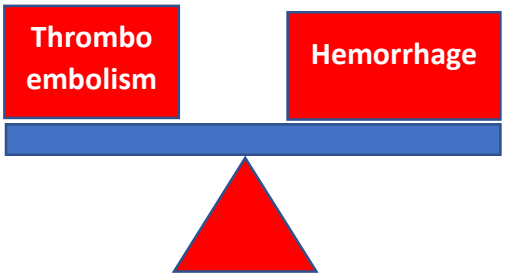
Perioperative Anticoagulation



Introduction:

-Oral anticoagulants include **vitamin K antagonists (VKAs)** and **direct oral anticoagulants (DOACs)**. Periprocedural management of patients on long-term oral anticoagulants (e.g., for the prevention of stroke and systemic thromboembolism**) is a field of ongoing research and there is currently no universal validated strategy.**

-Management of **anticoagulants** in the periprocedural period should be tailored **to the patient and the procedure in consultation with the proceduralist and anesthetist.**

-Although invasive procedures performed on patients receiving anticoagulants are associated with an increased risk of bleeding, discontinuing anticoagulants increases the risk of thrombosis.

-Therefore, anticoagulant therapy should not be routinely interrupted periprocedurally, but instead, the decision should be based on **the periprocedural bleeding risk and the periprocedural thrombotic risk.**

-Once interrupted, **VKAs** take time to achieve therapeutic anticoagulation on reinitiation, and hence, **bridging anticoagulation** with a short-acting **parenteral anticoagulant** is required in patients at high thrombotic risk.

-**Bridging anticoagulation** is not routinely required for patients on **DOACs**, as they **have a short half-life** and, if discontinued, can rapidly achieve therapeutic anticoagulation on reinitiation.

NOTE: For life-threatening periprocedural bleeding in patients on anticoagulants, see "Anticoagulant reversal."

-Surgery is generally safe when the INR value is below 1.5

-Patients whose INRs are maintained between 2.0 and 3.0 by the effect of warfarin normally require withholding of the medication for 5 days preoperatively.

Types of anticoagulants:

Oral anticoagulants:

1-VKA (warfarin)

-Inhibit hepatic **vitamin K epoxide reductase so prevent carboxylation of factors II, VII, IX, and X** as well as protein C and protein S.

- Disadvantages: Difficult to manage
  - Long half-life
  - **Regular monitoring** of the PT/INR required (as vitamin K antagonists affect the extrinsic coagulation pathway)
  - Requires periprocedural **bridging anticoagulation**
- Broad range of interactions (see "Warfarin interactions" below)
- Not suited for acute therapy of pulmonary embolism or deep vein thrombosis

  In cases of life-threatening bleeding:
  - Direct reversal by replacement (e.g., with **prothrombin complex concentrate**, **FFP**)
  - Indirect/delayed reversal by increasing production of coagulation factors (e.g., with vitamin K substitution)

2-DOAC:

Direct oral thrombin inhibitors (Dabigatran): Selective thrombin antagonist
Direct oral factor Xa inhibitors (Apixaban, Rivaroxaban, Edoxaban)

-Regular monitoring of coagulation parameters is not required → improved patient compliance

Parenteral anticoagulants:

1-Unfractionated heparin (UFH)

- **Drug**: heparin
- **Administration**
  - Prophylaxis: subcutaneous
  - Therapeutic: continuous intravenous infusion
- **Monitoring during therapy**: (**aPTT**) , platelet count (including baseline before treatment is started)
- **Clearance**: hepatic (preferred agent for patients with renal insufficiency)
- **Antidote**: **protamine sulfate**

2-Low molecular weight heparin (LMWH)

- **Drugs**: **enoxaparin**, dalteparin, tinzaparin, nadroparin, certoparin
- **Administration**: subcutaneous
- **Monitoring during therapy**: **anti-factor Xa activity** can be assessed in specific cases; not generally recommended
- **Clearance**: renal (contraindicated for patients with renal insufficiency)
- **Antidote**: **protamine sulfate** (partial reversal)

