Pharmacology Review Pre-Course: Anticoagulants and Reversal Agents in the Hospitalized Patient

Through thick and thin

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Disclosures

I have no relevant relationships with ineligible companies to disclose within the past 24 months

Educational Objectives

- Objectives:
- At the conclusion of this session, participants should be able to:
  - Identify clinical applications of anticoagulants in hospitalized patients
  - Identify appropriate reversal agents
  - Determine anticoagulant selection regimens upon discharge
  - Identify pitfalls of anticoagulant use in hospital medicine

Why is this lecture important

- **FIRST DO NO HARM**
  - Every decision made in the practice of medicine has benefits and risks that need to be addressed.
  - Through evidence-based practice, we are able to explain to patients the rationale for medical decision making and we engage the patient and or family in the decision-making process.
  - Hospital Medicine focuses on acute and life-threatening conditions that require hospitalization for further evaluation and management. Our duty to our patients is to consider the worst-case scenarios and prevent them when possible and to be prepared for them should the unfavorable situation present itself.

Clinical Impact

- Oral Anticoagulants (OACs) are associated with a significant reductions in stroke, intracranial hemorrhage, and mortality, and similar major bleeding as for warfarin, but increased gastrointestinal bleeding[2]

- About 20% of spontaneous ICH events are associated with OAC therapy[1]

- OAC-related major bleeding accounted for 15.5% of emergency department (ED) visits for adverse drug events based on 3661 surveillance cases in 2017[3]

What is Major bleeding?

- Any bleeding with hemodynamic compromise
- Any Bleeding in a non-compressible site
- Any bleeding with > 2g/dl from baseline or requiring 2 or more units of pRBC
  - Intracranial bleeding
  - GI Bleeds
  - Pericardium
  - Airway

[2]

Hospital Medicine Practice

- VTE Classifications
  - There are many ways of classifying DVT, such as proximal vs. distal, provoked vs. unprovoked, symptomatic vs. asymptomatic.
  - In general, proximal DVT (in the lower extremity, popliteal and proximal) carries a higher risk of both embolization and recurrence compared to isolated calf DVT.
  - Pelvic DVTs and those clots extending into the inferior vena cava generally are managed, at least at first, in the inpatient setting.

[4]

General Indications for hospitalization

- Proximal DVT's
  - Ileofemoral or higher
  - Presence of an Associated PE
  - Increased risk for bleeding(Patients on antiplatelets, History of bleeding issues-Ex:GI/GU)
  - Complexity of active comorbid conditions
  - Unprovoked VTE that are recurrent

Reference 2

General Indications for Outpatient management

- Hemodynamic stability
- oxygen saturation >95 percent on room air
- No requirement for narcotic analgesia
- a stable home situation (including unfettered access to medications, follow-up and emergency care
- other comorbidities that carry their own independent indication for admission, are currently stable.
  - As noted earlier in the discussion of DVT, it is likely unwise to move too quickly to outpatient management of patients with concomitant DVT and PE.

[4]

Scope in Hospital Medicine

- Focus is for prevention of propagation of clot burden and or recurrence.
    - Important to discuss with family that this is an anticoagulant(blood thinner)not a fibrinolytic(clot buster)
    - Another common question that patients/family ask is do we need to repeat imaging to ensure the clot has disappeared.
- Common clinical encounters as described on previous slides
    - High risk situations as described on previous slides
    - Mechanical Valves, hypercoagulable state, Malignancy
    - DVT+PE/Arterial Thrombosis

Hospital Medicine Clinical scenarios

- GI bleeding/Fractures
  - Common family questions to tackle include and not limited to
    - “Are we to continue/resume apixaban after admit?
    - “we as a family are concerned about holding anticoagulation due to risk for stroke given afib”(peri-operative management, GI bleeding, acute cva)
- Best points to discuss that I have picked up in clinical practice is explaining: Theoretical risk vs. Reality. (does fairly well 9/10 times) *Anecdotally : JMC*

