



Individualizing Anticoagulation in the Acutely Ill: A Case-based Approach

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Disclosures

Michael Gulseth:

- Janssen-Speaker
- BMS- Speaker and Consultant
- Pfizer-Speaker
- Portola-Speaker and Consultant
- Stago-Speaker

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Learning Objectives

- Identify unique characteristics of acutely ill patients that influence the approach to anticoagulation.
- Develop and implement an acute anticoagulation strategy for an acutely ill patient.
- Given a patient case, design a revised anticoagulation regimen and a follow-up assessment plan for an acutely ill patient.



Acutely Ill Anticoagulation Management – What's Different?

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Learning Objectives

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Patient Case

CC: ET is a 5' 6,"99 kg, 86 year-old female who presents to the hospital with a cold leg. She is diagnosed with acute lower extremity embolism in her common femoral artery.

Pertinent PMH: atrial fibrillation, on warfarin with a time in therapeutic range of 47%

Hospital course: Warfarin was fully reversed on admission using prothrombin complex concentrate (PCC) & vitamin K 10 mg IV) (INR was reduced to 1.2). She was treated with catheter-directed lysis. After the catheter is removed the following morning, the vascular surgeon prescribed rivaroxaban 15 mg orally twice daily (off label) for 21 days, followed by rivaroxaban 20 mg daily and permanently stops warfarin. It is now noon and the patient has minor oozing at the catheter site and the surgeon decides to draw an INR, which is 2.6. The surgeon orders 10 mg of oral vitamin K.

Question 1:

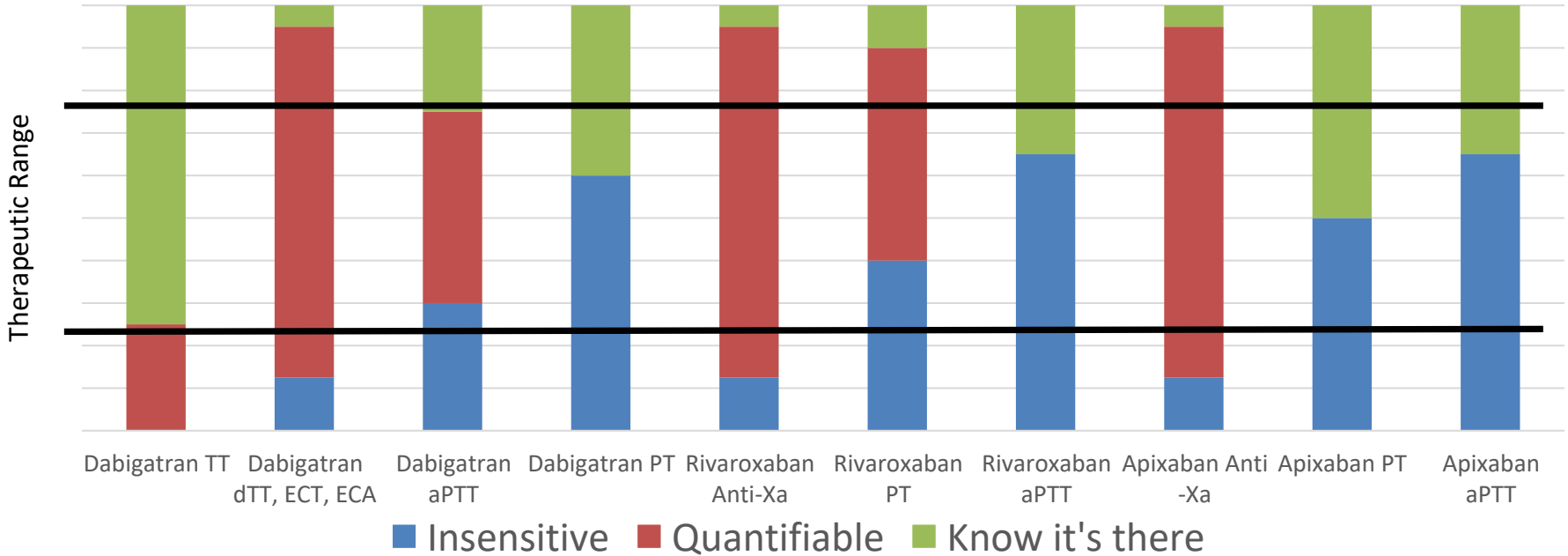
Which of the following is the most appropriate response to this vitamin K order by the pharmacist?

- A. Recommend reducing this dose of vitamin K to 2.5 mg because high doses of vitamin K can lead to anticoagulation resistance
- B. Recommend adding 1500 units of PCC since immediate reversal is needed
- C. Process the order since the patient is stopping warfarin and this will lower her INR
- D. Recommend not using vitamin K and instead use local measures to control oozing, and reassess if those efforts are not successful

Direct Oral Anticoagulants (DOACs) and Lab Test Interpretation

- Contemporary practice requires you to be able to interpret coagulation lab test results in the context of a patient's concurrent drug therapy
- Combining your knowledge of pharmacokinetics and the laboratory tests makes you an indispensable member of the patient care team

Effects of Common DOACs on Coagulation Labs



TT: Thrombin Time, dTT: Dilute Thrombin Time, ECT: Ecarin Clotting Time, ECA: Ecarin Chromogenic Assay, aPTT: Activated Partial Thromboplastin Time, PT: Prothrombin Time, Anti-Xa: Anti Factor Xa Activity Level

Cuker, A, et. al. *J Am Coll Cardiol.* 2014;64:1128-39.

