Management of Bleeding in Patients Receiving Direct Oral Anticoagulants

The use of any anticoagulant carries an inherent risk of bleeding, and bleeding complications can rapidly progress to life-threatening scenarios. Managing haemorrhage in individuals receiving direct oral anticoagulants (DOACs) presents unique clinical challenges, as routine coagulation assays cannot reliably determine the degree of anticoagulation, and reversal agents may be difficult to access whilst potentially introducing prothrombotic risks.

This presentation provides a comprehensive clinical approach to managing bleeding complications in patients receiving DOACs, incorporating evidence-based strategies, practical guidance on reversal agents, and considerations for resuming anticoagulation therapy.

RELATED TOPICS

Scope and Related Clinical Scenarios

DOAC-Associated Bleeding

- Intracerebral haemorrhage management
- Heavy menstrual bleeding in anticoagulated patients
- Prevention strategies and risk mitigation
- Perioperative anticoagulation management

DOAC Clinical Applications

- General prescribing considerations and contraindications
- Atrial fibrillation stroke prevention
- Venous thromboembolism treatment and prophylaxis
- Dosing adjustments in special populations

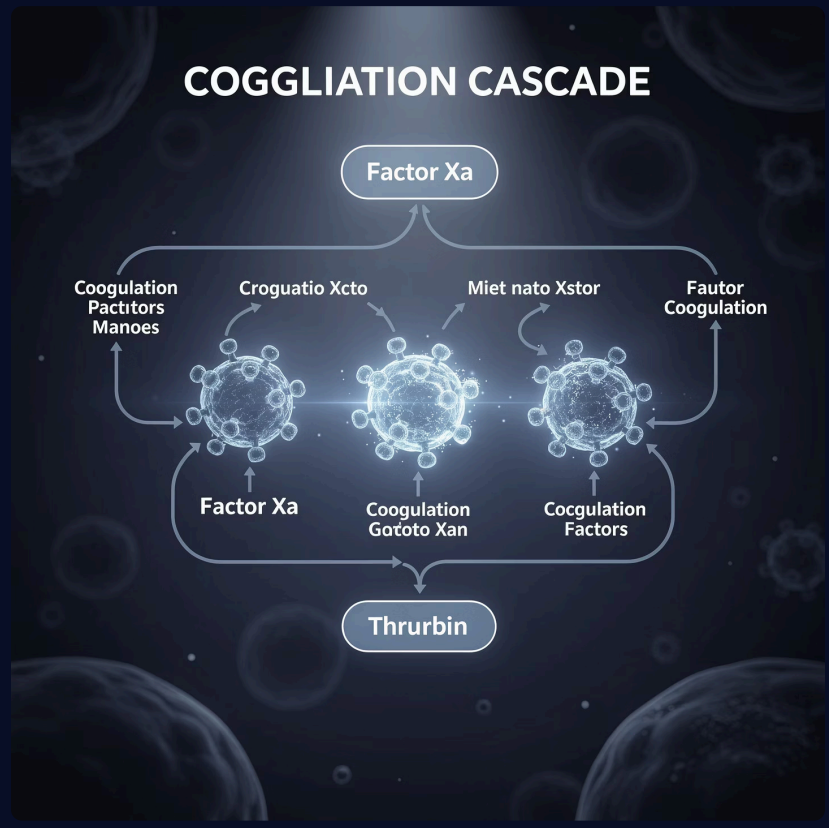
This presentation focuses specifically on the acute management of bleeding complications. Complementary topic reviews addressing prevention, specific bleeding sites, and therapeutic indications for DOACs are available in separate clinical resources.

Definition of Terms

Establishing clear terminology ensures precise clinical communication and appropriate therapeutic decision-making in anticoagulation management.

Direct Oral Anticoagulants: Mechanism and Classification

Direct oral anticoagulants (DOACs), also termed non-vitamin K oral anticoagulants (NOACs), are oral medications that directly inhibit specific enzymes in the coagulation cascade. These agents offer predictable pharmacokinetics without requiring routine monitoring, distinguishing them from traditional anticoagulants.



Direct Thrombin Inhibitor:

- **Dabigatran** (Pradaxa) – The only oral direct thrombin inhibitor available for clinical use, targeting factor IIa

Direct Factor Xa Inhibitors:

- **Rivaroxaban** (Xarelto)
- **Apixaban** (Eliquis)
- **Edoxaban** (Lixiana, Savaysa)

Note the naming convention: generic names for factor Xa inhibitors incorporate "xaban" (rivaro**xaban**, api**xaban**, edo**xaban**).

