NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Dabigatran, Management of Haemorrhage, Surgery or Other Invasive Procedures, Acute

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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Lead Author:	Cristina Coelho
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Important Note:

The Intranet 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.

Dabigatran: Management of haemorrhage, surgery and other invasive procedures

Contents

Introduction

Dabigatran (Pradaxa®) has a short half-life (8-12 hours), although longer in patients with renal impairment. In patients with normal renal function, for most elective procedures with a significant bleeding risk, omission of 2 days (48 hours) of dabigatran pre-operatively should suffice.

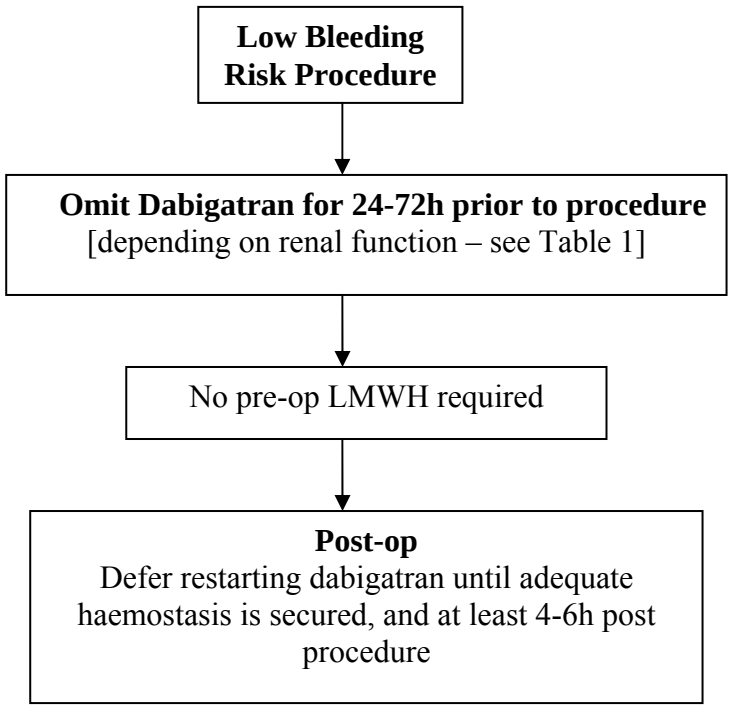
At the present time there is limited evidence on which to base guidance for the above situations, and a specific reversing agent is only recently licensed. Therefore the following advice is largely empirical with a pragmatic view towards balancing the thrombotic and haemorrhagic risks facing anticoagulated patients requiring invasive procedures or experiencing major bleeding.

Elective minor invasive procedures (for which warfarin would not have been discontinued)

This would include standard dental procedures, routine upper and lower GI endoscopy +/- simple biopsy, joint injections and cataract extraction with lens implantation (posterior segment eye surgery or surgery involving the iris should be regarded as major surgery).

Minor dental work: Dental procedures with low or no bleeding risk can usually be undertaken without interrupting dabigatran therapy, however for procedures with a higher bleeding risk the morning dose of dabigatran should be omitted. Undertake the dental procedure early in the day, limiting initial treatment area and assess bleeding before continuing. Actively consider suturing and/or packing. The evening dose of dabigatran should be taken at the usual time, but at least 4 hours after dental haemostasis has been achieved. See National guidance from SDCEP for further advice [http://www.sdcep.org.uk/published-guidance/anticoagulants-and-antiplatelets/].

Other minor procedures: For endoscopy, cataract surgery or joint injection it is recommended that this is delayed until 24h after the last dose of dabigatran. The next dose of anticoagulant should be deferred until 6h post procedure (or longer if haemostasis has not been achieved). If there is renal impairment (creatinine clearance [CrCl] <80 ml/min), dabigatran should be omitted for longer pre-procedure – see Table 1.



Elective procedures with a moderate or high risk of bleeding

These will include most operations with any risk of bleeding (including endoscopies involving sphincterotomy or polypectomy), and procedures using neuro-axial anaesthesia.