Risk Factors for Bleeding with UFH/LMWH

- Observational cohort study
- Receiving therapeutic UFH/LMWH between April 2006 and March 2007
 - Excluded cardiac surgery patients
- Bleeding classified using the GUSTO scale
- Risk factors associated with major bleeding in 3066 hospitalizations
 - Multivariate analysis: renal function, aPTT > 90 sec, and UFH instead of LMWH
- Remember the risk of bleeding associated with invasive procedures

UFH: unfractionated heparin
LMWH: low molecular weight heparin

Risk Factors for Bleeding with Warfarin

- Intensity of anticoagulation effect (higher INR targets)
- History of bleeding, particularly GI bleeding
- Patient age > 75 yr (primarily intracranial hemorrhage)
- Serious comorbid conditions:
 - Hypertension
 - Prior stroke
 - Heart disease
 - Renal insufficiency
 - Alcohol abuse
 - Liver disease
 - Malignancy
- Use of certain concomitant medications

HAS-BLED

Risk Factor	Score
Hypertension, SBP >160 mm Hg	1
Abnormal renal or liver function	1 each
Stroke	1
Bleeding history or predisposition	1
Labile INRs	1
Elderly: age ≥65 years	1
Drugs or alcohol	
--antiplatelets or NSAIDs	1
--alcohol use >8 servings/ <u>wk</u>	1
MAXIMUM	9

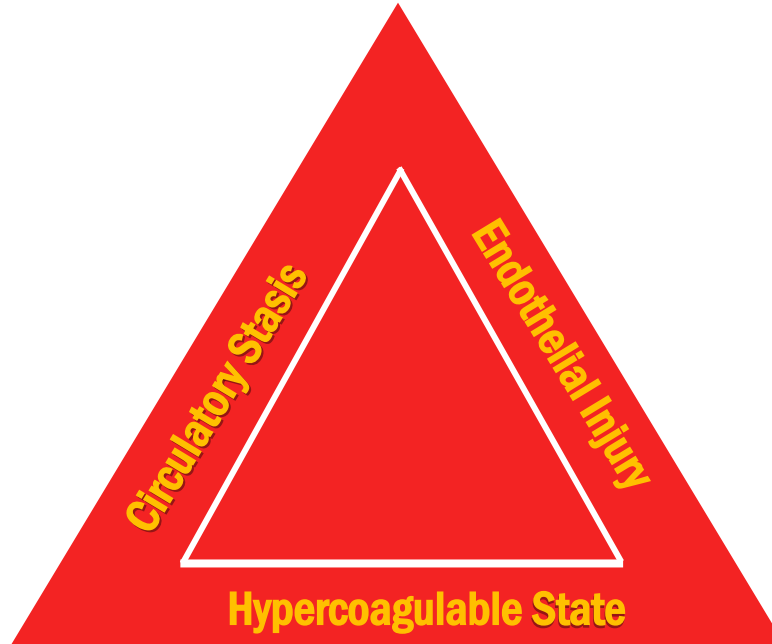
ATRIA

Risk Factor	Score
Anemia	3
Severe renal disease	3
Age ≥75 years	2
Any prior hemorrhage	1
Hypertension	1
MAXIMUM	10

Fang MC, et al. *J Am Coll Cardiol*. 2011;58:395-401.

Pisters R, et al. *Chest*. 2010;138:1093-1100.

Virchow's Triad



Balancing Stroke and Bleeding Risk in Atrial Fibrillation

CHADS₂ Score¹

Risk Factor	Score
Congestive heart failure	1
Hypertension	1
Age ≥75 yr	1
Diabetes	1
Stroke or TIA history	2
MAXIMUM	6

^a Prior myocardial infarction, peripheral arterial disease, or aortic plaque

^b Age is in two rows but is only counted once
 CHADS=congestive heart failure/hypertension/age ≥75/diabetes/stroke or TIA; CHA₂DS₂-VASc, CHADS + age 65-74 years + vascular disease; LV=left ventricle; TE=thromboembolism; TIA=transient ischemic attack

CHA₂DS₂-VASc Score²

Risk Factor	Score
Congestive heart failure/ <i>LV dysfunction</i>	1
Hypertension	1
Age ≥75 years	2
Diabetes	1
Stroke/TIA/TE history	2
Vascular disease ^a	1
Age 65-74 years	1
Sex category, female	1
MAXIMUM^b	9

Gage BF, et al. *JAMA*. 2001;285:2864-2870.

Lip GY, et al. *Chest*. 2010;137:263-272.

Patient Case

CC: TE is 5' 11", 140 kg, 74 year-old male who presents to the emergency department with abdominal pain and inability to pass stool the past week. After imaging, he is diagnosed with a complete bowel obstruction and taken to the OR.

Pertinent PMH: atrial fibrillation, type 2 diabetes mellitus, CKD (stage 3b), and hypertension. He was on dabigatran 150 mg twice daily prior to admission

Hospital course: Admission aPTT was 110 sec and this was reversed by idarucizumab prior to arrival at the OR. He had exploratory laparotomy with lysis of extensive adhesions. It is now the morning after surgery, and the team wants to restart anticoagulation to provide stroke prophylaxis (due to his atrial fibrillation) and venous thromboembolism (VTE) prophylaxis.

Question 2:

Which of the following is the most appropriate management recommendation by the pharmacist?

- A. Restart dabigatran 150 mg orally twice daily
- B. Give a 5000 unit IV bolus of UFH and start an infusion at 1000 units/hr
- C. Check an aPTT or TT to help with decision making
- D. Start enoxaparin 40 mg subcutaneously every 24 hrs

2017 American College of Cardiology (ACC) Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation

- Atrial fibrillation focus
- Covers anticoagulation restart issues which are critical for acute care pharmacists
- In our case, if no bleeding issue/complication and care is progressing normally, restarting “treatment” doses of anticoagulation 48-72 hours after surgery would be advised because the patient is at a high risk for bleeding
- Important to be familiar with the concepts in these guidelines

Only High Quality Bridging Data: The BRIDGE Trial

- Randomized, double-blind, placebo-controlled trial funded by NIH
- Evaluated patients with atrial fibrillation who needed interruption in warfarin therapy for an elective invasive procedure
- Patients were randomized to:
 - LMWH bridging
 - No bridging with placebo injections
- Warfarin was stopped 5 days prior to the procedure

BRIDGE Results

- Arterial thromboembolism
 - Bridging: 0.3%
 - No bridging: 0.4% p=0.01 for non-inferiority, NS for superiority
- Major bleeding
 - Bridging: 3.2%
 - No bridging: 1.3% p=0.005 for superiority

2017 ACC Decision Pathway for Periprocedural Management of Bleeding on Oral Anticoagulation

- Covers the critical issue of reversal of oral anticoagulants for major bleeding
- In life-threatening situations, recommends use of idarucizumab for reversal of dabigatran, four-factor PCC (PCC4) for reversal of warfarin and the Xa inhibitors
 - aPCC also an alternative for both dabigatran and Xa inhibitors
 - Released prior to approval of andexanet alfa
 - Recommended PCC4 dosing for warfarin reversal is per package insert or fixed dosing of 1000 units for any major bleeding or 1500 units for intracranial hemorrhage
- Important to be familiar with the concepts in these guidelines

Patient Case

CC: ZS is 6' 2", 85 kg, 80 year-old male who is admitted to the pulmonary medicine floor with suspected aspiration pneumonia.