Parenteral direct thrombin inhibitors (argatroban, bivalirudin) and indirect factor Xa inhibitors (heparins, fondaparinux) operate through different mechanisms and require distinct management approaches.

Defining Bleeding Severity

Bleeding exists on a continuum, and initial presentations can be misleading. What appears as massive lower gastrointestinal haemorrhage may prove less severe retrospectively, whilst occult bleeding–such as retroperitoneal haemorrhage–can present innocuously yet progress to significant morbidity or mortality. Clinical judgement remains paramount in assessing bleeding risk and trajectory.

Major/Serious Bleeding

Bleeding associated with transfusion risk, haemorrhage into critical closed spaces (intracranial bleeding, compartment syndrome), or requiring interventional procedures (surgery, interventional radiology, endoscopy). Carries significant immediate morbidity risk regardless of aetiology, with substantial risk of death during hospitalisation.

Minor Clinically Significant Bleeding

Bleeding requiring healthcare assessment or less invasive treatment, including heavy menstrual bleeding, ecchymosis, or epistaxis. Generally does not necessitate interruption of anticoagulant therapy but warrants clinical attention and monitoring.

Critical consideration: Haemoglobin determinations cannot initially measure bleeding severity. Development of anaemia is delayed until after fluid resuscitation or re-equilibration from body water, which may take several hours post-haemorrhage.

PATIENT ASSESSMENT

Clinical Evaluation Framework

Appropriate management of DOAC-associated bleeding depends on systematic risk stratification encompassing bleeding severity, anticoagulation status, and the underlying indication for anticoagulant therapy. This multifaceted assessment guides therapeutic decision-making and prioritisation of interventions.

Initial Clinical Assessment

We conduct a comprehensive evaluation addressing bleeding severity and haemostatic impairment, incorporating thorough history-taking and complete medication review.

01

Bleeding Characterisation

Severity assessment, anatomical location, and determination of active haemorrhage status

02

Anticoagulant Details

Specific agent identification, timing of last dose, and expected duration of anticoagulant effect

03

Overdose Assessment

Evaluation for intentional or unintentional anticoagulant overdose

04

Organ Function Status

History of renal or hepatic disease, underlying bleeding disorders potentially causing excessive anticoagulant effect

05

Concomitant Medications

Other medications affecting haemostasis (aspirin, clopidogrel, herbal supplements)

06

Comorbidity Evaluation

Conditions promoting bleeding (liver disease, uraemia, thrombocytopenia)

