McGill | Faculty of Medicine | Faculté de médecine

Centre Hospitalier de St. Mary – St. Mary's Hospital

Direct Oral Anticoagulants and Antiplatelet agents: Monitoring, peri-op management, reversal

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Transfusion Camp, Day 3

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- No conflicts of interest to declare

Objectives

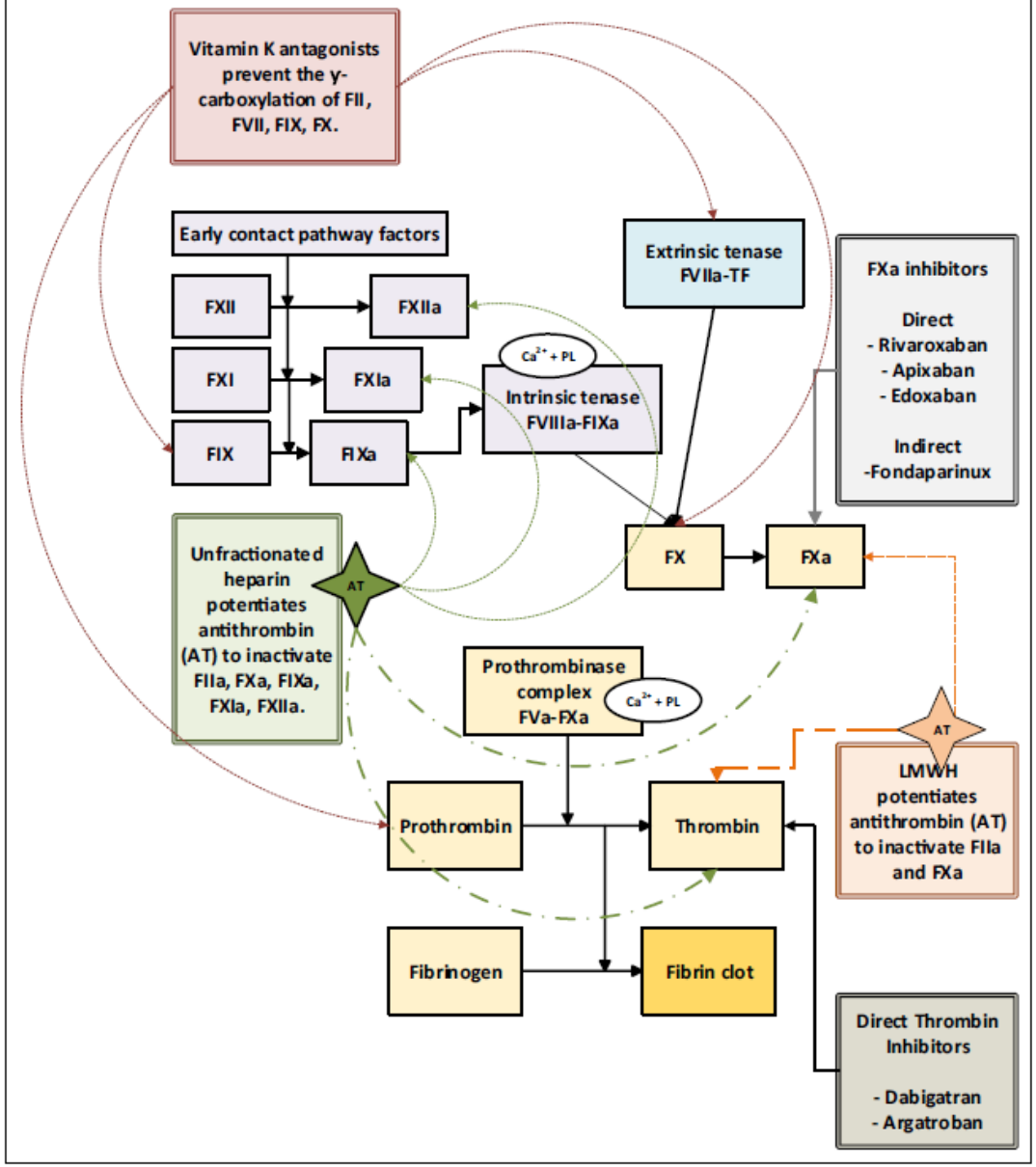
1. Brief overview of DOACs
2. Laboratory monitoring of DOACs
3. DOACs – Peri-operative management
4. DOACs – Management of bleeding
5. DOACs – Reversal with antidotes
6. Peri-operative management of antiplatelet therapy

Approved DOACs

- "Direct" oral anticoagulants
  - Dabigatran - Pradaxa®
  - Rivaroxaban - Xarelto®
  - Apixaban - Eliquis®
  - Edoxaban - Lixiana®

* Direct = no binding to antithrombin required to mediate effect

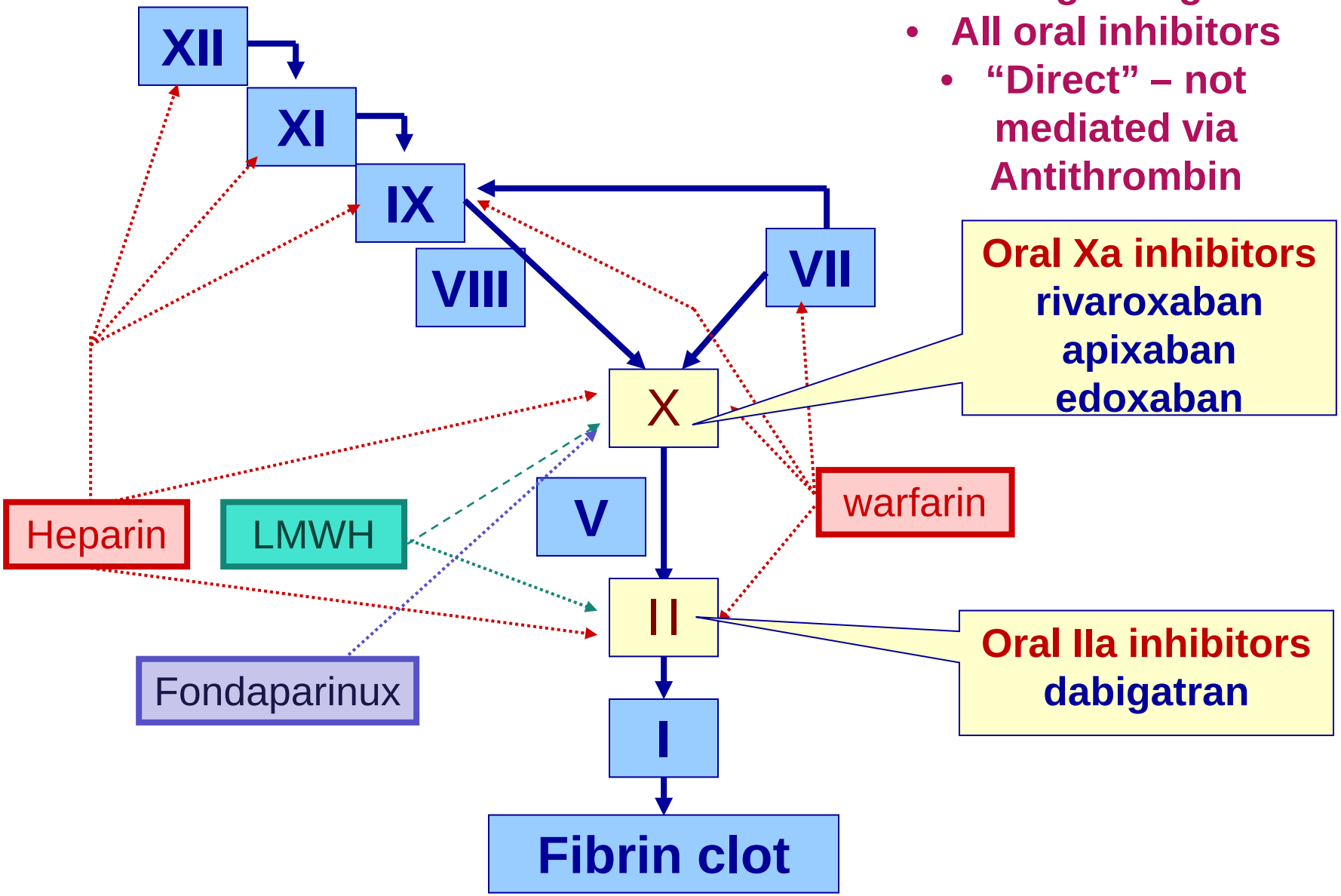
Coagulation cascade with sites of action of commonly used anticoagulants



Elbaz et al. RPTH, 2020

Mechanisms of actions of DOACs

- Single-target
- All oral inhibitors
- "Direct" – not mediated via Antithrombin



Meta-analysis: Stroke Prevention in NVAF

- RE-LY, ROCKET AF, ARISTOTLE, ENGAGE AF-TIMI 48
- 42,411 received DOAC, 29,272 received warfarin
- Compared to warfarin, DOACS:
  - Reduced stroke and systemic embolism (RR 0.81; 0.73-0.91; p<0.0001)
  - Reduced hemorrhagic stroke (RR 0.49, 0.38-0.64; p<0.0001)
  - Reduced ICH (RR 0.48, 0.39-0.59; p<0.0001)
  - Reduced all cause mortality (RR 0.90, 0.85-0.95; p=0.0003)
  - Increased GI bleeding (RR 1.25, 1.01-1.55; p=0.04)

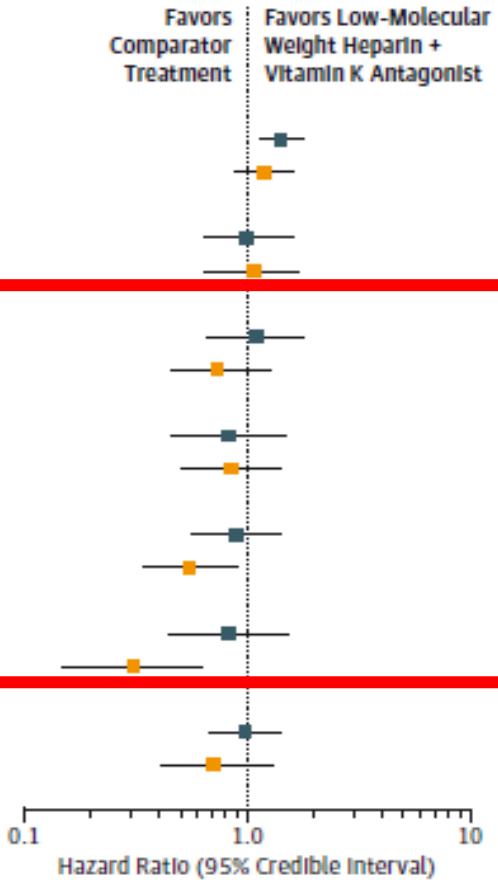
Ruff CT et al. Lancet 2014;383(9921):955-62