3-Synthetic heparin

- **Drugs**: **fondaparinux**
- **Administration**: subcutaneous
- **Monitoring during therapy**
  - Not generally recommended
  - **Anti-factor Xa activity** can be assessed in specific cases
- **Antidote**: possibly activated prothrombin complex concentrates (**aPCC**)

Complications of anticoagulants:

-General complications are hemorrhage. Risk factors for this often-fatal complication include INR intensity, older age, cerebrovascular disease, and hypertension

-As specific complication for certain drugs:

Unfractionated heparin: occur with bleeding and HTN, if bleeding occurs, heparin should be discontinued, and immediate assessment of the PT, PTT, and complete blood count (CBC). Ps its doses are 5,000 units in 5 mL concentration saline.

Warfarin: risk is estimated to be approximately 10% per year. Warfarin-induced skin necrosis, it can produce significant birth defects and fetal death and should not be used during pregnancy. Instead we use LMWH.

According to perioperative management:

There are two major complications of poor management of perioperative anticoagulation.
The first is bleeding, which occurs if the provider fails to interrupt anticoagulation therapy in an appropriate timeframe.
On the other hand, however, patients who have their anticoagulation interrupted too early in the perioperative period **are at high risk of thromboembolic events, as surgical procedures themselves induce a hypercoagulable state**.

-Thus, appropriate interruption of anticoagulation in the perioperative period is a delicate balancing act between the potentially severe complications of bleeding and thrombosis, requiring strict attentiveness of the managing provider.

Approach:

-The general approach to periprocedural management of **anticoagulant** therapy is described here.

-As guidelines vary, it is strongly encouraged to consult the proceduralist and the anesthetist early and to follow local protocols.

The decision to interrupt ongoing anticoagulation therapy should be tailored to the patient and the procedure.
The risk of periprocedural thrombosis should be weighed against the risk of periprocedural bleeding

Elective procedures

The following suggestions are based on the 2012 American College of Chest Physicians guideline and the 2017 American College of Cardiology (ACC) decision pathway, and apply to elective procedures.

- **7 days before the procedure**
  - Assess **periprocedural bleeding risk**.
  - Assess **periprocedural thrombotic risk**.
- **Low bleeding risk**: Anticoagulation may be continued; consult the proceduralist and anesthetist.
- **Increased bleeding risk**
  - Low thrombotic risk: **Interrupt oral anticoagulants (bridging anticoagulation** not required).
  - Moderate or high thrombotic risk
    - **VKAs**: Interrupt VKAs with **bridging anticoagulation** (use clinical judgment).
    - **DOACs**: Interrupt DOACs in most cases; preferably in consultation with specialists

NOTE:

Parenteral bridging anticoagulation is not required for DOACs

Emergency procedures

- **Low bleeding risk**: Anticoagulation may be continued; consult the proceduralist and anesthetist.
- **Increased bleeding risk**
  - Consider **anticoagulation reversal** before performing the procedure.
  - Determine the need for **postprocedural bridging anticoagulation based on the periprocedural thrombotic risk**.

Bleeding risk assessment:

Patient-related risk factors

The following factors are associated with an increased **risk of periprocedural bleeding**.

- Age > 65 years
- **Hypertension**
- Active cancer
- Abnormal renal function [4]
- **Abnormal liver** function [4]
- History of alcohol consumption (≥ 8 drinks per week) or recreational drug use [4]
- Chronic **bleeding diathesis**
- Quantitative or qualitative **platelet abnormality**
- Major bleeding or **ICH < 3 months** before planned procedure [3]
- History of **stroke** (i.e., ischemic stroke, spontaneous or traumatic ICH)
- History of or predisposition to major bleeding
- History of bleeding due to a similar procedure
- History of bleeding during **bridging anticoagulation**
- Concomitant therapy with **NSAIDs, steroids, antiplatelet, and/or anticoagulants**
- Labile **INR** or supratherapeutic **INR**

