Anticoagulation Periprocedural Management: Less Bridging and More Decisioning!

Richard Mullvain RPH, BCCP, BCPS (AQC), CCCC- Essentia Health

American Heart Association.

Anticoagulation Periprocedural Management..

Less Bridging and More Decisioning!

2:30 pm – 3:10 pm

Richard Mullvain, RPH, BCCP, BCPS (AQC), CCCC
Essentia Health Heart & Vascular Center

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Presenter Disclosure Information

Richard Mullvain, RPH, BCCP, BCPS (AQC), CCCC

FINANCIAL DISCLOSURE:
No relevant financial relationship exists

Certain Brand Names will be mentioned along with Generic Names to assist the audience in identification of different medications

Learning Objectives

Objectives:

- To improve knowledge and understanding of proper periprocedural management of oral anticoagulants in general

- To increase your skills and abilities to successfully make decisions on the timing of doses specifically for direct oral anticoagulants in a periprocedural setting

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Here with you

Richard Mullvain, RPH, BCCP, BCPS(AQC), CCCC

My Background:

- Clinical Pharmacist for 28 years
  - Board Certified Cardiology Pharmacist
  - Board Certified Pharmacotherapy Specialist
    - -With Added Qualifications in Cardiology
  - Certified Cardiac Care Coordinator
  - Anticoagulation Specialist
  - Provider of Medication Therapy Management (MTM)
  - 18 clinical publications

- Key author of the Essentia Health Anticoagulation Periprocedural Bridging Guidelines

- Fishing Problem
  - Founder of the Duluth Area Fishing League

Anticoagulation Periprocedural Management…

…Less Bridging and More Decisioning!

- Let’s make this interesting while learning about managing oral anticoagulants during periprocedural times

- While some bridging is still necessary, more decisions now need to be made with the direct oral anticoagulants

“It appears that the ingredients in your expensive supplement may increase your bleeding risk!”

“Oops, I forgot to ask…
…Is this patient on anticoagulation?”

Don’t be that guy!

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Case Study #1:

66 yo Male with A-Fib and Taking Warfarin (Coumadin) Needs a Colonoscopy

- Dr. requests that patient be “bridged” with Enoxaparin (Lovenox) before the procedure

- …stay tuned, and we’ll revisit this case at the end

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Case Study #2:

71 yo Male with A-Fib and Taking Rivaroxaban (Xarelto) Needs a Colonoscopy

- Dr. demands that patient be “bridged” with Enoxaparin (Lovenox) for 5 days before the procedure

- …stay tuned, and we’ll revisit this case at the end

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Anticoagulants

Parenteral (IV)

- Heparins
  - Unfractionated Heparin (UFH)
  - Low Molecular Weight Heparins (LMWH)
    - Enoxaparin (Lovenox)
    - Dalteparin (Fragmin)
    - Tinzaparin (Innohep)
- Direct Thrombin Inhibitors (DTI)
    - Bivalirudin (Angiomax)
    - Argatroban
- Direct Factor Xa Inhibitors
    - Fondaparinux (Arixtra)

Oral (PO)

- Vitamin K Antagonist
  - Warfarin (Coumadin)
- Direct Thrombin Inhibitors (DTI)
  - Dabigatran (Pradaxa)
- Direct Factor Xa Inhibitors
  - Rivaroxaban (Xarelto)
  - Apixaban (Eliquis)
  - Edoxaban (Savaysa)
  - Betrixaban (Bevyxxa)

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~~NOAC~~ or DOAC ?

- In some reports, use of the term **NOAC** has been misinterpreted as ‘No AntiCoagulation’

Recommendation statement for the use of DOAC

1. We suggest using the term ‘direct oral anticoagulant’ (DOAC) to reference the class of oral anticoagulants that directly inhibit a single target and have similar clinical properties (e.g. dabigatran, rivaroxaban, apixaban, edoxaban, and betrixaban).
2. We suggest that a drug’s specific mechanism of action (e.g. direct FXa inhibitor or direct thrombin inhibitor) should be used when it is clinically important to distinguish between the various DOAC medications.

http://onlinelibrary.wiley.com/doi/10.1111/jth.12969/full

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Direct, Novel or Non-Vitamin K Oral Anticoagulants (DOAC's)

(…sometimes called NOAC's)

- Dabigatran (Pradaxa)
- Rivaroxaban (Xarelto)
- Apixaban (Eliquis)
- Edoxaban (Savaysa)
- Betrixaban (Bevyxxa)

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To remember all 5 DOAC's…
…think "BEARD

- **B**etrixaban
- **E**doxaban
- **A**pixaban
- **R**ivaroxaban
- **D**abigatran

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PHARMACOLOGY OF DOACS

- Dabigatran is a competitive direct thrombin inhibitor
  - Acts through direct inhibition of thrombin

- Rivaroxaban, Apixaban, Edoxaban and Betrixaban inhibit factor Xa and prothrombinase activity
  - Thus inhibiting the conversion of prothrombin to thrombin

- Thrombin catalyzes the conversion of fibrinogen to fibrin; activates factors V, VIII, XI, and XIII; and activates platelets
  - Therefore, inhibiting thrombin decreases thrombus formation

Rafal et al; Management of Patients on Non-Vitamin K Antagonist Oral Anticoagulants in the Acute Care and Periprocedural Setting; Circulation. Published online Feb. 6th, 2017;135:00–00. DOI: 0.1161/CIR.0000000000000477

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Pharmacology

Properties of Oral Anticoagulants

Drug (Brand)	Protein Binding	Time to Peak Concentration	Half-Life
Warfarin (Coumadin)	99%	4 h	1 wk
Dabigatran (Pradaxa)	35%	1-6 h	12-17 h
Rivaroxaban (Xarelto)	92%-95%	2-4 h	5-11.7 h
Apixaban (Eliquis)	87%	3-4 h	6.8-15.2 h
Edoxaban (Savaysa)[a]	55%	1-2 h	10-14 h

Renal Clearance Dependent

https://www.uspharmacist.com/article/reversal-of-novel-oral-anticoagulants

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Clinical Pearls – DOAC's for A-Fib

- The novel direct oral anticoagulants currently approved by the FDA are:
  - Dabigatran (Pradaxa™)
  - Rivaroxaban (Xaralto™)
  - Apixaban (Eliquis™)
  - Edoxaban (Savaysa™)
  - Betrixaban (Bevyxa ™)

- The new oral anticoagulants are as effective as warfarin, but have significantly less intracranial bleeding risk

- Recent trial data triggered guidelines to reduce the use of "Bridging" for interruptions of anticoagulation therapy