Meta-analysis - Acute VTE treatment trials

Figure 3. Network Meta-analysis Comparing Low-Molecular-Weight Heparin–Vitamin K Antagonist Combination for Recurrent Venous Thromboembolism and Major Bleeding

A Recurrent venous thromboembolism and major bleeding

Comparator Treatment	Hazard Ratio (95% Credible Interval)
Unfractionated heparin + vitamin K antagonist	
Recurrent VTE	1.42 (1.15-1.80)
Major bleeding	1.19 (0.90-1.58)
Fondaparinux + vitamin K antagonist	
Recurrent VTE	1.01 (0.65-1.62)
Major bleeding	1.07 (0.65-1.70)
Low-molecular-weight heparin + dabigatran	
Recurrent VTE	1.11 (0.67-1.80)
Major bleeding	0.74 (0.46-1.26)
Low-molecular-weight heparin + edoxaban	
Recurrent VTE	0.83 (0.46-1.49)
Major bleeding	0.84 (0.51-1.39)
Rivaroxaban	
Recurrent VTE	0.90 (0.57-1.41)
Major bleeding	0.55 (0.35-0.89)
Apixaban	
Recurrent VTE	0.84 (0.46-1.51)
Major bleeding	0.31 (0.15-0.62)
Low-molecular-weight heparin alone	
Recurrent VTE	0.99 (0.70-1.42)
Major bleeding	0.71 (0.42-1.31)



Castellucci et al JAMA 2014;312(11):1122-35

LET’S GET TO KNOW THESE DRUGS

How to select the appropriate DOAC?

Indication: SPAF, VTE treatment	Age	Renal function
Thrombosis Risk or CHADS2 score	Bleed risk	Once a day vs. twice a day dosing
Cost (vs. warfarin)	Drug interactions	Need for concomitant antiplatelet agents

There’s an app for that !

Thrombosis Canada Management Tools
Anticoagulant selection and dosing in AF

TOOLS

Algorithms

- **Anticoagulant Dosing In Atrial Fibrillation**
- Perioperative Anticoagulant Management Algorithm
- Thrombophilia Testing Algorithm
- Diagnosing and Ruling Out VIPIT/VITT

Acute Management Algorithms

- Atrial Fibrillation
- Bleed Management
- Deep Vein Thrombosis
- Pulmonary Embolism

Checklists

- DOAC Follow-up

Calculators

Anticoagulant Dosing In Atrial Fibrillation

- Age (years) ____
- Weight (kg) ____
- Serum Creatinine (µmol/L) ____
- ☐ Congestive Heart Failure History
- ☐ Hypertension History
- ☐ Diabetes Mellitus History
- ☐ Previous stroke or TIA
- ☐ History of macrovascular disease (coronary, aortic or peripheral)
- ☐ Patient has another indication for warfarin therapy (for example, mechanical heart valve, LV thrombus, rheumatic valvular heart disease)
- ☐ Female Patient
- ☐ Concomitant use of P-gp inhibitors (except amiodarone and verapamil) ?

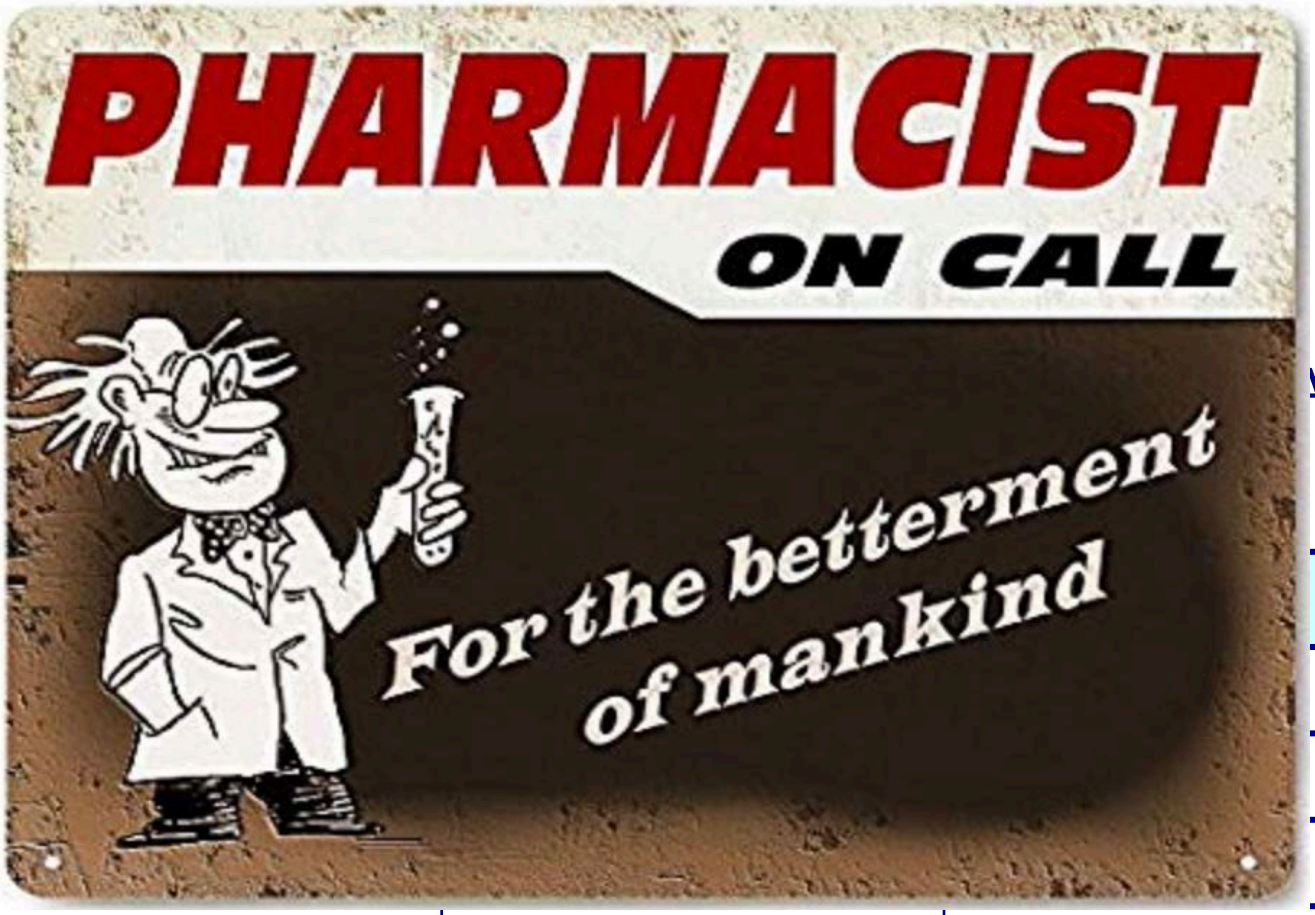
Drug-drug interactions : P-gp and CYP3A4 are important

- **P-gp** is a key drug efflux transporter (prevents absorption and increases excretion into bile and urine) → **MAY INCREASE DOAC LEVELS**
- **CYP3A4** metabolizes apixaban and rivaroxaban
- Many drugs induce both P-gp and CYP3A4 (phenytoin, carbamazepine, phenobarb, rifampin) → **MAY REDUCE DOAC LEVELS**

DOAC	P-gp	CYP3A4
dabigatran	Yes	No
apixaban	Yes	Yes
rivaroxaban	Yes	Yes
edoxaban	Yes	No

Drug-drug interactions : P-gp and CYP3A4 are important

- **P-gp** is a key drug efflux transporter (prevents absorption
  and
  INC
- **CY**
- Ma
  car
  LEV



DOAC		
dabig		
apixal		
rivaro		
edoxaban	Yes	No

Common P-gp and CYP3A4 inhibitors and inducers

		P-gp	CYP3A4
Inhibitors	↑ **DOAC effect**	Verapamil Dronedarone Itraconazole Ketoconazole Voriconazole Clarithromycin	Atazanavir Darunavir Itraconazole Ketoconazole Nefazodone Clarithromycin
Inducers	↓ **DOAC effect**	Rifampin Carbamazepine Phenytoin Barbiturates St. John's wort	Rifampin Carbamazepine Phenytoin Barbiturates St. John's wort

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Coagulation tests are not required to adjust DOAC dosing

