Thrombosis

Choice and Duration of Anticoagulation

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Disclosure

Faculty: Ben Schwartzentruber, UBC clinical instructor

Relationship with financial sponsors:

- No relationship with industry (speaking, honoraria, etc.)
- I am participating in the SSC funded Physician Quality Improvement curriculum focusing on thrombosis care, for which I receive sessional funding
- I am one of 4 internists participating in a pilot DVT pathway at RJH, a hospital funded clinic, and I get FFS for seeing patients there

Mitigating Bias

Faculty: Ben Schwartzentruber, UBC clinical instructor

Any recommendations I make are concordant with current guidelines or the pattern of practice of my thrombosis colleagues in areas not directly addressed by guidelines (Thrombosis Canada, ACCP, ISTH)

Choice of Anticoagulant

spoiler: DOACs

Choice of Anticoagulant

DOACs should be first line for the majority of patients

- in the major VTE trials, DOACs (esp. FXa inhibitors) have at least equal efficacy, and consistently lower bleeding risk compared to VKA
- RR for major bleed 0.61
- no monitoring, no bridging

Which DOAC?

- apixaban is generic, and no SA needed as of this month
- rivaroxaban is once daily (after 3/52)

Drug Interactions

PGP and CYP 3A4

- inducers (more clotting): rifampin, phenytoin, carbamazepine, some antiandrogens (*e.g.,* apalutamide)
- inhibitors (more bleeding): diltiazem, naproxen, -azoles, HIV protease inhibitors

PEARL: LMWH interacts with NOTHING, and has at least as good safety and efficacy as anything given orally

Choice of Anticoagulant

Special cases:

- rivaroxaban a/w more heavy menstrual bleeding than apixaban
- dabigatran/edoxaban may be options if there are drug interactions
  - *e.g.,* antiretroviral therapy
- LMWH preferred for anyone with GU and luminal GI malignancies
- limited DOAC data in patient with BMI > 40 or weight > 150 kg
  - guidelines suggest DOACs for all body weights based on retrospective data
  - more evidence for rivaroxaban than apixaban
- APLA: VKA

What about reversibility?

I don’t care that warfarin has an antidote

- it is MUCH better not to have a major bleed in the first place

The DOACs also have studied antidotes (andexanet alfa, idaracizumab)

- trials pharmacokinetic, drugs expensive and unavailable

Inpatients: same is true for UFH vs. LMWH!

- bleeding higher, HIT more frequent, more supra-, subtherapeutic

Dosing for VTE

DOACs:

- Apixaban 10 mg BID x 7 days then 5 mg BID for acute phase
- Rivaroxaban 15 mg BID x 21 days then 20 mg daily
- Dabigatran (LMWH x 5) then 150 mg BID
- Edoxaban (LMWH x 5) 60 mg daily or 30 mg daily (wt. > 60 kg)

Note: NO dose adjustment for renal impairment has been studied, unlike atrial fibrillation

- apix studied down to CrCl < 25; in practice CrCl >15
- riva CrCl 30

Dosing for VTE

LMWH

- dalteparin 200 units / kg - round to nearest prefill
- tinzaparin 175 units / kg - down to CrCl 20
- enoxaparin 1 mg / kg BID or 1.5 mg / kg daily (equivalent)

Warfarin

- who knows???

Duration of Anticoagulation

when and how to interrupt

Why I Treat VTE

Treat acute symptoms
Prevent chronic symptoms (PTS, CTED/CTEPH)
Prevent recurrent VTE
Prevent death

As long as I am not making things worse with bleeding

- major bleeding is a **contraindication** to anticoagulation!

Acute Phase

"Three to six months"

- the smaller and more provoked, the shorter I treat acutely
- the larger, more symptomatic, and less provoked, the longer I treat

Special cases:

- pregnancy - until 6 weeks postpartum for all

Note: AC should only be interrupted for emergencies in acute phase

- *e.g.,* biopsy for newly detected cancer, not dental stuff

Long Term Prevention

For people with high risk of recurrence, and low risk of bleed, may continue “long term” at reduced dose

- both apixaban 2.5 mg BID and rivaroxaban 10 mg daily studied
- studies lasted 1 year, showed no difference in efficacy or safety

Young, active: can interrupt for a weekend of mountain biking or mixed martial arts!

Long Term Prevention

Does everyone with unprovoked VTE need to be anticoagulated forever?