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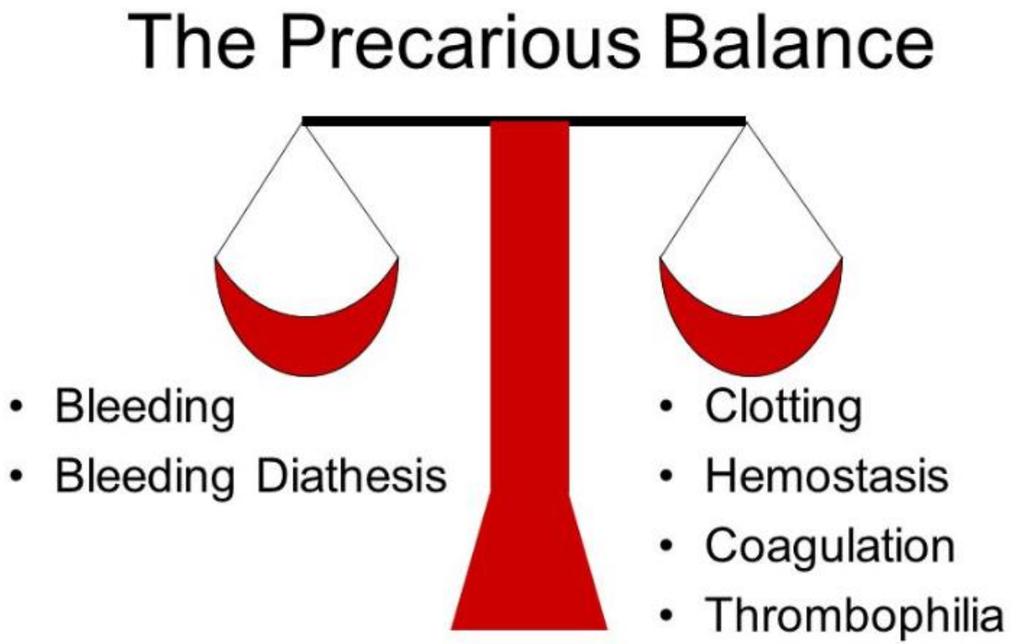
What does it mean to be “Bridged?”

At the End of the Day…
We Try to Balance the Risk of Clotting vs. Bleeding

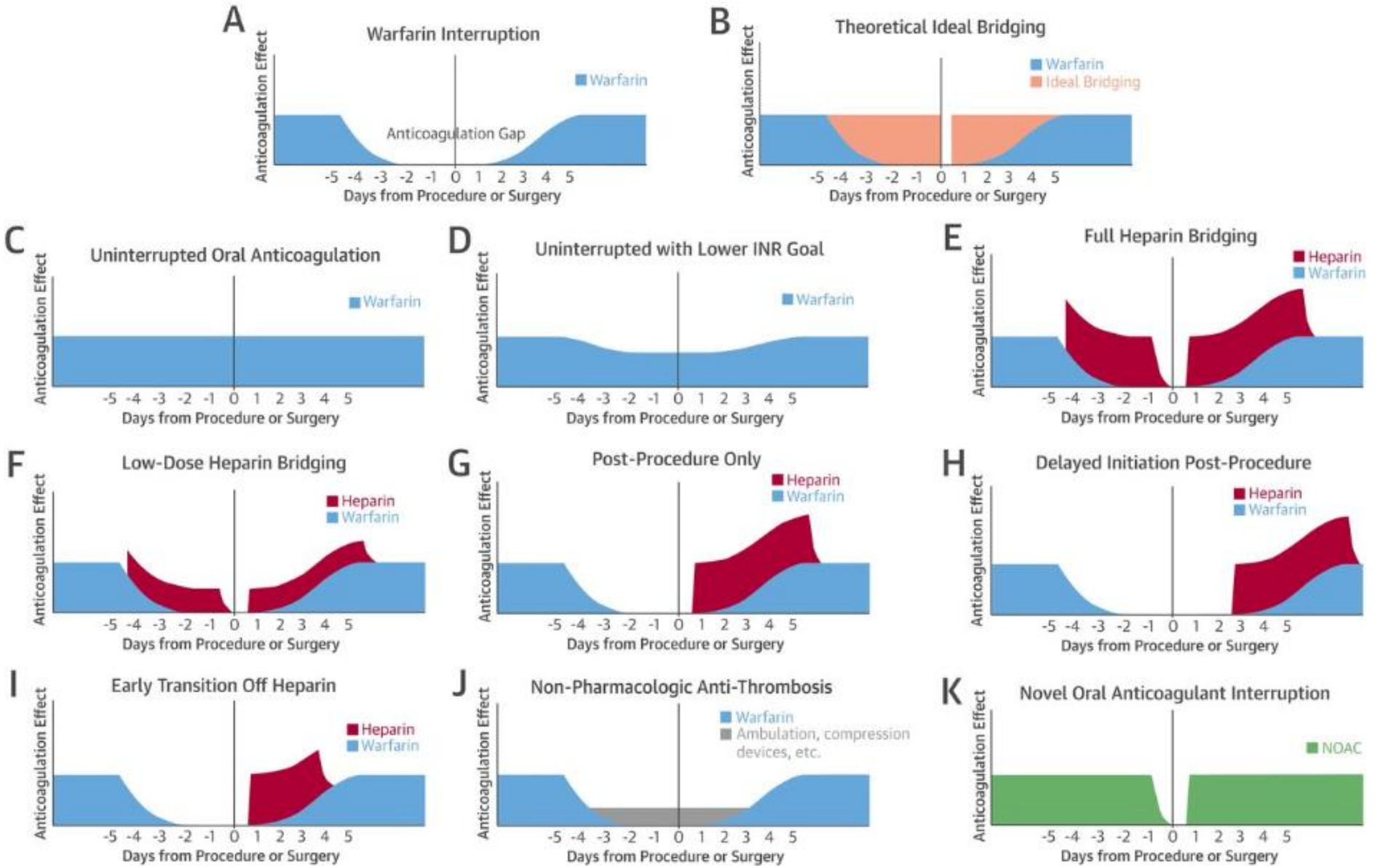


the anticoagulants vs. the procoagulants

To Bridge or NOT to Bridge?

- Are we “Over-Bridging”?

Bridging Anticoagulation



Rechenmacher et al.; Bridging Anticoagulation; JACC Vol. 66, Issue 12, Sept. 2016

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The PAUSE Study Approach

Low/moderate bleed risk – For low/moderate bleeding risk surgery, omit the DOAC one day before and resume one day (approximately 24 hours) after the procedure, provided hemostasis is secure. The total duration of interruption is two days.

High bleed risk – For high bleeding risk surgery, omit the DOAC two days before and resume two days (approximately 48 hours) after the procedure, provided hemostasis is secure. The total duration of interruption is four days. Waiting an additional one day before resumption may be appropriate in some cases.

Impaired kidney function – For individuals with impaired kidney function (creatinine clearance [CrCl] <30 to 50 mL/min) who are taking dabigatran, there is an additional one day interruption before low/moderate bleeding risk procedures and an additional two days interruption before high bleeding risk procedures. Direct factor Xa inhibitors (apixaban, edoxaban, rivaroxaban) do not require adjustments for kidney function.

Shaw, Li, Vanassche, et. al. Predictors of preprocedural direct oral anticoagulant levels in patients having an elective surgery or procedure. (PAUSE Study) Blood Adv. 2020;4(15):3520.

The PAUSE Approach…

Timing for interruption of a direct oral anticoagulant (DOAC) before and after elective surgery

HIGH BLEEDING RISK procedure			Day of surgery	No major bleeding		
Regular DOAC dose	X	X	X	X	Regular DOAC dose	Regular DOAC dose

LOW BLEEDING RISK procedure			Day of surgery	No major bleeding		
Regular DOAC dose	Regular DOAC dose	X	X	Regular DOAC dose	Regular DOAC dose	Regular DOAC dose

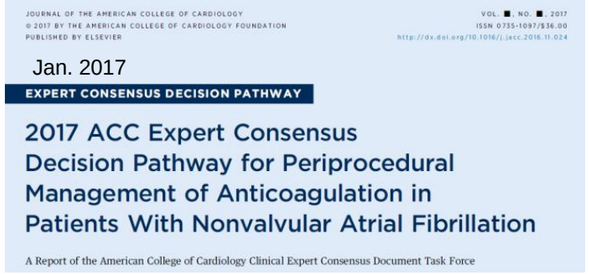
This strategy applies to all DOACs in individuals with normal kidney function (eg, CrCl >50 mL/min) and individuals taking apixaban, edoxaban, or rivaroxaban with CrCl 30 to 50 mL/min. For individuals taking dabigatran who have CrCl of 30 to 50 mL/min, omit an additional dose before the procedure. For any DOAC and a high bleeding risk procedure, it may be reasonable to omit the DOAC for an additional postoperative day (5 days total interruption). Refer to UpToDate for additional details.

