Blood Day for Primary Care

How long should I anticoagulate for after DVT or PE?

Marc Carrier MD MSc. FRCPC
Department of Internal Medicine, Division of Hematology, University of Ottawa

UNIVERSITY OF MANITOBA

Disclosures

Research Support/P.I.	Leo Pharma (PERIOP 01 Trial)
Employee	No relevant conflict of interest to declare
Consultant	No relevant conflict of interest to declare
Major Stockholder	No relevant conflict of interest to declare
Speakers' Bureau	No relevant conflict of interest to declare
Honoraria	Sanofi Aventis, Pfizer, Boehringer Ingelheim, Leo Pharma, Bayer.
Scientific Advisory Board	Sanofi Aventis, Leo pharma.

Objectives

1. Review risk stratification models aiming to help the decision of length anticoagulation therapy for patients with idiopathic/unprovoked venous thromboembolism (VTE)

2. Review the evidence supporting different secondary prevention strategies (anti-platelets, warfarin, novel oral anticoagulant (NOACs)

Who to stop?

1. **Answer is clear**- Discontinue after short term (3 months)
    - Clear temporary provoked
        - Post-surgical, casts, immobilization (>3 days)

2. **Answer is clear**- Continue long-term
    - Ongoing malignancy
    - Recurrent unprovoked VTE
    - Potent thrombophilia (e.g. APLA, anti-thrombin, etc.)

3. **Answer AMBIGUOUS**
    - Unprovoked proximal DVT and/or PE (i.e. major VTE)
    - Weakly provoked
        - Minor trauma, minor immobilization, ante-partum pregnancy, estrogens, prolonged flights, etc.

Mr. MT

50 year old ♂ completes 6 months of anticoagulant therapy for unprovoked proximal DVT.

Physical:

- BMI 25, hyper pigmentation and edema in the affected limb.

Labs:

- US shows a residual non-occlusive popliteal vein thrombus.
- D-Dimer of 200ng/ml while on anticoagulants and 350ng/ml off of anticoagulants 1 month later.

Mr. MT

You would recommend…

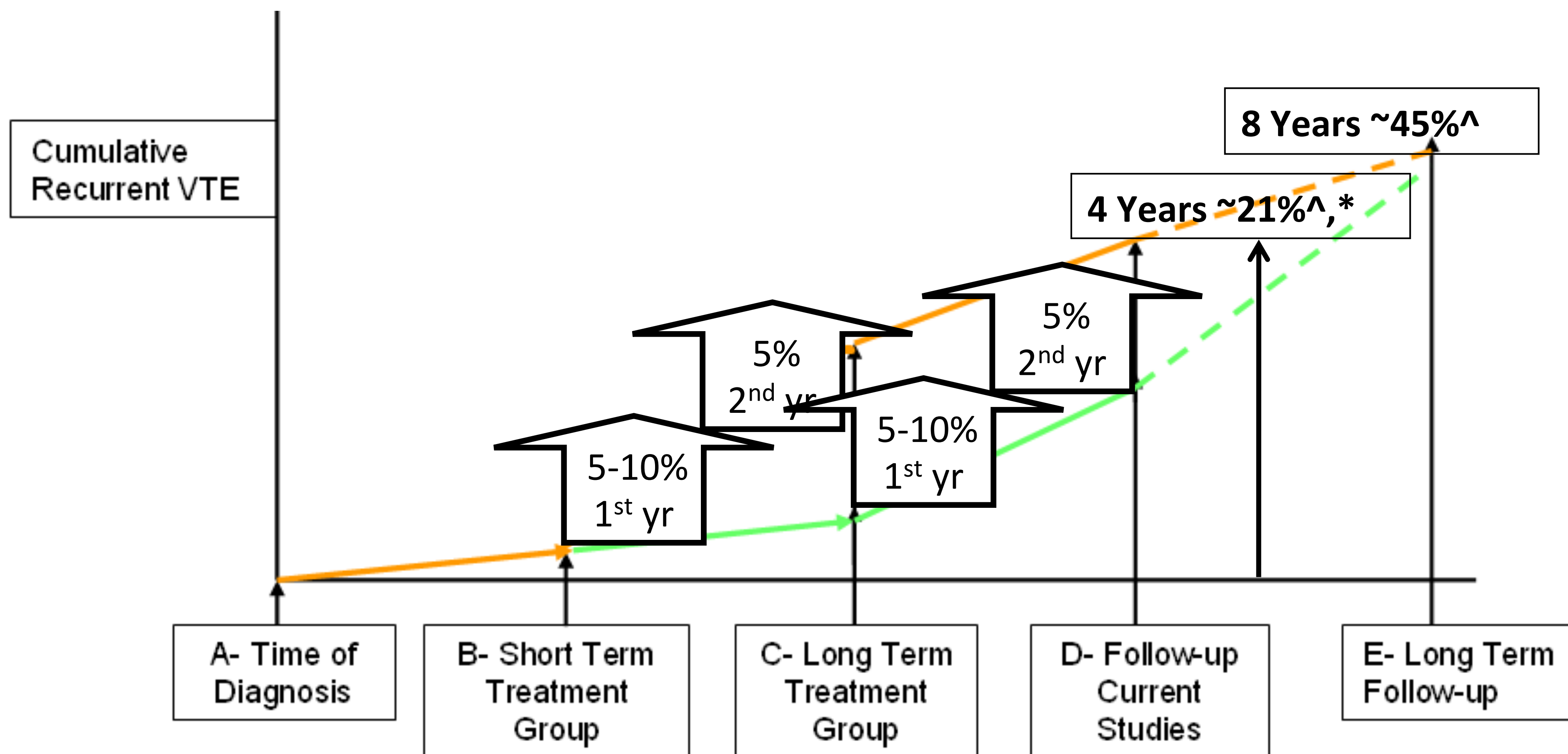
A. Discontinue anticoagulants
B. Continue anticoagulants for an additional 6 months
C. Continue anticoagulants an additional 1 year
D. Continue anticoagulants an additional 2 years
E. Continue anticoagulants indefinitely