Hospital Medicine Clinical scenarios

- Transitioning DOAC to heparin/LMWH
  - Guidelines recommend that when transition from either heparin drip or from LMWH
    - When next dose of DOAC is to be due, that is the time to start the heparin drip / LMWH
    - There are specific guidelines regarding indications of when to provide ongoing anticoagulation depending on risk level (Low, Intermediate, high risk)
- Bridging therapy
  - Typically, LMWH or heparin drip transitioning to oral VKA (warfarin)
  - *Be sure to overlap for 24hrs of coverage once therapeutic INR is achieved 2-3* common pitfall
  - When transitioning from warfarin to NOACs
    - Rivaroxaban: D/C warfarin and start when INR <2
    - Dabigatran and apixaban: D/C warfarin and start when INR <2
- Ischemic Stroke Patients: Requires specific Neurology recommendations regarding resuming therapeutic anticoagulation.

Critically ill Patients

- Caution regarding anticoagulation as many conditions may alter coagulation factors
  - Multiorgan failure
  - Coagulation factor depletion, Liver impairment, renal failure
  - Malnutrition (especially fat-soluble vitamins D,E,A,**K**)
- DIC
- Prolonged hospitalization

Anticoagulants

- Anticoagulants inhibit specific pathways of the coagulation cascade, which happens after the initial platelet aggregation but before the formation of fibrin and stable aggregated platelet products
  - -**Anti-factor Xa: enoxaparin, fondaparinux**
  - -DOAC: **rivaroxiban, apixaban, edoxaban, betrixaban**
  - -Vit K antagonist (**warfarin**)

    generally second line agent
  - -Anti-thrombins: **argatroban, bivalirudin, dabigatran**

Considerations: Mechanism of Action – Metabolism/Elimination

- Un-fractioned heparin
  - Metabolized by the Liver
- LMWH and Fondaparinux
  - Renal Elimination
- Warfarin alone therapy can induce protein C deficiency with a hypercoagulable state

Warfarin History

- Warfarin, which was initially approved as a rodenticide in the USA in 1952, and then for human use in 1954. The name warfarin is derived from *WARF* (Wisconsin Alumni Research Foundation) and *–arin* from coumarin.
- In 1955, warfarin's reputation as a safe and acceptable treatment was bolstered when President Dwight D. Eisenhower was successfully treated with it.

Other factors favoring Warfarin

- Warfarin
  - Considered First line agent
    - mechanical heart valves;
    - antiphospholipid antibody syndrome.
    - Otherwise, it is generally a second-line anticoagulant.

- Impaired renal function
  - Limited data for patients wih impaired CrCl < 30
  - NOACs not to be used in patients with CrCl, 15
    - In practice due to multiple external factors NOACs are used in ESRD however require renal adjustment.

INR

- Stands for International normalized ratio
  - A calculation of the patients PT in seconds / Mean Normal PT in seconds.

- Dosing
  - Check INR on Day 3
  - Takes:1-8 Days to eliminate; INR<1.5 in 93% patients in 5 days
  - INR 4.5-10 & no bleeding: no Vit K replacement
  - INR >10 & no bleeding: oral Vit K replacement
    *Vitamin K administration shortens correction time ~ 1-2 days

WARFARIN ADJUSTMENT W/TARGET INR OF 2-3

Starting dose 5mg(Consider < 5mg dose if elderly >75yrs of age, CHF, Malnutrition, hepatic impairment, recent surgery, on Amiodarone.)

INR	Initial Dose Adjustment for 1 Day	Maintenance Dose Adjustment	Check INR
1.1 – 1.4	Double dose (10mg) for 1 day	Increase 10-20% (6mg)	1 Week
1.5-1.7	Increase 50%(7.5mg) for 1 day	Increase 5-10% (5.5mg)	1 Week
1.8-1.9	No change in dose if stable for 2 prior values. If low in prior values Increase 5-10% (5.5mg)	No change in dose if stable for 2 prior values. If low in prior values Increase 5-10% (5.5mg)	1 Week
2.3	No change in dose	No change in dose	4 Weeks
3.1-3.2	No change in dose	No change in dose	1 Week
3.3-3.9	Decrease 50%(2.5mg) for 1 day	Decrease 5-10%(4.5mg) from day 3	2 Weeks
4-4.9	Hold warfarin for 2 days	Decrease 10-20%%(4) from day 3	1 Week

