

# Perioperative Management of Antiplatelet and Anticoagulant Therapy in Neurosurgical Patients: A Practical Review with Evidence-Based Flow Chart

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DOI: <https://doi.org/10.5281/zenodo.20486045>

Published Date: 01-June-2026

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**Abstract:** Background: For neurosurgery patients on antiplatelet or anticoagulation, there is a critical balance to be struck between the risks of bleeding and thromboembolic complications. A crucial distinction must be made, as the effects of even a small amount of over-bleeding are irreversible and fatal.

**Key Findings:** Aspirin can safely be continued for certain types of cranial or spinal procedures. P2Y12 inhibitors will need to be discontinued 5-10 days before operation. For Warfarin patients, the goal is an INR <1.4, and bridging is only recommended in extreme situations of thrombotic risk. All DOACs should be discontinued 48-72 hours before procedure, but emergency reversal is available if necessary (idarucizumab and andexanet alfa). Routine bridging anticoagulation should generally not be utilized.

**Conclusion:** Multidisciplinary, individualized decision making is necessary in each perioperative neurosurgical case; by accounting for the risks of bleeding from specific procedures versus individual thrombotic risks to a specific patient, one can provide adequate care. This review aims to offer a systematic evidence based approach to such a dilemma.

**Keywords:** anticoagulants; antiplatelet; neurosurgery; perioperative management; intracranial haemorrhage; bridging anticoagulation; DOAC reversal.

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## 1. INTRODUCTION

Both cardiovascular disease and cerebrovascular disease are on the rise globally, and significant proportions of patients undergoing neurosurgery will have been on long-term antithrombotic agents. Decisions about the perioperative management of antiplatelet or anticoagulation therapy in these patients is complex. Discontinuation of therapy increases the risk of ischemic stroke, myocardial infarction, venous thromboembolism, or mechanical prosthetic valve thrombosis. Conversely, continuation risks a potentially irreversible intracranial hemorrhage for which complete neurologic recovery will rarely occur. [1,4,15]

The implications of over-bleeding in the neurosurgical patient is of unique importance. The intracranial and spinal cavities do not tolerate volume in the same way as others. Over-bleeding only a few millimeters could cause catastrophic intracranial pressure elevations or spinal cord compression, resulting in irreversible neurological damage. Whereas an operation requiring the same extent of over-bleeding might be readily managed by re-exploration and drainage in the case of an abdominal procedure, re-bleeding intracranial will most likely lead to death. [11,13]

Optimal perioperative neurosurgical management requires an individualized and complete risk assessment which includes both the reason for which the patient is on antithrombotic therapy as well as time since the recent event/ placement of stent, the patient's renal and liver functions, as well as the particular drugs' own pharmacokinetics and the bleeding risk of the particular procedure itself. The expansion of DOACs—each with distinct half-lives, renal dependence, and reversal options—has further refined but also complicated this landscape. [5,9,28,29]

This review synthesises current evidence on perioperative antithrombotic management strategies in neurosurgery and presents a clinically applicable decision-support algorithm.

## 2. CLASSIFICATION OF ANTITHROMBOTIC AGENTS

### 1. Antiplatelet Drugs

Antiplatelet agents inhibit platelet activation and aggregation. Aspirin irreversibly acetylates cyclooxygenase-1 (COX-1), suppressing thromboxane A<sub>2</sub>-mediated platelet activation for the entire platelet lifespan (7–10 days). Clopidogrel, prasugrel, and ticagrelor are P<sub>2</sub>Y<sub>12</sub> receptor antagonists, widely prescribed in patients with acute coronary syndromes or coronary artery stents. Ticagrelor and prasugrel provide more potent and consistent platelet inhibition than clopidogrel. [6,7]