Duration of anticoagulation for unprovoked VTE?

1. One of the most important unanswered questions in clinical management of VTE
    - Short term (3-6 months) or forever
    - ACCP guidelines increasingly suggests longer term
        - Unless high bleeding risk (but don't tell us how to determine bleeding risk)
        - Not universally accepted

2. Clinicians/Patients
    - Balance 0.9-2.0% per year risk of major bleed with VKA, lifestyle (diet, monitoring, costs etc)

Oral anticoagulants are very effective at preventing recurrent VTE (>90% relative risk reduction) in "unprovoked" VTE… *while on therapy*



^Prandoni, Haematologica 92(2):199-205, 2007; * Rodger, ISTH, 2011

Balancing Risks...

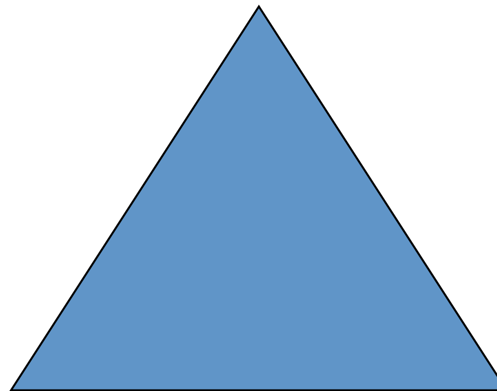
Major

Major
Bleed events are
3x more likely to

Decision ambiguous if long-term risk of recurrent VTE between 2.5-6.5% per year

95% CI 1.9-5.7)

CI 7.5-15.9)



Carrier M et al, Ann Int Med, 2010: 152(9):578-89.