Monitoring of INR

- It takes approximately 3 days to begin to see effects of change in INR after oral administration of warfarin
  - Can consider checking INR on day 3 of therapy known delay in effect of delta
  - Typically, more than half of patients will achieve therapeutic INR by Day 5
  - Follow up INR 3 times per week for the first week,
  - Two time per week for the second week for four weeks
  - Then every 2 weeks for 2 months
  - Then monthly thereafter

Bleeding on warfarin

- 1-8 Days to eliminate;
  - INR<1.5 in 93% patients in 5 days INR 4.5-10 & no bleeding: no Vit K replacement
  - INR >10 & no bleeding: oral Vit K replacement
    *Vitamin K administration shortens correction time ~ 1-2 days

MANAGING EXCESSIVE ANTICOAGULATION

INR	SYMPTOM	INTERVENTION
5-9	NO BLEEDING, LOW RISK FOR BLEEDING. RAPID REVERSAL NOT NEEDED	HOLD WARFARIN FOR 2 DAYS. MONITOR INR EVERY 1-2 DAYS UNTIL INR IS AT UPPER LIMIT OF THERAPEUTIC RANGE (3) AND RESTART AT LOWER DOSE
	HIGH RISK FOR BLEEDING, OR PREFER SLIGHTLY FASTER REVERSAL	HOLD WARFARIN ADMINISTER 1-2.5MG PO VITAMIN K
	MINOR BLEEDING, OR RAPID REVERSAL NEEDED (EX SURGERY)	HOLD WARFARIN, 2-4 mg PO vitamin K If INR REMAINS HIGH AT 24HRS. GIVE AN ADDITIONAL 1-2MG. PO VIT K
>9	NO BLEEDING	HOLD WARFARIN, VIT K 3-5MG X 1. EXPECT REDUCTION WITHIN 24-48HRS. M ONITOR INR DAILY, RESUME WARFARIN WHEN INR IS AT UPPER LIMIT OF THERAPEUTIC RANGE
>20	SERIOUS BLEEDING OR MAJOR WARFARIN OVERDOSE. LIFE THREATENING BLEEDING OR INTRACRANIAL BLEED (AT ANY INR	HOLD WARFARIN ADMINISTER 10MG VIT K IV(SLOW INFUCTIONS, PLUS PCC. OR RECOMBINANT FACTOR VII A VIT K INJECTIONS CAN BE REPEATED EVERY 12 HRS.

Benefits of NOAC's

- In general, dosed in fixed doses
- Rapid onset/offset
- Shown to be at least as efficacious as warfarin, but with improved safety profile
- No need for laboratory monitoring generally
- Less drug interactions
- Adherence to prescribed regimen as always is crucial to improved outcomes

Cost variations

Drug name	Average retail price	Lowest GoodRx price
warfarin	$18.59	$3.00
Brand (apixaban)	$556.15	$458.07
Brand (rivaroxaban)	$553.65	$461.93

(10) https://www.goodrx.com/classes/anticoagulants...

DOAC

- **rivaroxaban**, **apixaban**, dabigatran and edoxaban
  - Available literature review with results of Phase 3 studies were studied using rivaroxaban and apixaban which may be started immediately upon VTE diagnosis
  - In clinical practice, utilization of dabigatran and edoxaban are generally less ordered in the hospitalized patient. Dabigatran is likely more frequently encountered given patient preference and availability of pradaxabind.