### 2. Anticoagulants

Warfarin, a vitamin K antagonist (VKA), inhibits hepatic synthesis of coagulation factors II, VII, IX, and X. Its anticoagulant effect is reflected by the international normalised ratio (INR). DOACs include dabigatran (direct thrombin inhibitor) and rivaroxaban, apixaban, and edoxaban (factor Xa inhibitors). Low-molecular-weight heparin (LMWH) and unfractionated heparin (UFH) provide parenteral options critical in bridging strategies. [5,8,9]

## 3. NEUROSURGICAL BLEEDING RISK

Intracranial surgery carries among the highest haemorrhagic risk of any surgical subspecialty. Postoperative haematoma formation can cause rapid neurological deterioration requiring urgent re-operation. Procedures associated with greatest risk include intracranial tumour resection (particularly highly vascular tumours), aneurysm clipping, skull base surgery, deep-brain stimulation, and instrumented posterior spinal decompression. [11,13,35,38]

Even 'minor' spine procedures may result in epidural haematoma with cord compression. For this reason, accepted haemostatic thresholds in neurosurgery are substantially more stringent than in most other surgical disciplines.

## 4. PREOPERATIVE ASSESSMENT

A structured preoperative assessment must evaluate: (i) the specific indication for antithrombotic therapy and its associated thrombotic risk; (ii) time elapsed since thromboembolic events or coronary stent insertion; (iii) renal and hepatic function affecting drug clearance; (iv) haematological profile including INR, platelet count, and bleeding time; and (v) procedural urgency and expected intraoperative bleeding risk. Patients with mechanical mitral valves, atrial fibrillation with high CHA<sub>2</sub>DS<sub>2</sub>-VASc scores, recent venous thromboembolism (<3 months), or recently placed coronary stents represent the highest-risk subgroup for therapy interruption. [1,3,15]

## 5. MANAGEMENT OF ANTIPLATELET THERAPY

### *Aspirin*

Traditional practice dictated aspirin cessation 7–10 days before elective neurosurgery, matching the duration of irreversible COX-1 inhibition. However, a body of evidence has accumulated demonstrating that low-dose aspirin does not significantly increase intraoperative blood loss or postoperative haematoma rates in select cranial and spinal procedures. A landmark analysis by Rahman et al. found no significant increase in haemorrhagic complications in neurosurgical patients continued on aspirin. [2,16,17,18] Despite this, most high-volume centres continue to withhold aspirin before major intracranial operations given the catastrophic consequences of haemorrhage in this anatomical compartment.

### *Clopidogrel and P2Y12 Inhibitors*

The standard approach is clopidogrel cessation 5–7 days preoperatively, prasugrel 7–10 days, and ticagrelor at least 5 days. For patients with recently placed coronary stents (bare-metal stents within 6 weeks, drug-eluting stents within 6–12 months), premature dual antiplatelet therapy discontinuation poses a risk of life-threatening stent thrombosis. In these cases, elective neurosurgery should be deferred if clinically feasible. When deferral is not possible, a multidisciplinary conference involving cardiology, anaesthesia, and neurosurgery is mandatory. [19,20,21]

## **6. MANAGEMENT OF WARFARIN**

Warfarin is typically withheld approximately 5 days before elective surgery, targeting an INR below 1.4 on the day of the procedure. [8] The practice in patients who have a high thromboembolic risk (mechanical prosthetic valves, recent thromboembolism) has been to bridge with therapeutic LMWH or UFH. The results of the landmark BRIDGE trial (Douketis et al., 2015) clearly showed that in patients with atrial fibrillation, omitting bridging did not increase the risk of arterial thromboembolism and dramatically reduced major bleeding risk. [25] Current consensus reserves bridging anticoagulation for patients with mechanical heart valves, particularly those with mitral valve prostheses, or very recent venous thromboembolism. [10,23,24]

For urgent or emergent reversal of warfarin-related coagulopathy, four-factor prothrombin complex concentrate (4F-PCC) is the agent of choice, offering rapid, volume-efficient INR correction. Vitamin K (intravenous) provides sustained but delayed reversal. Fresh frozen plasma may be used when PCC is unavailable, though its use requires large volumes and carries transfusion-related risks. [26,27]