07

Thrombotic Risk

Anticoagulation indication and thrombosis risk during therapy interruption

Bleeding Assessment Protocol

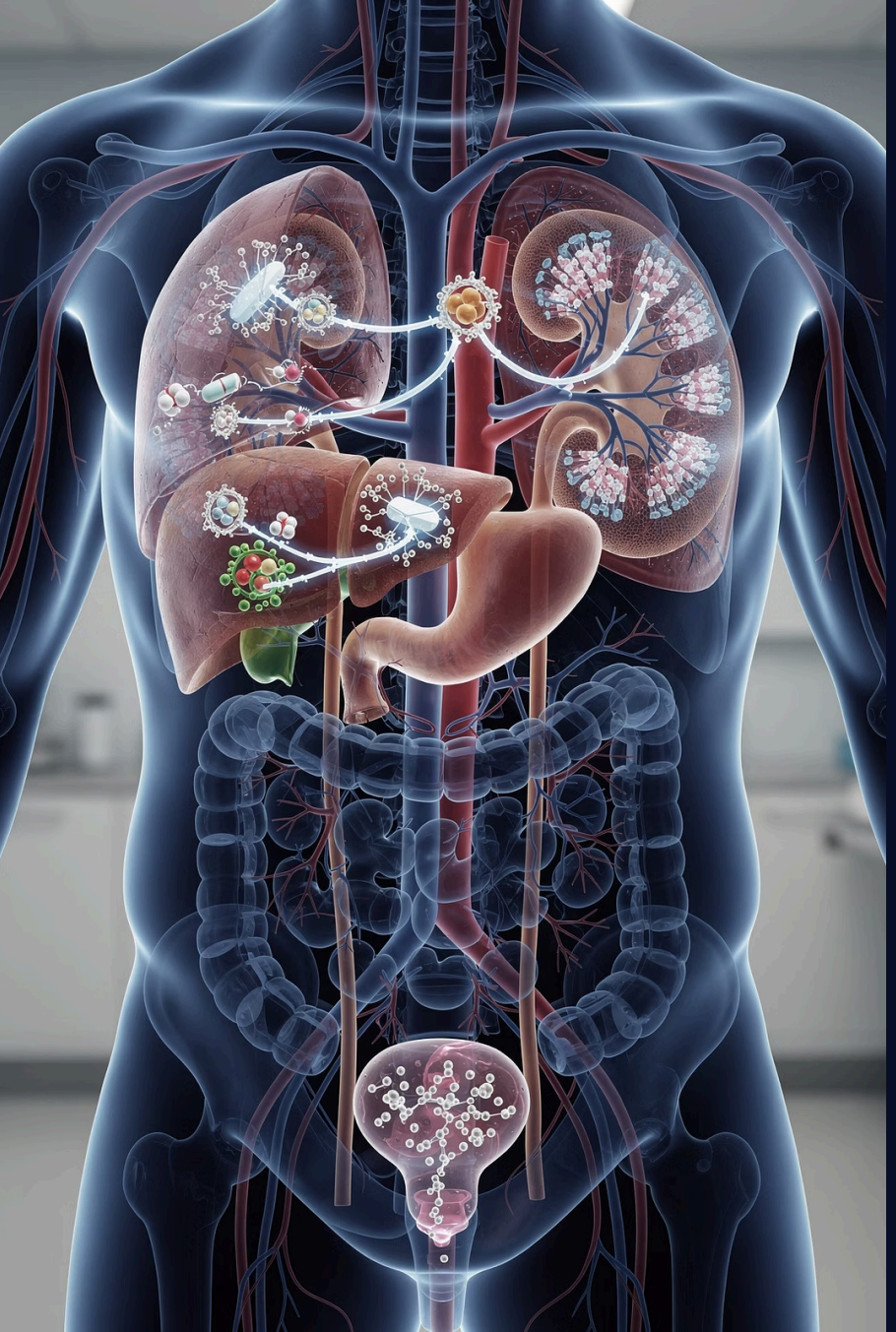
More severe bleeding necessitates increasingly aggressive interventions. We assess bleeding according to anatomical site, rate of haemorrhage, and magnitude of blood loss through thorough physical examination with serial vital signs measurement.

Assessment Components:

- Serial haemoglobin measurements for significant blood loss concerns
- Imaging studies (CT scanning for intracranial or retroperitoneal haemorrhage)
- Endoscopy for direct visualisation of bleeding sites

Many patients presenting with minor bleeding, slow blood loss, or simple anaemia without evidence of bleeding may not require DOAC reversal. Given the short half-lives of these agents, even brief but unnecessary therapy interruption could result in avoidable thrombosis.

Clinical pearl: Occasionally, bleeding appearing significant is not genuinely serious (some epistaxis or haemorrhoidal bleeds). In such cases, observation and local measures–ice and pressure–may allow bleeding resolution without aggressive treatments exposing patients to reversal strategy risks and potential thrombosis from anticoagulant withdrawal.



Assessing Anticoagulation Status

The degree of anticoagulation proves crucial both for predicting the bleeding episode course and determining required interventions. Anticoagulation status depends on the specific agent, dose, time since last administration, and renal (and to a lesser extent hepatic) function.

Half-Life Considerations and Time to Clearance

We consider anticoagulation fully resolved after five half-lives have elapsed since the last dose. The degree to which the anticoagulant impairs haemostasis dissipates continuously, occurring much more rapidly with DOACs than with vitamin K antagonists.

12-17h

Dabigatran Half-Life

Five half-lives elapsed by day 2.5 to 3.5 after last dose in normal renal function

5-9h

Rivaroxaban Half-Life

Five half-lives elapsed by day 1 to 2 after last dose in normal renal function

8-15h

Apixaban Half-Life

Five half-lives elapsed by day 1.5 to 3 after last dose in normal renal function

6-11h

Edoxaban Half-Life

Five half-lives elapsed by day 1.3 to 2 after last dose in normal renal function

Impact of Renal and Hepatic Function

DOAC half-lives depend significantly on kidney function and, to a lesser extent, liver function. Patients with renal disease and/or severe hepatic impairment may experience greater anticoagulation degree and/or duration compared with patients with normal organ function for equivalent dosing schedules.

