<table>
<tr><td>Guideline Number & Full Title:</td><td>2841 - Guideline for Patients on antiplatelet agents undergoing Elective, Non-cardiac Surgical Intervention</td></tr>
<tr><td>Contact Name and Job Title (author)</td><td>1. Sachin Jadhav – Consultant Cardiologist
2. Dr Ganesh Subramanian - Consultant Stroke Physician</td></tr>
<tr><td>Directorate & Speciality</td><td>Clinical Haematology</td></tr>
<tr><td>Date of submission</td><td>December 2023</td></tr>
<tr><td>Date on which guideline must be reviewed</td><td>December 2028</td></tr>
<tr><td>Explicit definition of patient group to which it applies (e.g. inclusion and exclusion criteria, diagnosis)</td><td>Adult patients taking oral antiplatelet agents who require an elective surgical procedure or intervention
Exclusions:
• Patients requiring emergency surgery
• Patients taking vitamin K antagonists
• Patients taking any of the direct oral anticoagulant drugs, rivaroxaban (Xarelto®), dabigatran (Pradaxa®), apixaban (Eliquis®) or edoxaban (Lixiana®)
• Children or pregnant patients
• Patients undergoing neurosurgical intervention
• Patients undergoing cardiac surgery or implantable cardiac devices
• Patients in the critical care unit
• Paediatric patients</td></tr>
<tr><td>Version</td><td>3</td></tr>
<tr><td>Abstract</td><td>The purpose of this document is to provide recommendations for the management of adult patients on antiplatelet agents who require interruption of treatment to allow a surgical procedure or intervention</td></tr>
<tr><td>Key Words</td><td>Antiplatelet, Perioperative Anticoagulation, Surgery</td></tr>
<tr><td>Statement of the evidence base of the guideline – has the guideline been peer reviewed by colleagues?

Evidence base: (1-6)
<table><tr><td>1</td><td>NICE Guidance, Royal College Guideline, SIGN (please state which source).</td></tr><tr><td>2a</td><td>meta analysis of randomised controlled trials</td></tr><tr><td>2b</td><td>at least one randomised</td></tr></table></td><td>Yes</td></tr>
</table>

Scope

The purpose of this document is to provide recommendations for the management of adult patients on anti-platelet therapy who may 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*, 2011) and expert opinion (Spyropoulos 2012).

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)
- Patients taking Vitamin K antagonists (eg warfarin)
- Children or pregnant patients
- Patients undergoing neurosurgical intervention
- Patients undergoing Cardiac surgery or implantable cardiac devices
- Patients in the critical care unit

Anti-platelet agents in clinical practice

There are several antiplatelet agents encountered in clinical practice:

Aspirin = cyclo oxygenase inhibitor. Inhibits platelets by reducing the production of arachadonic acid metabolites which activate platelets eg. Thromboxanes

Ticlopidine = first generation thienopyridine (irreversible platelet P2Y12 receptor blocker). Not in routine use given frequency of haematological sideeffects

Clopidogrel = second generation thienopyridine (irreversible platelet P2Y12 receptor blocker)

Prasugrel = third generation thienopyridine (irreversible platelet P2Y12 receptor blocker). Advantages over clopidogrel include rapid onset of action, more potent platelet inhibition and fewer "hypo-responders". Clinical trials suggest benefit over clopidogrel in patients undergoing percutaneous coronary intervention (PCI) following presentation with acute coronary syndrome (ACS)

Ticagrelor = first in class cyclo-pentyl-triazolo-pyrimidine (CPTP). This drug inhibits platelet function by reversibly blocking P2Y12 receptor. It has a similar pharmokinetic profile to prasugrel. Clinical trials have shown benefit over clopidogrel in patient presenting with ACS (irrespective of whether they underwent revascularisation)

Dipyridamole = inhibits platelet aggregation by reducing uptake of ADP into platelets and weak inhibition of cAMP phosphodiesterase leading to increased levels of intra-cellular cAMP

General points

This document provides guidance only. In all cases, the risks of stopping anticoagulant or antiplatelet therapy to prevent procedure related bleeding must be balanced against the risk of a further thromboembolic event.

It is important that these risks and benefits are clearly and openly discussed with the patient pre-operatively and this is the responsibility of the treating team

It is the responsibility of the surgical team to implement the plans outlined in this guidance; this includes informing the patient of the plan, prescribing any necessary medication and referring the patient back to the anticoagulation clinic/GP when discharged from hospital.

