Peri-operative management of oral anticoagulants and antiplatelets in elective and emergency cranial surgery

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Summary

- The aim of this document is to provide guidance on the management of oral anticoagulants (OAC) and antiplatelets (AP) in patients undergoing elective and emergency cranial surgery and enhance local policies.
- This guidance does not replace a patient specific management plan following discussion with involved clinicians, considering specific risks and the surgical procedure itself
- The risks to the patient with peri-operative intracranial haematoma include worsening neurological disability, raised intra-cranial pressure and can be life-threatening.
- The risk of stopping OAC / AP includes thromboembolic risk, ischaemic events, stent occlusion and valve thrombosis.
- Plan for recommencing OAC / AP agents will be dependent on the agent, the underlying surgical bleeding risk and the patient's risk of stopping the agent.
- Inform patients about the risk of continuation or cessation of OAC / AP (in addition to other complications) during the consent process.
- Preparation for cases with a high risk of stopping OAC / AP should include individualised discussion with the appropriate treating clinicians to ascertain the risks and benefits of delaying surgery or OAC / AP cessation.
- All patients undergoing elective and emergency cranial surgery should be screened for OAC / AP use and a clear visible plan documented for the perioperative period.
- All personnel involved in managing the patient should be aware of the decision making to reduce the risk of variance from the preoperative plan and prevent adverse consequences.
- The plan for recommencement of OAC / AP should be clearly outlined in the postoperative notes.
- The most important key message should remain the need to constantly evaluate the risk of thromboembolic events and bleeding for individual patients.

Abbreviations

AP	Anti-platelets
ACS	Acute Coronary Syndrome
EBL	Estimated blood loss.
eGFR	estimated Glomerular Filtration Rate
OAC	Oral Anti-Coagulants
POBL	Perioperative blood loss
POD	Post-operative drainage
SAH	Subarachnoid haemorrhage
SBNS	Society of British Neurological Surgeons
SR	Surgical Risk
TE	Thromboembolic
VTE	Venous Thromboembolism

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1. Who has developed this guideline?

This guideline has been developed in association with the Society of British Neurological Surgeons (SBNS), through review of recent literature and discussion of guidelines collated by the authors above amongst the SBNS council members.

2. Who does this guidance apply to?

Patient group
This guidance affects all patients undergoing emergency or elective cranial surgery who were previously on an OAC or AP.

Clinical staff
This guidance is relevant to neurosurgeons and the surgical team, emergency department teams, pre-assessment teams, theatre and recovery personnel, anaesthetic teams, nursing and pharmacy teams.

Managerial staff
Responsible ward managers, matrons, clinical leads / directors in cranial surgery.

3. Why is this guidance relevant?

The guidance is aiming to reduce the risks associated with managing OAC / AP in the perioperative period for patients who are having cranial surgery.

The risks to the patient who develops peri-operative intracranial haematoma include worsening neurological disability, raised intra-cranial pressure and eventually threat to life.

The risk of stopping OAC / AP includes thromboembolic risk, ischaemic events, stent occlusion and valve thrombosis.

4. The pathway for oral anticoagulant and antiplatelet management

All patients undergoing elective or emergency cranial neurosurgery should be screened for the use of OAC / AP.

In elective cranial surgery

- Patients should be screened during out-patient review for any elective cranial interventions and the use of OAC/AP highlighted.
- Screening should also take place during routine pre-operative assessment pathways and a clear management plan either be made following local policy or flagged to the operating surgeon for decision making.
- If appropriate, pre-operative discussion with relevant medical specialists (e.g. haematology/cardiology) should occur before surgery to guide decision making.
- A clear plan should be made and communicated to the patient prior to surgery to minimise risk of cancellation or prolonged time off OAC/AP.
- The risks and benefits of stopping OAC/AP and when to re-commence them post-operatively should be discussed with the patient and/or next-of-kin.

In emergency cranial surgery:

- Patients should be screened for use of OAC/AP at presentation in emergency department wherever possible.
- Local hospital protocols should be followed for stopping and commencing reversal if appropriate.
- The treating neurosurgeon should be aware of any OAC/AP use and reversal given prior to operative intervention.
- If appropriate, further discussion with medical specialists (e.g. haematology) and/or implementation of further management may be required before emergency surgical intervention can take place.
- Where possible the patient and/or next-of-kin should be made aware of the risks of surgery in relation to bleeding and those of cessing OAC/AP medications.