## **7. MANAGEMENT OF DIRECT ORAL ANTICOAGULANTS**

DOAC perioperative management depends on the specific agent, renal function (creatinine clearance), and procedural haemorrhagic risk. For high-risk neurosurgical procedures, factor Xa inhibitors (rivaroxaban, apixaban, edoxaban) are held for 48–72 hours; dabigatran requires a longer hold (72–96 hours or more) in patients with impaired renal function given its predominantly renal elimination. [5,28,29]

Two specific reversal agents have transformed emergency DOAC reversal: idarucizumab (a humanised monoclonal antibody fragment) provides complete and immediate dabigatran reversal; andexanet alfa (a modified recombinant factor Xa decoy) reverses factor Xa inhibitors. [30,31] When these agents are unavailable, 4F-PCC provides partial but clinically meaningful reversal of factor Xa inhibitors. Laboratory monitoring (anti-Xa levels, dilute thrombin time) assists in documenting drug clearance preoperatively.

## **8. BRIDGING ANTICOAGULATION**

Heparin bridging aims to maintain anticoagulant coverage during the perioperative window. In the neurosurgical context, bridging carries a substantially elevated risk of postoperative intracranial haematoma and must not be applied indiscriminately. A systematic review by Garcia et al. demonstrated that perioperative bridging increased major bleeding without a statistically significant reduction in thromboembolic events for most patient subgroups. [10] Existing guidelines from ACCP, AHA/ACC and the ESC recommend bridging anticoagulation for mechanical mitral valves only, or for previous venous thromboembolism within the last 3 months.

## **9. POSTOPERATIVE RESUMPTION OF ANTITHROMBOTIC THERAPY**

Restarting antithrombotics post-neurosurgery requires tailored decision making. Restarting too early can compromise haemostasis, too late can compromise safety against thrombosis. We can use the framework below (based on the current evidence) to guide the restarting of agents: [1,11,23]

Mechanical VTE prophylaxis should be implemented during surgery and continued until it is deemed safe to reintroduce pharmacological prophylaxis. LMWH prophylaxis doses can usually be restarted from 24–48 hours post-operatively after successful surgical haemostasis on clinical and radiological grounds. Full doses of anticoagulation are withheld for at least 48–72 hours and more likely post-intracranial procedures until postoperative imaging results are obtained. Antiplatelet agents can be restarted from 24–72 hours in selected individuals. Repeated CT scans should be performed post-operatively prior to the commencement of pharmacological anticoagulation.

## 10. DISCUSSION

The management of perioperative antithrombotic therapy in neurosurgery is among the most complex and critical issues faced by neurosurgeons today. The following central issues arise from the literature.

### *Individualised Risk Stratification*

There is no longer any rationale for a standard approach to antithrombotic management during the perioperative period. The change towards individually assessed risk-while considering simultaneously the individual patient's thromboembolic risk profile and the procedure's haemorrhagic risk-is based upon the developing consensus that both approaches at either extreme of this continuum-arbitrary continuation and universal cessation-result in death from distinct causes. The largest of these retrospectives including the Hamilton series, ACCP 2022, and others has shown that the optimal outcome occurs when the risk categories intersect: [1, 35]

### *The Aspirin Controversy*

The position of aspirin in perioperative neurosurgery continues to evolve and be debated. Historically based on apprehension regarding haemostasis in the surgical field, cessation of all perioperative neurosurgery no longer is automatic. Several studies including the one by Rahman et al and Korinth et al., have demonstrated that low-dose aspirin does not significantly increase clinically relevant haemorrhagic complications in elective cranial and spinal procedures. [17,18] Despite , the heterogeneity of neurosurgical interventions from surface tumour biopsies to complex aneurysm clipping—makes a blanket policy inappropriate. Prospective randomised data in high-risk intracranial procedures remain scarce.