Procedure-related risk factors

Low risk	High risk
Diagnostic endoscopy	Major intra-abdominal surgery
Cataract surgery	Major vascular surgery
Oral surgery/dental extraction	Major orthopaedic surgery
Arthrocentesis	Prostatectomy or bladder surgery
Cutaneous surgery	Neurosurgical procedures
Hernia repair	Heart valve replacement
Scrotal surgery	Coronary artery bypass graft surgery
Coronary angiography	Major intrathoracic surgery
	Major cancer surgery
	Pacemaker insertion/implantation
	Biopsy in a non-compressible tissue
	Puncture in a non-compressible artery

Thrombotic risk assessment:

Risk factors for periprocedural thrombosis

- **Patient-related factors**
  - Past history of **stroke** (especially within the past 3 months)
  - Past history of **VTE** or **risk factors for VTE**
  - Rheumatic **valvular heart disease**
  - **Atrial fibrillation**
  - Significant cardiovascular disease , especially within the past year
  - Active cancer
  - **Thromboembolism** during prior interruption of anticoagulation
- **Procedures associated with high risk of thromboembolism**: e.g., **carotid endarterectomy**, valve replacement, major vascular **surgery**

Common clinical scenarios

Atrial fibrillation, **mechanical heart valves**, and **VTE** are the most common conditions that require long-term anticoagulation.

-The following table provides guidance on determining the **periprocedural thrombotic risk** in patients with these conditions, but the ultimate decision of whether to discontinue anticoagulation **should be made on a case-by-case basis, ideally in consultation with relevant specialists.**

Before we should know what is CHA2DS2-VASc Score!

Is a validated scoring system for assessing the risk of stroke in nonvalvular Afib

Letter	Risk factor	Score
C	Congestive heart failure/LV dysfunction	1
H	Hypertension	1
A_2	Age ≥75	2
D	Diabetes mellitus	1
S_2	Stroke/TIA/thrombo-embolism	2
V	Vascular disease*	1
A	Age 65–74	1
S	Sex category (i.e., female sex)	1
	Maximum score	9

Congestive heart failure/LV dysfunction means LV ejection fraction ≤40%. Hypertension includes the patients with current antihypertensive medication. *Prior myocardial infarction, peripheral artery disease, aortic plaque. LV: left ventricular, TIA: transient ischemic attack

Risk of stroke:

- **0 points (male) or 0–1 point (female): low risk**
- **1 point (male) or 2 points (female): intermediate risk**
- **≥ 2 points (male) or ≥ 3 points (female): high risk**

Table 1. Thrombotic Risk Stratification

Risk	Anticoagulation reason		
	Prosthetic heart valves	**Atrial fibrillation**	**Venous Thromboembolism**
High	Mitral position Tricuspid position (includying biological valves) Aortic position Stroke/TIA < 6 months	CHA2DS2-VASc 7-9 Stroke/TIA < 3 months Rheumatic valvulopathy mitral	VTE < 3 months Severe thrombophilia (Leyden's factor V in homozygosis, 20210 prothrombin, protein C, S or antithrombin III deficiency, múltiples deficiencys, Antiphospholipid Syndrome)
Moderate	Aortic position + 1 Risk factor (AF, history of Stroke/TIA > 6 months, DM, congestive heart failure, Age >75 years)	CHA2DS2-VASc 5-6 Stroke/TIA > 3 months	VTE 3- 12 months Not Severe thrombophilia (Leyden's factor V in heterozygosis or 20210 A prothrombin mutation) Recurrent VTE VTE + active cancer
Low	Aortic position With no risk factors	CHA2DS2-VASc 1-4 with no previous Stroke/TIA	VTE > 12 months

TIA: Transient Ischemic Attack; AF: Atrial fibrillation; DM: Diabetes Mellitus; VTE: Venous thromboembolism. CHADSVASC: 1 point Congestive Heart Failure, 1 point High blood pressure, 1 point Age above 65 (two points if above 75), 1 poin t Diabetes, 1 point Previous stroke or Clot, 1 point Vascular disease, 1 point if woman.