Pre-op: Dabigatran will need to be discontinued prior to the procedure, however pre-operative bridging therapy with low molecular weight heparin (LMWH) should not be required. It should be remembered that dabigatran is contra-indicated in patients with CrCl <30 ml/min.

The duration for which dabigatran should be omitted pre-op is dependent on renal function:

Table 1

Renal Function	**Estimated half-life**	**Duration of omission of dabigatran before procedure / surgery**	
CrCl ml/min	***Hours***	***Standard or High bleeding risk procedures***	***Minor procedures (excluding dental)***
≥ 80	~13	48 hours	24 hours
≥ 50 < 80	~15	48 -72 hours	24 – 48 hours
≥ 30 < 50	~18	96 hours (4 days)	48 -72 hours

It is recommended that calculated CrCl is used (rather than eGFR) when determining dabigatran stopping time pre-surgery.

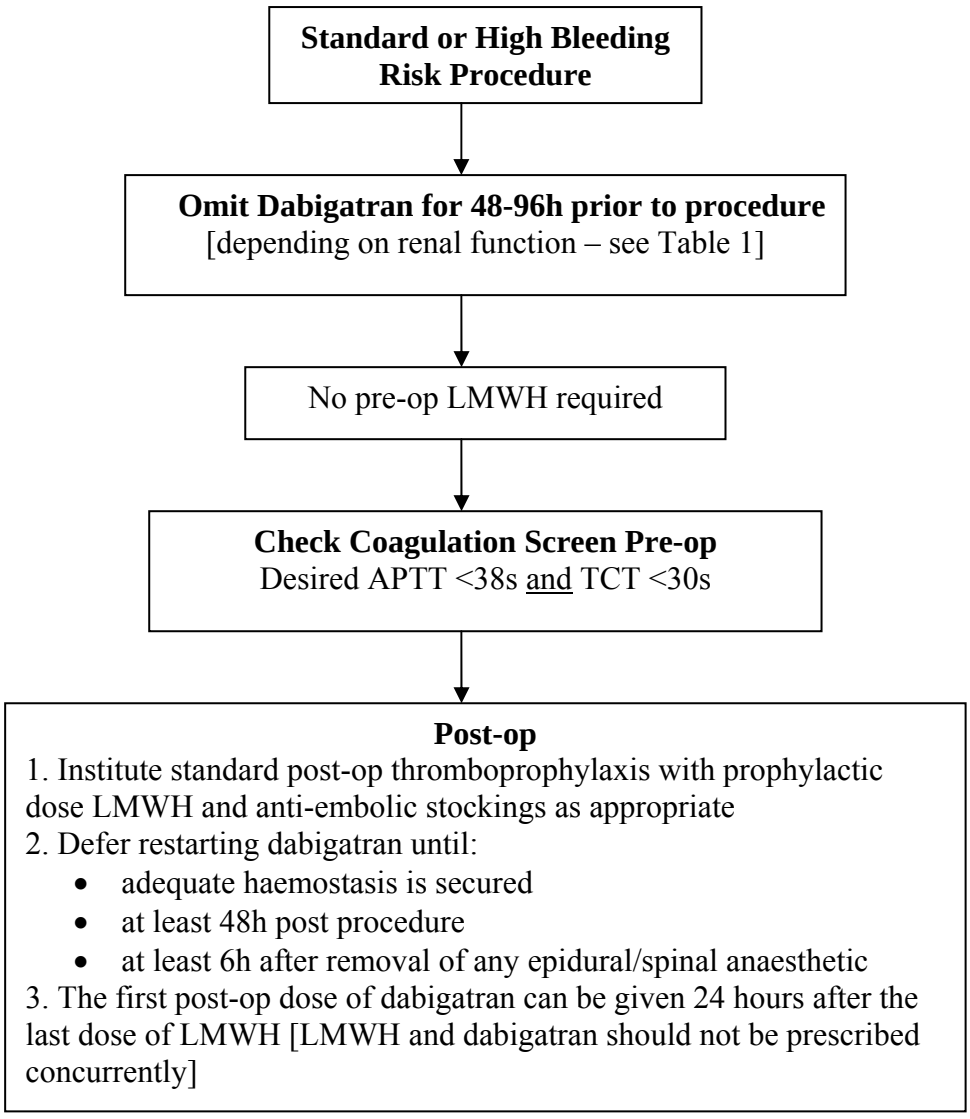
Pre-operative assessment of a routine coagulation screen may not accurately reflect the level of anticoagulation, although a normal Thrombin Clotting Time (TCT) would imply negligible dabigatran drug levels.