Coagulation tests are not required to adjust DOAC dosing

But that does not mean that coagulation tests are not affected

Interpreting routine coagulation screening tests

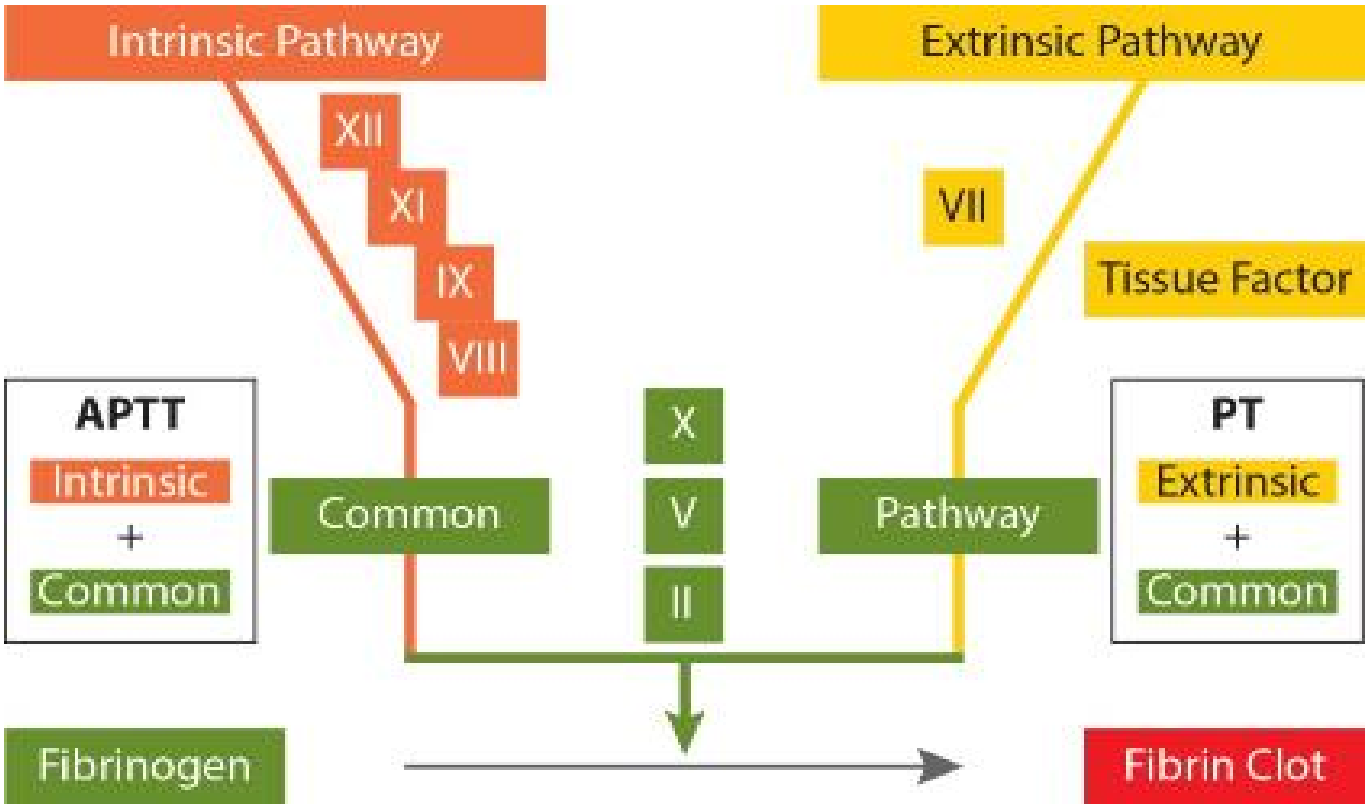
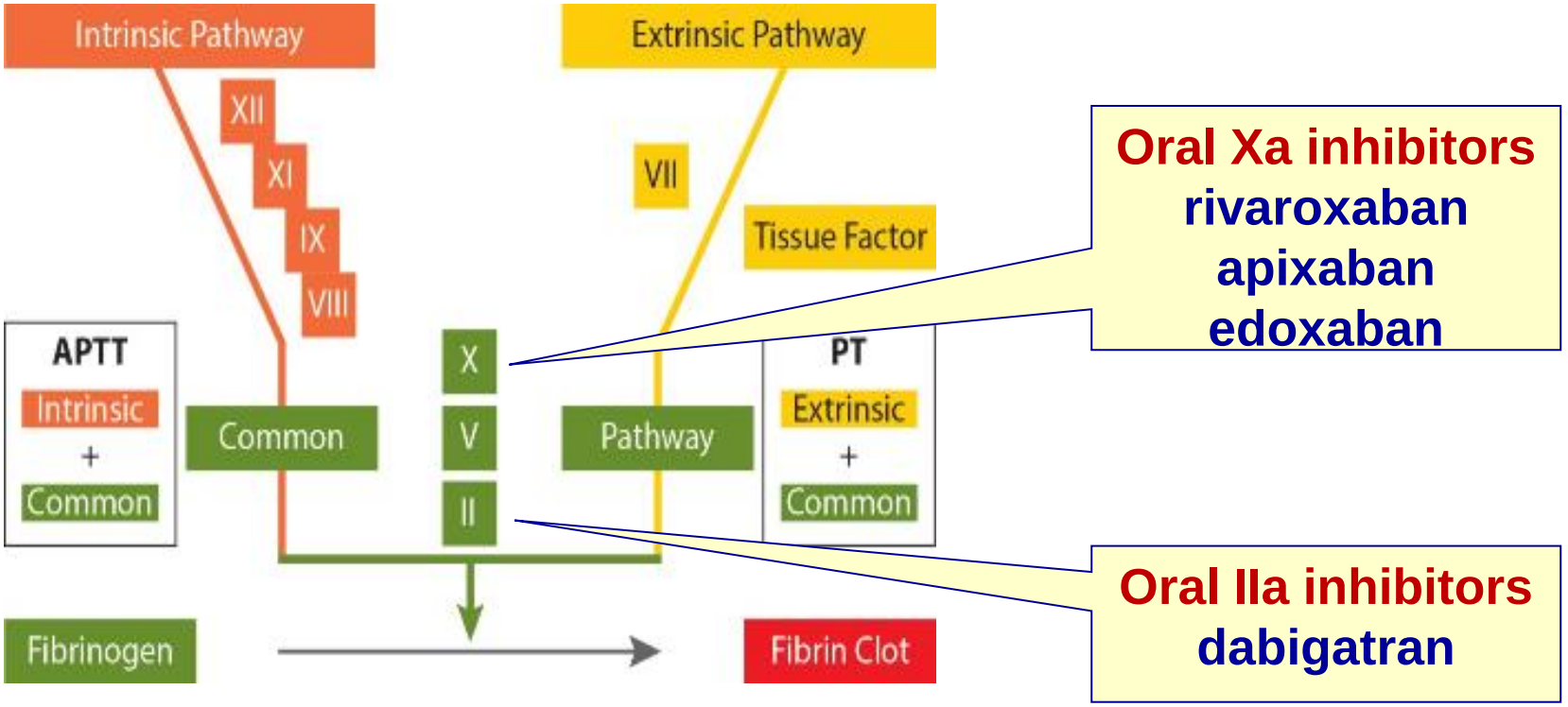


Image Source: BloodyEasy: *Coagulation Simplified, Second Edition*
Download at: www.transfusionontario.org

Interpreting routine coagulation screening tests



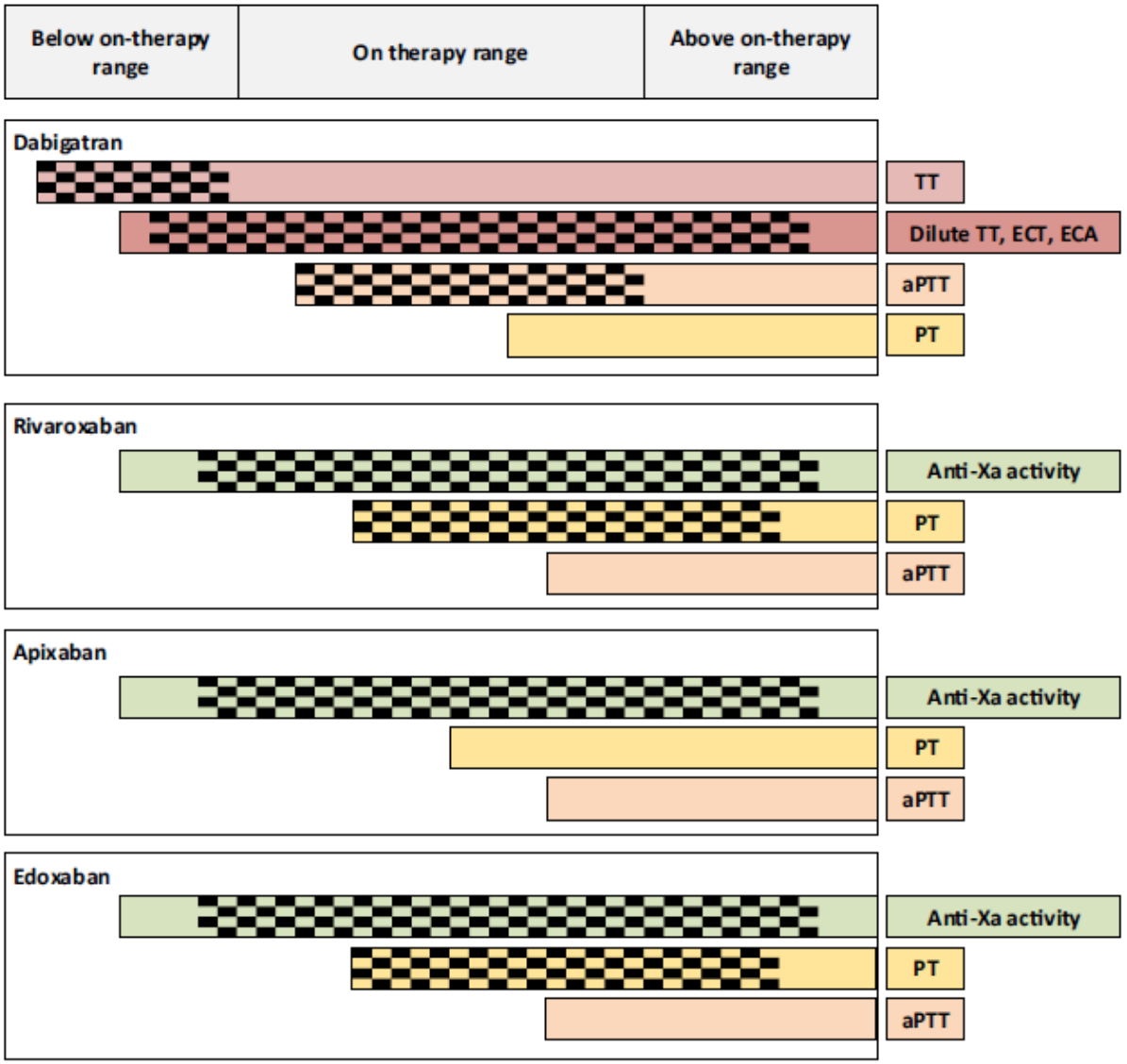
Since Factor X and Factor II are inhibited (both in the common pathway) both PT and PTT should be elevated