Single predictors that are not good enough to identify low risk group…

1. Normal D-Dimer off of anticoagulants

   - 3.6% per year
   - ~2 years follow-up

Verhovsek, M., Ann Intern Med 2008;149:481-490

2. Normal Compression Ultrasound at completion of therapy

   - ~6% per year
   - ~1 year follow-up

Donadini, M., Thrombosis Hemostaisis 2013;109:34-8

Clinical predictive rules – **"Men Continue and HERDOO2"**

- **Men continue** anticoagulants
  -13.9% annual risk of recurrent VTE
- Women with ≤ 1 point discontinue anticoagulants
  -1.6% annual risk of recurrent VTE
- **Women with ≥ 2 points continue** anticoagulants
  -14.1% annual risk of recurrent VTE

HERDOO Predictors

- Hyperpigmentation or Edema or Redness (HER) on exam either leg
- Vidas D-Dimer ≥ 250
- Obesity, BMI ≥ 30
- Older age ≥ 65 years

Rodger M, CMAJ 2008;179(5):417-26

Clinical predictive rules – **"DASH Score"**

DASH Score ≤1

3.1% annual risk of rVTE (95% CI: 2.3-3.9%)

51.6% of study patients

DASH Score =2

6.4% annual risk of rVTE (95% CI: 4.8-7.9%)

DASH Score ≥3

12.3% annual risk of rVTE (95% CI: 9.9-14.7%)

<u>*DASH* Predictors</u>

- Abnormal ***D***-Dimer after stopping anticoagulants=2 points
- ***A***ge < 50 years= 1 point
- Male ***S***ex= 1 point
- ***H***ormone associated index VTE= -2 points

Tosetto A, J Thromb Haemost. 2012;10:1019-25.

Mr. MT

50 year old ♂ completes 6 months of anticoagulant therapy for unprovoked proximal DVT.

Physical:
- BMI 25, hyper pigmentation and edema in the affected limb.

Labs:
- US shows a residual non-occlusive popliteal vein thrombus.
- D-Dimer of 200ng/ml while on anticoagulants and 350ng/ml off of anticoagulants 1 month later.

You would recommend…

1- Discontinue anticoagulants

2- Continue anticoagulants for an additional 6 months

3- Continue anticoagulants an additional 1 year

4- Continue anticoagulants an additional 2 years

5- **Continue anticoagulants indefinitely**

Oral anticoagulation (warfarin vs. NOAC) or ASA?

Odds ratio (95% CrI)

Treatment	Outcome	Odds ratio (95% CrI)
Standard adjusted dose VKA	Recurrent VTE	0.07 (0.03 to 0.15)
	Major bleeding	5.24 (1.78 to 18.25)
ASA 100 mg daily	Recurrent VTE	0.65 (0.39 to 1.03)*
	Major bleeding	1.29 (0.40 to 4.08)
Dabigatran 150 mg twice daily	Recurrent VTE	0.09 (0.04 to 0.21)
	Major bleeding	2.79 (0.79 to 11.69)
Apixaban 5 mg twice daily	Recurrent VTE	0.18 (0.08 to 0.38)
	Major bleeding	0.19 (0.01 to 1.78)
Apixaban 2.5 mg twice daily	Recurrent VTE	0.17 (0.08 to 0.36)
	Major bleeding	0.46 (0.05 to 2.82)
Rivaroxaban 20 mg daily	Recurrent VTE	0.17 (0.06 to 0.41)
	Major bleeding	20.79 (1.31 to 14 230)†
Low intensity VKA	Recurrent VTE	0.28 (0.13 to 0.57)
	Major bleeding	4.77 (1.38 to 19.49)