Dabigatran

Approximately 80-85% renal excretion

Highly dependent on kidney function for clearance

Rivaroxaban

Approximately 35% renal excretion

Severe hepatic impairment could result in bio-accumulation

Apixaban

Approximately 25% renal excretion

Severe hepatic impairment could result in bio-accumulation

Edoxaban

Approximately 35% renal excretion

Severe hepatic impairment could result in bio-accumulation

Coagulation Testing in DOAC Management

Coagulation testing is not routinely employed for determining anticoagulation status in patients receiving DOACs. With routinely available coagulation assays, prolonged clotting times can assist in determining residual anticoagulant effect; however, normal coagulation testing cannot necessarily confirm anticoagulant effect resolution or eliminate the need for aggressive interventions. Clinicians should consult local laboratories to determine whether rapidly available assays can exclude significant DOAC effect.

Standard Testing

- Prothrombin time/international normalised ratio (PT/INR)
- Activated partial thromboplastin time (aPTT)
- Thrombin clotting time (TT) for suspected dabigatran effect

Interpretation Guidance

If the relevant laboratory has validated that PT or aPTT is reliably prolonged by even low concentrations (30-50 ng/mL) of the agent in question, a normal value may provide reassurance. This requires consultation with laboratory personnel regarding institution-specific validated testing.

Specialised Coagulation Testing

Specialised testing possesses limited availability but may prove useful if available with rapid turnaround time from experienced laboratories. Testing may include anti-factor Xa heparin level, quantitative factor Xa inhibitor levels, and quantitative dabigatran levels.

Dabigatran-Specific Testing: Although we treat patients with persistent bleeding and normal basic coagulation testing as if they remain anticoagulated, an exception exists for patients receiving dabigatran with a normal TT—we consider this sufficient to eliminate continued dabigatran effect possibility. However, TT demonstrates extreme sensitivity to dabigatran effects and can be prolonged by trivial drug amounts. A calibrated dilute TT is preferable when available, correlating linearly with dabigatran concentration.

Factor Xa Inhibitor Testing: Specific anti-factor Xa activity assays are available in many institutions, though few clinicians possess timely access. Absent anti-factor Xa activity indicates no clinically relevant anti-factor Xa drug effect. Increased activity may reflect continued anticoagulant effect; however, unless the assay has been calibrated for the specific anticoagulant, the anticoagulant effect magnitude cannot be reliably determined.

- **Point-of-Care Testing:** Some laboratories offer rapid turnaround anti-factor Xa and thrombin time (DOAC screen); in some areas, rapid urine tests (DOAC dipstick) are available. These tests are unlikely to provide reliable quantitative drug levels but may guide reversal agent decisions.

We do not utilise thromboelastography (TEG) or related point-of-care coagulation tests to manage DOAC-associated bleeding, as data correlating these tests with drug concentration, clinical bleeding, and/or anticoagulant effect are lacking.

Additional Laboratory Evaluation

No additional laboratory testing is absolutely required beyond coagulation testing outlined previously. However, depending on bleeding severity, we often perform comprehensive assessment to guide transfusion decisions and identify contributing factors.

Complete Blood Count

Assessment of haemoglobin level and platelet count, as red blood cell and/or platelet transfusions may be indicated. Prudent to acquire pretransfusion testing sample (type and screen) when CBC is drawn if any likelihood exists of requiring blood product support.

Renal Function

Given DOAC clearance dependence on kidney function, creatinine determination and creatinine clearance calculation should be performed in all patients with significant, unexplained bleeding. Uraemia may also impair platelet function, further reducing haemostasis.

Hepatic Function

Assessment of liver synthetic function in patients with prolonged PT or signs/symptoms suggestive of liver disease, evaluating reduced clearance possibilities of direct factor Xa inhibitors partially metabolised hepatically. Diminished hepatic function may contribute to bleeding if coagulation factor synthesis is impaired.

DIC Evaluation

Patients with suspected disseminated intravascular coagulation in the setting of trauma or sepsis may require additional measurements including fibrinogen and D-dimer testing to guide comprehensive management strategies.

MAJOR BLEEDING

Overview of Major Bleeding Management

Patients with serious/major bleeding should be managed in intensive care settings with appropriate haemodynamic support. Management options include observation; drug removal with activated charcoal and/or haemodialysis; and active interventions including antifibrinolytic agent administration, clotting factor products (prothrombin complex concentrates, activated prothrombin complex concentrates), specific reversal agents (idarucizumab for dabigatran, andexanet alfa for direct factor Xa inhibitors), and/or surgery.