DOACs: Effect on coagulation assays

Laboratory Test¶	Dabigatran	Rivaroxaban, Apixaban or Edoxaban
Prothrombin time (PT) and International Normalized Ratio (INR)¶	Variable effect (usually INR<2.0 at peak blood levels)†	Rivaroxaban and edoxaban can increase PT/INR; apixaban has a minimal effect†
Activated partial thromboplastin time (aPTT)¶	Non-linear increase†	Rivaroxaban and edoxaban can increase aPTT; apixaban has a minimal effect†
Thrombin clotting time (TCT) (Not widely available)	Increases TCT‡. Normal TCT excludes the presence of dabigatran	No effect
Anti-factor Xa level (Not widely available)	No effect	Can be used to accurately quantify the anticoagulant effect. Specific apixaban, edoxaban, or rivaroxaban calibrators are required
Other specialized tests: Dilute thrombin time assay (dTT) Ecarin chromogenic assay (ECA) and Ecarin clotting time (ECT) (Not widely available)	dTT and ECA/ECT can be used to accurately quantify dabigatran levels	No effect

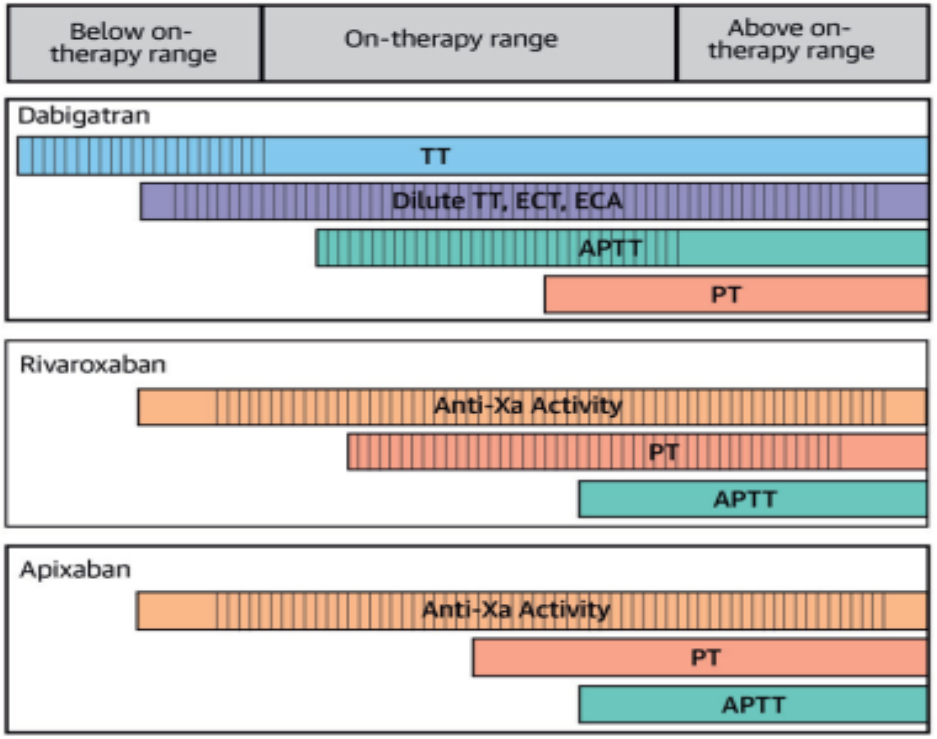
Adapted from Thrombosis Canada clinical guide

Effect of Direct Oral Anticoagulants on Hemostatic Tests



Elbaz et al. RPTH, 2020

DOACs: Effect on coagulation assays



CENTRAL ILLUSTRATION **Sensitivity and Linearity of Coagulation Assays to Below, Within, and Above Typical On-Therapy Concentrations of Dabigatran, Rivaroxaban, and Apixaban**

Horizontal bars and vertical hatching correspond to the approximate range of detectability (i.e., sensitivity) and linearity, respectively, of each assay to below, within, and above typical on-therapy concentrations of dabigatran, rivaroxaban, and apixaban. Ranges are approximations and may vary on the basis of choice of reagent. Typical on-therapy drug levels are shown in Table 1. APTT = activated partial thromboplastin time; ECA = ecarin chromogenic assay; ECT = ecarin clotting time; PT = prothrombin time; TT = thrombin time.

When might you need to obtain a DOAC level?

- **Urgent management / reversal needed**
  - **Bleed**
  - **Urgent surgery / procedure**
  - **Intentional overdose**
  - **Stroke on a DOAC and need to give tPA**

- Extremes of weight
- Renal dysfunction
- Malabsorption concerns / short gut
- Drug interactions

Quantitative DOAC levels

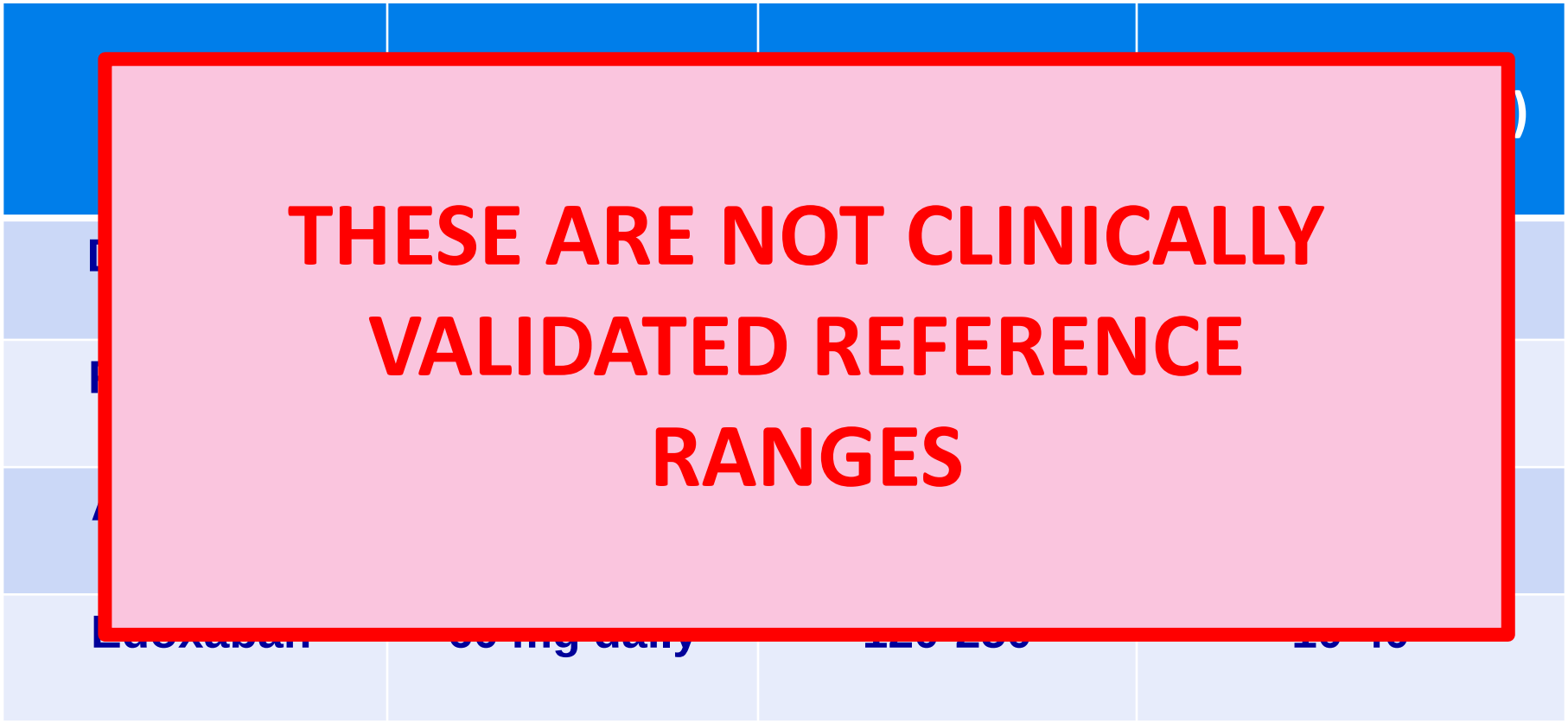
- For dabigatran – the Hemoclot® assay is based on the thrombin time and calibrated to dabigatran concentration
- For rivaroxaban, apixaban and edoxaban – Anti-Xa assays calibrated to the specific drug concentration
- In Ontario there are few academic centres offering these tests
- No immediate access to these tests in even large tertiary centres

Expected steady-state Peak & Trough concentrations of DOACs (A Fib)

Drug	Dose	Peak (ng/mL)	Trough (ng/mL)
Dabigatran	150 mg bid	64-443	31-225
Rivaroxaban	20 mg daily	189-419	6-87
Apixaban	5 mg bid	91-321	41-230
Edoxaban	60 mg daily	120-250	10-40

Derived from published pharmacokinetic analyses
Samuelson et al. Chest 2017;151(1):127-138

Expected steady-state Peak & Trough concentrations of DOACs (A Fib)



THESE ARE NOT CLINICALLY VALIDATED REFERENCE RANGES

Derived from published pharmacokinetic analyses
Samuelson et al. Chest 2017;151(1):127-138

Do DOAC levels correlate with clinical outcomes?