It is considered that 10% worth of platelet function recovers per day for aspirin after cessation, suggesting 10 days would be needed for full reversal of function. However, studies have also shown adequate haemostasis is possible with only 20% platelet function, or indeed that operating whilst on aspirin may not increase peri-operative haemorrhage risk.

5. Risks of stopping OAC/AP

- The risk of having a thromboembolic event resulting in a stroke, stent occlusion, valve thrombosis or other consequence should be considered.
- Risk calculators such as the CHA_2DS_2-VASc score can be used to assess the risk of stroke and stopping medication (low level of evidence for perioperative use)
- The acuity of a recent event or intervention (e.g. stroke or percutaneous coronary intervention) needs to be considered. In general, the risk of another event is felt to be higher within the first 3 - 6 months.
- Patients with high risk of having a thromboembolic event from stopping OAC / AP must be considered for deferring surgery when possible OR an individualised plan outlined after multidisciplinary discussion (between Neurosurgeons/Anaesthetists/Haematologist/Cardiologist/Stroke physicians, as appropriate)

Table 1; Risk of thromboembolic events.

High Risk	Low Risk
Mechanical heart valve (target INR 3.0-4.5)	Aortic bi-leaflet valve (target INR 2.0-3.0) with no other thromboembolic risk factors
Percutaneous coronary angioplasty < 2 wks.	Primary prevention antiplatelet therapy
Myocardial infarction / ACS < 6 weeks	Myocardial infarction / ACS > 6 months
Bare metal stent < 6 weeks	Bare metal stent > 6 weeks
Drug eluting stent < 12 months	AF with CHA_2DS_2-VASc score ≤4 and no stroke or TIA in last 3 months
Stroke < 3 months	Unprovoked VTE > 3 months
Stroke & high CHA_2DS_2-VASc score (≥5)	
VTE < 3 months	
VTE that occurred on OAC	
High risk pro-thrombotic conditions; anti-phospholipid syndrome and thrombophilia	
Patients on dual OAC or AP	
Any condition requiring warfarin with a target INR range above 2.0-3.0	

6. **Risks of bleeding and consequences in cranial neurosurgery**
    - Intra-operative haemorrhage control
    - Post-operative haematoma resulting in neurological deficits, seizures and delayed infection secondary to haematoma.
    - Risk of increased ICP secondary to haemorrhage, resulting in need for further surgery and risk to life if untreated.

Patients who have an elevated risk of bleeding (uncontrolled hypertension, age > 65 y, liver disease, renal disease, >8 alcohol drinks per week), prior major bleeding or predisposition to bleeding will need to be considered **high risk**.

7. **Management of OAC/AP in elective cranial neurosurgery**

Evidence

Systematic review of cranial neurosurgical operations (646 patients with mainly tumour and vascular pathology) found the same rate of haemorrhagic complications (3%) in the 62% that continued aspirin peri-operatively compared to those that discontinued it (***Rychen 2023***). The rate of thrombosis was half (3%) in the continuation group compared with those that discontinued aspirin (6%), but not statistically significant due to small numbers. Based on their systematic review of the literature, perioperative continuation of aspirin in elective craniotomies does not seem to be associated with a higher risk of haemorrhagic complications. There was also no evidence of increased intra-operative blood loss in patients who continued aspirin in one single-centre study (***Hanalioglu 2019***).

Concerning thromboembolic events, a pooled analysis shows a trend towards a beneficial effect of aspirin continuation; however, the results didn't reach statistical significance. Overall, the methodological quality of studies in this field is low and therefore this is not considered strong evidence.

Continuation of aspirin for extra-axial, transsphenoidal and shunt surgery, was not associated with any increase in haemorrhagic event in one subsequent series of 83 patients (***NF 2023***). All other cranial operations were associated with 2 days pre-operative cessation of aspirin, 7 days for clopidogrel and warfarin and 2-3 days for NOACs, with an overall haemorrhage rate of 4% (***NF 2023***).

It is challenging to balance the potential consequences of bleeding against those of thrombosis, of which stroke tends to be the most common complication. Overall, given the lack of evidence a safe stance would be to consider stopping aspiring for 0-5 days prior to lower risk interventions and a minimum of 5 days for higher risk interventions, based on limited evidence.