### *Bridging Anticoagulation: Falling Out of Favour*

The publication of the BRIDGE trial marked the first major turning point in perioperative anticoagulant management [25]. This evidence was practice changing when non-inferiority of a no-bridging strategy was shown in AF patients having a haemostatic procedure. The cost of postoperative haemorrhage in the field of neurosurgery is unlike any other discipline, and this study provides overwhelming argument against bridging as standard practice in this specialty. Bridging only becomes necessary in patients with mechanical mitral valve or who are less than three months from a DVT or PE, and even then only following discussion in the MDT.

### *DOAC Management: A Rapidly Evolving Landscape*

The increased use of DOACs have complicated, yet solved problems for the perioperative neurosurgeon; specific reversal agents for dabigatran (idarucizumab) and for factor Xa inhibitors (andexanet alfa) have greatly improved the neurosurgeon's ability to deal with emergency and elective cases[30,31]; the ANNEXA-4 study has confirmed haemostatic effectiveness of andexanet alfa in factor Xa inhibitor-associated intracranial haemorrhage; neurosurgical units with complex patients should have clear procedures for quick availability of these agents

### *Special Populations*

Three neurosurgical subgroups merit specific mention. Patients undergoing intracranial tumour surgery face compounded risk from tumour-related coagulopathy, neovascularity, and post-resection cavities; anticoagulation restart should be guided by sequential imaging. Patients with spinal epidural haematoma, a rare but devastating complication of spine surgery in anticoagulated patients, require immediate surgical decompression; prevention through meticulous haemostatic timing is paramount. [41,42] Finally, patients with flow diverters or intracranial stents who require urgent surgery represent perhaps the most challenging subgroup, requiring close coordination with neuro-interventionalists to weigh stent thrombosis risk against surgical haemorrhage risk. [43,44]

### *Limitations and Future Directions*

Despite growing evidence, perioperative antithrombotic management in neurosurgery remains largely guided by extrapolation from general surgery trials, pharmacokinetic modelling, and single-centre retrospective data. High-quality prospective randomised controlled trials specifically addressing neurosurgical populations are markedly lacking. Future research should prioritise: (i) randomised trials of aspirin continuation versus cessation in high-risk cranial procedures; (ii) prospective evaluation of DOAC reversal agent protocols in the emergency neurosurgical setting; and (iii) development of validated risk-scoring systems that integrate both thromboembolic and haemorrhagic risk with procedure-specific data.

### 11. CLINICAL ALGORITHM: PERIOPERATIVE ANTITHROMBOTIC MANAGEMENT

Figure 1 presents a structured decision-support algorithm for perioperative antithrombotic management in neurosurgical patients, integrating haemorrhagic risk stratification, thromboembolic risk evaluation, drug-specific interruption protocols, emergency reversal pathways, and postoperative restart guidance.

