

# PERIOPERATIVE ANTICOAGULANT DRUGS

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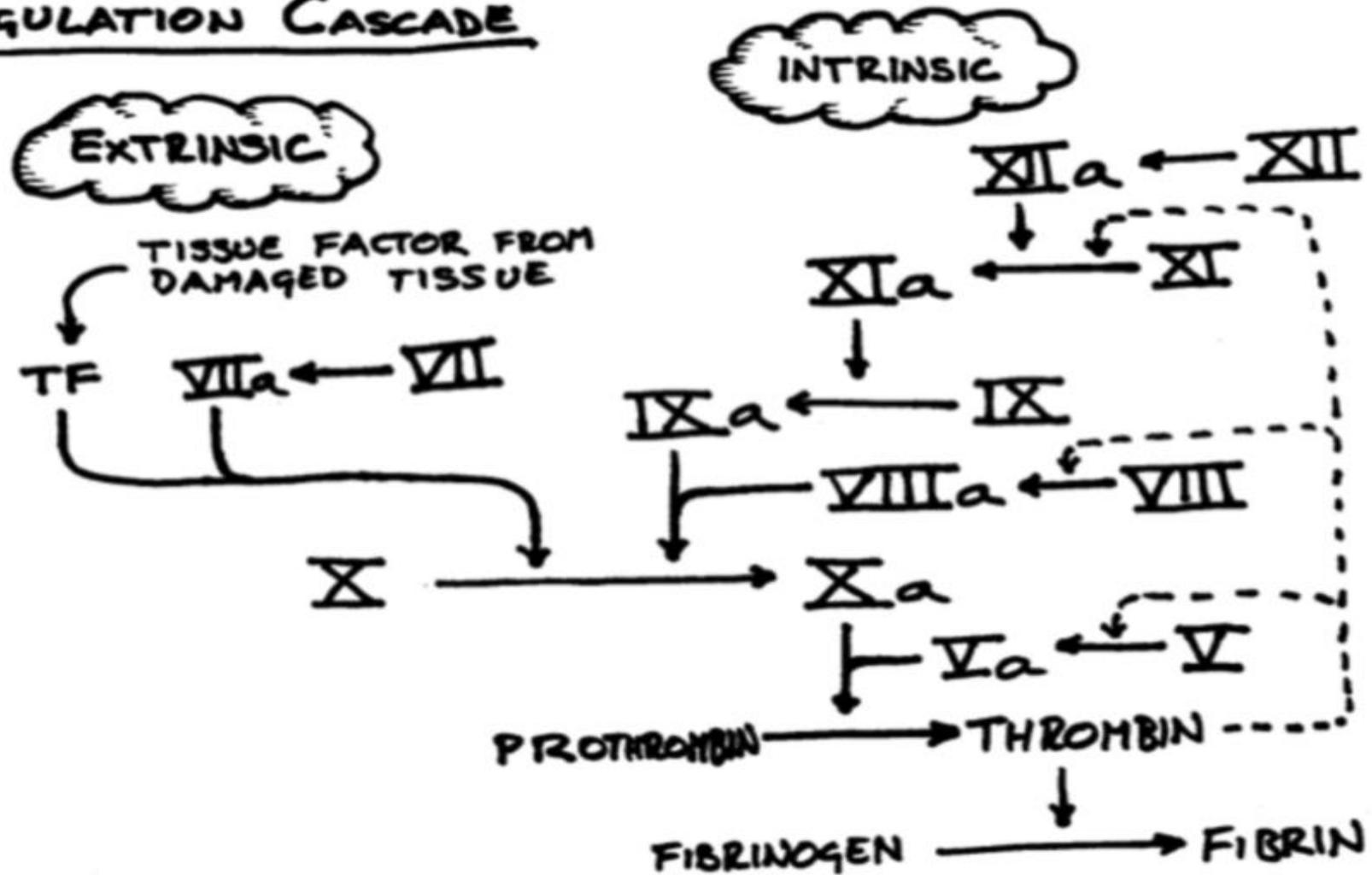
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- At the end of this session, participants will be able to:
  - To review the most recent literature on perioperative anticoagulant management
  - To review current recommendations around perioperative anticoagulant management
  - To present patient cases and develop perioperative plans with respect to anticoagulants

# COAGULATION CASCADE



# INTRODUCTION

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- -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.