Periprocedural management of VKA (warfarin):

Approach

- Consult specialists and follow institutional protocols if available.
- Assess the need to interrupt **VKAs** based on **periprocedural bleeding risk**.
- If **VKAs** are to be interrupted:
  - Determine the timing of **VKA interruption** based on preprocedural **INR** levels.
  - Determine the need for **bridging anticoagulation** based on **periprocedural thrombotic risk**.
- Resume **VKAs** 12–24 hours after the procedure; consider delaying **VKA** resumption if **postprocedural bleeding risk** is high

NOTE:
Periprocedural bridging anticoagulation involves the temporary administration of a short-acting **parenteral anticoagulant** after **VKA interruption** for an invasive procedure. The timing of **bridging anticoagulation** initiation (i.e., pre- or post-procedurally) is based on **periprocedural bleeding risk**. Protocols may vary between institutions.

VKA interruption

VKA interruption is the temporary discontinuation of **VKAs** a few days before an elective invasive procedure to minimize periprocedural bleeding risk.

- **High periprocedural bleeding risk**: Interrupt VKA.
- **Uncertain periprocedural bleeding risk**
  - Patient-related factors for periprocedural bleeding present: Interrupt VKA
  - No patient-related factors for bleeding: Consider interruption.
- **Low periprocedural bleeding risk**: VKAs may be continued.
  - Patient-related factors for periprocedural bleeding present: Consider interruption.
  - No patient-related factors for bleeding: Do not interrupt VKA.
- **Timing** (if VKA is interrupted): Assess **INR** 5–7 days before the procedure.
  - **INR** 1.5–1.9: Interrupt VKA 3–4 days before the procedure.
  - **INR** 2.0–3.0: Interrupt VKA 5 days before the procedure.
  - **INR** > 3.0: Interrupt VKA ≥ 5 days before the procedure.

Periprocedural management of DOACS:

DOAC interruption

The decision of whether to interrupt **DOAC** therapy is based on **periprocedural bleeding risk**.

- **High or uncertain periprocedural bleeding risk** (patient and procedure-related): Interrupt DOAC.
- **Low periprocedural bleeding risk** (patient and procedure-related)
  - Interruption may not always be necessary (consult proceduralist and anesthetist).
  - The procedure should be timed to coincide with the lowest plasma concentration of the DOAC.

Bridging anticoagulation with a parenteral agent is typically not required for DOACs.

Timing:

The timing of DOAC interruption is based on **periprocedural bleeding risk and creatinine clearance.**

DOAC reinitiation

- Consult the proceduralist before reinitiating DOACs.
- Ensure procedural site **hemostasis**.
- Consider reinitiating of DOAC 24–72 hours after the procedure, depending on the **postprocedural bleeding risk and postprocedural creatinine clearance**.

Timing:

Timeframe for preoperative discontinuation of factor Xa inhibitors [2]		
Creatinine clearance	Periprocedural bleeding risk	
	Low	High or uncertain
≥ 30 mL/min	≥ 24 hours	≥ 48 hours
15–29 mL/min	≥ 36 hours	No data
< 15 mL/min	Unknown	

Timeframe for preoperative discontinuation of dabigatran [2][7]		
Creatinine clearance	Periprocedural bleeding risk	
	Low	High or uncertain
≥ 80 mL/min	≥ 24 hours	≥ 48 hours
50–79 mL/min	≥ 36 hours	≥ 72 hours
30–49 mL/min	≥ 48 hours	≥ 96 hours
15–29 mL/min	≥ 72 hours	≥ 120 hours
< 15 mL/min	No data	No data