Esperienza Londinese nella gestione della terapia antitrombotica

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Guy's and St Thomas' NHS
NHS Foundation Trust

Clinical Guideline

Perioperative bridging of warfarin in adult patients undergoing elective surgery

When in doubt seek advice from Bridging Clinic (ext 82802) or Thrombosis StR (bleep 0122)

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Perioperative Bridging of Warfarin in Adult Patients Undergoing Elective Surgery

Key:
CrCL- creatinine clearance
UFH - unfractionated heparin
VTE - venous thromboembolism

(A) Low risk:
- Target INR 2.0-3.0 *unless* VTE with:
  - active cancer – intermediate risk
  - VTE within last 3 months - intermediate risk
  - VTE within last 6 weeks - high risk: ideally avoid surgery, consider use of temporary IVC filter
- non valvular AF target INR 2.0-3.0 *unless*:
  - TIA/CVA within the last 3 months (ideally avoid surgery) - intermediate risk

(B) Intermediate risk:
- DVT/PE target INR 2.0 - 3.0 but VTE 6 -12 weeks ago
- Valvular AF (even if INR target 2.0 - 3.0)
- TIA/CVA within the last 3 months (ideally avoid surgery)

(C) High risk:
- VTE within the last 6 weeks – ideally avoid surgery, consider use of temporary IVC filter
- Any indication with target INR 3.0 - 4.0, unless mechanical cardiac valves when very high risk

(D) Very high risk:
- Mechanical cardiac valves

(E) Bridging therapy in renal failure:
- **Refer to table F for prophylactic dalteparin dosing in renal failure and box H for anti-Xa level testing**
- **Refer to table G for treatment dalteparin dosing in renal failure and box H for anti-Xa level testing**

Consult Thombosis StR for patients undergoing cardiac valve insertion

Pre-op **ALL** patients should take their last dose of warfarin 4 days before the procedure (day -4)

Does the patient have antithrombin deficiency or antiphospholipid antibodies?
Does the patient have allergy to heparin/history of HIT?

Yes → Contact Bridging Clinic (ext 82802) or Thrombosis StR (0122/via switchboard)

No

Is the patient low risk (A) , intermediate risk (B), high risk (C) or very high risk (D) ?

Low risk (A)	**Intermediate risk (B)**	**High risk (C)**	**Very High Risk (D)**
Pre-op: No alternative anticoagulation required	**Pre-op:** dalteparin prophylactic dose OD according to patient weight and renal function – see table (F) at 9am on day -3, -2 and -1. Omit on the morning of surgery	**Pre-op:** dalteparin treatment dose according to patient weight and renal function - see table (G) at 9am on day -3, -2 and -1. Omit on the morning of surgery	**Pre-op:** Admit patient on day -3. Start IV UFH infusion when INR < 2.0 (see heparin guideline). Stop 4 hours before surgery *Treatment dose LMWH can be considered (check renal function-see (E) but this is an UNLICENSED option so obtain patient consent
Post-op: Start prophylactic dalteparin OD according to patient weight and renal function-see table (F) Give first dose 6-12 hours post wound closure (Restart warfarin as below)	**Post-op:** Start prophylactic dalteparin dose OD according to patient weight and renal function-see table (F) Give first dose 6-12 hours post wound closure (Restart warfarin as below)	**Post-op:** Restart dalteparin treatment dose according to patient weight and renal function-see table (G). Give first dose 6-12 hours post wound closure (Restart warfarin as below)	**Post-op:** Restart IV UFH infusion immediately post-op as soon as bleeding has stopped. (Allow 2 hours post epidural insertion OR 24 hours if traumatic epidural insertion). Continue until target INR on TWO consecutive occasions

If traumatic epidural catheter insertion- wait **24 hours** after insertion before restarting dalteparin / UFH

Note: If the patient has renal failure (eg: CrCL < 30 mL/min)
-See **Bridging therapy in renal failure (E)**

Continue Subcut dalteparin (as in- or out-patient) until discharge, or oral anticoagulant re-started and INR in range

Continue Subcut dalteparin / (as in- or out-patient) or IV UFH (as in-patient) until oral anticoagulant re-started and INR in range *on two consecutive occasions*

(F) Prophylactic dalteparin dosing

Weight	CrCL > 30ml/minute Prophylaxis	CrCL<30ml/minute Prophylaxis - see (H)
30-39 kg	2500 units OD	1250 units OD
40-49 kg	2500 units OD	2500 units OD
50-99 kg	5000 units OD	2500 units OD
100-139kg	7500 units OD	5000 units OD
140-179kg	5000 units BD	5000 units OD
>180kg	Seek Haematology Advice	