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- -Management of anticoagulants in the periprocedural period should be tailored to the patient and the procedure in consultation with the proceduralist and anesthesiologist.
  - Although invasive procedures performed on patients receiving anticoagulants are associated with an increased risk of bleeding, discontinuing anticoagulants increases the risk of thrombosis,
  - The decision of the anticoagulant therapy periprocedurally should be based on the periprocedural bleeding risk and periprocedural thrombotic risk.

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- -Once the anticoagulation therapy is 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

# HOW TO BRIDGE

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- During the preoperative period:
- Discontinue warfarin five days before surgery.
- Three days before surgery, start subcutaneous LMWH or unfractionated heparin) UFH), (depends on the renal function of the patient at therapeutic doses.
- Two days before surgery assess INR, if greater than 1.5 vitamin K can be administered at a dose of 1 to 2 mg.
- Discontinue LMWH 24 hours before surgery or 4 to 6 hours before surgery if UFH.

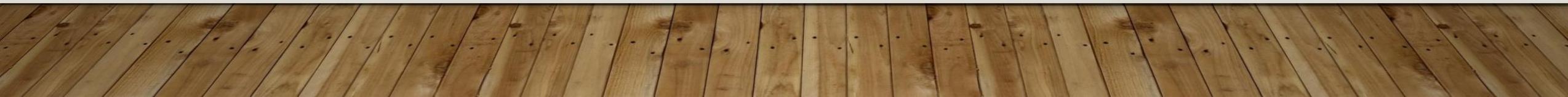
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- During the postoperative period:
  - If the patient is tolerating oral intake, and there are no unexpected surgical issues that would increase bleeding risk, restart warfarin 12 to 24 hours after surgery.
  - If the patient received preoperative bridging therapy and underwent a minor surgical procedure, resume LMWH or UFH 24 hours after surgery
  - If the patient underwent a major surgical procedure, resume LMWH or UFH 48 to 72 hours after surgery.
  - Always assess the bleeding risk and adequacy of homeostasis before the resumption of LMWH or UFH

NOTE: FOR LIFE-THREATENING PERIPROCEDURAL BLEEDING IN PATIENTS ON ANTICOAGULANTS, SEE “ANTICOAGULANT REVERSAL.”

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- 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.

## What's INR?!

- INR stands for International Normalized Ratio. It is a laboratory measure used to monitor and adjust the effectiveness of blood-thinning medications, such as warfarin.
  - INR testing is typically done by taking a blood sample and sending it to a laboratory for analysis. The test is used primarily to monitor patients on blood-thinning medications, but it can also be used to investigate abnormal bleeding or to assess liver function.
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# TYPES OF ANTICOAGULANTS:

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- Oral anticoagulants:
- I -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, 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 COAGULATIONFACTORS (E.G., WITH VITAMIN K SUBSTITUTION)
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- **2-DOAC:** Direct oral thrombin inhibitors (Dabigatran) selective thrombin antagonist and Direct oral factor Xa inhibitors (Apixaban, Rivaroxaban, Edoxaban)
  - Regular monitoring of coagulation parameters is not required -> improved patient compliance

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- Parenteral anticoagulants:

- I-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

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## 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)