- **Likely, yes**
  - Subanalysis of RELY study – correlation with dabi plasma concentrations and ischemic stroke and bleeding
  - Subanalysis of ENGAGE AF-TIMI 48 study – relationship between edoxaban dose, drug level and clinical outcomes
  - Prospective Italian Registry, n=565, DOAC levels and followed for clinical outcomes; mean trough levels in patients with high CHADS-VASC scores correlated with thrombosis & mean peak levels with bleeding
  - DOAC levels changed clinical management in 77% of cases

Reilly et al, J Am Coll Cardiol 2014;63:321-8
Ruff et al, The Lancet 2015;385:2288-95
Testa et al, J Thromb Haemost 2018;16:842-8
Testa et al, J Thromb Haemost 2019;17:1064-72
Winthen-Larsen et al, Thromb Res 2019; 175:40-45

“Evidence” for “safe” DOAC levels

- < 30ng/mL for high risk surgery
- > 50 ng/mL + serious bleeding = consider reversal / antidote
- < 100 ng/mL – for IV tPA
- > 200 ng/mL – concentration associated with a consistent peri-procedural bleeding risk

BASED ON PK DATA, PUBLISHED SUB-ANALYSES OF THE PHASE 3/4 RANDOMIZED CLINICAL TRIALS, SMALL RETROSPECTIVE STUDIES AND “EXPERT OPINION” GUIDELINES FROM VARIOUS SOCIETIES = “WEAK EVIDENCE”

Levy et al, J Thromb Haemost 2016;14:623-7
Pernod et al, Arch Cardio Dis 2013;106:382-393
Steiner et al, Clin Res Cardiol 2013;102:399-412
Seiffge et al, Circulation 2015; 132:1261-9

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Pre-Procedure Stopping of DOACs

- Consider procedure:
  - **Bleeding risk** associated with surgery/procedure
  - Whether patient is to receive **spinal/epidural anesthesia**

- Consider patient factors :
  - Effects of **renal function** on drug elimination half life
  - Concomitant meds: **antiplatelets**

- Consider drug factors :
  - Drug elimination **half life** (with normal renal function)
  - Lab tests accurately measuring anticoagulant effect not widely available and not recommended
  - The correlation between anticoagulant levels and bleeding (or thrombosis) is not well established

TABLE 2] Suggested Risk Stratification for Procedural Bleed Risk, Based on ISTH Guidance Statements[25]

High-bleed-risk surgery/procedure[a] (30-d risk of major bleed ≥ 2%)	Major surgery with extensive tissue injury Cancer surgery, especially solid tumor resection (lung, esophagus, gastric, colon, hepatobiliary, pancreatic) Major orthopedic surgery, including shoulder replacement surgery Reconstructive plastic surgery Major thoracic surgery Urologic or GI surgery, especially anastomosis surgery Transurethral prostate resection, bladder resection, or tumor ablation Nephrectomy, kidney biopsy Colonic polyp resection Bowel resection Percutaneous endoscopic gastrostomy placement, endoscopic retrograde cholangiopancreatography Surgery in highly vascular organs (kidneys, liver, spleen) Cardiac, intracranial, or spinal surgery Any major operation (procedure duration > 45 min) Neuraxial anesthesia[b] Epidural injections
Low-to-moderate-bleed-risk surgery/procedure[c] (30-d risk of major bleed 0%-2%)	Arthroscopy Cutaneous/lymph node biopsies Foot/hand surgery Coronary angiography[d] GI endoscopy ± biopsy Colonoscopy ± biopsy Abdominal hysterectomy Laparoscopic cholecystectomy Abdominal hernia repair Hemorrhoidal surgery Bronchoscopy ± biopsy
Minimal-bleed-risk surgery/procedure[e] (30-d risk of major bleed approximately 0%)	Minor dermatologic procedures (excision of basal and squamous cell skin cancers, actinic keratoses, and premalignant or cancerous skin nevi) Ophthalmologic (cataract) procedures Minor dental procedures (dental extractions, restorations, prosthetics, endodontics), dental cleanings, fillings Pacemaker or cardioverter-defibrillator device implantation

ISTH = International Society on Thrombosis and Haemostasis.

Peri-procedure management of DOACs

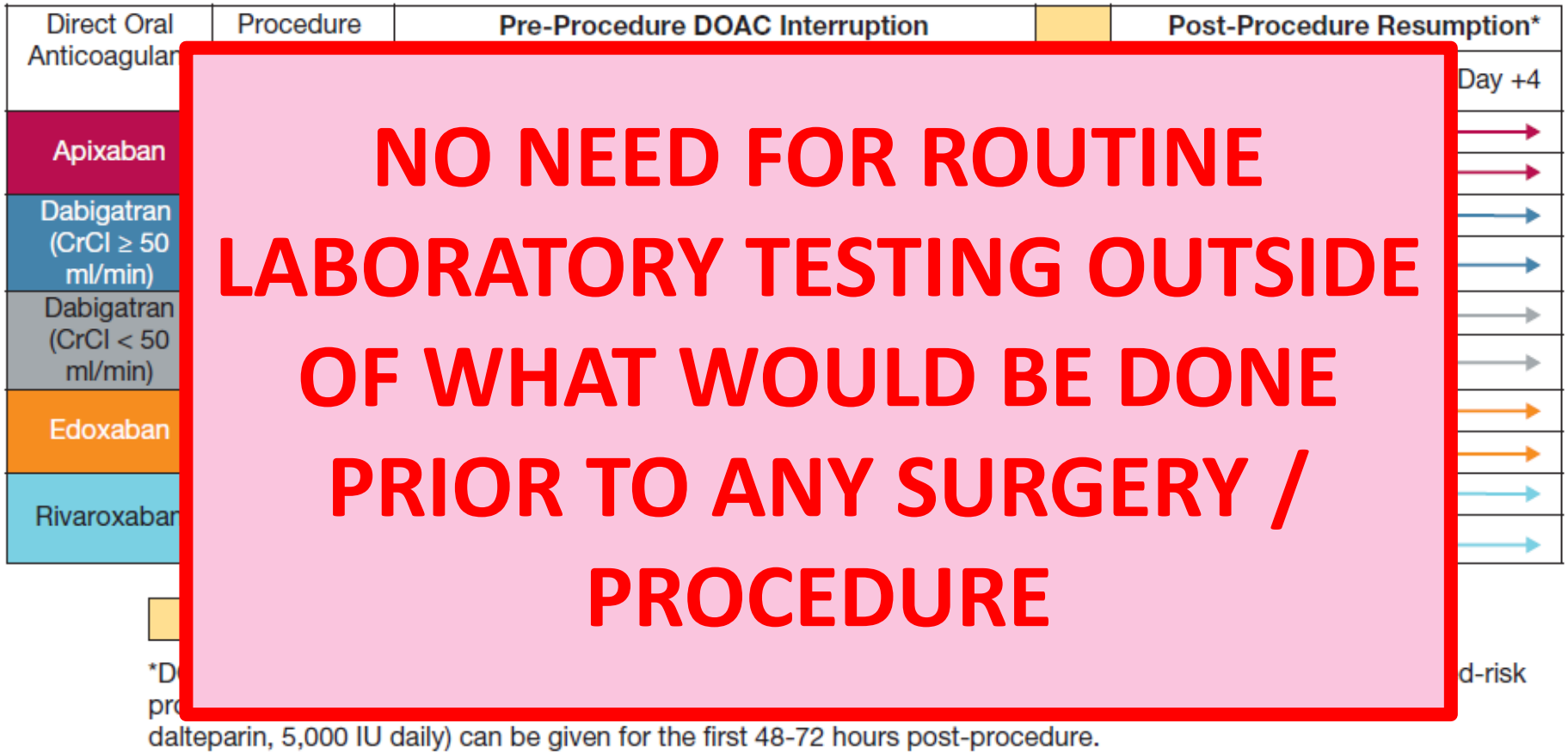

Figure 2 – *Perioperative management of direct oral anticoagulants (DOACs). CrCl = creatinine clearance.*

ACCP 2022

PAUSE : Perioperative Anticoagulation Use for Surgery Evaluation

Patients

3007 patient with atrial fibrillation

Mean CHADS2 2.0-2.2

Anticoagulation

Apixaban (n=1257)

Rivaroxaban (n=1082)

Dabigatran (n=668)

Procedure

Elective surgery

High vs. low risk bleed procedure

1/3 high risk bleeding

Intervention:

- **DOAC omitted 1 day before low risk bleeding procedure and 2 days before high risk bleeding procedure**
- **DOAC resumed 1 day after low risk bleeding procedure and 2-3 days after high risk bleeding procedure**
- **CrCl < 25 mls/min for apix and < 30 mls/mi for riva and dabi excluded**

Douketis et al, JAMA Internal Medicine. 2019

PAUSE : Outcomes at 30 days post op

DOAC	Major bleeding	Arterial thrombosis	Residual DOAC <50ng/mL
Apixaban	1.35%	0.16%	90.5%
Rivaroxaban	1.85%	0.60%	96.8%
Dabigatran	0.90%	0.37%	95.1%

1007 patients had a high risk bleeding procedure (1/3 of the cohort)

832 (82.6%) had DOAC level assessed – 98.8% were < 50 ng/mL

Bleeding after high bleed risk procedures:

2.96% (95% CI, 0%-4.68%) - apixaban cohort
2.95% (95% CI, 0%-4.76%) - rivaroxaban cohort