An online survey regarding the perioperative management of AP and OAC medication took place with most responders practicing neurosurgery in Europe or high-income countries (79%). Responders reported in 59% and 49% respectively, to have institutional guidelines for the perioperative management of AP and OAC medications. Preoperative interruption time was reported heterogeneously for the different types of AP and OACs, with 40% of responders interrupting aspirin for 4 - 6 days and 46% interrupting clopidogrel for 6 - 8 days. Around half of the responders considered aspirin safe to be continued or resumed within 3 days for bypass (55%) or vascular (49%) surgery, but only few for skull base or other tumour craniotomies in general (14% and 26%, respectively). Three quarters of the responders (74%) did not consider OAC safe to be continued or resumed early (within 3 days) for any kind of craniotomy. Aspirin was considered to have the lowest risk of bleeding. Nearly all responders (93%) agreed that more evidence is needed concerning AP and OAC management in neurosurgery.

Recommencement
Recommencement of OAC/AP within 3 days post-operatively does not appear to be related to a higher bleeding risk (***NF 2023***). Extra-axial skull base tumours have been shown to have a higher thromboembolic risk and therefore early recommencement should be considered particularly in these patients (***Hanalioglu 2019***).

Case considerations

- Transphenoidal surgery for pituitary tumours:
  Some studies have suggested that discontinuation of antithrombotic therapy may be unnecessary before an uncomplicated transsphenoidal surgery.

  Furthermore, the risk of a thrombotic event in patients with Cushing's has been reported to be up to 10 times higher than that of the general population therefore preop therefore decisions on AC preop and on recommencement should individualised following discussion between surgeon, anaesthetic and endocrine teams.

- Expanded transsphenoidal surgery for other pathologies, i.e. chordoma etc. the perceived risk may be higher therefore a more careful approach is required.

- Functional Neurosurgery: The clinical consequences of deep haemorrhage in patients who already have significant neurological impairment (Parkinson disease / tremor / dystonia) are significant. Moreover, these are minimally invasive stereotactic procedures where it is not possible to employ the usual haemostatic neurosurgical methods that are available with direct visualisation.
  There is well-documented evidence of low haemorrhagic risks when a strict approach is followed: A publication from a large series from the
  National Hospital advocates stopping NSAIDs and Aspirin 2 weeks before AND
  after the procedure as well as stopping DOACs 4 days before surgery and wait 2
  weeks before restarting and take specific advice from local haematology team (Zrinzo L et al)

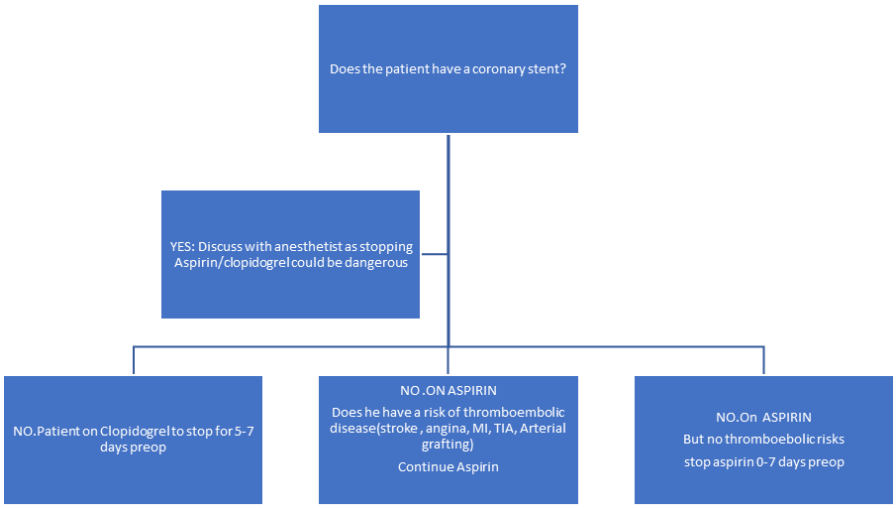
- Low risk procedures:

Some cranial surgical interventions could be considered **lower risk** than others so reducing the period of discontinuing OACs maybe reasonable, however surgeon's preference my vary therefore this should be individualised.

Indicative cases below:

- Extra-axial tumours
- Shunts

All patients taking chronic low-dose aspirin or Clopidogrel.