Pertinent PMH: atrial fibrillation, hypertension, chronic heart failure, and coronary artery disease, s/p myocardial infarction. He recently had a stroke (2 months ago) and has had trouble swallowing and been noncompliant with a soft diet at home. As an outpatient, he was on warfarin 5 mg orally daily for stroke prevention, with a stable INR.

Hospital course: Warfarin was withheld at admission for gastric (G) tube placement, causing the INR to fall. Three days after admission, he had a G-tube placed for long-term enteral tube feeding. He currently receives continuous feedings at 60 mL/hr. After the tube was inserted, he was started on enoxaparin 80 mg SC twice daily, and warfarin 5 mg daily was restarted. Three days later his INR is still 1.1 (same level as before surgery).

Question 3:

What is the most appropriate management by the pharmacist?

- A. Continue warfarin 5 mg daily and stop enoxaparin because bridging is not indicated
- B. Stop enoxaparin and warfarin and start dabigatran 150 mg twice daily by G-tube
- C. Continue enoxaparin and continue warfarin at 5 mg daily
- D. Continue enoxaparin and increase warfarin dose to 10 mg daily

DOAC Administration Via Tubes

- **Dabigatran**
 - Capsules cannot be opened because it leads to a significant 75% increase in absorption
- **Rivaroxaban**
 - Gastric tube placement is necessary, crush and suspend in 50 mL of water followed by enteral feeding
- **Apixaban**
 - Can be crushed and suspended in 60 mL of water or dextrose 5% in water and given via nasogastric tube
- **Edoxaban**
 - Can be crushed and suspended in 2-3 ounces of water and given in a gastric tube
- **Betrixaban**
 - No information published, but company letter says it can be dissolved in water and given via tube, followed by enteral feeding

Dabigatran US Prescribing Information. Boehringer Ingelheim; 2018

Rivaroxaban US Prescribing Information. Janssen Pharmaceuticals; 2017.

Apixaban US Prescribing Information. Bristol Myers Squibb; 2018.

Edoxaban US Prescribing Information. Daiichi Sankyo; 2015.

Portola, Data on File.

Warfarin and Enteral Tube Feeding

- Warfarin/enteral tube feeding resistance issues are well described in the literature, and not likely due to the vitamin K content of the enteral formulas
 - Most patients are unlikely to receive more than 160 mcg/day of vitamin K
- Binding of warfarin by protein in enteral formula has been proposed
- Recent data shows warfarin may bind to the tubes at lower pH levels; tube binding likely cannot be saturated
 - Holding enteral tube feeding is likely not the answer
- What is for sure, you will likely need significantly higher warfarin doses, usually big increases in dose!
 - Must know when enteral tube feeding is stopped

Williams, NT. *Am J Health Syst Pharm.* 2008; 65: 2347-2357.

Dickerson RN. *Nutrition.* 2008; 24: 1048-1052.

Klang M, et. al. *J Parenter Enteral Nutr.* 2010; 34: 300-4.

Obese Evaluations of DOAC Phase 3 Trial Participants

Medication	Clinical Trial	Weight/BMI Threshold	Number (%)
Dabigatran	RE-COVER 1	≥ 100 kg BMI ≥ 35 kg/m ²	502 (20) 306 (12)
	RE-COVER 2	> 100 kg BMI > 35 kg/m ²	438 (34.2) 302 (23.6)
	RE-LY	≥ 100 kg	3099 (17.1)
	RE-MEDY	≥ 100 kg	299 (20.9)
	RE-SONATE	≥ 100 kg	122 (17.9)
Rivaroxaban	EINSTEIN DVT	> 100 kg	245 (14.2)
	EINSTEIN PE	> 100 kg	345 (14.3)
	EINSTEIN EXTENSION	> 100 kg	85 (14.1)
	ROCKET-AF	> 90 kg BMI > 35 kg/m ²	2035 (28.5) 972 (13.6)
Apixaban	AMPLIFY	≥ 100 kg BMI > 35 kg/m ²	522 (19.4) 349 (13.0)
	ARISTOTLE	BMI ≥ 40 kg/m ²	1006 (5.6)*
Edoxaban	HOKUSAI VTE	> 100 kg	611 (14.8)

Schulman S et. al. *N Engl J Med.* 2013 Feb 21;368(8):709-18.

Einstein Investigators. *N Engl J Med.* 2010;363:2499-2510.

Patel MR et al. *N Engl J Med.* 2011;365(10):883-891.

Sandhu RK, et. a. *Eur Heart J* (2016) 37, 2869–2878, post hoc.

Schulman S et al. *N Engl J Med.* 2009; 361:2342-52.

Schulman S et al. *Circulation.* 2014;129:764-72.

Connolly SJ, et al. *N Engl J Med.* 2009;361:1139-51.

EINSTEIN Investigators et al. *N Engl J Med.* 2010; 363:2499-510.

EINSTEIN-PE Investigators et al. *N Engl J Med.* 2012; 366:1287-97.

Agnelli G et al. *N Engl J Med.* 2013;369:799-808.

HOKUSAI-VTE Investigators et al. *N Engl J Med.* 2013;369:1406-15.