(G) Treatment dalteparin dosing

Weight	CrCL >30ml/minute Treatment 200 units/kg	CrCL<30ml/minute 140 units/kg - see (H)
Wt <46 kg	7500 units OD	5000 units OD
46-56 kg	10 000 units OD	7500 units OD
57-68 kg	12 500 units OD	10 000 units OD
69-82 kg	15 000 units OD	10 000 units OD
>83 kg	18 000 units OD (dose capped)	12 500 units OD

(H) Anti-Xa level testing in renal failure (SEND ON ICE)
- Dalteparin levels can accumulate in renal failure over time.
- Check anti-Xa levels if there are concerns about bleeding or bruising after 7 days of dalteparin.
- If trough (pre-dose) anti-Xa level is >0.2 international units/mL, please discuss with Thrombosis StR (bleep 0122 / switchboard)

Re-starting oral anticoagulant

If there is no excessive bleeding (and epidural catheter has been removed), ideally restart on the evening of surgery (obtain surgical consultant/ StR approval first) once oral intake established.

Providing INR less than 1.5, restart with a loading dose of 1.5 x patient's usual dose for 3 days, then continue on usual dose (e.g. a patient who usually takes warfarin 5 mg, should receive 7.5 mg for 3 days and then continue on 5 mg).

If INR more than 1.5, contact clinical pharmacist / Thrombosis StR for advice

Note: If any medications that interact with warfarin have been started/stopped during admission contact ward pharmacist for advice as usual maintenance dose may need altering.
Refer to local anticoagulation clinic within 3 days of discharge if only one INR in range pre discharge; within 5 days if two consecutive INR's in range

2. PROCESSO DECISIONALE

Prevede una serie di passaggi (steps):

- Stratificare il rischio trombotico del paziente **(Step 1)**
- Valutare il rischio emorragico correlato al tipo di intervento chirurgico **(Step 2)**
- Valutare il rischio emorragico personale di ogni singolo paziente **(Step 3)**
- Consultare il diagramma di flusso per scegliere il tipo di terapia da impostare **(Step 4).**

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(D) Very high risk:

- Mechanical cardiac valves

Step 1: stratificazione del rischio trombotico*

CATEGORIA RISCHIO	PROTESI VALVOLARI	FA (fibrillazione atriale)	VTE (tromboembolismo venoso)
Elevato /medio	qualsiasi protesi meccanica	CHA_2DS_2-VASc≥4	VTE<12 mesi
	Protesi biologica di recente inserzione (< di 3 mesi)		VTE + Trombofilia ad alto rischio**
	Plastica mitralica (< di 3 mesi)		VTE recidiva
Basso		CHA_2DS_2-VASc≤3	VTE>12 mesi (non recidiva, non trombofilia)

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- Maggiore frammentazione legata al VTE timing
- Nessun cardiologo nel gruppo di Lavoro UK
- Eventi ischemici cerebrali

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation

James D. Douketis, M.D., Alex C. Spyropoulos, M.D., Scott Kaatz, D.O., Richard C. Becker, M.D., Joseph A. Caprini, M.D., Andrew S. Dunn, M.D., David A. Garcia, M.D., Alan Jacobson, M.D., Amir K. Jaffer, M.D., M.B.A., David F. Kong, M.D., Sam Schulman, M.D., Ph.D., Alexander G.G. Turpie, M.B., Vic Hasselblad, Ph.D., and Thomas L. Ortel, M.D., Ph.D., for the BRIDGE Investigators*

Suggested Risk Stratification: Atrial Fibrillation

High Risk

- CHADS2 score = 5-6
- Recent (within 3 months) stroke or TIA
- Rheumatic valvular heart disease

Moderate Risk

- CHADS2 score = 3-4

Low Risk

- CHADS2 score = 0-2 *and* no prior stroke or TIA

From “To Bridge or Not to Bridge” ISTH 2015, kindly provided by Prof Ortel

Suggested Risk Stratification: Mechanical Heart Valves

High Risk

- Any mitral valve prosthesis
- Older (caged-ball or tilting disc) aortic valve prosthesis
- Recent (within 6 months) stroke or TIA

Moderate Risk

- Bileaflet aortic valve and at least one of:
- Atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age >75 years

Low Risk

- Bileaflet aortic valve without atrial fibrillation and no other risk factors for stroke