The appropriate approach depends on ongoing bleeding severity assessment. Early involvement of appropriate specialists is vital for definitive interventions at bleeding sites, which can be both diagnostic and therapeutic. The consulting endoscopist, interventional radiologist, or surgeon should be notified immediately regarding potential intervention need in patients with bleeding that is (or may become) severe.

Essential Management Components for Major Bleeding

1

Discontinue Anticoagulation

Immediate discontinuation of all anticoagulant and antiplatelet therapy must be clearly documented in medical records and ordering systems, including avoidance of routine venous thromboembolism prophylaxis orders

2

Haemodynamic Monitoring

Rapid and continuous haemodynamic assessment with establishment of effective airway and large-bore intravenous access

3

Physiological Optimisation

Optimisation of body temperature, blood pH, and electrolyte balance, including calcium levels

4

Transfusion Support

Transfusions if required: red blood cells for severe anaemia or ongoing blood loss; platelets for thrombocytopenia and/or severe platelet dysfunction; plasma for trauma-associated coagulopathy

Site-Specific Major Bleeding Considerations

Intracerebral Haemorrhage

ICH represents a critical concern as bleeding increases intracranial pressure, and haematoma expansion is common. Clinical features generally cannot distinguish ischaemic stroke from haemorrhagic stroke with intracerebral bleeding; ICH diagnosis must be confirmed by non-contrast computed tomography or magnetic resonance imaging, whichever is fastest.

However, empiric treatment for suspected ICH without intracranial imaging may be appropriate in some cases when time delay in obtaining imaging could be life-threatening. Management, including anticoagulant reversal, is discussed in separate topic reviews specific to intracranial haemorrhage.

Other Major Bleeding Sites

Other major bleeding sites may include:

- Retroperitoneal bleeding
- Compartment syndrome
- Massive gastrointestinal haemorrhage
- Traumatic haemorrhage

Additional considerations in managing these types of major bleeding are discussed in detail in separate clinical resources addressing specific anatomical sites and clinical scenarios.

REVERSAL STRATEGIES

General Strategy for Anticoagulant Reversal

Reversal of anticoagulation is generally considered desirable in patients with serious or life-threatening bleeding who remain actively anticoagulated with a DOAC, although randomised trial data supporting this practice are lacking.

Specific Reversal Agents

Idarucizumab for dabigatran; andexanet alfa for oral direct factor Xa inhibitors

Nonspecific Agents

Prothrombin complex concentrates (PCCs) and activated PCCs

Antifibrinolytic Agents

Tranexamic acid and epsilon-aminocaproic acid

Drug Removal

Activated charcoal, desmopressin, haemodialysis (dabigatran only)

Balancing Reversal Benefits and Risks

High-quality evidence from randomised trials is lacking for reversal strategies; thus, our practice is based on clinical experience and data from case series. Our approach attempts to balance the risk of life-threatening bleeding with thrombosis risk, which may be increased based on the underlying condition for which anticoagulation was prescribed and/or prothrombotic effects of some therapies (andexanet alfa, PCCs).

In most cases of major (life-threatening or uncontrolled) DOAC-associated bleeding, we suggest using a pro-haemostatic agent (PCC or specific antidote if available), an antifibrinolytic agent (for all anticoagulants), and/or oral activated charcoal (for all recently ingested anticoagulants).

Therapies We Avoid: We generally avoid recombinant activated factor VII (rFVIIa), plasma, or cryoprecipitate in DOAC-associated bleeding due to lack of supporting data and associated risks (thrombosis, volume overload, transfusion reactions). An exception is using these products to correct coexisting coagulopathy from trauma or other settings with decreased clotting factors and/or fibrinogen levels.

Critical consideration: PCCs, especially activated product FEIBA, and some antidotes may possess thrombotic potential at doses used to treat bleeding. Available data consist largely of non-bleeding volunteers, case reports, and preclinical models. We avoid pro-haemostatic agents in patients with less severe bleeding.

Dabigatran Reversal with Idarucizumab

Idarucizumab (Praxbind) is a humanised anti-dabigatran monoclonal antibody fragment that can be used for emergency reversal of dabigatran's anticoagulant effect. We administer this agent, if available, for patients for whom more conservative bleeding management measures have been ineffective and who have life-threatening bleeding or require surgery on an urgent/emergency basis. We only administer idarucizumab to patients with convincing evidence of significant dabigatran levels based on clinical history of ingestion or laboratory testing. Idarucizumab should not be administered to patients with normal thrombin time.

