframes are met:

Table 9: Timeframes and requirements between anticoagulant doses and neuro-axial anaesthesia

Anticoagulant	**Timeframe or requirement prior to insertion or removal of an epidural catheter or spinal/deep anaesthetic block**
Therapeutic dose LMWH	No earlier than 24h after last dose
Prophylactic dose LMWH	No earlier than 12h after last dose
DOAC	Follow timelines in Table 6 above
Warfarin	INR ≤1.4

Restarting anticoagulation after neuro-axial anaesthesia

• There should be an interval of at least 6 hours after the removal of an epidural catheter before the **reintroduction** of anticoagulation (DOAC, LMWH, or Warfarin) and frequent observations for neurological signs and symptoms of epidural haematoma must be made.

Lumbar puncture

Table 10: Timeframes and requirements between anticoagulant doses and lumbar puncture

Anticoagulant	**Timeframe or conditions prior lumbar puncture**
Therapeutic dose LMWH	No earlier than 24h after last dose
Prophylactic dose LMWH	No earlier than 12h after last dose
DOAC	When using Apixaban up to 10mg/day and Rivaroxaban up to 20mg/day, lumbar punctures can be performed 24 hours after last anticoagulant dose, as long as CrCl ≥50ml/min. For patients with creatinine clearance < 50ml/min or on dabigatran, the cases should be discussed with haematology.
Warfarin	INR ≤1.4

4b) Bridging therapy with unfractionated heparin (UFH), for high thrombotic risk patients, in the peri-operative period

Use of UFH may occasionally be preferable to using LMWH e.g. when the ability to ensure rapid and complete reversal of heparin is required, where significant renal impairment exists or where standard monitoring of heparin effect is necessary. If an UFH infusion is required, and the patient is already on therapeutic dose LMWH, the LMWH should be stopped and the UFH infusion started when the next dose of LMWH was scheduled.

1. Commence UFH according to the schedule detailed in the Drug Therapy section of the **Diagnosis and Treatment of Venous Thromboembolism guideline**.
2. Monitor APTT ratio and adjust UFH dose in line with the guideline above to achieve a result of 1.8-2.8.
3. Stop UFH 6 hours pre-operatively.
4. Recommence UFH 8 hours post-op (assuming haemostatic) at 50% of prior therapeutic dose. **N.B.** Do not give a loading dose post-operatively.
5. Assess APTT ratio on day +1 and **slowly** adjust UFH dose to achieve a ratio of 1.5-2.0
6. Only after any epidural has been removed, restart usual dose of warfarin as soon as it is safe and GI tract function is judged adequate.
7. Stop UFH for 6 hours prior to removal of any epidural catheters
8. On day +2 monitor APTT ratio and, only after any epidural has been removed, slowly adjust UFH to achieve a ratio of 1.8-2.8.
9. Continue UFH until INR is ≥2.

If good haemostasis has been secured and maintained for 2-3 days post-procedure it may be reasonable to switch from IV UFH to therapeutic dose LMWH. LMWH dosing should be chosen based on thrombotic risk (table 2 & table 5) and should be commenced 4 hours after cessation of the UFH infusion. If exposure to UFH (and LMWH) exceeds 4 days, monitor platelet count every 2-3 days from day 4 to 14, or until heparin is stopped. Be alert for evidence of HIT.

Appendix 1: Heparin Prescribing Information

PROPHYLACTIC HEPARIN DOSING

For dose adjustments in adult patients < 34kg or > 120kg, refer to the GGC Guideline 'Heparin Dose Adjustment in Adult Patients with Very High or Low Body Weight.'			
	Creatinine Clearance (ml/min) **GGC Creatinine Clearance (CrCl) calculator available here.**		
Low Molecular Weight Heparin	**≥ 30 ml/min**	**≥15 ml/min - <30ml/min**	**< 15 ml/min**
Enoxaparin	40mg once daily	20mg once daily	AVOID if CrCl < 15 ml/min Use an alternative LMWH
Dalteparin	5,000 units once daily	5,000 units once daily	2,500 units once daily

THERAPEUTIC HEPARIN DOSING

For dose adjustments in adult patients < 34kg or > 120kg, refer to the GGC Guideline 'Heparin Dose Adjustment in Adult Patients with Very High or Low Body Weight.'			
	Creatinine Clearance (ml/min) **GGC Creatinine Clearance (CrCl) calculator available here.**		
Low Molecular Weight Heparin	**≥ 30 ml/min**	**≥10 ml/min - 30ml/min**	**< 10 ml/min**
Dalteparin **(weight-banded dosing)**	200 units/kg once daily [max 18,000 units] Consider dalteparin 100 units/kg twice daily in patients with high bleeding risk.	200 units/kg once daily [max 18,000 units] Consider dalteparin 100 units/kg twice daily in patients with high bleeding risk.	Due to lack of evidence suggest use of UFH* *In the renal unit enoxaparin 1mg/kg once daily is regarded as an acceptable alternative.
Enoxaparin	1.5 mg/kg once daily Consider enoxaparin 1mg/Kg twice daily in patients with high bleeding risk or patients perceived to be at high risk of recurrent VTE	1 mg/kg once daily AVOID if CrCl < 15 ml/min Use an alternative LMWH	