From “To Bridge or Not to Bridge” ISTH 2015, kindly provided by Prof Orte

Suggested Risk Stratification: Venous Thromboembolism

High Risk

- Recent VTE (<3 months ago)
- Severe thrombophilia (eg, antiphospholipid antibodies)

Moderate Risk

- VTE within the past 3-12 months
- Nonsevere thrombophilia (eg, heterozygous factor V mutation)
- Recurrent VTE
- Active cancer (treated within 6 months or palliative)

Low Risk

- Prior VTE >12 months ago and no other risk factors

From “To Bridge or Not to Bridge” ISTH 2015, kindly provided by Prof Ortel

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Clinical Guideline

Perioperative Bridging of New Oral Anticoagulants in Adult Patients Undergoing Elective Surgery

Key:
CrCL- creatinine clearance
VTE - venous thromboembolism
NOAC – new oral anticoagulant

Peri-operative Surgical Bridging Protocol for patients receiving New Oral Anticoagulants (NOACs)

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Identify indication for NOAC (either prevention of stroke in non-valvular AF or VTE treatment or secondary prevention)

NOACs for AF or VTE occurred > 6 weeks ago

NB: Patients with VTE in last 6 weeks
Discuss with Thrombosis team (bleep 0122)

Pre-operative: Is the procedure minor or major?

Minor: e.g. ophthalmological & dental procedures

Timing of last NOAC dose pre procedure:		
Renal function (as calculated CrCl[a])	Dabigatran (minimum)	Rivaroxaban / apixaban / edoxaban (minimum)
>80ml/min	24h	24h
50-80 ml/min	36h	24h
30-50 ml/min	48h	36h

Major: e.g. cardiac, chest or abdominal surgery

Timing of last NOAC dose pre procedure:		
Renal function (as calculated CrCl[a])	Dabigatran (minimum)	Rivaroxaban / apixaban / edoxaban (minimum)
CrCl>80ml/min	48h	48h
CrCl 50-80 ml/min	72h	48h
CrCl 30-50 ml/min	96h	48h

Post-operatively: Assess patient's bleeding risk and risk of VTE

Haemostasis achieved & no further surgery planned:

Day 0: Restart pre-admission dose 6-8 hours post-wound closure (Adjust dose as per SPC if renal function has altered)

Ongoing bleeding risk postoperatively:

Day of procedure:

- Bridge with prophylactic dalteparin. Give first dose 6-12 hours post wound closure, if haemostasis achieved.
  If traumatic epidural catheter insertion- wait **24 hours** after insertion before restarting dalteparin

Weight	Prophylactic dose if calculated CrCL≥ 30ml/minute	Prophylactic dose if calculated CrCL< 30ml/minute
30-39 kg	2500 units OD	1250 units OD
40-49 kg	2500 units OD	2500 units OD
50-99 kg	5000 units OD	2500 units OD
100-139kg	7500 units OD	5000 units OD
140-179kg	5000 units BD	5000 units OD
>180kg	Seek Haematology Advice	

- Once bleeding risk reduced, restart NOAC **12-24 hours after last dose of dalteparin (determined by surgeon)**
- If renal function has deteriorated, please review dose of NOAC
- Ensure patient has not been started on any drugs that could potentially interact with NOAC e.g. cytochrome P-450 3A4 inhibitors and P-glycoprotein inhibitors - contact ward pharmacist / resident pharmacist for advice.

DTC Reference: 15015p

Review by: January 2018

Tabella 2 - Tempistica di sospensione preoperatoria dei NOACs in chirurgia elettiva

GFR (ml/min)	Dabigatran		Apixaban-Rivaroxaban	
	Per le procedure minori con bassissimo rischio emorragico e/o possibile adeguata emostasi locale(es. odontoiatriche semplici) sospendere il trattamento 12-24 ore prima			
	Basso rischio	**Alto rischio**	**Basso rischio**	**Alto rischio**
>80	≥ 24 ore	≥48 ore	≥24 ore	≥48 ore
50-80	≥36 ore	≥72 ore	≥24 ore	≥48 ore
30-50*	≥48 ore	≥96 ore	≥24 ore	≥48 ore
15-30	Non indicato		≥36 ore	≥48 ore
<15	Non indicato			

Minor: e.g. ophthalmological & dental procedures

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CrCl 50-80 ml/min	72h	48h
CrCl 30-50 ml/min	96h	48h

- Estrema semplificazione della stratificazione
- Rapida applicabilità
- Scarsa attenzione alle problematiche non trombotiche

- Maggiore attenzione alla stratificazione del paziente, anche in base al tipo di procedura
- Approccio multidisciplinare