Anticoagulant laboratory evaluation

- Parenteral agents
  - Dalteparin, enoxaparin, fondaparinux
- Oral agents
  - Rivaroxaban(CrCl>50mL/Minute: No dosage adjustment necessary. CrCl 15-50ml/minute: 15mg once daily with the evening meal. No data on trials for patients with CrCl<30mL/Minute. CrCl<15 mL/minute. AVOID USE)
  - Apixaban: (Dose adjustments necessary if patient is > 80 years of age and eighter weight < 60kg or has a serum Cr of > or equal to 1.5mg/dl.)
  - Betrixaban
  - Edoxaban

Laboratory analysis

- PT-Prothrombin Time (VKA-warfarin)
- INR: International normalized ratio *(A calculation of the patients PT in seconds / Mean Normal PT in seconds.)*
  - Therapeutic goal
    - Dvt/pe/afib: 2-3
    - Mechanical valves/failed treatment: 2.5-3.5
- PTT(heparin drip)
  - PTT, Drip protocol
    - Drip protocols per facility. Variance in loading dose/drip titrations/targeted PTT depending on Diagnosis
- Xa levels: Used to assess for efficacy/response to LMWH. Not routinely checked since weight-based dosing has appropriate correlation. At times can be checked in morbidly obese patients > 150kg since >150 units of LMWH is not recommended
- It is not routinely recommended to use LMWH in Impaired renal function.

Labs continued

- DOAC
  - Do not require routine laboratory testing
  - Do obtain baseline labs (CBC, aPTT, PT, Serum Cr, and Liver function tests prior to initiation)

- DOSING AJUSTMENTS
  - Rivaroxaban(CrCl>50mL/Minute: No dosage adjustment necessary. CrCl 15-50ml/minute: 15mg once daily with the evening meal. No data on trials for patients with CrCl<30mL/Minute. CrCl<15 mL/minute. AVOID USE)
  - Apixaban: (Dose adjustments necessary if patient is > 80 years of age and eighter weight < 60kg or has a serum Cr of > or equal to 1.5mg/dl.)
    - Dosing in Kidney Impairment
      - Serum Cr: <1.5, no dose adjustment necessary UNLESS Age >80, Body weight < 60kg=reduce dose to 2.5mg twice daily
      - Serum Cr:>1.5, and EITHER Age > 80 or body weight < 60kg=reduce dose to 2.5mg twice daily
      - Severe or End Stage Kidney Disease: NOT requiring dialysis: CrCl 15-20=reduce dose to 2.5mg twice daily
      - ESRD on HD: Although manufacturer suggests no dosage adjustment necessary unless either > 80yrs of age or body weight <60kg, then reduce to 2.5mg twice daily.
        - In clinical practice 2.5mg po bid is typically dose that is chosen by most clinicians. Requires close assessment of comorbid conditions.Overall very limited data available.

Bleeding with heparin and derivatives

- Unfractionated heparin
  - half-life ~2-4 h; Protamine sulfate
- Low Molecular Weight Heparin
  - half-life 4-5 h; little protamine sulfate effect, Could use Andexanet Alfa if available.
- Fondaparinux
  - half-life 18 h; PCC or rFVIIa if bleeding (protamine sulfate is NOT effective.)

Clinical Indications Discussion with patient/family

- General Awareness of treatment duration/outcome discussion with your patients
  - Provoked dvt: ”You will likely be on this medication of 3 months”
  - Unprovoked dvt: “follow up with pcp/hematology clinic for outpatient work up
- Discussing validated risk stratification models that exist in determining if anticoagulation is warranted or not

HASBLED

- This is a scoring system developed to assess 1-year risk of major bleeding in people taking anticoagulants for atrial fibrillation (AF).
- It was developed in 2010 with data from 3,978 people in the Euro Heart Survey.
- Major bleeding is defined as being intracranial bleedings, hospitalization, hemoglobin decrease > 2 g/dL, and/or transfusion.

[13]

HASBLED

Condition	Points	
H	Hypertension: (uncontrolled, >160 mmHg systolic)	1
A	Abnormal renal function: Dialysis, transplant, Cr >2.26 mg/dL or >200 µmol/LAbnormal liver function: Cirrhosis or Bilirubin >2x Normal or AST/ALT/AP >3x Normal	1 1
S	Stroke: Prior history of stroke	1
B	Bleeding: Prior Major Bleeding or Predisposition to Bleeding	1
L	Labile INR: (Unstable/high INR), Time in Therapeutic Range < 60%	1
E	Elderly: Age > 65 years	1
D	Prior Alcohol or Drug Usage History (≥ 8 drinks/week)Medication Usage Predisposing to Bleeding: (Antiplatelet agents, NSAIDs)	1 1

CHADVASC2

This is a clinical prediction model for estimating the risk of stroke in patients with nonvalvular Atrial Fibrillation.