This guidance is divided into 2 sections based on the indication for antiplatelet therapy. In general, patients taking antiplatelet therapy for neurological indications should follow the Stroke guidance (section 2) and patients taking antiplatelet therapy for a vascular indication should follow the Cardiology guidance (section 1). If in doubt, please seek advice directly from the relevant specialty

Section 1: Cardiology

Perioperative management of patients on antiplatelet agents - Cardiology indications

1.1 Cardiology indications for antiplatelet therapy

There are 3 main indications for antiplatelet therapy in the context of coronary artery disease:

- **Primary prevention of myocardial infarction** (MI)
  Generally anti-platelet monotherapy with aspirin (or clopidogrel if aspirin intolerant/allergic). In general, this can be stopped perioperatively if required with minimal risk

- **Secondary prevention following MI**
  Dual antiplatelet therapy (DAPT) is typically prescribed for 12 months. This comprises aspirin + one of clopidogrel/prasugrel or ticagrelor

- **Following percutaneous coronary intervention (PCI)**
  DAPT is prescribed to avoid stent thrombosis which is generally a lifethreatening event. This is needed for a period of between 1-6 months (until endothelialisation of the stent has occurred). Exact duration depends on the type of stent used. In general, DAPT can be interrupted after 1 month for most stent types in favour of single antiplatelet therapy and restarted as soon as feasible after any procedure has been completed

1.2 Stopping Dual Antiplatelet Therapy

- **Secondary Prevention:**

In patients taking DAPT for secondary prevention of MI one antiplatelet agent can be stopped/interrupted 7 days pre-procedure with relative safety (usually clopidogrel, prasugrel or ticagrelor) such that only aspirin is taken perioperatively. Stopping aspirin is not recommended routinely unless bleeding risk is deemed extremely high.

- **Post PCI:**

In patients who have had a coronary stent implanted > 6 months ago - one antiplatelet agent can usually be stopped safely 7 days pre-procedure. Aspirin ought not to be discontinued in these patients

In patients who have had a coronary stent implanted <6 months ago – see table below. If further discussion is required please contact Cardiology. In

general the best point of contact is the Interventional Cardiologist who performed the PCI procedure.

Platelet reactivity takes 5-7 days to return to baseline following discontinuation of antiplatelet agents - it takes this long for marrow to liberate new uninhibited platelets into the circulation. Hence, it is recommended that anti-platelet drugs are stopped 7 days pre-procedure to allow “normal” platelet reactivity to return. If an emergency procedure is required then platelet reactivity can be restored to some extent sooner with a platelet transfusion - these cases should be discussed with Haematology

1.3 Stopping antiplatelet agents in other clinical situations

CLINICAL SCENARIO	ADVICE
1. Myocardial infarction or PCI >12 months previously	Most patients ought to be taking single antiplatelet therapy with aspirin (or clopidogrel if aspirin intolerant) Single antiplatelet therapy is advisable peri-procedure unless excessive bleeding risk (clopidogrel could be changed to aspirin temporarily if required unless true aspirin allergy – this change should be made at least 7 days pre-procedure) If patient remains on DAPT >12 months then please discuss with Cardiology (unless stopping DAPT was clearly intended at 12 months)
2. Secondary prevention post MI (medically managed) within last 12 months. Discuss with Cardiology if < 1month	Remain on aspirin (unless excessive bleeding risk) Interrupt clopidogrel/prasugrel/ticagrelor 7 days pre-procedure aiming to restart as soon as haemostasis is secure post procedure to complete 12 months
3. PCI <1 month ago [Elective for stable angina or following acute coronary syndrome (ACS)]	Dual antiplatelet therapy must not be interrupted. If exceptional circumstances please discuss with Interventional Cardiologist
4. PCI 1-6 months ago [Elective for stable angina or following acute coronary syndrome (ACS)]	DAPT <u>may</u> be interrupted periprocedure (remain on aspirin) – stop clopidogrel/prasugrel/ticagrelor 7 days pre-procedure. Please discuss case with the Interventional Cardiologist Restart 2nd antiplatelet agent post procedure as soon as haemostasis is secure to continue for originally intended duration

6. PCI >6 months ago [Elective for stable angina or following acute coronary syndrome (ACS)]	If still on DAPT, this can be interrupted periprocedure (remain on aspirin) – stop clopidogrel/prasugrel/ticagrelor 7 days pre-procedure Restart 2nd antiplatelet agent post procedure as soon as haemostasis secure to continue for originally intended duration
7. Previous CABG	If >12 months then single antiplatelet therapy needed – ought to remain on Aspirin or Clopidogrel peri-procedure unless bleeding risk outweighs risk of peri-procedural MI If < 12 months then discuss with Cardiology or Cardiac Surgery

If any doubt remains or further information is required please discuss with a Cardiologist; the preferred point of contact is:

- Cardiology team on-call via Cardiology SpR
  (Contact via ACU on 76213 or via switchboard)

- Interventional Cardiologist who performed the PCI procedure

Section 2: Stroke

Perioperative management of patients on antiplatelet agents – stroke indications

There is very little evidence for using antiplatelet agents in the primary prevention of stroke or TIA and hence it is not routinely recommended.