DOAC: direct oral anticoagulant; CrCl: creatinine clearance.

Graphic 130000 Version 1.0

uptodate.com/contents/perioperative-management-of-patients-receiving-anticoagulants

Shaw, Li, Vanassche, et. al. Predictors of preprocedural direct oral anticoagulant levels in patients having an elective surgery or procedure. (PAUSE Study) Blood Adv. 2020;4(15):3520.



…In this document, we aim to:

1) validate the appropriateness of the decision to chronically anticoagulate
2) guide clinicians in the decision of whether to interrupt anticoagulation
3) provide direction on how to interrupt anticoagulation with specific guidance for vitamin K antagonists and direct-acting oral anticoagulants
4) evaluate whether to bridge with a parenteral agent peri procedurally
5) offer advice on how to bridge
6) outline the process of restarting anticoagulation post-procedure

Doherty JU, Gluckman TJ, Hucker WJ, Januzzi JL, Ortel TL, Saxonhouse SJ, Spinler SA, Periprocedural Management of Anticoagulation Writing Committee. 2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation: A Report of the American College of Cardiology Clinical Expert Consensus Document Task Force. Journal of the American College of Cardiology. 2017 Jan 9.

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AHA SCIENTIFIC STATEMENT March 2017

Management of Patients on Non–Vitamin K Antagonist Oral Anticoagulants in the Acute Care and Periprocedural Setting

A Scientific Statement From the American Heart Association

- Healthcare institutions should adopt a NOAC reversal and **perioperative management protocol** developed with multidisciplinary input

Raval AN, Cigarroa JE, Chung MK, Diaz-Sandoval LJ, Diercks D, Piccini JP, Jung HS, Washam JB, Welch BG, Zazulia AR, Collins SP. Management of Patients on Non–Vitamin K Antagonist Oral Anticoagulants in the Acute Care and Periprocedural Setting: A Scientific Statement From the American Heart Association. Circulation. 2017 Mar 7;135(10):e604-33.

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Essentia Health Bridging Guidelines: Periprocedural Management of Anticoagulation and Antiplatelet Therapies

Updated: **July 13th, 2017**
By: Ramin Artang, MD, Mary Heiken, Pharm D, Richard Mullvain, RPh, Jim Tomsche, Pharm D.
(Thank you to the many others who contributed!)

*Also known as NOAC's (New or Novel, or Non-Vitamin K Antagonist, Oral Anticoagulants)

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Essentia Health Bridging Guidelines:
Periprocedural Management of Anticoagulation and Antiplatelet Therapies

Updated: **July 13th, 2017**
By: Ramin Artang, MD, Mary Heiken, Pharm D, Richard Mullvain, RPh, Jim Tomsche, Pharm D.
(Thank you to the many others who contributed!)

Purpose:

- The purpose of this guideline is to offer assistance in determining a reasonable **bridging** plan for periprocedural management of anticoagulation and antiplatelet therapies

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- There are times when temporary interruption of oral anticoagulation and antiplatelet therapies may be necessary
- This usually includes the vitamin K antagonist (VKA) warfarin, but in some cases now may include a direct oral anticoagulant agent (DOAC)
- These chronic therapies may need to be interrupted to reduce the risk of bleeding due to a procedure

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- In an attempt to reduce the risk of thromboembolism during the period of time when a patient is off of their oral anticoagulant…
- …often times a bridging regimen of subcutaneous low molecular weight heparin (LMWH), such as enoxaparin, or unfractionated heparin (UFH), may be used

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Bridging Anticoagulation

- The administration of a short-acting anticoagulant therapy with (SC) LMWH or SC / IV UFH for approximately 10-12 days surrounding a procedure…
- …during which time anticoagulant therapy is interrupted and its anticoagulant effect is not within target range

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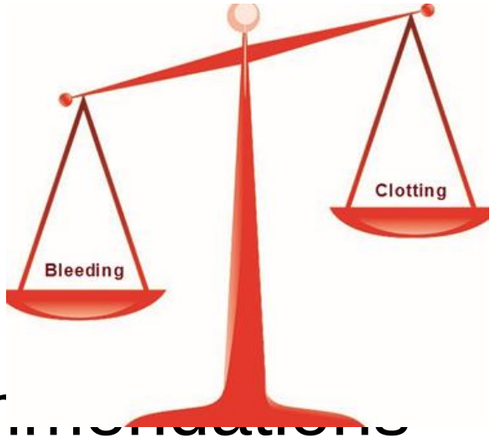
Patient Selection



- Bridging anticoagulant therapy recom…[illegible] are based on a patient's risk of thromboembolism balanced with a patient's risk of bleeding based on the procedure type

  – This is often not clearly defined and will require clinical judgment by a provider based on a patient's specific medical history and circumstances

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Steps to determine best periprocedural approach:

1. Is interruption of antithrombotic therapy in the perioperative period needed?
   - Bleeding risk associated with procedures (Page 3 of this document)
2. If antithrombotic therapy is interrupted, what is risk of thromboembolism?
   - Patient risk for thromboembolism (Page 4 of this document)
   - Balance of thromboembolic vs. bleeding risk (clinical judgment)
3. Based on thromboembolic risk is periprocedural bridging appropriate?
4. If the answer to step three is “yes” then what is the most appropriate bridging agent and dose based on patient and procedure risk factors?

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Procedure Bleeding Risk Assessment

- Consultation with the surgeon / provider is **always** encouraged to determine bleeding risk associated with a procedure!

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Surgeries and procedures associated with **HIGH** bleeding risk during perioperative antithrombotic drug administration include:

Urologic procedures consisting of:

-Transurethral prostate resection

- Bladder resection or tumor ablation

- Nephrectomy; or kidney biopsy in part due to untreated tissue damage (after prostatectomy) and endogenous urokinase release

- Prostate biopsy

Colonic polyp resection, typically of large (greater than 1-2 cm long) sessile polyps

Surgery and procedures of highly vascular organs (i.e. kidney, liver, and spleen)

Bowel resection

Major surgery with extensive tissue injury (i.e. cancer surgery, joint arthroplasty, reconstructive plastic surgery)

Intracranial or spinal surgery, intracerebral or epidural bleeds can have serious clinical consequences

Cardiac catheterization via femoral artery

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Procedures associated with **MODERATE** bleeding risk during perioperative antithrombotic drug administration include:

- Supraventricular tachycardia (SVT) ablation
- Implantable cardioverter-defibrillator (ICD) implant
- Cardiac catheterization via radial artery

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Procedures associated with **LOW** bleeding risk during perioperative antithrombotic drug administration include:

- Minor Dental Procedures
  - e.g. tooth extractions and endodontic (root canal) procedures
- Minor Dermatologic Procedures
  - e.g. excisions of basal and squamous cell carcinomas, actinic keratoses, and malignant or premalignant nevi
- Minor Ophthalmologic Procedures
  - e.g. cataract extraction
- Pacemaker or implantable cardioverter-defibrillator device implantation
- Endoscopy without planned biopsy

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CHA_2DS_2VASc score calculation:

	Condition	Points
C	Congestive Heart Failure	1
H	Hypertension	1
A_2	Age ≥ 75 years	2
D	Diabetes mellitus	1
S_2	Prior stroke or transient ischemic attack or thromboembolism	2
V	Vascular disease (i.e. myocardial infarction, aortic plaque)	1
A	Age 65 – 75 years	1
Sc	Sex category: female gender	1

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Patient Thromboembolic Risk Assessment and Stratification

Thromboembolic Risk Stratum	Indication for Bridging for Patients on Warfarin^		
	Mechanical Heart Valve	**Atrial Fibrillation (AFib)**	**VTE**
High	• Any mitral valve prosthesis • Aortic valve prosthesis (old caged-ball* or tilting disc**) • Recent stroke or TIA (within 6 months) • Bileaflet*** aortic valve prosthesis **AND** one of the following: ▪ AFib ▪ CHF ▪ HTN ▪ Age > 75 yr ▪ DM ▪ prior stroke or TIA	• $CHA_2DS_2VASc^a$ score of ≥7 • $CHA_2DS_2VASc^a$ score of 5 or 6 with history of prior stroke or TIA • History of stroke or TIA, regardless of $CHA_2DS_2VASc^a$ score • Rheumatic valvular heart disease	• Recent VTE within 3 months • Recurrent unprovoked VTE • Prior thromboembolism during temporary interruption of anticoagulation • Active cancer (treated within 6 months or palliative) • Severe thrombophilia: ▪ Deficiency of protein C, protein S or antithrombin ▪ Antiphospholipid antibodies ▪ Multiple abnormalities
	Bridging of Moderate- to Low-Risk Patients is Generally **NOT** Recommended		
Moderate		• $CHA_2DS_2VASc^a$ score of 3 to 6 **AND** no history of prior stroke or TIA	• VTE within 3-12 months • Non-severe thrombophilia: ▪ Heterozygous factor V Leiden mutation ▪ Prothrombin gene mutation
Low	• Bileaflet*** aortic valve prosthesis without AFib **AND** no other risk factors for stroke	• $CHA_2DS_2VASc^a$ score of 0 to 2 **AND** no prior stroke or TIA	• VTE >12 months prior **AND** no other risk factors

CHF=congestive heart failure; DM=diabetes mellitus; HTN=hypertension; TIA=transient ischemic stroke; VTE=venous thromboembolism

^ for periprocedureal management of DOACs, refer to Section 4 on page 8.
* Starr-Edwards valve
** Bjork-Shiley, Medtronic-Hall or Omnicarbon valve
*** St. Jude or Carbomedics

- Unless use of aspirin is contraindicated, any interruption of anticoagulation (with or without bridging), should be covered by low-dose aspirin (81 mg/day) for patients with:
  - Any type of mechanical valve
  - Known coronary artery disease
  - AFib with CHA_2DS_2VASc score ≥ 3

Refer to Section 3 on Page 7 for perioprocedural management of antiplatelet therapy

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Warfarin Periprocedural Anticoagulation Management

- Step 1: Determine bleeding risk associated with procedure (page 3)
- Step 2: Determine thromboembolic risk associated with interruption of warfarin (page 4)
- **Step 3: Based on**
  the analysis of bleeding risk with procedure
  versus
  thromboembolic risk,
  determine if bridging is appropriate (see chart below)

- **Step 4: Select most appropriate bridging agent (enoxaparin or UFH) and dose based on patient and procedure risk factors**

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Warfarin Periprocedural Anticoagulation Management

Thromboembolic Risk	Anticoagulation management
High	Bridge With Therapeutic-dose SC LMWH OR IV UFH
Moderate	Bridging of Moderate-Risk Patients is Generally **NOT** Recommended*
Low	NO bridging

*If additional decision support is needed, consult Cardiologist.

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Warfarin Periprocedural Anticoagulation Management

Enoxaparin Baseline Lab Monitoring and Dosing Options:

MUST obtain hemogram to assess platelet count – the incidence of heparin induced thrombocytopenia (HIT) is lower with enoxaparin than with UFH but enoxaparin has nearly 100% cross-reactivity with heparin antibodies, so should be avoided in patients with established diagnosis or history of HIT.
MUST obtain serum creatinine (SCr) and calculate renal function with Cockcroft-Gault method – may use SCr reported in last 90 days if stable (see Appendix B for calculation)

- Therapeutic-dose SC LMWH: Enoxaparin 1 mg/kg SC every 12 hrs **OR** 1.5 mg/kg SC every 24 hrs
  (**Evidence suggests twice daily dosing may be preferred over the once daily regimen**)
- Intermediate dose SC LMWH: Enoxaparin 40 mg SC every 12 hrs
- Low-dose SC LMWH: Enoxaparin 30 mg SC every 12 hrs **OR** Enoxaparin 40 mg SC every 24hrs

Enoxaparin Dose Adjustments

- Enoxaparin should be dosed based on actual body weight
- **Capping doses** of LMWH may be unsafe due to the risk of **under-dosing** in the obese.
- Females less than 45 kg, or males less than 57 kg, consider decreasing prophylactic dose to 30 mg SC once daily
- Patient weight greater than 150 kg or BMI greater than 40 kg/m^2, consider increasing prophylactic dose to 40 mg SC EVERY12 hrs
- If CrCl less than 30 ml/min
  - Consider using SC unfractionated heparin
  - Reduce prophylactic dose of enoxaparin to 30 mg SC every 24 hrs
  - Decrease therapeutic dose of enoxaparin to 1 mg/kg SC once daily and monitor anti-Xa activity level
- Hemodialysis or Peritoneal Dialysis: If patient is receiving either therapy, the estimation of creatinine clearance is no longer a meaningful calculation. Enoxaparin use should be avoided in this population. Heparin is the preferred anticoagulant for bridging in this case because it is not renally eliminated and thus may be safer.

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Warfarin Periprocedural Anticoagulation Management

Unfractionated Heparin Dosing Options:

- Therapeutic-dose IV UFH: Dose-adjusted IV infusion to achieve a target anti-Xa heparin therapeutic range as defined by current heparin dosing nomogram based on indication

- SC UFH: 250 Units/kg SC BID **Consider in renal insufficiency when CrCl less than 30 ml/min;
  -Generally does NOT require aPTT or anti-X_a monitoring
  -If active VTE, consider load with 333 Units/kg SC x 1 dose, then 250 Units/kg SC twice daily

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Warfarin Periprocedural Anticoagulation Timeline Recommendations

Order INR measurement 5 – 7 days prior to procedure, and evaluate below:		
Supratherapeutic	**Therapeutic**	**Subtherapeutic**
• Discontinue ≥5 days before procedure depending on current INR, time to procedure and desired INR for procedure • Recheck INR 24 hours before procedure	• Discontinue 5 days before procedure depending on current INR, time to procedure and desired INR for procedure • Recheck INR 24 hours before procedure	• Discontinue 3-4 days before procedure • Initiate alternative anticoagulant (if indicated) when INR becomes subtherapeutic • Recheck INR 24 hours before procedure if a normal INR is desired

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Warfarin Periprocedural Anticoagulation Timeline Recommendations