C	Congestive heart failure (or Left ventricular systolic dysfunction)	1
H	Hypertension: blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	1
A_2	Age ≥75 years	2
D	Diabetes Mellitus	1
S_2	Prior Stroke or TIA or thromboembolism	2
V	Vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque)	1
A	Age 65–74 years	1
Sc	Sex category (i.e. female sex)	1

CHADSVASC2

Annual stroke risk (%)			
CHA_2DS_2-VASc score	Friberg 2012	Lip 2010	95%
0	0.2	0.0	0.0–0.0
1	0.6	0.6	0.0–3.4
2	2.2	1.6	0.3–4.7
3	3.2	3.9	1.7–7.6
4	4.8	1.9	0.5–4.9
5	7.2	3.2	0.7–9.0
6	9.7	3.6	0.4–12.3
7	11.2	8.0	1.0–26.0
8	10.8	11.1	0.3–48.3
9	12.2	100	2.5–100

CHADSVASC2

Score	Risk	Anticoagulation Therapy	Considerations[18][27]
0 (male) or 1 (female)	Low	No anticoagulant therapy	No anticoagulant therapy
1 (male)	Moderate	Oral anticoagulant should be considered	Oral anticoagulant, with well controlled vitamin K antagonist (VKA, e.g. warfarin with time in therapeutic range >70%), or a direct oral anticoagulant (DOAC, e.g. dabigatran, rivaroxaban, edoxaban or apixaban)
2 or greater	High	Oral anticoagulant is recommended	Oral anticoagulant, with well controlled vitamin K antagonist (VKA, e.g. warfarin with time in therapeutic range >70%), or a direct oral anticoagulant (DOAC, e.g. dabigatran, rivaroxaban, edoxaban or apixaban)

CHADSVASC2

- Medical Decision making in prescribing anticoagulant therapy for patients with *Non-Valvular AF
- For a CHA2DS2-VASc score ≥2 in males or ≥3 in females
  - recommend chronic OAC.
- For a CHA2DS2-VASc score of 1 in males and 2 in females
  - the specific nonsex risk factor present and the documented burden of AF influences decision making. For patients with CHA2DS2-VASc score of 1 in males and 2 in females based on age 65 to 74 years, recommend chronic OAC. Age 65 to 74 years is a stronger risk factor than the other factors conferring one CHA2DS2-VASc score point
- For patients with other risk factors, the decision to anticoagulate is based upon the specific nonsex risk factor and the burden of AF.
  - For patients with very low burden of AF (eg, AF that is well documented as limited to an isolated episode that may have been due to a reversible cause such as recent surgery, heavy alcohol ingestion, or sleep deprivation), it may be reasonable to forgo chronic OAC and institute close surveillance for recurrent AF, although it may not be possible to reliably estimate AF burden from surveying symptoms or infrequent monitoring. The frequency and duration of AF episodes vary widely over time and episodes are often asymptomatic. For patients with a CHA2DS2-VASc of 0 in males or 1 in females, ASA can be used as secondary prevention
  - we suggest against anticoagulant therapy. Patient values and preferences may impact the decision. For example, a patient who is particularly stroke averse and is not at increased risk for bleeding may reasonably choose anticoagulation, particularly if the patient is a candidate for treatment with a direct oral anticoagulant (DOAC).
- For all potential candidates for OAC, bleeding risk and related possible contraindications to OAC should be reviewed. The appropriate use of bleeding risk assessment is to draw attention to modifiable bleeding risk factors that can be mitigated, and to flag patients with high bleeding risk for early review and follow-up and to identify potential candidates for left atrial appendage occlusion

**(without severe or clinically significant rheumatic mitral stenosis [mitral valve area ≤1.5 cm2], a bioprosthetic valve [surgical or bioprosthetic] within the first three to six months after implantation, or a mechanical valve)*

