

Handling Anticoagulants for Stroke Prophylaxis in Different and Challenging Clinical Situations

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DEAR EDITOR,

Managing anticoagulation for stroke prophylaxis requires a delicate balancing act between thrombotic risk (preventing a stroke) and hemorrhagic risk (preventing a life-threatening bleed). The clinical focus has shifted heavily toward personalized medicine and individualized approaches and the use of Direct Oral Anticoagulants (DOACs) over VKA (vitamin K antagonist), though certain "grey area" scenarios remain challenging.

The Extreme Scenarios:

1. An ongoing life-threatening bleeding, significantly deranged coagulation abnormality/thrombocyte count or function prognosticating a life-threatening bleeding, or a drop in hemoglobin of more than or equal to two gm/dl requiring two or more units of blood transfusions.
2. A mechanical valve demanding support of oral anticoagulation to maintain a target INR to ensure its normal functioning to prevent a life-threatening thrombotic event at any cost.

There are few clinical scenarios when starting anticoagulants as stroke prophylaxis is challenging:

The High Bleed Risk Patient (HAS-BLED vs. CHA₂DS₂-VASc): When a patient has a high stroke risk but also a history of gastrointestinal bleeds or frequent falls, the decision becomes difficult.

The Strategy: We need to focus on modifiable risk factors (uncontrolled hypertension, NSAID use, alcohol consumption). Alternatively, if long-term anticoagulation is contraindicated due to recurrent life-

threatening bleeds, Left Atrial Appendage Occlusion (LAAO)—like the Watchman device—is the primary non-pharmacological alternative.

DOAC Selection: Low-dose options (e.g., apixaban 2.5 mg BID) are often preferred over warfarin in elderly "fall-risk" patients due to a lower incidence of intracranial haemorrhage [1].

Chronic Kidney Disease (CKD) and Dialysis: Renal impairment significantly complicates DOAC metabolism.

Renal status and preferred Agent:

- CrCl > 30 mL/min: Any DOAC standard dosing (adjust for age/weight).
- CrCl 15–30 mL/min: Apixaban or Edoxaban requires careful dose reduction.

ESRD/Dialysis:

Warfarin or Apixaban data is still evolving; warfarin has traditionally been the gold standard, but apixaban 2.5 mg BID is increasingly used based on recent registry data.

Post-Intracranial Hemorrhage (ICH):

Timing: Current consensus suggests waiting 4 to 8 weeks post-ICH, provided the source of the bleed is controlled (e.g., blood pressure) and the hematoma has stabilized [2].

Lobar Versus Non-Lobar: Lobar bleeds (often associated with amyloid angiopathy) have a higher recurrence risk, making LAAO a more attractive option than restarting drugs.

Triple Therapy (Post-PCI in Patients with Atrial Fibrillation) [3]: Handling a patient with atrial

fibrillation who just received a coronary stent is a "triple threat" (anticoagulant + aspirin + P2Y12 inhibitor).

The Modern Shift: "Triple therapy" is now kept as short as possible (often 1 to 7 days or just the duration of the hospital stay).

The "Dual" Approach: most patients are transitioned quickly to "Dual Therapy": a DOAC + a P2Y12 inhibitor (usually Clopidogrel) for 6–12 months.

Anticoagulation in Cancer Patients: Anticoagulation selection in cancer patients balances thrombosis risk with bleeding risk. Active, progressive cancer often warrants continued anticoagulation. Venous thromboembolism, stroke and myocardial infarction contribute to 25.8% of overall mortality in cancer patients often requiring lifesaving anticoagulation. Key factors under consideration for the choice of anticoagulation type are cancer type/activity, renal/platelet function, drug interactions with chemotherapy, and patient preference.

Key Considerations- in cancer patients:

Bleeding Risk: High-risk areas (gastrointestinal and genitourinary cancers), low platelets, or recent surgery often favour LMWH.

Drug Interactions: Avoid DOACs with strong interactions (e.g., some chemotherapeutic drugs like ibrutinib).

Renal Function: Adjust DOAC doses for renal impairment; LMWH may be better for severe impairment.

Practical approach- in cancer patients:

Initial Choice: LMWH or a DOAC (e.g., apixaban/rivaroxaban) for most, tailored to risk, monitor & re-evaluation.

Regular checks (platelets, renal function, bleeding) are crucial; we need to adjust therapy as cancer/patient status changes.

Multidisciplinary Care: We need to involve haematology/oncology for complex cases, discuss with patient/ family and need to respect their wishes.

Anticoagulation in CVT (Cerebral Venous Thrombosis) and Secondary Intracerebral Haemorrhage:

Approximately 30% to 40% of CVT patients present with ICH (intracerebral haemorrhage) at the time of diagnosis. Pathophysiology: ICH in CVT results from high venous pressure causing venule rupture or hemorrhagic transformation of a venous infarct. Large-scale observational data suggest that OAC treatment in CVT patients with ICH does not significantly increase the risk of hematoma expansion. However, we cannot give OAC for patients where OACs are strictly contraindicated for some reasons or who show rapid clinical deterioration despite treatment, endovascular therapy (EVT) or decompressive craniectomy may be considered as rescue options.