International Society on Thrombosis and Haemostasis (ISTH) Statement on Obesity

- Recommend not using DOACs in patients with a BMI of > 40 kg/m² or a weight of > 120 kg
 - Due to limited clinical efficacy and safety data and available pharmacokinetic/pharmacodynamic data suggesting that underdosing could be an issue
 - If used, suggests using drug specific calibrated levels
 - Peak and trough
 - Switch to warfarin instead of adjusting DOAC dose if level is below expected range

Studied Weight Maximums/Minimums

Agent	Highest Weight	Lowest Weight
Enoxaparin	196 kg	45 kg
Dalteparin	190 kg	Unknown
Fondaparinux	215 kg	Unknown
Tinzaparin	165 kg	Unknown
Dabigatran	222 kg	32 kg
Rivaroxaban	209 kg	33 kg
Apixaban	210 kg	28.9 kg
Edoxaban	NA	NA
NA: not available		

Source: Reprinted with permission from Hellwig T, Dager W. Considerations in special populations. In: Dager, WE, Gulseth MP, Nutescu EA, eds. *Anticoagulation therapy; a clinical practice guide*. Bethesda: ASHP; Copyright ©2018: 251-279.

KEY TAKEAWAYS

1) KEY TAKEAWAY

It is critical you can interpret coagulation laboratory assays in the DOAC era

2) KEY TAKEAWAY

You constantly need to be weighing the risk of bleeding versus thrombosis

- Risk varies day to day

3) KEY TAKEAWAY

The acutely ill will regularly fall into special populations that may necessitate unique care for the individual patient

Thank you!

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Skills for Specialized Anticoagulation Therapy Decisions and Plans

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Learning Objective

- Given a patient case, design a revised anticoagulation regimen and a follow up assessment plan for an acutely ill patient.

Making Decisions in the Acutely Ill

- Literature
- Clinical Trial Support
- Evidence Based and Institution Guidelines
- Other Resources
- Practical Experience
- Hard outcomes vs surrogate markers

Making an individualized decision



Skill: Starting at a Point of Reference

- Patient Case: TL is a 70 yo, obese, 140kg (Ideal Body Weight 70kg) Chinese male admitted with acute heart failure
- PMH: Lung Cancer, Pulmonary Embolism (5 years ago), Heart Failure (EF 25%) and GI Bleed (1 year ago). Has a new proximal DVT and the physician asks for advice about a treatment regimen
- A Colonoscopy is requested, but patient has a DVT on hospital day 2. Baseline INR is 1.5, CrCl 40 mL/min

Question 4:

Which approach would you use for the new DVT?

- A. Enoxaparin 60 mg subcutaneous every 12 hr; Warfarin 5 mg today
- B. UFH 5000 unit bolus and infusion at 18 units/kg/hr. Target Anti-Xa of 0.3 to 0.5 units/mL. Withhold 6 hours prior to colonoscopy
- C. Warfarin 5mg for one dose, then 2mg/day; INR in 2 days
- D. Apixaban 2.5mg orally twice daily, withhold morning of colonoscopy.

Anticoagulation Considerations in the Acutely Ill

- Change can occur rapidly – clinical presentation in flux
 - Can return to prehospital condition once acute influencing factors are resolved
- Influencing factors for decisions are subject to rapid change
- Bleeding: active, history, need for invasive procedures
- Thrombosis: acute, history
- Dosing routes/choices: access, formulary, guidelines/policy
- Elimination (organ dysfunction, drug interactions, disease influences)

Initiating Anticoagulation

- **Efficacy and Safety – Multiple Choices & ↑ Potential for Confusion**
 - What about using a DOAC?
- **Many “Special” Populations (Acute and Chronic)**
- **Complex Patients**
 - ? Need to modify typical target
 - Need for invasive procedures
 - May be excluded from clinical trials (ICU, high risk...)
 - ↑ bleeding risk acutely
 - Contraindications present
- **Monitoring Challenges: use of surrogate indicators for outcomes**
- **Comprehensive Plan: Finish what you start...**



Anticoagulation in Special Populations with Chronic Conditions or Needs

Many excluded from Clinical Trials

- Renal dysfunction (Chronic)
- Obesity
- Cancer
- Dietary influences
- Ethnic groups
- Age: elderly and pediatrics
- History of bleeding/falling
- Quality of management - Poor follow-up and support system
- Mechanical devices (Heart valves, Left Ventricular Assist Device “LVAD”)
- Hypercoagulable conditions



Causes of Cancer-related VTE

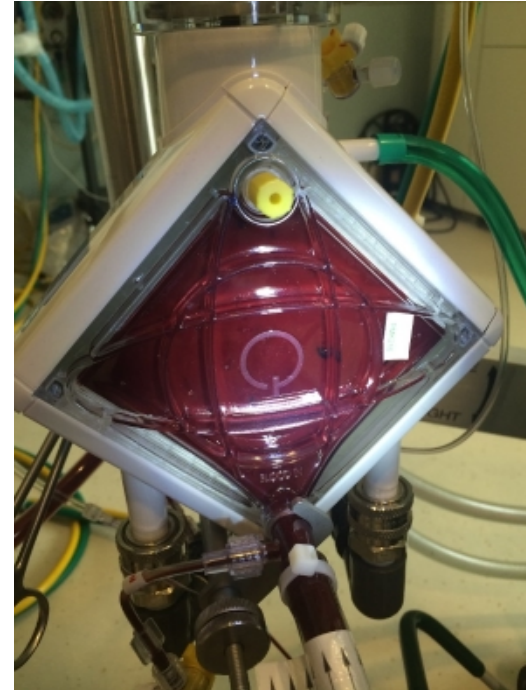
- Stage of Cancer
- Surgery
- Central Venous Catheters
- Radiation therapy
- Chemotherapy/Hormone therapy, Targeted Antibodies
- Supportive Agents (growth factors, heparins, IgG)
- Interaction between Chemotherapy and Anticoagulation
 - Assessment considers both directions