Axis: 0.01, 0.1, 1, 10, 100

Favours treatment | Favours placebo or observation

CancerCareManitoba

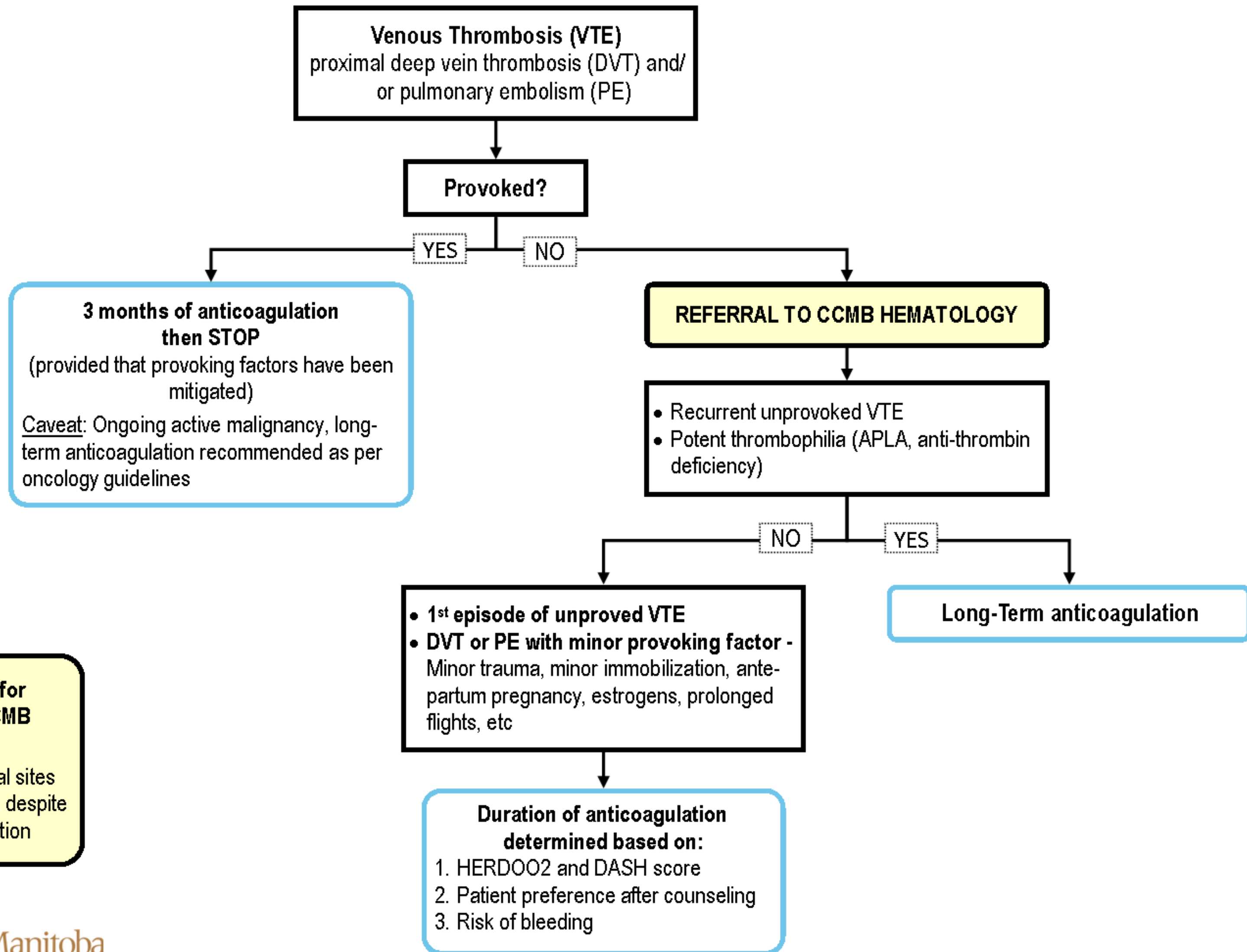
Take Home Messages

- Predictors that identify patients with long-term risk of <3% annual risk should be used to discontinue anticoagulants
- To risk stratify unprovoked VTE patients
  - Don't use:
    - D-Dimer off anticoagulants alone
    - Residual vein imaging alone
  - Consider:
    - "Men Continue and HERDOO2"
    - DASH Score

Duration of Anticoagulation after DVT/PE

PRACTICE POINTS: Typical Provoking factors → • a post operative state or trauma (within 4 weeks) • immobilization >3 days (casting, hospitalization, bed ridden) • active malignancy • peripherally inserted central catheter (PICC) or central venous access device (CVAD)

Risk of major bleeding on anticoagulation ~0.9-2% per year



Other indications for REFERRAL TO CCMB HEMATOLOGY

1. Thrombosis at unusual sites
2. Recurrent thrombosis despite adequate anticoagulation

CancerCare Manitoba
ActionCancerManitoba

Pathways are subject to clinical judgment and actual practice patterns may not always follow the proposed steps in this pathway.

Feb.6, 2015: ©Hematology DSG FINAL (Zarychanski)

When to consider referral to hematology

- Unprovoked VTE
- Thrombosis at unusual sites
- Recurrent thrombosis despite adequate anticoagulation

Questions?

Marc Carrier
mcarrier@toh.on.ca