Douketis et al, JAMA Internal Medicine. 2019


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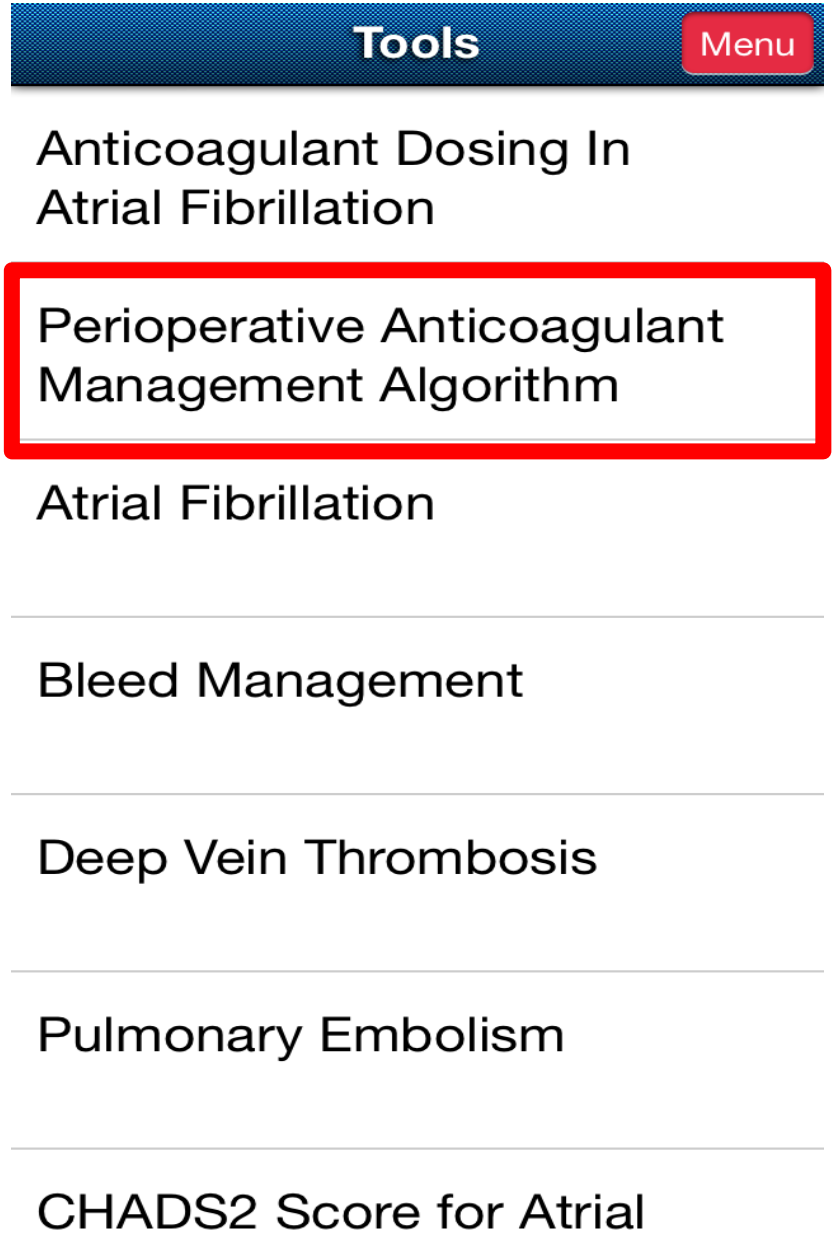
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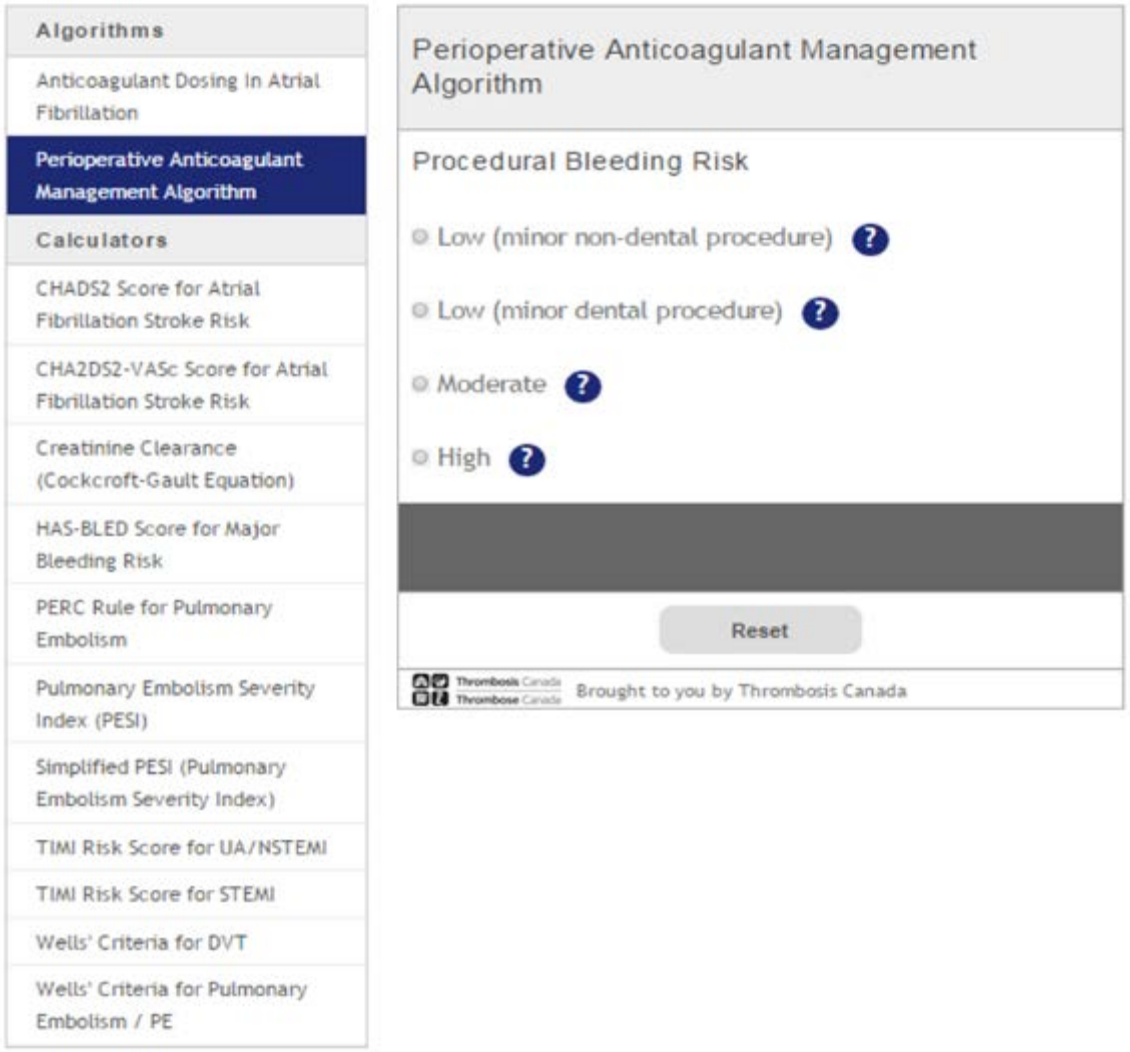
CHADS2 Score for Atrial

Thrombosis Canada Management Tools
Perioperative anticoagulant management algorithm



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In DOAC associated bleeding, consider the following

What drug is the patient on?

When was the last dose?

Is the patient taking drugs that inhibit platelet function?

Is there known kidney disease?

Calculate the CrCl

DOACs – Non major Bleeding Management

- **Bruising, hemorrhoidal bleeding, subconjunctival bleed, self limited epistaxis etc**
  - Don’t hold DOAC
  - Confirm dose appropriate based on indication, age, weight, CrCl
  - Consider checking CBC, renal function (CrCl)
  - Review concomitant meds which may be contributing (ASA, NSAIDS)

https://thrombosiscanada.ca/clinicalguides/#

DOACs – Major, Non Life-threatening Bleeding Management

- **Stable GI bleed, severe menorrhagia, severe epistaxis, hematuria requiring medical attention / interventions**
  - Hold DOAC
  - Apply local hemostatic measures if applicable
  - Obtain CBC, PT/INR, PTT, Creatinine (calculate CrCl)
  - Determine "likely" drug presence and expected elimination rate – time of last dose, half-life and CrCl
  - ? Drug level if available
  - ? Tranexamic acid
  - Transfusion (RBC for symptomatic anemia, platelets if less than 50, Fib concentrate if concomitant low fib), endoscopy etc as indicated
  - Review concomitant meds (ASA, NSAIDS) – ?hold, reassess, d/c

https://thrombosiscanada.ca/clinicalguides/#

DOACs – Major, Life-threatening, into a critical organ Bleeding Management

- **Unstable GI bleed, ICH etc**
  - Hold DOAC, Resuscitate, Consult expert
  - Apply local hemostatic measures if applicable
  - Obtain STAT CBC, PT/INR, PTT, Creatinine (calculate CrCl)
  - Determine "likely" drug presence and expected elimination rate – time of last dose, half-life and CrCl
  - Transfusion, tranexamic acid*, endoscopy, surgery, procedural intervention as indicated
  - Drug level IF RAPIDLY AVAILABLE – if less than 30-50 ng/mL – no reversal needed
  - ANTIDOTE if available; PCC / FEIBA infusion if not
  - Review concomitant meds (ASA, NSAIDS)

* *May exacerbate prothrombotic effect when given with other prothrombotic products; consider if giving antidotes or PCC*

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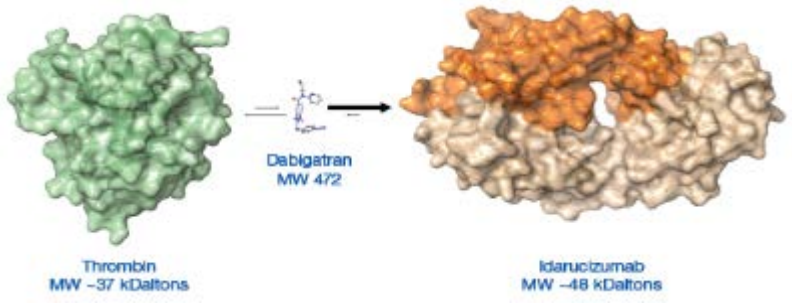
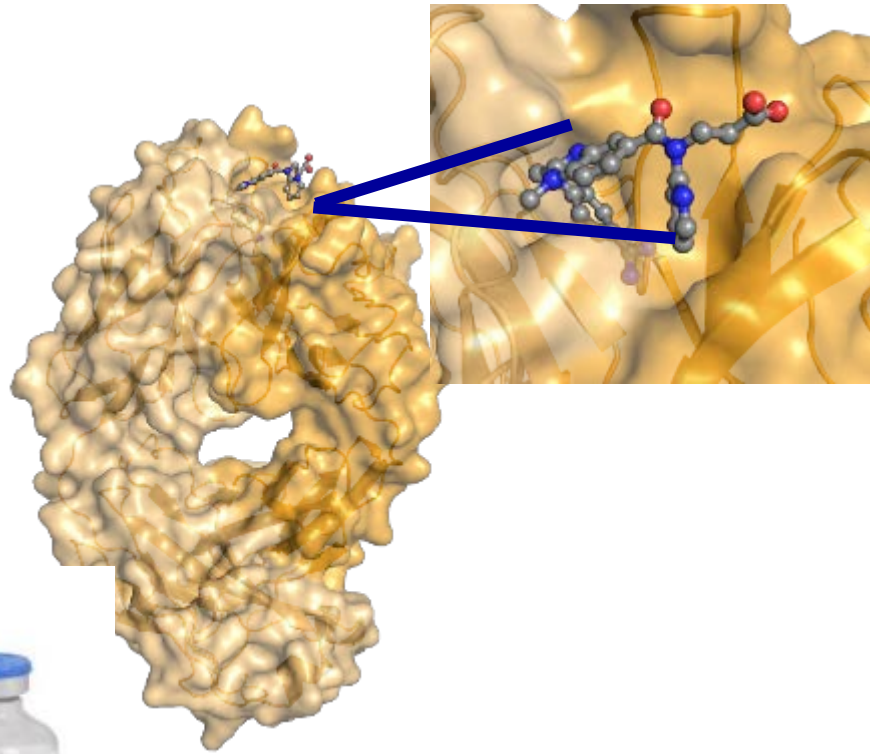
Idarucizumab (Praxbind®): Dabigatran Antidote