1. **Perioperative Management and Timing of LMWH / UFH *Before* Surgery**
   - If using 1 mg/kg SC EVERY12 hour enoxaparin regimen
     - Administer the last dose (1 mg/kg) 24 hours prior to surgery
   - If using 1.5 mg/kg SC once daily enoxaparin regimen
     - Administer only one-half dose (0.75 mg/kg) 24 hours prior to surgery
   - If using SC UFH, administer the last dose 24 hours prior to surgery
   - If using heparin IV infusion, the infusion should be stopped 4-6 hours prior to surgery

2. **Perioperative Management and Timing of LMWH / UFH *After* Surgery**
   - If bleeding risk is low, post-operative bridging anticoagulation should not be started until 24 hours after the procedure when hemostasis is achieved
   - If the bleeding risk of the procedure is felt to be high (i.e. craniotomy, spinal surgery, partial organ removals, etc.), delaying bridging anticoagulation therapy even further may be appropriate
     - Consider either delaying the initiation of either low-dose, or therapeutic-dose LMWH/UFH for 48 to 72 h after surgery when hemostasis is secured, or completely avoiding LMWH or UFH after surgery
   - It is strongly recommended to discuss the appropriate time to restart therapy with the surgeon

3. **Resumption of Warfarin After Surgery:**
   - 12-24 hours post-op pending adequate hemostasis

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What About Interruption of the Direct Oral Anticoagulants? (DOAC's)

- **Bridging is NOT usually needed** with apixaban, dabigatran, edoxaban, and rivaroxaban due to short time to offset and onset

*http://pharmacistsletter.therapeuticresearch.com/pl/ArticleDD.aspx?nidchk=1&cs=CEPDA&s=PL&pt=2&fpt=31&dd=301213&pb=PL&searchid=55361766&segment=7856

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SECTION 3: DOAC PERIPROCEDURAL MANAGEMENT

Periprocedural Management of Direct Oral Anticoagulants (DOACs)

NOTE: This is to be used as a guide; patients may be using alternate dose regimens so each plan must be based on clinical judgment using patient specific factors and dosing regimens. Full dosing guidelines for each of these new agents can be found at: http://intraeast/Clinical_Services/Anticoagulation/PoliciesandGuidelines.html

Pre-procedural interruption of DOAC's

1. Prior to decision making, determine the renal function by calculating a Creatinine Clearance (CrCl), preferably using the Cockroft Gault equation*
2. Next determine the estimated bleeding risk of the procedure (Low vs. Uncertain/Intermediate/High Risk)
3. Based on CrCl, see table for recommended amount of time to hold DOAC prior to procedure

	DOAC: Dabigatran					DOAC: Apixaban, Edoxaban, or Rivaroxaban		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13 h	15 h	18 h	27 h	30 (off dialysis)	6-15 h	Apixaban: 17 h Edoxaban: 17 h Rivaroxaban: 9 h	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk	Hold Dabigatran for:					Hold Apixaban, Edoxaban, or Rivaroxaban for:		
Low bleed risk	≥24 h	≥36 h	≥48 h	≥72 h	No Data	≥24 h	≥36 h	No Data
Uncertain, intermediate, or high bleed risk	≥48 h	≥72 h	≥96 h	≥120 h	No Data	≥48 h	No Data	No Data

NOTE: The duration for withholding is based upon the estimated DOAC half-life withholding times of 2 to 3 half-lives for low procedural bleeding risk and 4 to 5 drug half-lives for uncertain, intermediate, or high procedural bleeding risk.

*DOAC = direct-acting oral anticoagulant (Also known as NOAC's (New or Novel, or Non-Vitamin K Antagonist, Oral Anticoagulants)

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SECTION 3:
DOAC PERIPROCEDURAL MANAGEMENT

Post-procedural resumption of DOAC's

Drug	Low bleeding risk procedure	Moderate to High bleeding risk procedure
Dabigatran (Pradaxa®)	Resume 24 hr after procedure	Discussion with provider about resumption 48-72 hr after procedure
Rivaroxaban (Xarelto®)		
Apixaban (Eliquis®)		
Edoxaban (Savaysa®)		

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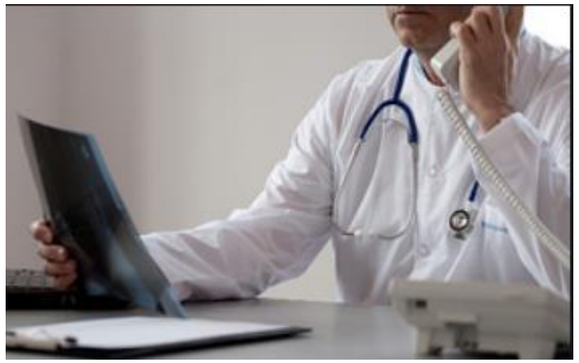
Antiplatelet Medications

If You Are Not Sure If or When to Stop Aspirin or a P2Y12 Inhibitor…

- *Please ask the Cardiologist!*



And don’t stop Aspirin for a patient with Coronary Artery Disease unless absolutely necessary!

SECTION 4: ANTIPLATELET THERAPY PERIPROCEDURAL MANAGEMENT

Guidelines for Interruption of Antiplatelet Therapy

When appropriate, a cardiology consult is strongly recommended to evaluate patient risk for cardiac events and to provide advice on proper periprocedural management of antiplatelet therapies.

I. **Non-Cardiac Surgery**

a. **Aspirin**

i. Minor (low bleeding risk) procedures: Dental, Dermatologic, and Ophthalmologic

a) Aspirin use for Primary Prevention: In general if CV risk is felt to be low then stop aspirin 7-10 days before procedure (i.e. AFib with $CHA_2DS_2VASc^a$ score ≤ 2)

b) **Aspirin for Secondary Prevention: Continue aspirin without interruption**

a. **Do NOT discontinue aspirin without Cardiology consult**

ii. Major (high bleeding risk) procedures

a) ***Patients at low risk for cardiac events***[a]: Recommend interruption of aspirin 7-10 days before surgery

b) ***Patients at high risk of cardiac events***[b]: Continue aspirin without interruption

b. **P2Y12 Inhibitors:** In patients with a drug-eluting coronary stent who require surgery within 12 months of stent placement, or a bare metal stent who require surgery within 6 weeks of stent placement (discouraged!), recommend continuing dual antiplatelet therapy in the perioperative period or interrupting dual antiplatelet therapy only after obtaining Cardiology consult.

i. ticagrelor**: STOP 5 days before procedure
ii. clopidogrel: STOP 5 days before procedure
iii. prasugrel: STOP 7 days before procedure

c. **Aspirin/Dipyridamole (Aggrenox) or Cilostazol (Pletal):**

i. Follow aspirin recommendations above

Ticagrelor Discontinuation Qualifying Statement: The prescribing information from AstraZeneca regarding discontinuation of Ticagrelor is 5 days prior to an elective surgery. However, Ticagrelor has a short duration of action and an offset of action of 1-2 days. Due to this discrepancy it is recommended to weigh bleed risk with embolic / re-stenosis risk. A cardiology consult is recommended.

