Anticoagulation Tips and Pitfalls in 2023

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Case:

John is a 64 male who is currently receiving adjuvant chemotherapy for resected colorectal cancer (curative intention). He presents to primary care clinic with a swollen left leg. He denies chest paint or SOB. D-dimer significantly elevated. Doppler ultrasound confirms proximal DVT. No prior thrombosis. No family history of thrombosis. No active bleeding
PMHx: chronic kidney disease (GFR 40 mL/min), seizure disorder, hypertension,
Medications: FOLFOX, Dilantin, Amlodipine, chlorthalidone
Weight 67 kg

Questions:

Was d-dimer testing the right place to start?
What is the duration of anticoagulation?
Should he receive LMWH or DOAC?
Does he need thrombophilia testing?

Obesity

- Obesity highly correlated with VTE risk (component of validated HERDOO2 score)
- Higher doses of warfarin and LMWH typically needed for patients with elevated BMI
- Older (2016) ISTH guidance statement suggests avoiding DOAC if weight >120kg or BMI > 40 kg/m^2
- ISTH updated guidelines in 2021= No known "weight ceiling" now for DOAC (Apixaban and Rivaroxaban have best data)
  - Based on retrospective studies and post-hoc analysis from EINSTEIN Trial
- No role for routine anti-Xa levels
- Avoid DOAC following bariatric surgery (possible reduced absorption)

Renal Impairment

- DOACs have variable hepatic metabolism and renal clearance
- DOAC trials excluded patients with CrCl <30 mL/min (<25mL/min for Apixaban)
  - Risk of drug accumulation and bleeding
- Health Canada approved Rivaroxaban and Apixaban with CrCl >15mL/min but VERY limited prospective data
- Most LMWHs also not recommended with CrCl < 30 mL/min
  - Tinzaparin is the LMWH with highest molecular weight and least renal clearance
  - consider anti-xa monitoring

Drug/Drug Interactions

- a common culprit for "anticoagulation failure" or major bleeding
- Apixaban/Rivaroxaban depend on both CYP and P-gp pathways while Dabigatran/Edoxaban mostly reliant on P-gP
- Common drugs to be mindful of
  - INCREASE DOAC levels: Cyclosporine, fluconazole. Tacrolimus, amiodarone, verapimil, clarithromycin
  - DECREASE DOAC levels: Carbamazepine, Dilantin, Rifampin
- Tip: ensure patients are using single pharmacy for prescriptions

GI related Cancer

- Evidence for efficacy and safety of DOAC for cancer thrombosis continues to grow
- Excess bleed risk in DOAC trials mostly attributed to GI bleeding with GI tumors
  - i.e. HOKUSAI-VTE = 12.7% (Edoxaban) vs 3.6% (LMWH)
- Highest bleeding risk seen with endoluminal (unresected) GI tumors
  - Canadian Expert Consensus recommends LMWH
  - Many patients willing to accept higher bleeding risk to avoid daily LMWH
- Caution: be careful with DOAC post GI cancer surgery (absorption *may* be impacted)

Anticoagulant	Nonvalvular AF - stroke prophylaxis*	VTE treatment[¶]	VTE primary prophylaxis[Δ]
Dabigatran (Pradaxa)	150 mg twice daily	Parenteral anticoagulation for 5 to 10 days; then dabigatran 150 mg twice daily	110 mg for the first day, then 220 mg once daily
Apixaban (Eliquis)	5 mg twice daily	10 mg twice daily for one week, then 5 mg twice daily	2.5 mg twice daily
Edoxaban (Savaysa, Lixiana)	60 mg once daily	Parenteral anticoagulation for 5 to 10 days; then edoxaban 60 mg once daily	
Rivaroxaban (Xarelto)	20 mg once daily with the evening meal	15 mg twice daily with food for three weeks; then 20 mg once daily with food	10 mg once daily, with or without food

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