Dosing

5 grams (two 2.5 g vials), administered either as two consecutive infusions or as a bolus injection

RE-VERSE AD Study Evidence

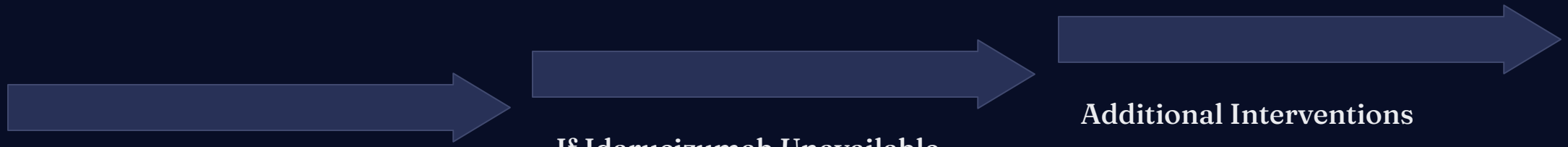
Final report described outcomes in 503 patients: 68% of bleeding patients had documented cessation of bleeding within 24 hours; 93% of surgical patients had normal haemostasis; mortality approximately 14% at one month

Reversal Efficacy

Anticoagulant effect completely reversed within first 15 minutes of treatment in almost all patients, with reversal maintained for 24 hours in most

Idarucizumab is dabigatran-specific and has no known activity against direct factor Xa inhibitors, other thrombin inhibitors, or other anticoagulants.

Dabigatran Bleeding Management Algorithm



Life-Threatening Bleeding

For patients at imminent risk of death, we suggest idarucizumab administration. We would not combine idarucizumab with procoagulant reversal agents such as activated prothrombin complex concentrate.

If Idarucizumab Unavailable

Weak preference for administering activated PCC (FEIBA) at fixed dose or weight-based dose of 50-80 units/kg. If aPCC unavailable, unactivated 4-factor or 3-factor PCC at fixed dose or weight-based dose of 25-50 units/kg represents reasonable alternative.

Additional Interventions

Use strategies for less severe bleeding, including antifibrinolytic agent, oral activated charcoal and/or haemodialysis when appropriate, and drug discontinuation.

Important: Treatment with activated PCCs carries real and substantial prothrombotic risk. These agents have not been studied adequately in patients receiving dabigatran, so we avoid their use except in extreme clinical circumstances.

FACTOR XA INHIBITORS

Overview of Factor Xa Inhibitor Reversal

Available factor Xa inhibitors include apixaban, edoxaban, and rivaroxaban. Our management approach balances bleeding control with thrombotic risk.

1

Life-Threatening Bleeding

For patients at imminent risk of death: maximal supportive care, withholding Xa inhibitor, antifibrinolytic agent, oral activated charcoal when appropriate, andexanet alfa OR unactivated 4-factor PCC (but not both)

2

Dosing Specifications

Andexanet: based on factor Xa inhibitor dose and time since last dose (low or high dose regimen). 4-factor PCC: fixed dose of 2000 units or weight-based dose of 25-50 units/kg

3

Agent Selection

If both andexanet and PCCs available, care should be tailored to individual patient. In exsanguinating haemorrhage, andexanet may be preferred; in patients at high thrombotic risk, 4-factor PCC may be preferred

4

Major Bleeding

For most patients without imminent death risk, we suggest not using andexanet or PCC, based on lack of high-quality evidence that benefits outweigh risks

Factor Xa Inhibitor Management: Additional Strategies

Antifibrinolytic Therapy

For patients with major bleeding, including life-threatening bleeding, we suggest administering an antifibrinolytic agent (tranexamic acid, epsilon-aminocaproic acid). These agents may also be appropriate in individuals with less serious bleeding if the patient has ongoing bleeding or other comorbidities increasing bleeding risk.

Activated Charcoal Administration

We suggest activated charcoal administration to remove unabsorbed drug from the gastrointestinal tract if the last anticoagulant dose was within the previous two hours and the patient can tolerate enteral administration (not vomiting, adequate mental status, or via gastric tube if tracheally intubated).

Special Considerations for Overdose

In a patient with major bleeding following an intentional excessive ingestion within the previous six hours, we suggest charcoal administration since prolonged absorption has been reported. We advise consultation with a medical toxicologist or regional poison control centre for patients with intentional ingestion.