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SECTION 4:
ANTIPLATELET THERAPY PERIPROCEDURAL MANAGEMENT

II. **Cardiac Surgery**

a. **Aspirin / P2Y12 Inhibitors**

i. **For patients scheduled for CABG:**

a) Recommend continuing aspirin up to and beyond the time of CABG;

b) In general, if receiving:

i. Ticagrelor**: STOP 5 days before procedure

ii. clopidogrel: STOP 5 days before procedure

iii. prasugrel: STOP 7 days before procedure

ii. **For patients with coronary stent**:

a) Who are receiving dual antiplatelet therapy[c] and require surgery, recommend deferring surgery for at least:

i. 6 weeks after placement of a bare-metal stent

ii. 6 months after placement of a drug-eluting stent

b) In patients with a bare-metal coronary stent who require surgery within 6 weeks of stent placement, recommend continuing dual antiplatelet therapy in the perioperative period

c) In patients with a drug-eluting coronary stent who require surgery within 12 months of stent placement, recommend continuing dual antiplatelet therapy in the perioperative period or interrupt dual antiplatelet therapy only after obtaining cardiology consult.

****Ticagrelor Discontinuation Qualifying Statement**: The prescribing information from AstraZeneca regarding discontinuation of Ticagrelor is 5 days prior to an elective surgery. However, Ticagrelor has a short duration of action and an offset of action of 1-2 days. Due to this discrepancy it is recommended to weigh bleed risk with embolic / re-stenosis risk. A cardiology consult is recommended.

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SECTION 5 Switching Between Anticoagulant Agents

Parenteral Agent Conversions

Agent	Conversion to parenteral anticoagulant	Conversion from parenteral anticoagulant
Dabigatran Pradaxa®	Based on renal function: CrCl greater than 30 ml/min: start parenteral agent 12 hours after last dose of dabigatran CrCl less than 30 ml/min: start parenteral agent 24 hours after last dose of dabigatran	**START** dabigatran 0 to 2 hours before the next dose of the parenteral drug was due to be administered or at the time of discontinuation of a continuously administered parenteral drug (i.e. IV UFH)
Rivaroxaban Xarelto®	Discontinue rivaroxaban and start the parenteral anticoagulant at the time the next scheduled dose of rivaroxaban would have been given	**START** rivaroxaban 0 to 2 hours before the next evening dose of the parenteral drug was to be administered or at the time of discontinuation of a continuously administered parenteral drug (i.e. IV UFH)
Apixaban Eliquis®	Discontinue apixaban and begin the parenteral agent at the next scheduled dose of apixaban or 12 hours after last apixaban dose	Begin apixaban when the next scheduled dose of parenteral agent was due or at the time of discontinuation of a continuously administered parenteral drug (i.e. IV UFH)
Edoxaban Savaysa®	Discontinue edoxaban and start the parenteral anticoagulant at the time of the next dose of edoxaban	Discontinue LMWH and start edoxaban at the time of the next scheduled administration of LMWH Discontinue heparin infusion and start edoxaban 4 hours later

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SECTION 5

Switching Between Anticoagulant Agents
Key Points:

- During a transition from oral factor Xa inhibitor therapy to treatment with unfractionated heparin or low-molecular weight heparin (ie. enoxaparin), the use of an anti-Xa assay for anticoagulation monitoring can yield inaccurate or unquantifiable results
  - Especially during the first 12-24 hours after taking a DOAC, but effect can last up to 72 hours in those with poor renal function
- The oral factor Xa inhibitors also have unpredictable (negligible to moderate) effects on global coagulation assays, which measure activated partial thromboplastin time (aPTT) or prothrombin time
- Despite that, the use of an aPTT assay may be more appropriate during transitions from oral factor Xa inhibitor therapy to UFH infusion therapy
  - (Of note, Rivaroxaban appears to have a stronger impact on aPTT levels than does Apixaban).
    - For further clarity, see reference #10 (page 12):"Managing transitions from oral factor Xa inhibitors to unfractionated heparin infusions."
- For Dabigatran, consider monitoring anti-Xa levels instead of aPTT

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DOAC Conversions to and from Warfarin

- Increased risk of stroke when anticoagulant is stopped
  - especially in the setting of non-valvular Afib!

- It is recommended to overlap warfarin with a parenteral anticoagulant until warfarin is therapeutic

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DOAC	Conversion to Warfarin	Conversion From Warfarin
Dabigatran Pradaxa®	Based on renal function (CrCl), start warfarin **2 – 3** days before discontinuing dabigatran: CrCl greater than 50 ml/min: 3 days before CrCl 31-50 ml/min: 2 days before CrCl less than 30: No recommendation available ****Dabigatran affects the INR****	Discontinue warfarin and start dabigatran when INR less than 2
Rivaroxaban Xarelto®	Discontinue rivaroxaban and ***start warfarin plus a parenteral anticoagulant*** at the time of the next dose of rivaroxaban dose. Continue the parenteral anticoagulant until INR at goal. ****Rivaroxaban affects the INR****	Discontinue warfarin and start rivaroxaban when INR less than 3
Apixaban Eliquis®	Discontinue apixaban and ***start warfarin plus a parenteral anticoagulant*** at the time of the next apixaban dose. If no parenteral anticoagulant is to be used, then start warfarin roughly 72 hours prior to last dose of apixaban ****Apixaban affects INR****	Discontinue warfarin and start apixaban when INR less than 2
Edoxaban Savaysa®	Discontinue edoxaban and ***start warfarin plus a parenteral anticoagulant*** at the time of the next scheduled edoxaban dose. Once a stable INR ≥ 2.0 is achieved the parenteral anticoagulant should be discontinued and the warfarin continued If no parenteral anticoagulant is to be used: • For patients taking 60 mg of edoxaban, reduce the dose to 30 mg and begin warfarin concomitantly • For patients receiving 30 mg of edoxaban, reduce the dose to 15 mg and begin warfarin concomitantly Once a stable INR ≥ 2.0 is achieved, edoxaban should be discontinued and the warfarin continued ****Edoxaban affects INR****	Discontinue warfarin and start edoxaban when the INR is ≤ 2.5

While all DOAC's can impact the INR, note that Dabigatran would be expected to most significantly elevate the INR lab test. But it is likely an artificial inflation of the INR value, and does not represent a therapeutic INR while the blood levels of Dabigatran remain on board.

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Abbreviations

aPTT = activated partial thromboplastin time
ASA = aspirin
CABG = coronary artery bypass graft
CHF = congestive heart failure
CrCl = creatinine clearance
CVA = cerebrovascular accident
DM = diabetes mellitus
DOAC = direct oral anticoagulant (formerly known as New (or Novel) Oral Anticoagulants (NOACs); also known as Non-Vitamin K Antagonist Oral Anticoagulants)
FDA = Food and Drug Administration
HIT = heparin-induced thrombocytopenia
HTN = hypertension
GI = gastrointestinal
IBW = ideal body weight
INR =international normalized ratio
IV = intravenous
LMWH = low-molecular-weight heparin
MOA = mechanism of action
P2Y12 = antiplatelet agents (clopidogrel, ticagrelor, prasugrel)
pt = patient
SC = subcutaneous
SCr = serum creatinine
TIA = transient ischemic attack
UFH = unfractionated heparin
VKA = vitamin K antagonist
VTE = venous thromboembolism

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APPENDIX B
Creatinine Clearance Calculation

Estimating Renal Function Use the Cockcroft-Gault equation for estimating drug dosing/intervals (Not MDRD)

To estimate Creatinine Clearance (CrCl) from serum creatinine (SCr), first determine the body weight (BW) to use in the equation:

- Use ideal body weight (IBW) with the exception of the following:
  - If Actual BW is less than IBW, use Actual BW
  - If Actual BW is greater than 120% of IBW, use Adjusted BW

Ideal body weight (IBW):

- Men = 50 kg + 2.3 (inches greater than in height than 60)
- Women = 45.5 kg + 2.3 (inches greater than in height than 60)

Adjusted BW :

- Multiply 0.4 (Actual BW-IBW) + IBW

Cockcroft Gault Equation:

- Men→[(140-age)BW] ÷ [(72)(SCr*)] = CrCl
- Women→ (Men's result)(0.85) = CrCl

*In patients older than 65 and/or if malnourished or frail, consider substituting 1 for serum creatinine (SCr) if the measured value is less than 1 to avoid overestimating clearance in a patient with suspected decreased muscle mass

Call a pharmacist at Essentia Health if you need assistance with this calculation.