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## 3-Synthetic heparin

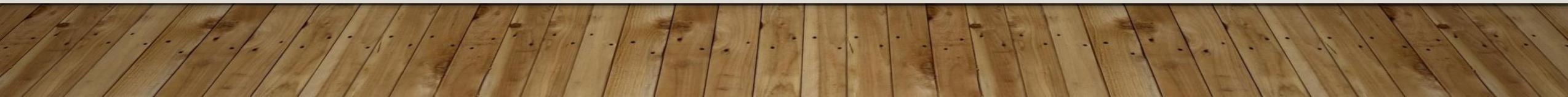
Drugs: fondaparinux

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)



# COMPLICATION

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- -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 5,000units 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

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- **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 hypercoagulability 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

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- -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 anesthesiologist.
- **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

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- **Low bleeding risk:** Anticoagulation may be continued; consult the proceduralist and anesthesiologist.
- **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:

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- 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
  - Abnormal liver function
  - History of alcohol consumption or recreational drug use
  - Chronic bleeding diathesis

# BLEEDING RISK ASSESSMENT:

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- Quantitative or qualitative platelet abnormality
- Major bleeding or ICH < 3 months before planned procedure
- 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

Diagnostic endoscopy  
Cataract surgery  
Oral surgery/dental  
extraction  
Arthrocentesis  
Cutaneous surgery  
Hernia repair  
Scrotal surgery  
Coronary angiography

### High risk

Major intra-abdominal surgery  
Major vascular surgery  
Major orthopaedic surgery  
Prostatectomy or bladder surgery  
Neurosurgical procedures  
Heart valve replacement  
Coronary artery bypass graft  
surgery  
Major intrathoracic surgery  
Major cancer surgery  
Pacemaker insertion/implantation  
Biopsy in a non-compressible  
tissue  
Puncture in a non-compressible  
artery

# THROMBOTIC RISK ASSESSMENT:

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- 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 and Atrial fibrillation
  - Significant cardiovascular disease , especially within the past year
  - Thromboembolism during prior interruption of anticoagulation
  - Procedures associated with high risk of thromboembolism: e.g., carotid endarterectomy, valve replacement, major vascular surgery

# THROMBOTIC RISK ASSESSMENT:

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- 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 <sub>2</sub>	Age $\geq 75$	2
D	Diabetes mellitus	1
S <sub>2</sub>	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

### Risk of stroke:

- 0 points (male) or 0–1 point (female): low risk
- 1 point (male) or 2 points (female): intermediate risk
- $\geq 2$  points (male) or  $\geq 3$  points (female): high risk

**Table 1. Thrombotic Risk Stratification**

Risk	Anticoagulation reason		
	Prosthetic heart valves	Atrial fibrillation	Venous Thromboembolism
High	Mitral position  Tricuspid position (including 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, multiples deficiencies, 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

# PERIPROCEDURAL MANAGEMENT OF VKA (WARFARIN):

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- 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 24-12hours after the procedure; consider delaying VKA resumption if postprocedural bleeding risk is high

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- 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.

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- 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.

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- **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 2 5 days before the procedure.

# PERIPROCEDURAL MANAGEMENT OF DOAC:

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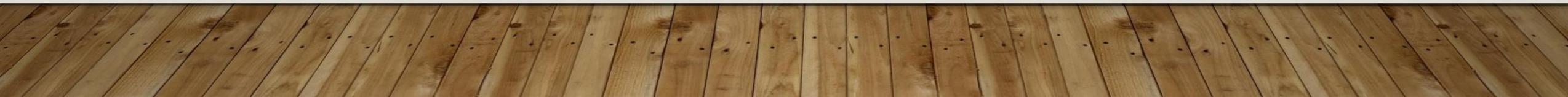
- DOAC interruption
- The decision of whether to interrupt DOAC therapy is based on periprocedural bleeding risk.
- **High or uncertain** periprocedural bleeding risk (patient and procedure-related): Interrupt DOAC.
- **Low** periprocedural bleeding risk (patient and procedure-related)
  - Interruption 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**

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- **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.
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# REFERENCES

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- Amboss. Com
- National Library of Medicine

**THANK YOU**