Special Populations with Acute Conditions or Needs

- Many excluded from Clinical Trials -

- Acute Kidney Dysfunction
- New bleeding/falling/clotting risks
- Acute illness (Heart Failure, Liver Failure, ICU admission, infection)
- New Mechanical Devices (Heart Valves, LVAD, Extracorporeal Life Support “ECLS”)
- Hypercoagulable Conditions (Heparin Induced Thrombocytopenia)
- Need for IV route of administration or loss of oral route
- Acute infection, organ failure
- Acute comorbid conditions
- Hypothermia
- Acute thrombocytopenia
- Thrombolysis



Question 5:

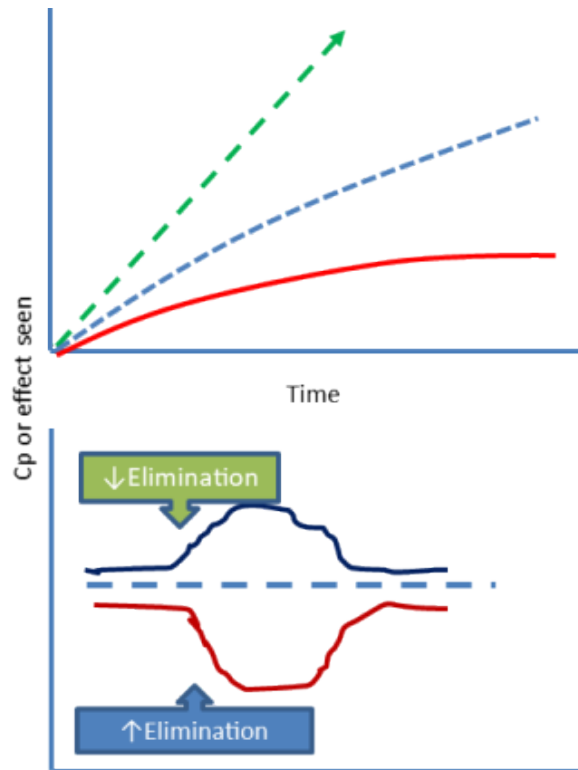
LM started Warfarin – His INR the morning after the first 5mg dose was 3.5. Which of the following interventions would you recommend at this time?

- A. Hold the next warfarin dose
- B. Stop the LMWH
- C. Repeat the INR
- D. Consider vitamin K and Fresh Frozen Plasma

Developing a Management Plan

- Set goals (short- vs long-term)
- Make sure the plan can be implemented
- Identify and implement a follow-up plan
 - May consider frequent data and adjust as needed

You can always change your mind



Skill: Time/Measure for the Greatest Success

- Baseline labs and clinical assessment
- Allow sufficient time for a response
- Reliance on electronic medical records vs bedside observations
- Make it easy for the nurse or patient to implement the plan
- Avoid missing doses (automated dispensing cabinet \neq ingested)
- Keep it simple – will a bleed or clot happen within the next few hours?

Anticoagulant Dosing Considerations

- Initial dose
 - How fast do you need a response?
 - Any reasons to withhold therapy?
 - (epidural catheter present?)
 - Presence of factors associated with ↑ sensitivity
- Wait for adequate response
 - **(10-12 hours for INR)**
- Monitoring Pearls
 - Plausibility of result – Steady state vs. rising or falling
 - Assay errors
 - Was the anticoagulant actually received?
 - Initiate order for RN to witness patient ingesting



Pick a Starting Point (Point of Reference)

- Severe obesity is a risk factor for PE, very few bleed to death
- Warfarin – 5 mg daily is a common dose – but LM may require a lower dose as he is Chinese and has heart failure
- Enoxaparin – 120 mg q 12hr or possibly 150 mg once daily (CrCl = 40 mL/min)



Look at the Big Picture

- Where do you want to end up?
- What needs to be planned out to get there?



- Acute Changes
- Goal Changes
- Invasive Procedures
- Discharge Plans

JT, a 70 year old, 45 kg patient is admitted with a history of nausea and vomiting for 5 days and is noted to be in atrial fibrillation.
His Scr in the ED was 4.5 mg/dL. and is being started on amiodarone.

Question 6:

Which statement is CORRECT regarding renal function and anticoagulant management?

- A. Patients with end stage renal disease are typically included in phase III trials.
- B. The ideal body weight should be used for estimating renal function and oral anticoagulation dosing.
- C. Renal failure is associated with both increased risk for bleeding and thrombosis.
- D. A 50% enoxaparin dosing reduction for an estimated CrCl <30 mL/min is appropriate even for patients with acute kidney injury or stage V chronic kidney disease

Dosing in Renal Failure

- How was the dose determined?
- What CrCl equation and body weight should be used? (Cockcroft-Gault and total body weight ?)
- Were data obtained from patients with renal failure or extrapolated from another population ?
 - 50% enoxaparin dose for CrCl < 30 ml/min
 - Any additional drivers not present in other populations?

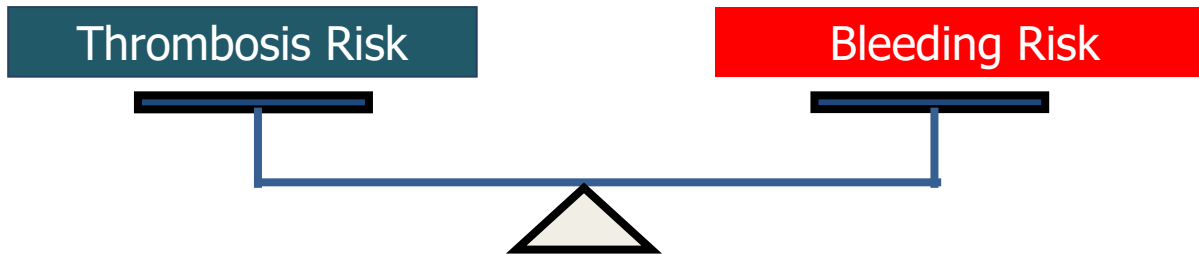


Bleeding and Thrombosis Risk in Renal Disease

Bleeding	Thrombosis
<p>Excessive anticoagulation (including excess dosing as elimination declines, drug interactions)</p> <p>Fibrinogen fragments</p> <p>Blood pressure (poorly controlled Hypertension)</p>	<p>Tissue factor expression</p> <p>vWF (von Willebrand Factor)</p> <p>High Hemoglobin with ESA use</p> <p>Plasminogen activating inhibitor 1</p>
<p>Impaired platelet function</p> <p>Anemia (hereditary and acquired)</p> <p>Frequent blood draws</p> <p>Antiplatelet therapy</p> <p>Dialysis Circuit</p> <p>- Shear wall stress on platelets by dialyzer</p>	<p>Endothelial changes</p> <p>Hemodialysis-induced platelet aggregation</p> <p>Inadequate prophylaxis during acute risk periods (acute illness)</p> <p>Prothrombotic microparticles</p> <p>Nephrotic Syndrome</p>