- Humanized mouse monoclonal antibody fragment (Fab) – specifically and potently binds dabigatran (~350x higher affinity than for thrombin)
- Approved and licensed in Canada since 2016
- Dose – 5 g provided in 2 separate vials with 2.5 g/50 ml at 15 min interval





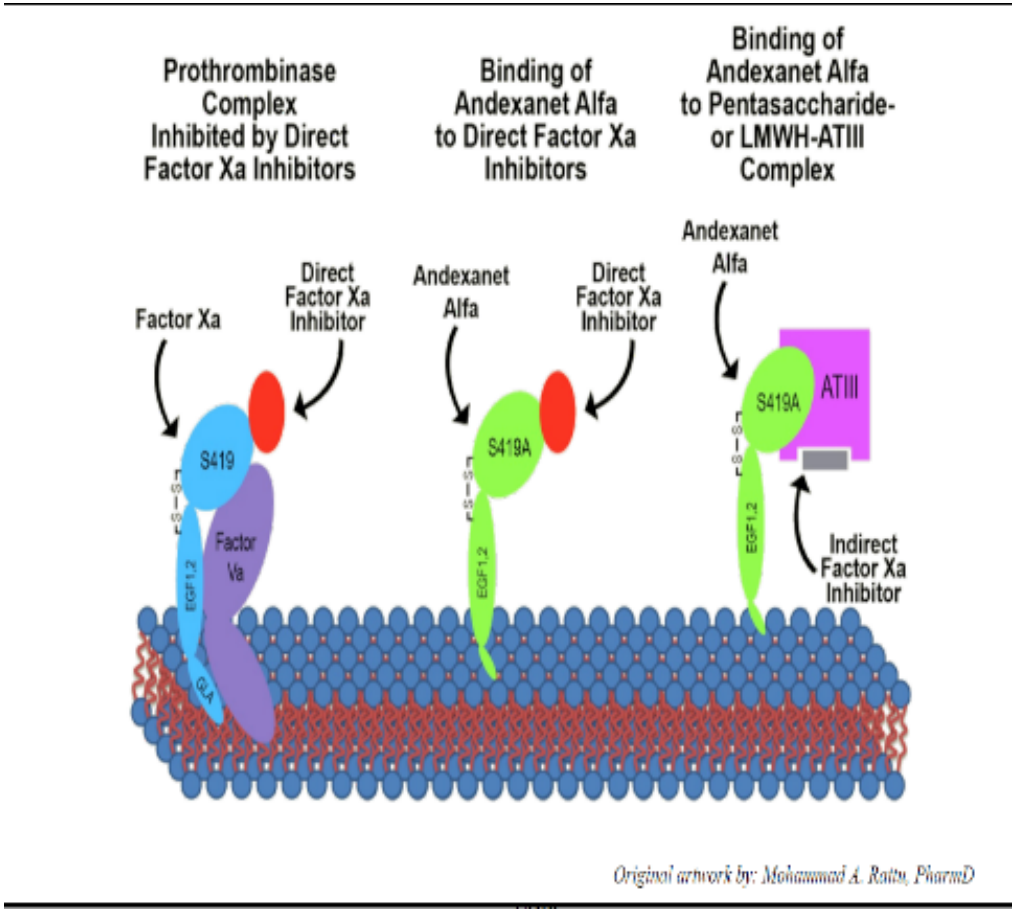
Idarucizumab – Real world effectiveness

- Denmark, Netherlands, Toronto cohort studies
  - Used for bleeding – 43%, 60% and 76% respectively
  - Commonest - GI bleeding followed by ICH
  - Commonest OR's requiring anticoagulant reversal were GI, Orthopedic, CV
  - Mortality was almost double (20-25%) in real-world cohorts compared to REVERSE-AD clinical trial (13.5%)
  - 1-3% thrombotic outcomes – ATE and VTE
  - Time to administration ~ 4 hours (Toronto experience)

Van der Wall et al. Europace 2019
Haastrup et al. Thromb Res 2021
Abdulrehman et al. RPTH. 2021

Andexanet Alfa (AnnexXA): Universal Factor Xa inhibitor antidote

- Recombinant, human Factor Xa "decoy"
- Binds and neutralizes Factor Xa inhibitors and LMWH / pentasaccharide-FXa complexes
- Given as a bolus followed by a 2 hour infusion



Andexanet Alfa: Current Status

- **ANNEXA-4**
  - Prospective cohort study
  - Population: 352 adults with acute major bleeding on apixaban, rivaroxaban, edoxaban, enoxaparin
  - Intervention: bolus of andexanet, followed by a 2-hour infusion
  - Outcome:
    - 82% "efficacy" in achieving good to excellent hemostatic control in 12 hours (**all surrogate outcomes – hematoma volumes, hemoglobin values, Anti-Xa activity**)
    - No clinical outcomes like disability (after ICH) / LOS etc
  - Anti-Xa activity **did not** correlate with bleeding outcomes
  - **2018** - FDA approved based on this study for apixa and riva
  - **2019** – Open label RCT commenced to compare Andexanet to usual care in ICH assessing clinical outcomes (***ClinicalTrials.gov Identifier: NCT03661528)***
  - Costs in US - $25,000 (low dose) to $50,000 (high dose) – selected availability

Connolly et al. N Engl J Med 2019

PCCs and Xa inhibitors

- **UPRATE** study – Prospective cohort in 84 patients using PCC in management of major bleeding with FXa inhibitors
  - 2014-2016 - Consecutive patients, 25 Swedish hospitals, major bleeding, on Riva or Apix, 70% ICH, 15.5% GI
  - 1500-2000 U PCC (25 IU/kg)
  - "Hemostatic effectiveness" – **58 (69.1%) effective;** 26 (30.9%) ineffective
- **Meta-analysis** of 340 patients in single arm studies – **69 to 77%** hemostatic efficacy, 16% all-cause mortality, 4% thrombosis
- **Large, multicentre retrospective cohort** study – 633 patients with ICH (2015-2019), 433 patients included in efficacy analysis (82% good to excellent hemostasis) with 3.8% thrombosis, majority within 14 days of PCC

Majeed et al; Blood August 2017
Piran et al. Blood Adv 2019
Panos Circulation 2020