Does the patient have a coronary stent?
YES: Discuss with anesthetist as stopping Aspirin/clopidogrel could be dangerous
NO.Patient on Clopidogrel to stop for 5-7 days preop
NO .ON ASPIRIN
Does he have a risk of thromboembolic disease(stroke , angina, MI, TIA, Arterial grafting)
Continue Aspirin
NO.On ASPIRIN
But no thromboebolic risks
stop aspirin 0-7 days preop

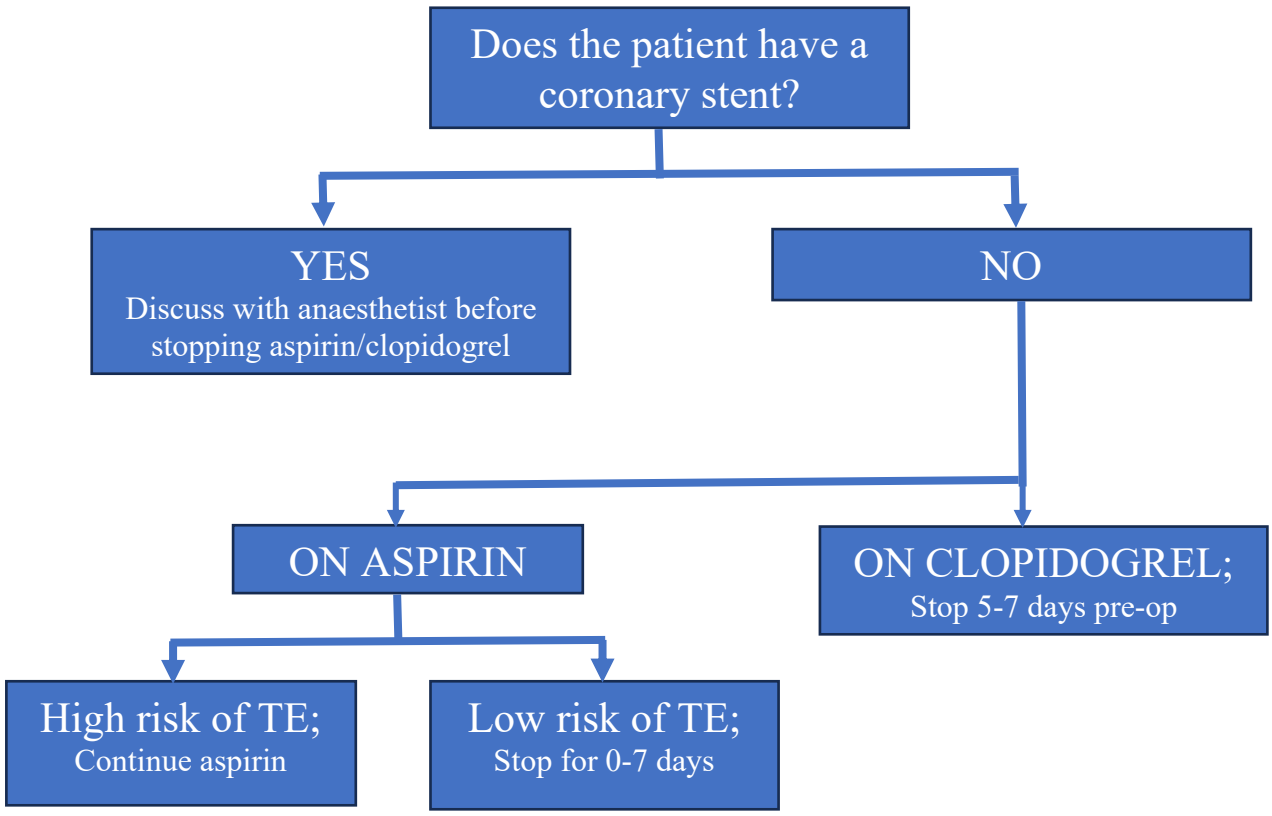

Does the patient have a coronary stent?
YES
Discuss with anaesthetist before stopping aspirin/clopidogrel
NO
ON ASPIRIN
ON CLOPIDOGREL;
Stop 5-7 days pre-op
High risk of TE;
Continue aspirin
Low risk of TE;
Stop for 0-7 days

Table 2; Recommendation for stopping and recommencing OAC/AP in elective procedures; should we be aiming for INR <1.2?