Factors Affecting your Anticoagulation Management Decisions

- What may lead you to be “aggressive” with the dosing ?
 - (i.e., use larger doses)
 - Obesity
 - Cancer
- What may lead you to use a lower dose?
 - Bleeding issues
 - Renal Failure
 - Advanced age
 - Don't want to overshoot on bridge therapy



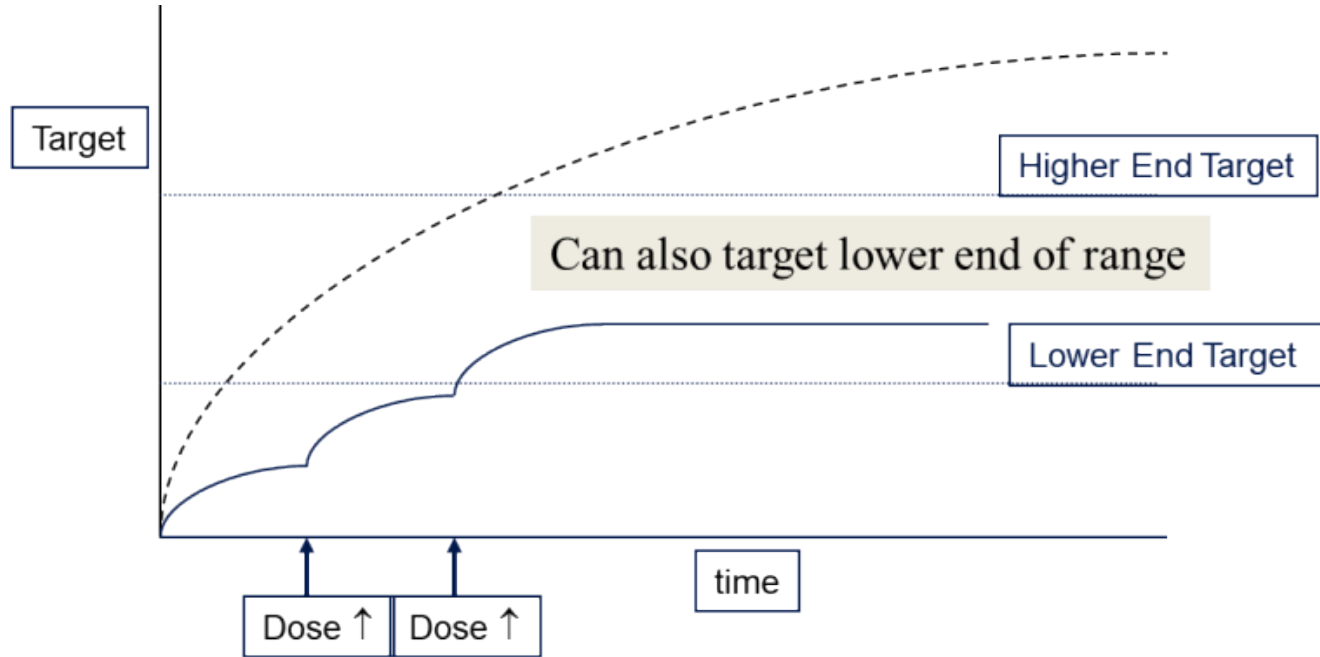
Skill: Think Outside the Box

A 70-kg patient is admitted with an intracranial hemorrhage after a fall while skiing. The baseline aPTT is 30 seconds. Two days later, the patient develops PE, and the physician wants to start UFH after consultation with several experts and the neurosurgery staff.

- UFH aPTT range for anti-Xa of 0.3 to 0.7 IU/mL is 50 to 100 seconds at your hospital.
- UFH order set in your hospital system suggests 80 units/kg bolus and 18 units/kg/hr – target aPTT is 80-100 seconds.

Don't want to overshoot

(high bleeding concerns present)
Dose is lower than the estimated dose



Unfractionated Heparin

Dosing

- Is a bolus needed?
 - 50-80 units/kg vs. 2,000-3,000 units
- Wt: Actual vs Modified

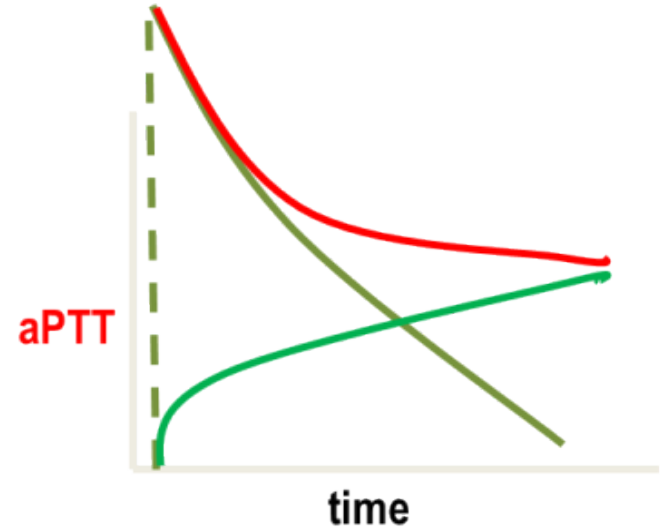
Monitoring (aPTT, Anti-Xa)

- On DOAC → ↑ baseline anti-Xa activity

Target lower end (0.3-0.5 units/mL)