Thrombosis Canada
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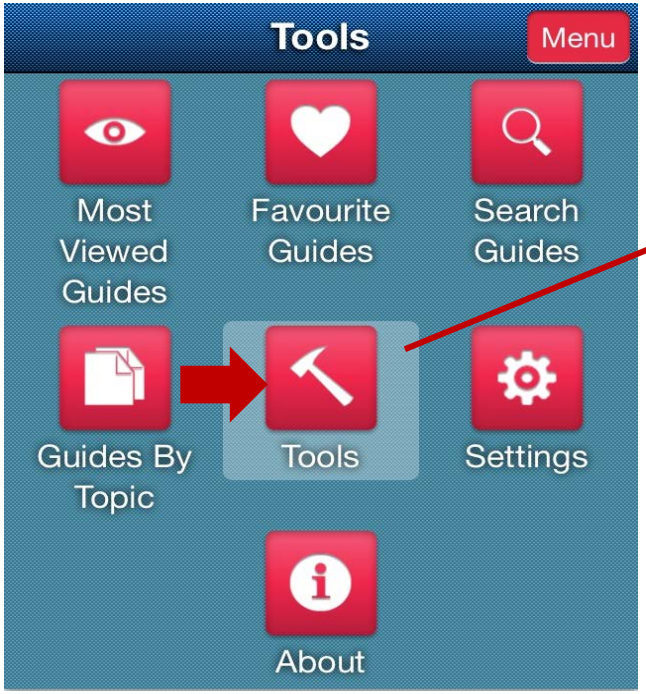
Tools
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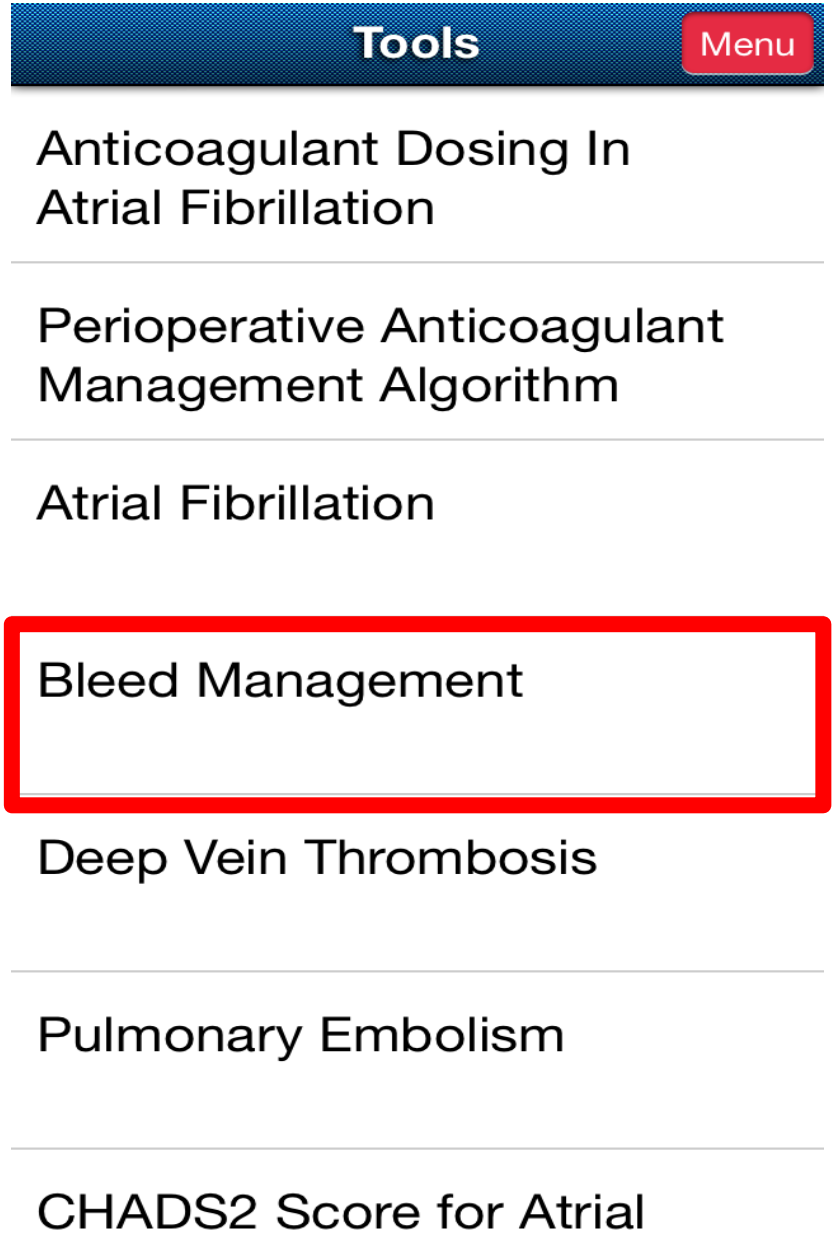
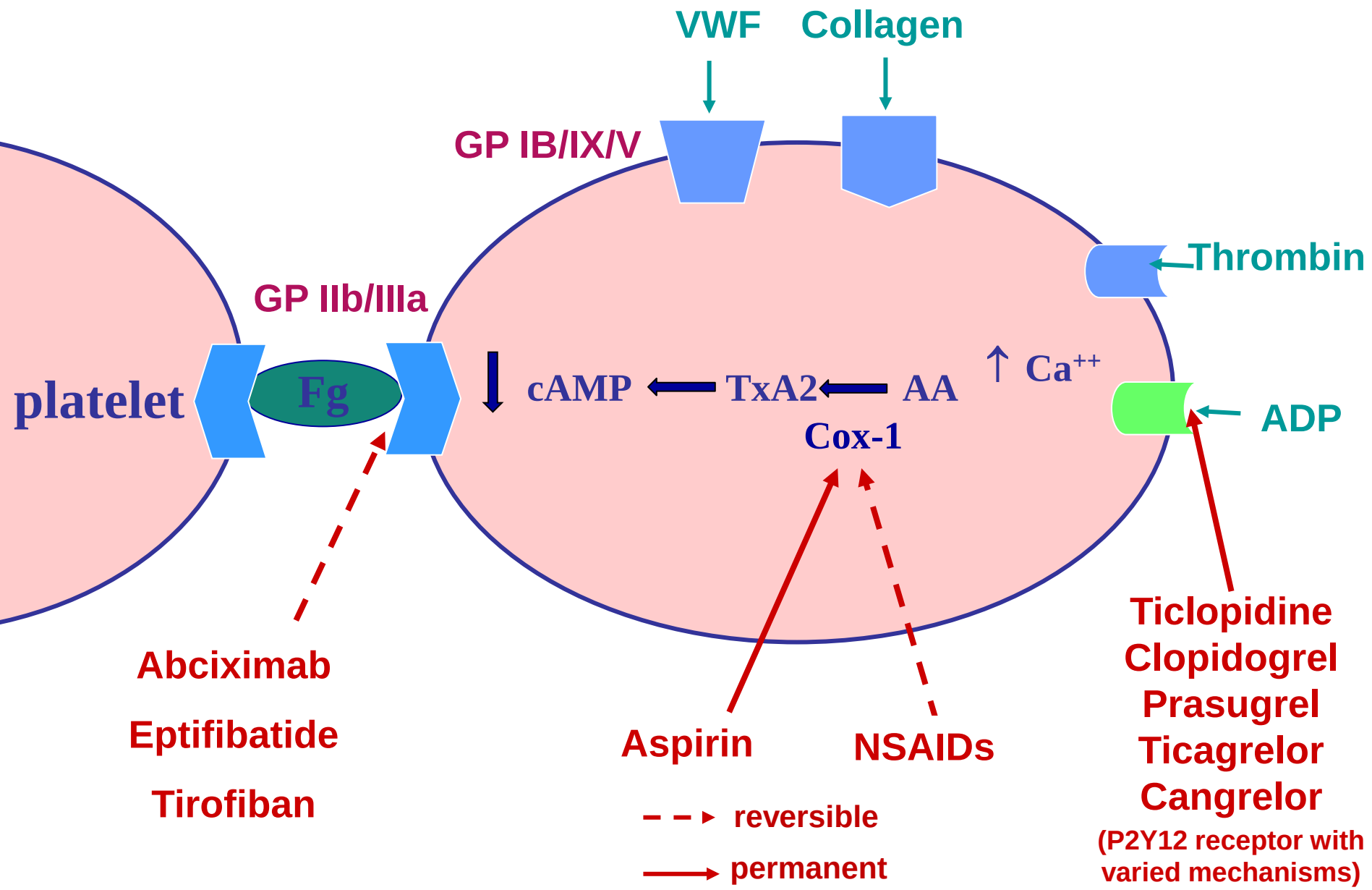

Tools
Menu
Anticoagulant Dosing In Atrial Fibrillation
Perioperative Anticoagulant Management Algorithm
Atrial Fibrillation
Bleed Management
Deep Vein Thrombosis
Pulmonary Embolism
CHADS2 Score for Atrial

Objectives

- Brief overview of DOACs
- Laboratory monitoring of DOACs
- DOACs – Peri-operative management
- DOACs – Management of bleeding
- DOACs – Reversal with Antidotes
- Peri-operative management of Antiplatelet therapy

Mechanisms of Actions of available Antiplatelet drugs



Anti Platelet Therapy and Minor Procedures

- **Dental, Cataract, Skin (biopsy, cancer excision)**
  Low bleeding risk diagnostic procedures
  - Continue ASA
  - P2Y12 inhibitor monotherapy – safety of continuing unknown so reasonable to hold for 3-4 days
  - Dual Anti platelet therapy – Continue ASA, Hold P2Y12 for 5-7 days

https://thrombosiscanada.ca/clinicalguides/#

Antiplatelet therapy and neuraxial procedures:
American Society of Regional Anesthesia Guidelines 2018
4th edition

- **Prior to and after neuraxial anesthesia (single injection, catheter techniques, post-op monitoring, catheter removal)**
  - **NSAIDS/ASA: no specific concerns** (unless additional bleeding risks identified)
  - Hold **10 d for ticlopidine**, **5-7 d for clopidogrel**, **7-10 d for prasugrel**, Resume 24 hours post-op
  - **Clopidogrel / Prasugrel:** Can keep catheter in for 1-2 days and resume drug immediately after catheter removal as long as no loading dose administered (if yes, wait 6 hours to remove catheter)
  - **Ticagrelor:** Hold 5-7 days pre-neuraxial procedure, Resume 24 hours post-op, Do not keep catheter in because of rapid onset of action & resume drug immediately after catheter removal as long as no loading dose administered (if yes, wait 6 hours to remove catheter)

Horlocker et al. 2018 Reg Anesth Pain Med;43: 263–309

Patients without Coronary Stents: Elective / Non Urgent Non-Cardiac Surgery

- **POISE-2 Study – RCT on Peri-op APT management in non cardiac surgery in 10,000 patients**
  - Continuing ASA did not reduce major adverse CV events or mortality but increased major bleeding
  - Only 4% had coronary stent
  - **Excluded:** carotid endarterectomy, recent coronary artery stent (6 weeks for BMS, 12 months for DES)

- **D/C ASA 7-10 days prior and resume 8-10 days after** (except in patients excluded above)

Devereaux PJ et al. New Engl J Med 2014; 370:1494-1503
Mehta et al. 2018 CCS/CAIC Focused Update of Guideline for use of APT. Can J Cardiol 2018

Patients with Coronary Stents: Elective / Non Urgent Non-Cardiac Surgery

- **Sub-study of POISE-2 Study – 470 patients with previous PCI and cardiac stents**
  - Continuing ASA will prevent 59 MI but cause 8 major bleeds / 1000 patients
- **PCI with BMS –** Delay surgery for at least 1 month after PCI, Continue ASA peri-op when possible, Hold clopidogrel and ticagrelor for 5-7 days and prasugrel 7-10 days
- **PCI with DES –** Delay surgery for at least 3 months; if semi-urgent at least 1 month after PCI. Continue ASA, Hold clopidogrel and ticagrelor for 5-7 days and prasugrel 7-10 days.
- Restart maintenance dose DAPT as soon as deemed safe by surgeon

Devereaux PJ et al. New Engl J Med 2014; 370:1494-150
Mehta et al. 2018 CCS/CAIC Focused Update of Guideline for use of APT. Can J Cardiol 2018

Patients on DAPT undergoing CABG

- **Continue ASA in all ACS patients who need CABG**
- **Ticagrelor and Clopidogrel –**
  - **Semi-urgent CABG – minimum interruption of 48-72 hours**
  - **Elective CABG - 5 days**
- **Prasugrel –**
  - **Semi-urgent CABG – minimum interruption of 5 days**
  - **Elective CABG - 7 days**

Mehta et al. 2018 CCS/CAIC Focused Update of Guideline for use of APT. Can J Cardiol 2018

Urgent / Emergent Reversal of antiplatelet therapy

- **Consider Desmopressin** – meta-analysis of RCTs to reverse platelet dysfn after cardiac surgery - reduced RBC, blood loss and re-operation
- **Platelet transfusion for ICH –** Neurocritical Care Society and Society of CCM guidelines (2016) , PATCH trial (2016)
  - DO NOT GIVE PLTS UNLESS NEUROSURGERY PLANNED (regardless of drug, platelet function testing, hemorrhage volume or neuro exam)
  - Give pre-neurosurgery for ICH after platelet function testing if available, empirically if not available; If lab documented function is normal DON'T GIVE PLTS
  - Post NSAID or Gp2b3a inhibitors – NO PLTS EVEN IF NEUROSURG
  - Yes for Desmopressin

Desborough et al. 2017 JTH;15:263-72
Frontera et al. 2016 Neurocrit Care;24(1):6-46
PATCH trial, Lancet;387:2605-13

Urgent / Emergent Reversal of antiplatelet therapy

- **Consider Tranexamic acid**
  - Strong evidence supporting safety and efficacy in many severe bleeding indications
  - Easily available
  - Inexpensive
  - Meta-analysis of 7 trials using TXA to reduce surgical bleeding related to antiplatelet monotherapy or DAPT showed reduction in blood loss, re-operation, blood/platelet transfusion (2020)

- **Specific reversal agents for antiplatelet agents**
  - Phase 3 clinical trials

Fischer et al. Cureus 2020; 12(9):e10290. doi: 10.7759

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DISCUSSION