The available oral direct factor Xa inhibitors cannot be dialysed because they are highly protein-bound. Charcoal haemofiltration has been suggested but not evaluated or used in patients with bleeding complications.

Andexanet Alfa: Evidence and Considerations

Andexanet alfa (AndexXa; coagulation factor Xa, inactivated-zhzo) is a recombinantly produced, catalytically inactive form of factor Xa that acts as a "decoy" to bind and sequester the anticoagulant. Approved by the US FDA in May 2018 for reversing anticoagulation by rivaroxaban and apixaban in individuals with life-threatening or uncontrolled bleeding.

Dosing Regimens

Low dose: 400 mg bolus at 30 mg/minute, followed by 480 mg infusion at 4 mg/minute for up to 120 minutes

High dose: 800 mg bolus at 30 mg/minute, followed by 960 mg infusion at 8 mg/minute for up to 120 minutes

Boxed Warning

Risks of arterial and venous thromboembolic and ischaemic events including myocardial infarction, ischaemic stroke, cardiac arrest, and sudden death

ANNEXA-I Trial Results

Randomly assigned 530 individuals with intracerebral haemorrhage who had taken a factor Xa inhibitor. Haemostatic efficacy (haematoma expansion ≤35%) was better with andexanet: 67% versus 53% with usual care (P=0.003). However, thrombosis rate was higher with andexanet (10% versus 6%), with increased ischaemic stroke (7% versus 2%) and myocardial infarction (4% versus 2%). Survival rates were not statistically different.

ANNEXA-4 Study Results

Single arm study of andexanet for acute factor Xa inhibitor-associated major bleeding in 352 patients. Haemostasis was excellent in 69% and good in 13% of evaluable patients. Anti-factor Xa activity was reduced by 92% for apixaban and rivaroxaban. Thromboses occurred in 10% of patients, with 3% within 5 days after receiving andexanet. Mortality within 30 days was 14%.

Clotting Factor Products: PCCs and aPCCs

Unactivated prothrombin complex concentrates (PCCs) and activated PCCs (aPCCs) both contain clotting factors purified from human plasma, differing in composition and whether coagulation factors are in inactive or activated forms.

Unactivated PCCs

3-factor PCCs contain factors II, IX, and X; 4-factor PCCs contain factors II, VII, IX, and X, along with protein C and S. Optimal dosing uncertain. Fixed dose and weight-based dosing have not been compared in randomised trials. In rare instances where we prescribe unactivated PCC for imminently life-threatening bleeding, we prescribe fixed dose of 2000 units or weight-based dose of 50 units/kg.

Activated PCCs (FEIBA)

FEIBA is the only aPCC available in the United States. Contains at least one factor in activated form (factor VII mostly activated). When we use FEIBA, we start at dose of 50 units/kg. Total daily dose should not exceed 200 units/kg. Higher risk of thrombosis compared with unactivated products.

Critical consideration: PCCs and aPCCs are potentially prothrombotic. Clinical judgement is required in determining individual bleeding and thrombotic risks on a case-by-case basis. These products do not "reverse" the anticoagulant effect; they provide a "work-around" (bypass) of the coagulation block produced by the DOAC.

Antifibrinolytic and Pro-Haemostatic Therapies

Tranexamic Acid

Oral dose: 1-1.5 grams every 8-12 hours for bleeding duration

Intravenous doses: 10-20 mg/kg as IV bolus followed by 10 mg/kg IV every 6-8 hours for major bleeding. After cardiac surgery: 10-15 mg/kg IV bolus followed by 1 mg/kg per hour for 6-10 hours

Excretion highly dependent on kidney function; dosing interval increased in chronic kidney disease

Epsilon-Aminocaproic Acid

Dose depends on urgency of bleeding reversal

Typical starting dose: 2 grams IV every 6 hours

Aggressive dosing: As much as 1 gram IV every hour

Oral administration: 3 grams three to four times per day

Desmopressin (DDAVP)

Used for impaired platelet function in uraemia or antiplatelet agent settings

Typical dosing: 0.3 mcg/kg given subcutaneously or intravenously (in 50 mL normal saline over 15-30 minutes if IV)

May improve platelet function for several hours. Usually do not give more than two doses due to tachyphylaxis and hyponatraemia risk

High-quality data are lacking regarding these agents' efficacy in DOAC-related bleeding. However, given their low thrombosis risk, low cost, and widespread availability, these agents may be appropriate in patients with major or life-threatening DOAC-associated bleeding. A systematic review found no increased thrombosis risk with tranexamic acid in non-surgical patients.