Drug	High risk of TE	Low risk of TE	Surgical risk*	Discontinuation pre-op (minimum)	Recommence post-op
Aspirin	Consider continuing	Stop pre-op	Stop if high risk, can continue if lower risk.	0 days in low-risk surgery 5 days in high risk	Day 3
Clopidogrel	Consider switch to aspirin	Stop-pre op	Stop or switch for all cases	7 days	Day 5
Warfarin	Stop Warfarin 5 days pre-op & use **bridging LMWH** 72hrs pre-op Stop bridging LMWH 24hrs pre-op **Aim for INR <1.5 on day of surgery**	Stop Warfarin 5 days pre-op No bridging required **Aim for INR <1.5 on day of surgery**	Stop Warfarin 5 days pre-op where able Check INR **<1.5** before day of surgery If INR ≥ 1.5 on day before surgery use Vitamin K 1-2 mg orally and recheck INR	5 days For high TE and high surgical risk consider intermediate dose LMWH e.g. dalteparin 5000 u bd **Check INR <1.5** before day of surgery If INR ≥ 1.5 on day before surgery use Vitamin K 1-2 mg orally and recheck INR	**Prophylactic LMWH;** start 24 hrs post-op **Treatment dose LMWH**; 48 hrs post-op if high SR & high TE risk OR 24 hrs post-op for low SR & high TE risk Start **warfarin** 48 hrs postop (unless concerns) & bridge until INR in range.
Apixaban, Rivaroxaban, Edoxaban	Can stop, or delay surgery	Can stop	Stop for all, no bridging	**GFR >30,** stop 2 days **GFR <30,** stop 3 days	**Prophylactic LMWH** as per warfarin. Restart NOAC 48 hrs post-op
Dabigatran	Can stop, or delay surgery	Can stop	Stop for all, no bridging	GFR >50, 2 days pre-op GFR <50, 4 days pre-op	Restart 72 hrs post-op
Unfractionated Heparin (UFH)	Can stop if surgery cannot be delayed	Can stop	Stop pre-op	4-6 hours	24 hrs post-op if low SR 48 hrs post-op if high SR
LMWH – therapeutic doses	Can stop For VTE < 30 days consider IVC filter	Can stop	Stop pre-op	If OD omit dose 24hrs pre-op If BD omit dose 12hrs pre-op	24 hrs post-op if low SR 48 hrs post-op if high SR
LMWH – prophylactic doses	Can stop	Can stop	Stop pre-op	12 hours	Start 24 hrs post-op unless concerns.

***Surgical Risk** = Patients who have a high risk of bleeding (uncontrolled hypertension, age > 65 y, liver disease, renal disease, >8 alcohol drinks per week, prior major bleeding or predisposition to bleeding will need to be considered high risk.

Management of OAC/AP in Emergency Cranial Neurosurgery

This advice relates to any emergency neurosurgical procedure and includes but is not limited to emergency craniotomy, decompressive craniectomy, external ventricular drain placement and burr hole surgery.

In general, it is accepted that all OAC/AP should be stopped and reversed on admission with an emergency neurosurgical pathology unless there is a strong reason not to. In some cases, it may be preferable to continue OAC/AP or switch to an alternative bridging treatment, and this should generally be done under specialist guidance.

Due to the nature of haemorrhagic underlying pathology, a separate review of evidence and guidelines are provided for;

a. Traumatic head injury
b. Spontaneous intracerebral haemorrhage (sICH)
c. Spontaneous subarachnoid haemorrhage

All other non-haemorrhagic emergency pathologies are treated as one group for the purpose of this guideline.

Current evidence on sub-specialty areas.

a. Traumatic head injury

This includes all types of traumatic intracranial haemorrhage (tICH) such as extradural haematoma (EDH), acute subdural haematoma (ASDH), traumatic subarachnoid haemorrhage (tSAH) and traumatic intra-parenchymal haemorrhage (IPH) or contusions.

This section does not include chronic subdural haematoma (CSDH), which should be considered separately.

In the presence of acute tICH, all AP and OACs should be stopped and reversed where possible to minimise the risk of haemorrhage expansion which occurs in approximately 25% of haemorrhages, mostly within the first 72 hours (***Edlmann 2023***). The highest risk group for haemorrhage expansion is in ASDH patients, particular care should be taken to pursue adequate reversal in these patients (***Pandaya 2018***).