Assay Changes

- Time post bolus: 6-8 hr (4-6 hr if no bolus)



Heparin Induced Thrombocytopenia (HIT)

- Scoring (4T vs Cardiothoracic Surgery)
- Acute HIT: new onset
 - Initial phase with low platelets
 - Post platelet recovery period
- Isolated HIT (HIT without thrombosis)
- HITTS (+ HIT-related thrombosis)
- History of HIT

Timing after heparin exposure:
Rapid – Immediate (hours)
Typical – 5-10 days
Delayed – up to 40 days after stopping

- Direct Thrombin Inhibitor Therapy – Target range for aPTT testing based on risk: 1.5- 2.5 x control value
- Transition to long-term therapy

Skills or Lessons Learned

- Can adapt guidelines to meet patient needs
- When increased bleeding is a concern, lower end of target range can be considered
- Monitor/measure lab values more frequently if necessary
- Can adjust therapy to provide a high intensity if desired as risk for bleeding declines

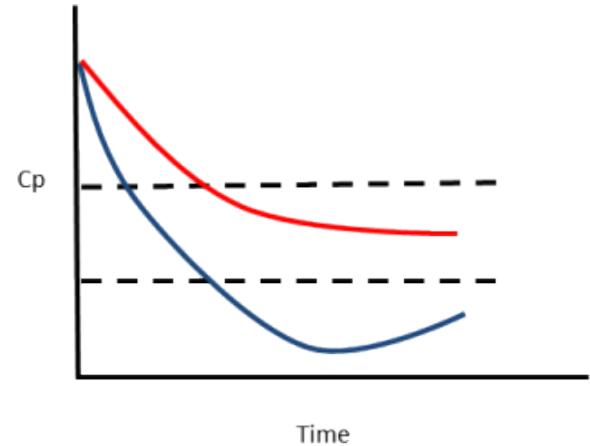
Question 7:

A patient with acute heart failure arrives with GI bleeding on a DOAC. Her INR is 2.0, and does not have liver failure. Which of the following is not a consideration in managing her anticoagulation?

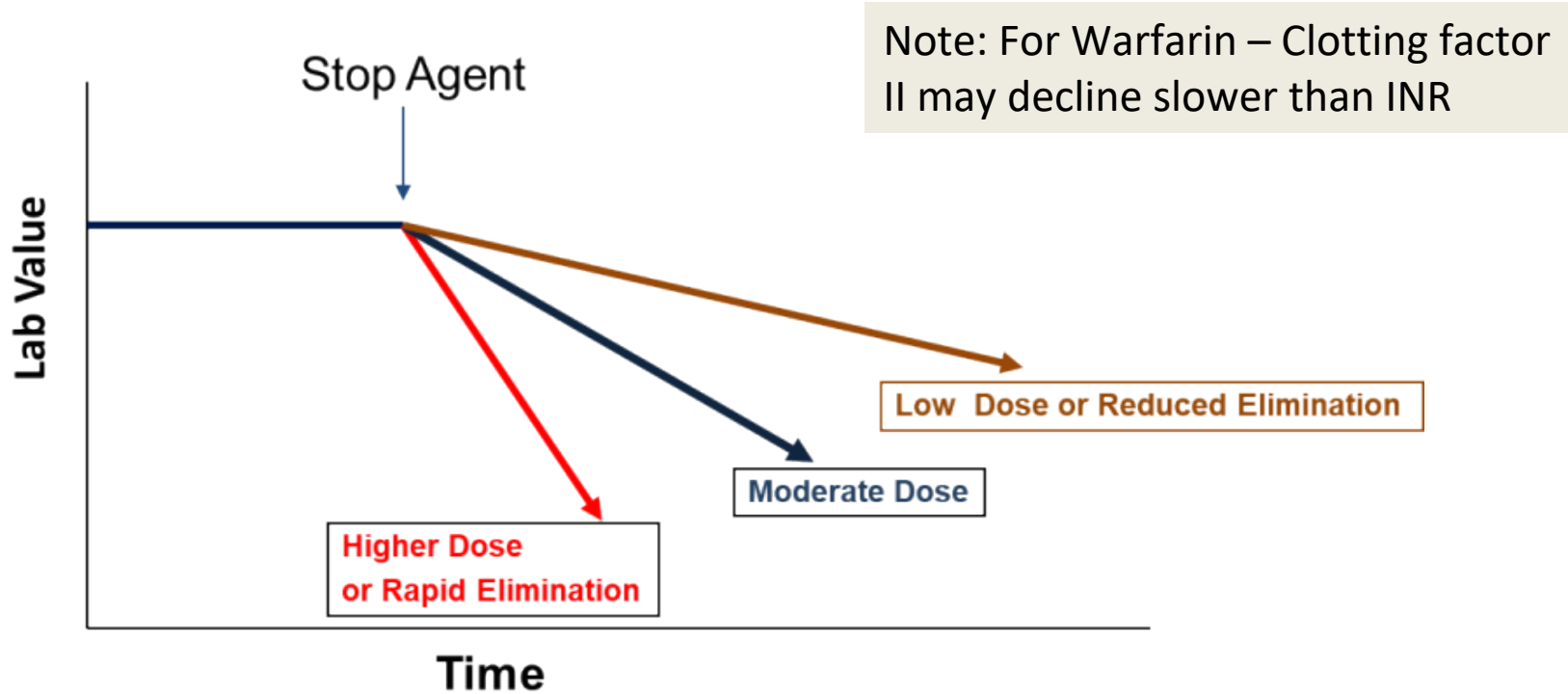
- A. INR Values are not elevated by DOAC's
- B. The heart failure may have caused a high DOAC level
- C. The DOAC effects may last for several days
- D. INR Values can be elevated by DOAC's