Transfusion Support Strategy

Transfusions are a critical component of supportive care for severe bleeding, requiring careful assessment of haematological parameters and clinical status.

Red Blood Cells

RBC transfusion may be required depending on bleeding rate and blood loss magnitude. Haemoglobin thresholds for transfusion in haemodynamically stable patients are discussed in separate topic reviews

Platelets

Platelet transfusion is not used to reverse DOAC anticoagulant effect in patients with normal platelet count. However, thrombocytopenic patients with bleeding should receive platelet transfusions if thrombocytopenia is severe and bleeding is major or life-threatening

Plasma Products

Fresh Frozen Plasma or Plasma Frozen Within 24 Hours may be given as part of massive transfusion protocol to replace coagulation factors lost by bleeding. No evidence supports FFP use as a reversal strategy in DOAC-associated bleeding

Minor Bleeding Management

Minor bleeding (epistaxis, bruising, slow gastrointestinal bleeding) can be managed conservatively using local haemostatic measures such as mechanical pressure. Decisions to temporarily discontinue the anticoagulant must balance bleeding and thrombotic risks for each patient on a case-by-case basis.

Clinical approach: Local haemostatic measures often suffice for minor bleeding episodes. These include:

- Direct mechanical pressure
- Topical haemostatic agents
- Ice application
- Elevation of affected area

Careful monitoring for progression to more serious bleeding remains essential in all cases.

Conservative Management Approach

The use of antifibrinolytic agents may occasionally be appropriate for individuals with less serious bleeding if the patient has ongoing bleeding or other comorbidities increasing bleeding risk; however, these agents generally are not required for minor bleeding.

We do not administer prothrombin complex concentrates for minor bleeding. Antifibrinolytic agents appear particularly effective for heavy menstrual bleeding.

Surgery and Invasive Procedures

Given the short half-lives of DOACs, it is often possible to delay procedures long enough to allow most or all anticoagulant effect to dissipate spontaneously in patients with normal renal or hepatic function. However, if urgent or emergency surgery is required with insufficient time to allow anticoagulant effect dissipation, reversal strategies discussed herein may be appropriate.

Timing Considerations

Decisions regarding reversal need are individualised based on urgency and bleeding risk of the procedure

Emergency Surgery

Emergency surgical interventions should proceed regardless of anticoagulation status or receipt of reversal agents. Strategies to ameliorate anticoagulant effect can be implemented intraoperatively if required

Risk-Benefit Analysis

High-quality data lacking to inform use of andexanet alfa or PCCs for managing bleeding risk in patients requiring urgent/emergency surgery. Surgeon must weigh benefits based on procedure bleeding risk and available reversal agents' thrombotic risk

Perioperative management of DOACs in the setting of elective surgery is discussed in separate clinical resources addressing comprehensive perioperative anticoagulation strategies.

RESUMPTION STRATEGY

Resuming Anticoagulation After Bleeding

In all patients, a plan to decide about restarting the anticoagulant should be established. Resumption should be delayed until rebleeding risk is minimised and may be permanently deferred in selected patients with very high recurrent bleeding risk.

Evidence Supporting Resumption

A large database study involving nearly 7,000 adults >65 years who experienced bleeding whilst receiving anticoagulation found that, compared with not resuming the anticoagulant, resuming anticoagulation was associated with:

- Lower risk of thrombosis (adjusted HR 0.60)
- Higher risk of rebleeding (HR 1.88)
- Lower mortality (adjusted HR 0.54)

Approximately 70% of patients resumed their anticoagulant, with a median time of 46 days.

Decision-Making Framework

Each decision regarding resumption of anticoagulation following a bleed is individualised based on:

- Risks and benefits for the specific patient
- Patient's values and preferences
- Underlying indication for anticoagulation
- Thrombotic risk during therapy interruption
- Bleeding site and recurrence risk

We are less likely to restart the anticoagulant in individuals with low risk of first or recurrent thromboembolism or whose underlying lesion strongly predisposes to recurrent bleeding.

If anticoagulants are to be restarted, this can generally be done sooner than the median time identified in observational studies. The optimal time for restarting anticoagulation after gastrointestinal bleeding appears to be 7–14 days, although details depend on the cause and site of bleeding and the risks of rebleeding and thrombosis.