Risk of recurrent [fatal] VTE after initial treatment (Khan et al. 2019)

- year 1: 10.3% [0.4%]
- year 2: 16.0% [0.7%]
- year 5: 25.2% [1.0%]
- year 10: 36.1% [1.5%]
- treatment reduces recurrence risk by ~80%
- men have 1.4 x recurrence risk as women

Long Term Prevention

Does everyone with unprovoked VTE need to be anticoagulated forever?

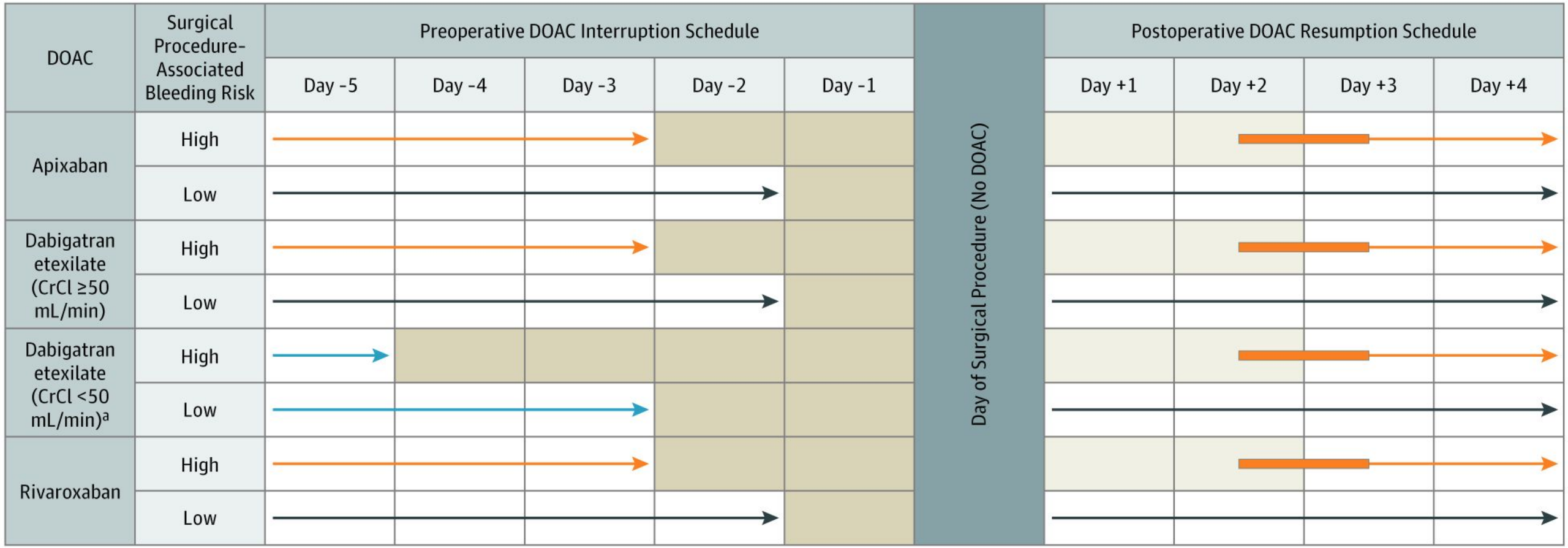
Risk of major bleeding [fatal] on treatment (Khan et al. 2021):

- VKA year 1: 2.00% [0.18%] DOAC: 1.20% [0.11]
- VKA year 2: 3.6% [0.4%]
- VKA year 5: 6.3% [1.0%]
- bleeding risk: age > 65, CrCl < 50, pts on antiplatelet, anemia, female
- if 2+ RFs for bleeding, consider stopping anticoagulation

Interruption

Bleeding Risk:

https://thrombosiscanada.ca/wp-uploads/uploads/2019/01/Risk-of-Periop-Bleeding-e1547756533302.png



When to Workup Thrombophilia

Don't! Recurrence risk comes from provoking event (or lack thereof)
But for unprovoked VTE, please update malignancy screening

- case detection by history, physical, labs, +/- imaging for covert malignancy (SOME trial, 2015)

Exceptions:

- I send antiphospholipid testing for unprovoked VTE < age 60
- Patient who could become pregnant or who have 1st degree relatives who could (would affect prophylaxis in pregnancy)

When to Refer

Whenever you need help with decision-making or the patient needs to hear another doctor agree with you!

- I am happy to see these referrals at UMAC
- Pacific Hematology is also happy to see these patients

Thank You!

Questions?

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