Or consider utilizing an online calculator for Creatinine Clearance:

- http://www.globalrph.com/crcl.htm or
- http://www.micromedexsolutions.com/micromedex2/librarian/CS/2EB4FD/ND_PR/evidenceexpert/ND_P/evidenceexpert/DUPLICATIONSHIELDSYNC/F967F5/ND_PG/evidenceexpert/ND_B/evidenceexpert/ND_AppProduct/evidenceexpert/ND_T/evidenceexpert/PFActionId/pf.ShowPage/PageId/calc.CreatinineClearance

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Quiz Time…

Example 1

For a patient on Dabigatran with a CrCl = 90 ml/min, and procedure is low bleed risk:

- Suggest holding for at least 24 hours, but no longer than 36 hours

	DOAC: **Dabigatran**					DOAC: **Apixaban, Edoxaban, or Rivaroxaban**		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13 h	15 h	18 h	27 h	30 (off dialysis)	6-15 h	Apixaban: 17 h Edoxaban: 17 h Rivaroxaban: 9 h	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk	Hold Dabigatran for:					Hold Apixaban, Edoxaban, or Rivaroxaban for:		
Low **bleed risk**	≥24 h	≥36 h	≥48 h	≥72 h	No Data	≥24 h	≥36 h	No Data
Uncertain, intermediate, or high **bleed risk**	≥48 h	≥72 h	≥96 h	≥120 h	No Data	≥48 h	No Data	No Data

Example 2
For a patient on Dabigatran with a CrCl = 45 ml/min, and procedure is high bleed risk:

- Suggest holding at least 96 hours, but no longer than 108 hours

	DOAC: **Dabigatran**					DOAC: **Apixaban, Edoxaban, or Rivaroxaban**		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13 h	15 h	18 h	27 h	30 (off dialysis)	6-15 h	Apixaban: 17 h Edoxaban: 17 h Rivaroxaban: 9 h	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk	Hold Dabigatran for:					Hold Apixaban, Edoxaban, or Rivaroxaban for:		
Low **bleed risk**	≥24 h	≥36 h	≥48 h	≥72 h	No Data	≥24 h	≥36 h	No Data
Uncertain, intermediate, or high **bleed risk**	≥48 h	≥72 h	≥96 h	≥120 h	No Data	≥48 h	No Data	No Data

Example 3
For a patient on Rivaroxaban with a CrCl = 60 ml/min, and procedure is low bleed risk:

- Suggest holding for at least 24 hours, but no longer than 48 hours

	DOAC: **Dabigatran**					DOAC: **Apixaban, Edoxaban, or Rivaroxaban**		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13 h	15 h	18 h	27 h	30 (off dialysis)	6-15 h	Apixaban: 17 h Edoxaban: 17 h Rivaroxaban: 9 h	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk	Hold Dabigatran for:					Hold Apixaban, Edoxaban, or Rivaroxaban for:		
Low **bleed risk**	≥24 h	≥36 h	≥48 h	≥72 h	No Data	≥24 h	≥36 h	No Data
Uncertain, intermediate, or high **bleed risk**	≥48 h	≥72 h	≥96 h	≥120 h	No Data	≥48 h	No Data	No Data

Example 4
For a patient on Rivaroxaban, with a CrCl=24 ml/min, and procedure bleeding risk is uncertain:

- No Data

- Suggest holding for longer than 36 hours, and consult cardiology and/or operator to weigh risks and decide hold time

	DOAC: **Dabigatran**					DOAC: **Apixaban, Edoxaban, or Rivaroxaban**		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13 h	15 h	18 h	27 h	30 (off dialysis)	6-15 h	Apixaban: 17 h Edoxaban: 17 h Rivaroxaban: 9 h	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk	Hold Dabigatran for:					Hold Apixaban, Edoxaban, or Rivaroxaban for:		
Low **bleed risk**	≥24 h	≥36 h	≥48 h	≥72 h	No Data	≥24 h	≥36 h	No Data
Uncertain, intermediate, or high **bleed risk**	≥48 h	≥72 h	≥96 h	≥120 h	No Data	≥48 h	No Data	No Data

Example 5
For a patient on Apixaban, with a CrCl = 45 ml/min, and procedure is **high** bleed risk:

- Suggest holding at least 48 hours, but no longer than 60 hours

	DOAC: **Dabigatran**					DOAC: **Apixaban, Edoxaban, or Rivaroxaban**		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13 h	15 h	18 h	27 h	30 (off dialysis)	6-15 h	Apixaban: 17 h Edoxaban: 17 h Rivaroxaban: 9 h	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk	Hold Dabigatran for:					Hold Apixaban, Edoxaban, or Rivaroxaban for:		
Low **bleed risk**	≥24 h	≥36 h	≥48 h	≥72 h	No Data	≥24 h	≥36 h	No Data
Uncertain, intermediate, or high **bleed risk**	≥48 h	≥72 h	≥96 h	≥120 h	No Data	≥48 h	No Data	No Data

Example 6
For a patient on Apixaban, with a CrCl = 25 ml/min, and procedure is low bleed risk:

- Suggest holding at least 36 hours, but no longer than 48 hours

	DOAC: **Dabigatran**					DOAC: **Apixaban, Edoxaban, or Rivaroxaban**		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13 h	15 h	18 h	27 h	30 (off dialysis)	6-15 h	Apixaban: 17 h Edoxaban: 17 h Rivaroxaban: 9 h	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk	Hold Dabigatran for:					Hold Apixaban, Edoxaban, or Rivaroxaban for:		
Low **bleed risk**	≥24 h	≥36 h	≥48 h	≥72 h	No Data	≥24 h	≥36 h	No Data
Uncertain, intermediate, or high **bleed risk**	≥48 h	≥72 h	≥96 h	≥120 h	No Data	≥48 h	No Data	No Data

Example 7
For a patient on Apixaban and Dabigatran, with a CrCl = 15 ml/min, and procedure is High bleed risk:

- **Trick Question!**
- Stop Apixaban and Dabigatran,
- …and find out what moron put them on both medications!!!
- …consider warfarin after procedure?