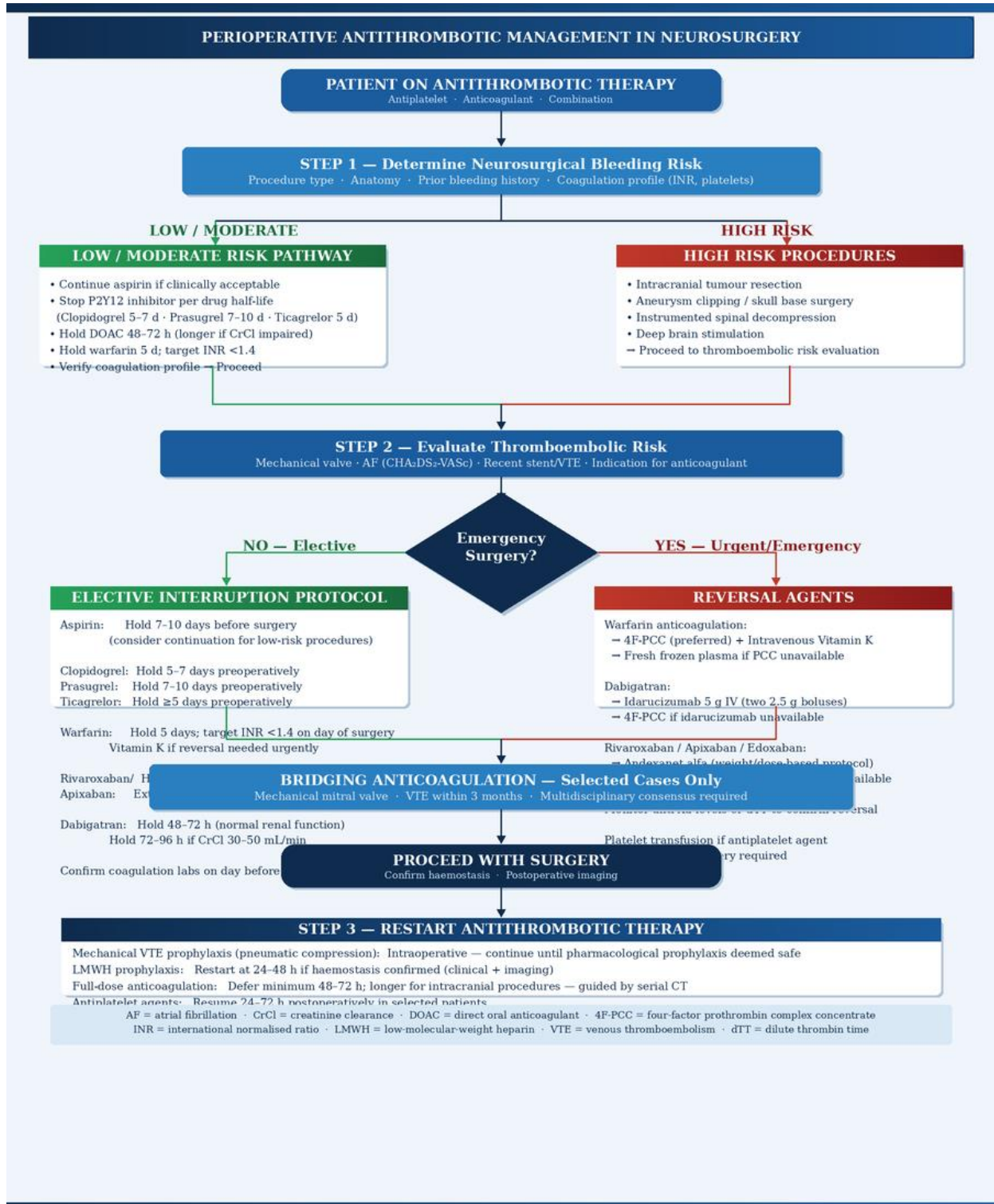


Figure 1. Evidence-based perioperative antithrombotic management algorithm for neurosurgical patients. AF = atrial fibrillation; CrCl = creatinine clearance; DOAC = direct oral anticoagulant; INR = international normalised ratio; LMWH = low-molecular-weight heparin; 4F-PCC = four-factor prothrombin complex concentrate; VTE = venous thromboembolism.

## 12. CONCLUSION

A well informed, individualised approach to perioperative antithrombotic management of neurosurgical patients is required and can only be achieved with an appropriate knowledge of drug pharmacology and procedure-specific haemorrhagic risk. The central principles governing this are; bridging anticoagulation limited to the high-risk thrombotic subgroups, the use of aspirin in chosen elective scenarios, use of the relevant drug-specific cessation period and appropriate monitoring of renal function for individual DOACs, availability of immediate antidotes for acute surgery, and the reintroduction of anticoagulation based on clinical and radiological evaluation of haemostasis. Collaboration between neurosurgeons, cardiologists, haematologists and anaesthetists will be key. There remains a research gap in robust trial data relating to the neurosurgical population. [1,11,13,14

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