Post-op: initial thromboprophylaxis will be most simply achieved with LMWH at prophylactic doses (starting at the later of 4h post-op or at 6pm on day of surgery, assuming adequate post-op haemostasis). Once post-op haemostasis is safely secured and bleeding risk has subsided therapeutic dose anticoagulation could be re-introduced 48h post-op. Dabigatran can be restarted 24h after the last dose of LMWH. If the bleeding risk persists,

or there are concerns about restarting the DOAC at this time, a cautious approach, assuming any epidural has been removed, would be to continue LMWH at a prophylactic or intermediate dose LMWH (e.g. enoxaparin 1mg/Kg od) at this time for a few days, before switching back to therapeutic dose dabigatran.

Neuro-axial anaesthesia

Neuro-axial and deep local anaesthetic blocks should be regarded as major invasive procedures for the purposes of this guidance. Catheter-directed local anaesthetic techniques should not be used during dabigatran treatment. There should be an interval of at least 6 hours after the removal of an epidural catheter before the introduction of dabigatran and frequent observation for neurological signs/symptoms of epidural haematoma must be made.



Haemorrhage & Emergency invasive procedures

The specific reversal agent Idarucizumab [Praxbind®] is now licensed and available in the emergency drug cupboard/fridge in GRI, QEUH, RAH and IRH. It binds to Dabigatran with very high affinity and instantly reverses its anticoagulant effect. It should be considered in cases of major haemorrhage or when surgery cannot be delayed, and only prescribed after discussion with haematology.

Key principles in managing these situations are:

1. Assess coagulation screen and renal function. A normal Thrombin Clotting Time (TCT) implies no significant residual dabigatran anticoagulant effect.
2. Ascertain time of the most recent dose of anticoagulant, and administer no further doses. If very recent ingestion (≤ 2h), consider administration of oral activated charcoal to inhibit further drug absorption.
3. Maintain adequate diuresis (to aid dabigatran renal excretion)
4. If significant dabigatran effect, as assessed by coagulation screen (e.g. APTT >38s and Thrombin time [TCT] >30s), consider the possibility of delaying major surgery until anticoagulant effect has sufficiently dissipated
5. Consider use of dabigatran reversing agent (Idarucizumab) – see below

In the presence of major bleeding, or if surgery has to proceed, in the face of significant anticoagulant effect [also see Appendix 1]:

- Ensure haemostatic platelet count & fibrinogen level & satisfactory pre-op Hb
- Consider administration of idarucizumab 5g iv (in two doses of 2.5g in 50ml over 5mins each, one after the other) to reverse dabigatran effect. This should be approved by the consultant in charge.
- Emergency supplies of Idarucizumab [Praxbind®] are located within the fridge section of the Emergency Drugs Cupboard at GRI, QEUH, RAH and IRH.
- Treat any additional causes of coagulopathy
- Consider general haemostatic measures (e.g. iv tranexamic acid)

- If idarucizumab is not available or if despite the above measures there is significant peri- or post-op bleeding, discuss with haematologist and consider administration of prothrombin complex concentrate (e.g. Beriplex® 50 units/Kg)
- In the presence of major bleeding, in addition to the above, follow general major haemorrhage principles

Once haemostasis secured and/or invasive procedure completed

- continue to monitor haemostasis (recurrence of dabigatran effect has been reported in some patients, who may then require a second dose of idarucizumab)
- introduce thromboprophylaxis with LMWH when appropriate
- if dabigatran is to be re-introduced this should be deferred until 24h after the last dose of LMWH.

Appendix Management of haemorrhage in dabigatran-treated patients