	DOAC: **Dabigatran**					DOAC: **Apixaban, Edoxaban, or Rivaroxaban**		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13 h	15 h	18 h	27 h	30 (off dialysis)	6-15 h	Apixaban: 17 h Edoxaban: 17 h Rivaroxaban: 9 h	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk	Hold Dabigatran for:					Hold Apixaban, Edoxaban, or Rivaroxaban for:		
Low **bleed risk**	≥24 h	≥36 h	≥48 h	≥72 h	No Data	≥24 h	≥36 h	No Data
Uncertain, intermediate, or high **bleed risk**	≥48 h	≥72 h	≥96 h	≥120 h	No Data	≥48 h	No Data	No Data

Case Study #1:

66 yo Male with A-Fib and Taking Warfarin (Coumadin) Needs a Colonoscopy

- Dr. requests that patient be “bridged” with Enoxaparin (Lovenox) before the procedure

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Case Study #1:

66 yo Male with A-Fib and Taking Warfarin (Coumadin) Needs a Colonoscopy

- Step 1: Determine bleeding risk (page 3)
- Step 2: Determine thromboembolic risk (page 4)
- Step 3: Determine if bridging is appropriate (see chart)

- Step 4: Select most appropriate bridging agent (enoxaparin or UFH) and dose based on patient and procedure risk factors

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Case Study #1:

66 yo Male with A-Fib and Taking Warfarin (Coumadin) Needs a Colonoscopy

(Normal Renal Function)

- Stop Warfarin 5 days prior to procedure
- Start Enoxaparin (1 mg/kg SQ Q12h) 3 days prior to procedure
- Check INR 1 day prior to procedure
  - If INR>1.5 consider oral Vitamin K 1 mg
- Hold Enoxaparin 24 hours prior to procedure

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66 yo Male with A-Fib and Taking Warfarin (Coumadin) Needs a Colonoscopy
(Normal Renal Function)

- Resume Warfarin 12-24 hours after procedure
  - (Increase dose for first 3 days to equal normal weekly dose)
    - ie. 2 mg daily = 14 mg per week…so give 5 mg daily x 3 days, then resume 2 mg daily if INR coming into range
- Doctor approves restarting Enoxaparin 48 hours after procedure
- Check INR on day 3 and day 5, then as needed
- Stop Enoxaparin when INR therapeutic for 2 days
  - May take 5 or more days after procedure

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Case Study #2:

71 yo Male with A-Fib and Taking Rivaroxaban (Xarelto) Needs a Colonoscopy with Expected Biopsies

- Dr. demands that patient be “bridged” with Lovenox for 5 days before procedure

- RN calls clinical pharmacist to find out how to “Bridge” a Rivaroxaban patient with Enoxaparin (Lovenox)

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Case Study #2:

71 yo Male with A-Fib and Taking Rivaroxaban (Xarelto) Needs a Colonoscopy

- RN flustered, as the doctor doesn't seem interested in the new (evidence based) guideline, and wants a 5 day "washout" of the Rivaroxaban

- Pharmacist suggests **NOT** bridging with Enoxaparin (Lovenox), but rather simply figure out how long to hold the Rivaroxaban before the colonoscopy with expected biopsies

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Case Study #2:

71 yo Male with A-Fib and Taking Rivaroxaban (Xarelto) Needs a Colonoscopy

- After RN tells the doctor that the pharmacist (Co-Author of the Anticoagulation Bridging Guidelines) strongly advises to not bridge with Lovenox…
  - Consider holding 24 to 48 hours prior to procedure

- …Doctor agrees to skip the Lovenox, and to hold Rivaroxaban for 2 doses (approximately 36-40 hours) prior to colonoscopy

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Question #1:

For a typical bridge of Warfarin with Enoxaparin, when do you stop the Warfarin and when do you start the Enoxaparin?

- A.) Stop Warfarin 5 days out and start Enoxaparin 5 days out
- B.) Stop Warfarin 5 days out and start Enoxaparin 3 days out
- C.) Stop Warfarin 3 days out and start Enoxaparin 5 days out
- D.) Stop Warfarin 3 days out and start Enoxaparin 3 days out

Answer = B

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Question # 2:

An otherwise healthy 55 yo Male with A-Fib is taking Apixaban (Eliquis) 5 mg q12h.
He is having a dental procedure with low bleeding risk, but interruption is requested.
How long should you recommend they hold Apixaban before the procedure?

- A). ≥ 12 hours
- B). ≥ 24 hours
- C.) ≥ 48 hours
- D). ≥ 72 hours

	DOAC: **Dabigatran**					DOAC: **Apixaban, Edoxaban, or Rivaroxaban**		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13 h	15 h	18 h	27 h	30 (off dialysis)	6-15 h	Apixaban: 17 h Edoxaban: 17 h Rivaroxaban: 9 h	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk	Hold Dabigatran for:					Hold Apixaban, Edoxaban, or Rivaroxaban for:		
Low **bleed risk**	≥24 h	≥36 h	≥48 h	≥72 h	No Data	≥24 h	≥36 h	No Data
Uncertain, intermediate, or high **bleed risk**	≥48 h	≥72 h	≥96 h	≥120 h	No Data	≥48 h	No Data	No Data

Answer = B

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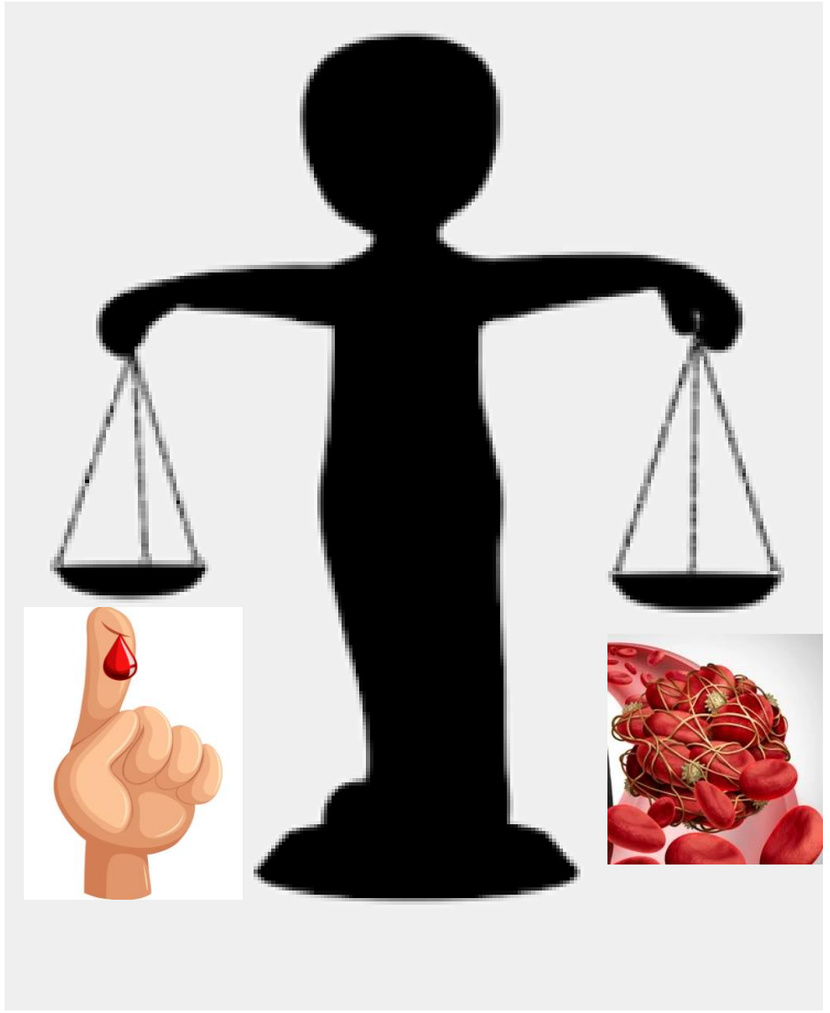
Thank You!



Any Questions?

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Here with you