It is also clear that this patient population have a high risk of thrombotic events, with a 4-5% stroke risk at 30 days, and therefore timely recommencement, within 7-14 days, should be considered (***Edlmann 2023***). Several large studies also show a lower risk of both thrombosis and overall mortality in the longer term if OACs are recommenced after traumatic brain injury (***Staerk, Puckett, Albrecht***). There is a lack of evidence surrounding the exact timing of recommencement and therefore currently a patient-centred approach should be taken. There is evidence that warfarin is associated with a greater risk of haemorrhage in trauma than DOACs, and therefore where appropriate patients should be switched to a DOAC from warfarin (***Scotti, Shin, Feeney***). A randomised trial on early (1 week) versus late (4 weeks) recommencement of DOACs after traumatic Intracerebral hematoma has started recruitment in the UK in 2025 and where appropriate, recruitment to this trial will inform on future practice.

b. Spontaneous ICH

Patients with spontaneous ICH (sICH) are largely managed under stroke physicians, and medical treatment decisions should be led by them. In a small number of cases, admission to a neurosurgical unit for observation or intervention is appropriate and decisions about management of OAC/APs is required. In nearly all situations OAC/AP are discontinued on diagnosis of a sICH to minimise the risk of clot expansion. There is a small group of patients who are at very high risk of thrombosis where this may not be the case or where bridging therapy may be needed upon discussion with local haematologists.

For the majority of patients in whom OAC/AP have been withheld, a decision about timing of recommencement is required. The RESTART trial found that recommencement of anti-platelets after sICH was not associated with a significantly higher rate of intracerebral haemorrhage but the secondary outcome of all major vascular events (including non-fatal MI, non-fatal stroke and death from vascular cause) was reduced by anti-platelet therapy, suggesting an overall balance to favouring recommencement (***Al-Shahi Salman 2019***). The median time to recommencement in this study was 76 days (IQR 29-146) suggesting only that AP recommencement is safe at approximately 10 weeks (earliest 4 weeks) post-sICH.

In relation to OAC recommencement after sICH is also likely to be on net-benefit regarding reduction of ischaemic stroke risk and overall mortality, but currently the data is very limited in this field with no RCTs published (***Hawkes 2018***). One pilot trial suggested OAC recommencement at a median of 16 weeks (IQR 7-38 weeks) had higher rates of intracranial haemorrhage (8% versus 4%) but there was also some evidence for benefit in reducing major vascular events (***Al-Shahi Salman 2021***). A more recent meta-analysis suggested benefit in restarting OACs within 2-4 weeks resulted in significant reduced ischaemic events and death with no increase in haemorrhage (***Huang 2022***). Another summary paper supported this, whilst recommending careful judgement for higher risk locations (e.g. brainstem/cerebellum) and the use of post-operative imaging to help guide decisions (***Li 2018***).

c. Spontaneous Subarachnoid Haemorrhage (SAH)

The early initiation of prophylactic LMWH (within 48hours) following aneurysm treatment, results in more favourable outcomes (with GOS) at 12 months due to reduced systemic ischaemia and has no impact on re-bleeding rates or cerebral ischaemia (***Hantsche 2021***). Therefore, this should occur in all SAH patients, unless there is a significant concern about bleeding risk such as a large clot.

Being on either aspirin or an OAC prior to aSAH does not appear to significantly increase the risk of a poor outcome, once the patient has survived to make hospital treatment (***Veldeman 2023, Dasenbrock 2017***). However, it is important that the underlying reason for the OAC is not forgotten, and treatment reinstated at a reasonable time point, although there is little data in the literature to guide the timing of this. The use of APs (including dual APs) post-aneurysm coiling has become more common place with the increase in stent-assisted coiling and flow-diversion to prevent post-procedural TE events (***Enomoto 2023***). Systematic review has also demonstrated that APs can be beneficial following aSAH regardless of the treatment (clipping/coiling) with reduction in delayed cerebral ischaemia and mortality and without increased bleeding (***Lee 2023***). Whilst research is on-going in this field and there are no randomised control trials, this data supports re-starting APs early in patients who already have risk factors indicating their use. The exception to this may be in patients requiring external ventricular drainage (EVD), where there is a bleeding risk of replacing or removing the drain.