Anticoagulant “Lowering Intensity or Reversal” Strategy

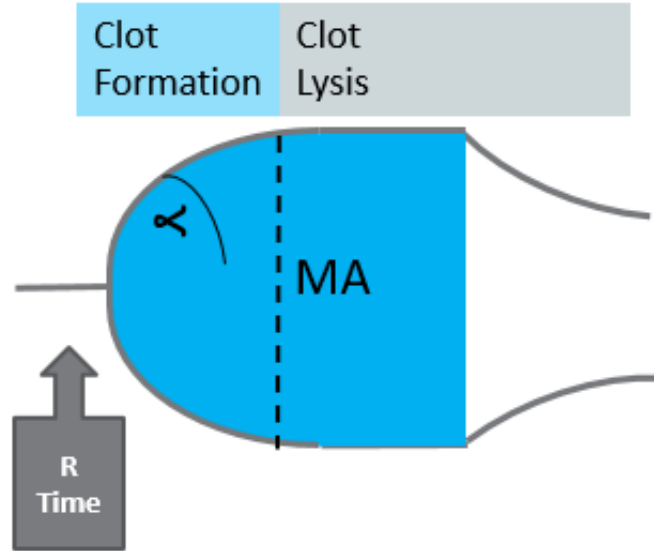
- Withhold Anticoagulation
- Bleeding?
 - Site and severity – may influence outcomes
- Create a plan and request necessary follow up
 - Stop or slow anticoagulant administration to locate and treat bleeding
- Mechanical Intervention (Surgery)
- Pharmacological intervention
 - Topical Agents
 - Neutralize the drug
 - Reverse the effects of the drug independently – Hemostatic agents
- Replace blood losses
- Optimize management of comorbid situations



Estimating Rate of Decline in Anticoagulation Effects



Thromboelastography



Situation	Thromboelastography	Action
Normal		
Coagulopathy Anticoagulants	Longer R 	Stop Anticoagulant Clotting Factors
Hypercoagulable	Short R High MA 	Start Antithrombotic
Reduced Platelet Function		Cryoprecipitate Platelets
Primary Fibrinolysis		Antifibrinolytic
DIC Hypercoagulable state		
DIC Hypocoagulable state		

Patient Case

CC: RA is 5' 3" 45 kg 79 yo male who presents to the emergency room with chest pain. He is diagnosed with a new Pulmonary Embolism

Pertinent PMH: Atrial fibrillation, diabetes mellitus, CKD (stage 3), heart failure, CAD (a drug-eluting stent "DES" was placed 1 month ago with a GI Bleeding during that admission) and hypertension. He was on apixaban 2.5 mg twice daily (last dose 24 hr ago), amiodarone 200 mg once daily, aspirin 325 mg once daily, and clopidogrel 75 mg once daily, all of which were taken orally

Hospital course: Admission INR was 1.5, and a UFH infusion was started. The baseline anti-Xa was 1.2, and aPTT was 35 seconds. Platelet count was 250,000/mm³. He was also noted to have acute kidney injury, with an increase in SCr from 1.6 mg/dL at baseline to 2.8 mg/dL.

Question 8:

Which of the following interventions is most appropriate at this time based on the elevated anti-Xa level?

- A. Withhold UFH and check anti-Xa in 6 hours
- B. Withhold UFH and check liver function studies
- C. Adjust UFH based on the aPTT
- D. Give vitamin K 5mg IV and PCC4 – 50 units/kg IV

Question 9:

Four days later (Saturday) the team decided to start oral anticoagulation, but the platelets suddenly dropped this morning from 100,000 to 50,000/mm³. Which of the following approaches would you recommend?

- A. Stop UFH and start rivaroxaban 15mg/day
- B. Stop UFH and give 5mg warfarin once with subsequent dosing based on INR
- C. Change UFH to enoxaparin 40mg SC once daily
- D. Consider switching UFH to a direct thrombin inhibitor.

What else would you consider in this case?

CC: RA is 5' 3" 45 kg 79 yo male who presented to the emergency room with chest pain and diagnosed with a new pulmonary embolism.

Pertinent PMH: Atrial fibrillation, diabetes mellitus, CKD (stage 3), heart failure, CAD (a drug-eluting stent "DES" was placed 1 month ago with a GI Bleeding during that admission) and hypertension. He was on apixaban 2.5 mg twice daily (last dose 24 hr ago), amiodarone 200 mg once daily, aspirin 325 mg once daily, and clopidogrel 75 mg once daily, all of which were taken orally

Hospital course: Admit INR was 1.5, heparin infusion started. The baseline Anti-Xa was 1.2 and aPTT 35 seconds. Platelet count dropped from 250 to 50 mm³. He was also noted to have AKI with a Scr increased from 1.6 to 2.8.

What else would you consider in this case?

CC: RA is 5' 3" 45 kg 79 yo male who presented to the emergency room with chest pain and diagnosed with a new pulmonary embolism.

Pertinent PMH: Atrial fibrillation, diabetes mellitus, CKD (stage 3), heart failure, CAD (a drug-eluting stent "DES" was placed 1 month ago with a GI Bleeding during that admission) and hypertension. He was on apixaban 2.5 mg twice daily (last dose 24 hr ago), amiodarone 200 mg once daily, aspirin 325 mg once daily, and clopidogrel 75 mg once daily, all of which were taken orally

Hospital course: Admit INR was 1.5, heparin infusion started. The baseline Anti-Xa was 1.2 and aPTT 35 seconds. Platelet count dropped from 250 to 50 mm³. He was also noted to have AKI with a Scr increased from 1.6 to 2.8.

- **What increased the baseline Anti-Xa? Can you measure this?**
- **How long will Apixaban effects last?**
- **What drug drug interactions are present ?**
- **Should we stop the Anti-platelet therapy?**
- **Would you repeat the platelet count before starting the Direct Thrombin Inhibitor?**
- **Are all heart failures the same?**

KEY TAKEAWAYS: What skills have we explored?

- 1) We looked at the big picture
- 2) Watched trends
- 3) Picked a starting point and tailored approach to the individual
- 4) Explored errors in the literature
- 5) Individualized treatment based on risk for thrombosis and bleeding risk
- 6) Adapted short and long term goals as necessary
- 7) Evaluated laboratory tests and potential limitations present – don't base all your decisions on a single lab value





Questions?