[11],[12]

Risk Considerations

- Non-modifiable risk factors
  - Increasing age
  - Valvular heart disease
- Modifiable risk factors
  - Use of nsaids
  - Alcohol use
  - Uncontrolled hypertension > 160/90

Reversal Agents

- Idarucizumab –Pradaxabind
  - Dabigatran-Pradaxa

- Andexanet Alpha
  - Inhibits all anti-Fxa agents
  - FDA approved 2018
- PCC
  - Not FDA approved for anti Xa agents, however widely available.
    - Has no effect on dabigatran

Recommended reversal agents

Dabigatran (Thrombin/factor IIa inhibitor)	Idarucizumab 5 g IV **If unavailable: activated PCC 50 units/kg IV**
Rivaroxaban or apixaban[1] (Factor Xa inhibitor)	Andexanet alfa dosed according to the US FDA label **If unavailable: 4-factor PCC 2000 units**
Edoxaban or betrixaban[1] (Factor Xa inhibitor)	Off-label treatment: High-dose andexanet alfa **if unavailable 4-factor PCC 2000 units**
Warfarin[5,6] (Vitamin K antagonist)	4-factor PCC + Vitamin K (10 mg IV) **If unavailable: Consider PCC or FFP**

Reversal agents

- aPCC: Before andexanet alfa, aPCC's were considered useful for factor Xa reversal[8] (Connolly SJ, et al N Engl J Med. 2016: 14:14-623-627)
- Andexanet alfa is a recombinant human factor Xa decoy protein that binds to oral factora Xa inhibitors with similar afifinity to native factor Xa
- Non-activated Prothrombin Concentrate complex (PCC)
  - Kccentra: 4 factor PCC
  - Ex: Intracerebral Hemorrhage
    - INR 2Dose U/KG if INR is 2-<
    - Kcentra : 4 factor PCC
      INR 2-<4: 25 U/kg (max 2500 U) INR 4-6: 35 U/kg (max 3500 U) INR > 6: 50 U/kg (max 5000 U)
    - rFVIIa 10-30 µg/kg IV FFP 5-10 ml/kg
- Issue regarding Availability : adnexastat is non-formulary in many facilities

Gearing up for discharge

- Warfarin
  - Least expensive
  - Tedious INR labs
  - Bridging
    - Overlap for 24 hrs after therapeutic inr
  - INR clinics
  - Information regarding Drug Drug interactions and Dietary intake of vitamin K

Gearing up for discharge

- DOAC
  - No need for routine coagulation panel
  - Outpatient monitoring
    - Monitor for spontaneous bleeding
  - Cost
    - Covered by most insurance plans based on DRG
    - Prior authorization requests
      - Some-times required, explain clinical scenario/failed outpatient regimen
      - Don’t delay discharge planning
        - Begin discharge planning from day one of admit
        - Send Rx early to pharmacy and or call pharmacy to assess available coverage
  - Coupons:
    - Generally, OAC’s are covered by most insurance plans, and coupons are generally available (including uninsured patients)

Take home points

- YOU ARE NOT ALONE !!!
  - Multidisciplinary team may include emergency medicine clinicians, cardiologists, pharmacists, trauma specialists, and critical care clinician

Take Home Points

- *When to use what?*
  - *NOAC's,DOAC's,OAC's are generally considered to be safer for most patients*
  - *There are specific situations when Warfarin is considered a first line agent*
- *Reversal and blood product (RX)*
  - *Regarding OAC's. The reversal agent adnexastat is not always readily available due to cost. Be familiar with best practices in absence of specific antidotes*
- *What fits best for the patient ie. monitoring or insurance concerns (prior authorization)?*
  - Generally OAC's are covered by most insurance plans, and coupons are generally available (including uninsured patients)
- *What will work when they go home?*
  - *DOAC's will achieve desired effects for most patients withing our scope of hospital medicine.*
  - *Bridging treatments/educations of LMWH injections prior to discharge is key*
- *Do they need blood draws?*
  - *As mentioned previously. Routine Labs are recommended for patients on DOAC's. INR monitoring was discussed previously in detail.*