Oral Anticoagulant / antiplatelet reversal for Emergency Cranial Neurosurgery
Where surgery can be safely delayed, this is the recommended action to reduce the bleeding risk. The following recommendations are for scenarios whereby surgery cannot be delayed.

Reversal in emergency scenarios should be performed with local haematology advice and following local protocols where appropriate.

Table 3; reversal recommendations in emergency cranial neurosurgery

Agent	Reversal
Anti-platelet agents	Give 1 g tranexamic acid intraoperatively. Request 2 pools of donor platelets and give first pool pre-operatively in anaesthetic room and second pool as and when required intra-operatively.
Warfarin	10mg Vit K intravenously and four-factor prothrombin complex concentrate (PCC) – if not available then give Fresh Frozen Plasma
Rivaroxaban, apixaban, edoxaban	1g Tranexamic acid intraoperatively (repeat if necessary) PCC use is controversial but can be considered if bleeding risk is high * *For patients with intracranial haemorrhage, PCC 25 to 50 IU/kg would be recommended and usually go for the higher dose of PCC 50 IU/Kg (if the last dose of DOAC was taken within 24 hours of presentation. If last dose of DOAC more than 24 hours but significantly impaired renal function, then discuss with Haematologist) The evidence for use of Andexanet alfa is not recommended in intracranial haemorrhage. (NICE currently recommends it for life threatening GI bleeding).
Dabigatran	1g Tranexamic acid intraoperatively (repeat if necessary) 5g IV infusion of idarucizumab followed by another 5g if required. PCC use for dabigatran is controversial.
UFH and LMWH	For UFH stopping the agent may be sufficient. Protamine can be used for both UFH and LMWH If last dose UFH > 4 hours nothing further may be required If last dose UFH ≤ 4 hours, then use protamine 1mg per 100u heparin slowly (especially if SC UFH; IV regimen stopped > 2 hrs may not need protamine) If last dose LMWH ≥ 12 hours (eGFR normal) nothing further may be required If last dose LMWH 8-12 hours consider protamine 0.5mg/100 u heparin slowly If last dose LMWH < 8 hours give protamine 1mg per 100u heparin slowly

Table 4; Recommendations on Oral Anticoagulant / antiplatelet recommencement after emergency cranial neurosurgery

Pathology	Medication	High risk TE	Low risk TE
Traumatic intracranial haemorrhage	Anti-platelets	Consider restarting day 7-14 depending on bleeding risk.	Consider restarting at 2-6 weeks depending on injury severity and patient factors.
	Warfarin	Change to DOAC where possible, consider re-starting day 7 depending on bleeding risk (or recruit to trial)	Change to DOAC where possible, start 1-4 weeks depending on injury severity and patient factors.
	DOACs	Re-start day 7 depending on bleeding risk (or recruit to trial)	Re-start 1-4 weeks depending on injury severity and patient factors

Spontaneous intracerebral haemorrhage	Anti-platelets	Restart by 10 weeks	Stroke team to determine on follow-up in relation to risk factors
	Warfarin	Change to DOAC where possible, restart from 4 weeks	MDT decision based on risk factors
	DOACs	Change to DOAC where possible, restart from 4 weeks	MDT decision based on risk factors
Subarachnoid haemorrhage	Anti-platelets	Within 48 hours of treatment unless bleeding concern.	Within 48 hours of treatment unless bleeding concern.
	Warfarin	Start prophylactic LMWH within 48 hours unless bleeding concern. Warfarin decision on MDT basis.	Start prophylactic LMWH within 48 hours unless bleeding concern. Warfarin decision on MDT basis.
	DOAC	Start prophylactic LMWH within 48hours unless bleeding concern. DOAC decision on MDT basis.	Start prophylactic LMWH within 48hours unless bleeding concern. DOAC decision on MDT basis.
Non-haemorrhagic emergency neurosurgery	Anti-platelets	Day 3-5 if unlikely to need further surgery	MDT decision based on risk factors and underlying pathology
	Warfarin	Recommence 48hrs if unlikely to need further surgery	MDT decision based on risk factors and underlying pathology
	DOAC	Recommence 48hrs if unlikely to need further surgery (72hrs for Dabigatran)	MDT decision based on risk factors and underlying pathology

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