Clopidogrel is the first choice agent for long term secondary prevention of ischaemic strokes and TIA (aspirin 300 mg od is the recommendation for the first 14 days after an ischaemic stroke). Alternatives would include either aspirin monotherapy or dual therapy with aspirin and dipyridamole MR (these are used in case the patient is intolerant of clopidogrel). There is some evidence for ticagrelor monotherapy, but the risk of haemorrhage is much higher than other antiplatelets. Hence, it should not be used without prior discussion with the on call stroke physician.

2.1 Antiplatelet usage/stoppage prior to non-cardiac interventions

The risk of blood ooze is considerable with clopidogrel. It is therefore recommended that clopidogrel is switched to aspirin 75 mg od for at least 7 days prior to any planned surgical intervention (including endoscopies and dental extractions). The patient needs to be counselled that aspirin 75 mg od *may* be slightly inferior to clopidogrel 75 mg od (as the evidence for this not robust in all patients although it is clear in some subset of populations – and hence the term ‘may’ should be used whilst counselling).

The antiplatelet activity of dipyridamole is less than that of aspirin and clopidogrel. Moreover, its action is wholly reversible and ceases about 24 hours after the drug is discontinued. Daily use of dipyridamole does not appear to increase blood loss significantly during surgical procedures, and so unless the bleeding risk from the procedure is deemed exceptionally high, dipyridamole need not be stopped pre-operatively.

In case of emergency procedures (e.g. endoscopies, surgery, etc), clopidogrel should be discontinued as long as (if at all) possible prior to the procedure. The patient should be counselled about the higher risk of operative site haematoma which may or may not require further intervention.

2.2 Anti-platelet usage post procedure

Antiplatelet agents should be restarted as soon as possible, preferably, 24 hours post procedure. However, if the patient has undergone a complex surgical procedure, or where there is a high risk of postoperative bleeding, the decision to restart anti-platelet agents should be made by the surgical team when it is deemed safe to so.

Following low risk procedures such as PEG tube placement (unless there are complications during or after the procedure) or after vascular interventions (e.g. stent placement or carotid endarterectomy), antiplatelets should be restarted after 24 hours (unless advised by the endoscopist, interventional radiologist or vascular surgeons otherwise) and the drug of choice would be clopidogrel.

After complex or high risk surgical procedures, aspirin should be started as soon as it is safe to do so from a surgical perspective. Aspirin should subsequently be changed to Clopidogrel after a week (unless advised otherwise by the surgical team).

carotid stenting is not the treatment of choice for carotid stenosis. However, it may be part of mechanical thrombectomy (for acute ischaemic stroke with large vessel occlusion) if they have tandem stenosis or occlusion. In this scenario, patient should be commenced on dual antiplatelets (as guided by the interventional neuroradiologist) 24 hours post procedure (unless advised otherwise by the Interventional Neuroradiologist or there is evidence of Hyperperfusion syndrome characterized by intracerebral bleed). Treatment should be continued for 6 months, but further advice can be obtained from the interventional neuroradiologist.

Post mechanical thrombectomy without any stent insertion (for acute ischaemic stroke), the patient should be commenced on aspirin 300 mg od (unless advised otherwise by either the stroke physicians or interventional neuro-radiologists). Longer term antiplatelet therapy will usually be recommended but specific instruction will be issued by the Stroke Team

References

Veitch, A.M., Baglin,T.P., Gershlick,A.H., Harnden,S.M., Tighe,R., & Cairns,S. Guidelines for the management of anticoagulant and antiplatelet therapy in patients undergoing endoscopic procedure Gut 2016, **57**, 1322-1329.

Di Vincenzo V, Cappelletti L, Acciai N, Bosco G, Scipioni G, Zecchini F et al The effect of dipyridamole and aspirin on postoperative blood loss after myocardial revascularization. J Cardiothorac Anesth 1989; 3(5 Suppl 1):88.