Anticoagulant in a State of Disarray of Coagulation State in the Body Secondary to Infection/Sepsis, Hematological Disorder:

Sepsis causes hepatic dysfunction, which reduces clotting factor production. We need to keep in mind the interaction of anticoagulants with antibiotics. Common sepsis-treating antibiotics can interact with anticoagulants, causing unpredictable, dangerously high INR levels. Some of our commonly used antibiotics, such as piperacillin/tazobactam, ampicillin/sulbactam, tigecycline, and cephalosporins with NMTT or MTD side groups, fall in this category. Besides this, any long-term antibiotic therapy can also lead to vitamin K deficiency and coagulation dysfunction secondary to dysbiosis of the intestinal flora and abnormal liver function.

How to tackle the situation:

1. It is generally recommended to hold oral anticoagulant therapy (like warfarin) immediately upon suspicion of sepsis.
2. Switch to parenteral anticoagulation: If the indication for anticoagulation is high-risk (e.g., active pulmonary embolism/deep venous thrombosis, mechanical valve), switch to therapeutic-dose low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH). UFH is often preferred in acute renal failure or unstable patients due to its short half-life and reversibility.
3. Prophylactic Dosing: If the patient was taking anticoagulants for lower-risk indications (e.g., stable AF) or simply for venous thromboembolism (VTE) prophylaxis, switch to prophylactic-dose LMWH or UFH.
4. Monitor Coagulation Closely: Daily monitoring of PT/INR, PTT, fibrinogen, and platelets is necessary to detect the development of Disseminated Intravascular Coagulation (DIC).
5. Identify "Sepsis-Induced Coagulopathy" (SIC): If a patient develops DIC (specifically, SIC), anticoagulants might actually improve mortality, contrary to the general rule.
6. Resuming Anticoagulation: - Resume or switch back to the oral agent only after the sepsis has resolved, organ function has stabilized, and the patient is no longer receiving interacting antibiotics. Ensure that the INR has returned to the desired therapeutic range.
7. Consider restarting the anticoagulant 1-4 weeks after the major bleeding has stopped, balancing the thrombosis and bleeding risk and the patient's background co-morbidities.
8. It may also happen that we may never restart the OAC after detailed discussion with the treating team.

The "Extremes" of Body Weight:

1. Obesity (BMI > 40 or Weight > 120 kg): recent guidelines now support the use of apixaban or rivaroxaban in these patients.
2. Underweight (< 60 kg): Requires mandatory dose reduction for most DOACs to avoid over-anticoagulation.

Treatment adherence to anticoagulant:

1. Treatment adherence to oral anticoagulants is an ongoing issue, and one in three patients adhering to their DOAC <80% of the time, which was associated with poor clinical outcomes in nonadherent patients.^[4]
2. Clinical practitioners must actively involve patients in treatment processes involving anticoagulants in stroke.
3. Use of pillboxes to regularly monitor the drug intake may be helpful.
4. A more active and widespread implementation of patient education programs is required, and the cost of the anticoagulants needs to be affordable to all.

Quantitative Assessment of Anticoagulant (Measurement/Monitoring)

Definition: Quantitative assessment of anticoagulant provides a specific, precise measurement of the anticoagulant concentration (e.g., ng/mL) or a direct measurement of the drug's activity (e.g., IU/mL).

1. Anti-Factor Xa is calibrated to specifically measure the concentration of rivaroxaban, apixaban, or edoxaban.
2. Diluted Thrombin Time (dTT) / Ecarin Clotting Time (ECT): Used for precise quantification of dabigatran.

Qualitative Assessment of Anticoagulant (Measurement/Monitoring)

Definition: Determines the presence, absence, or approximate qualitative range (e.g., normal, low, high) of an anticoagulant.

1. Prothrombin Time (PT/INR): Can qualitatively detect the presence of factor Xa inhibitors like rivaroxaban.
2. Activated Partial Thromboplastin Time (aPTT): Used for detecting the presence of dabigatran or heparin.

3. Thrombin Time (TT): Highly sensitive for detecting the presence of dabigatran.

In conclusion, the management of anticoagulation for stroke prophylaxis rarely follows a uniform approach.

1. A discussion with the patient and family is required regarding this chronic treatment process, regarding possible ups and downs during the course of the treatment and how to handle them.
2. A careful follow-up regarding stringent adherence to the drug is necessary.
3. Monitoring of medical comorbidities and the dynamic metabolic/coagulation parameters is required. Such variables may affect drug selection, the dose of the anticoagulant, or temporary/permanent stoppage of the drug.
4. More widespread educational programs are required to ensure updated knowledge about the importance of anticoagulants in stroke prophylaxis. The possible options and pros and cons of their usage need to be discussed to bring both confidence and compliance towards the treatment.

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