Question#1

- Patient is a 37 y/o female who was diagnosed with a proximal iliofemoral. Patient has is in Medicaid pending status and will be discharged on warfarin. INR has finally trended to a therapeutic level and patient is asking about discharge. What is the best next step?
  a. Discharge the patient on current dose of warfarin
  b. Keep the patient for ongoing inpatient monitoring for another 24 hrs
  c. Discharge patient with therapeutic enoxaparin injections and instruct patient to follow up in an INR clinic (crossing fingers she can find an INR clinic and in hopes she can be seen in INR clinic in 24hrs.
  d. Repeat a venous duplex ultrasound and if DVT has resolved discharge with no anticoagulation regimen
  e. Keep the patient in order to improve HCAHPS

Question #2

- You recently discharged a patient from the inpatient setting on coumadin for atrial fibrillation given elevated chadsvasc score. Now presents to the ED after a mechanical fall resulting in a non-displaced intertrochanteric hip fracture. The patient is admitted to the trauma service and Internal Medicine has been consulted for co-management of medical conditions and INR reversal. Patient is scheduled for surgery in a.m. INR is 2.5. What is your recommendation for pre-operative optimization?
  a. Oral Vit K
  b. IV vit K
  c. Protamine sulfate
  d. Hold warfarin and check INR in a.m.
  e. Hold warfarin and have patient eat as much green leafy salads as possible prior to midnight as patient is npo past midnight.

Question # 3

- You are called to admit a 73 y/o female with a medical history hypertension, dm type 2, sent to ED by PCP for palpitations. ED work up reveals atrial fibrillation with rvr. She is started on a diltiazem drip. Initial work up in the ED reveals no evidence of an acute cva. Patient has no history of falls, and or bleeding disorders. Hepatic function panel is within normal limits and serum Cr is 0.8 with estimated GFR >60. The patient is insured and will be admitted for management of atrial fibrillation with rvr. What anticoagulant do you choose to start the patient on during hospitalization?
  a. Rivaroxaban 20mg at bedtime
  b. Apixaban 5mg po bid
  c. LMWH for now with plans to ”bridge treatment” to warfarin
  d. ASA 325mg po daily
  e. Dabigatran 50 bid
  f. Apixaban 10mg bid x 7 days then 5mg bid thereafter.

QUESTION # 4

You admitted a patient for new onset right hemiplegia and slurred speech. She has a history of atrial fibrillation and is on apixaban for stroke prevention. She tells you she was forgot to take her meds for 7 days, because she went on a trip to a Bingo tournament and forgot her home medications. The patient asks you if she will be given her apixaban, since she is due for her nighttime dose. What do you tell the patient?

a. NO!.... and offer no further explanation.
b. Tell her YES !, we will be resuming apixaban tonight without any reservations and mention that you are proud of her for demonstrating willingness to comply with prescribed medication regimen.
c. Recommend transition to coumadin with LMWH bridge to warfarin as she seemingly failed Apixaban for stroke prevention.
d. Discuss with the patient a need for LMWH bridge to warfarin as she seemingly failed DOAC's.
e. Discuss with patient that you will need to collaborate with the primary Neurology team on the case (in-person or remote) regarding safety in resuming anticoagulants.

Homework-Land Mark Trials

- ARISTOTLE=Apixaban for the prevention of stroke in subjects with Atrial Fibrillation
- ATLAS ACS 2 – TIMI 51 = Anti-Xa therapy to lower cardiovascular events in addition to standard therapy in subjects with Acute Coronary Syndrome ACS 2- Thrombolysis in Myocardial Infarction 51
- EINSTEIN-DVT = Oral Direct Factor Xa Inhibitor Rivaroxaban in patients with Acute Symptomatic Deep-Vein Thrombosis or Pulmonary Embolism
- ROCKET AF = Rivaroxaban-Once-Daily, Oral , Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation
- ENGAGE AF- TIMI 48 = Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation- Thrombolysis in Myocardial Infarction Study

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