MAYO CLINIC | School of Continuous Professional Development

Thrombophilia Testing

WHEN TO ORDER

Robert D McBane II MD
Gonda Vascular Center

DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INDUSTRY

- Nothing to disclose

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

Learning Objectives: 3 questions

To determine whether thrombophilia test results will…..

- help explain the ***thrombosis mechanism***?
- inform management ***decision making***?
- impact ***treatment duration***?

First patient

75 y/o female

Three weeks ago, she underwent ***left total knee arthroplasty*** and recovered well. She then noted ***new pain*** and ***swelling*** of the left leg.

Past history: Hypertension, osteoarthritis

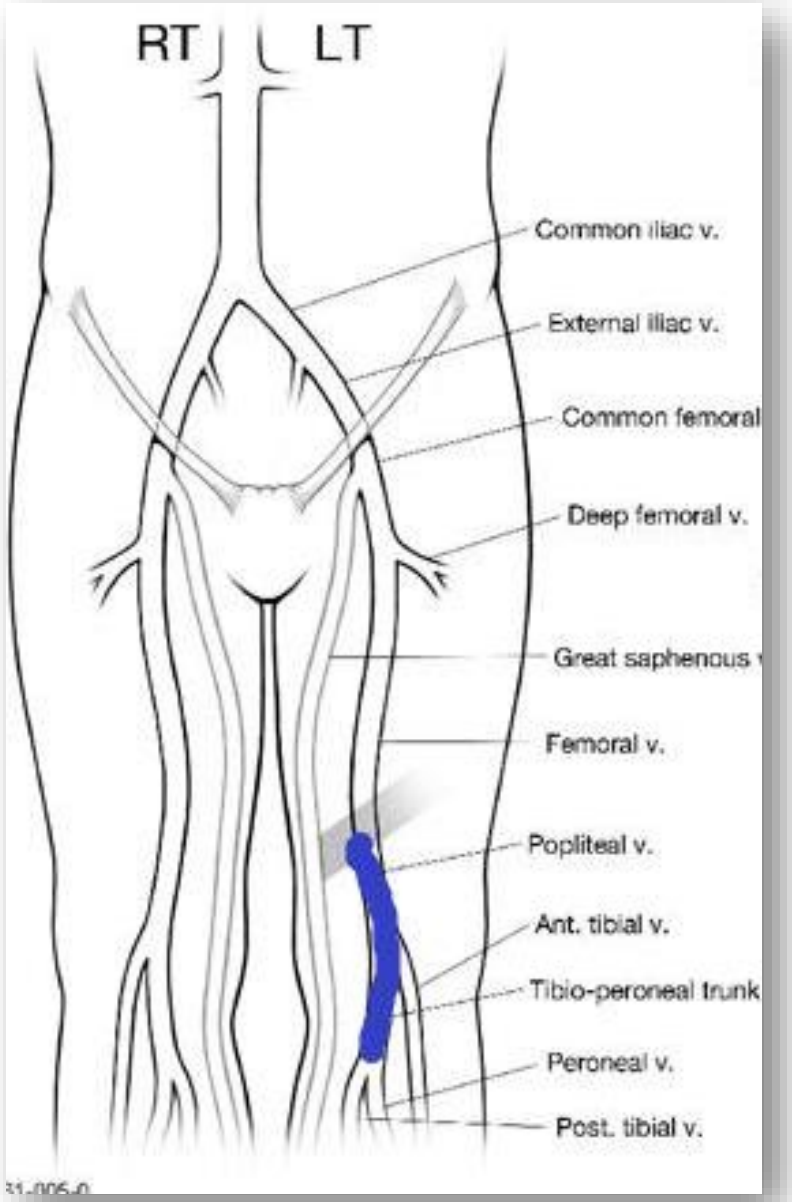
Examination: Comfortable

BP 144/80 P 97

COR: no JVD or RV Lift. No murmurs

Extr: ***left leg edema***

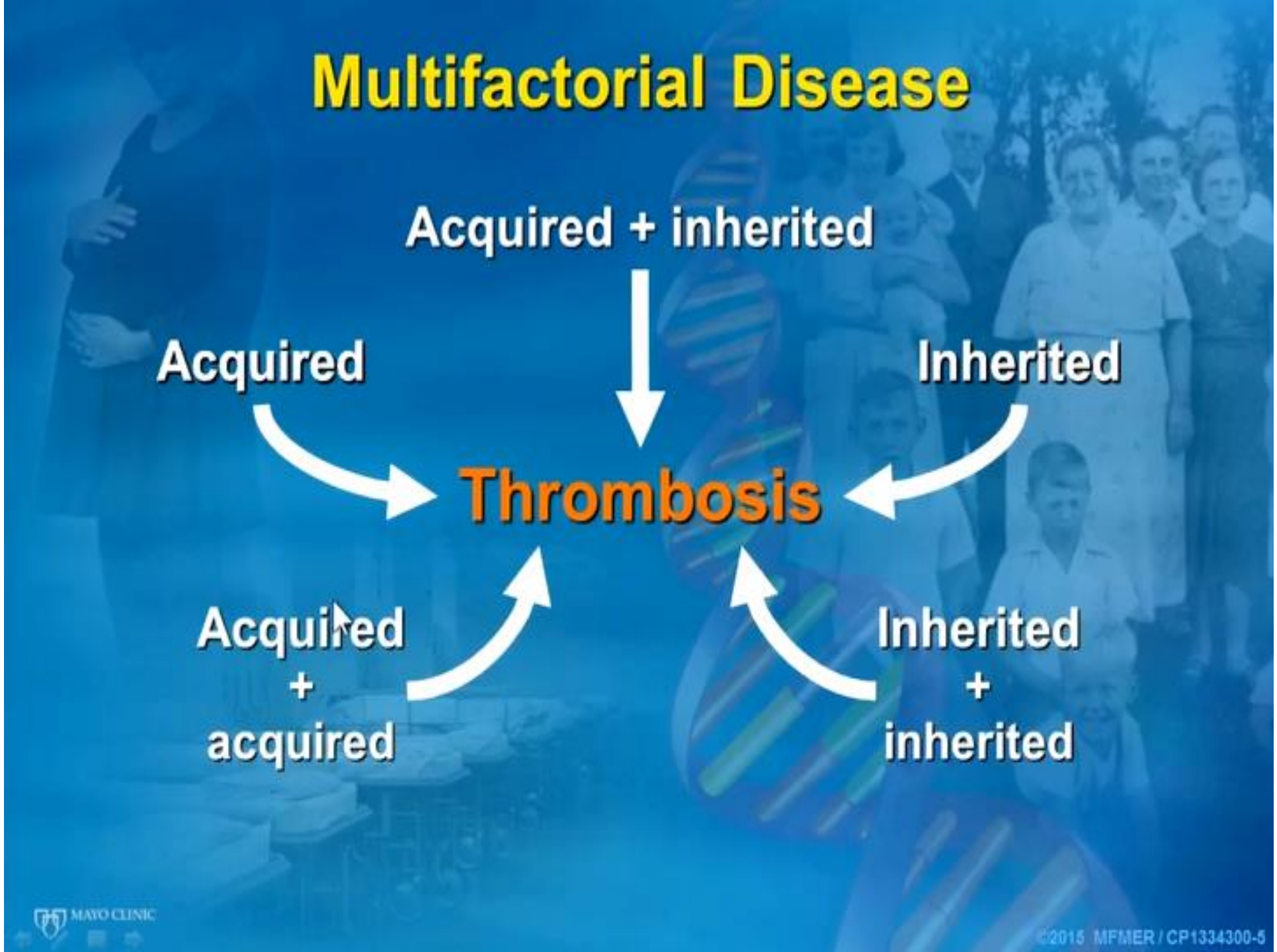
Ultrasound Results



Blue is bad

75 year old female with left popliteal DVT. ***After 3 months*** of ***apixaban***, what are your recommendations?

1. Stop apixaban
2. Stop apixaban and begin low dose aspirin
3. Continue apixaban at 5 mg twice daily
4. Continue apixaban but reduce dose to 2.5 mg twice daily
5. Stop apixaban and obtain thrombophilia Testing


Multifactorial Disease
Acquired + inherited
Acquired
Inherited
Thrombosis
Acquired + acquired
Inherited + inherited
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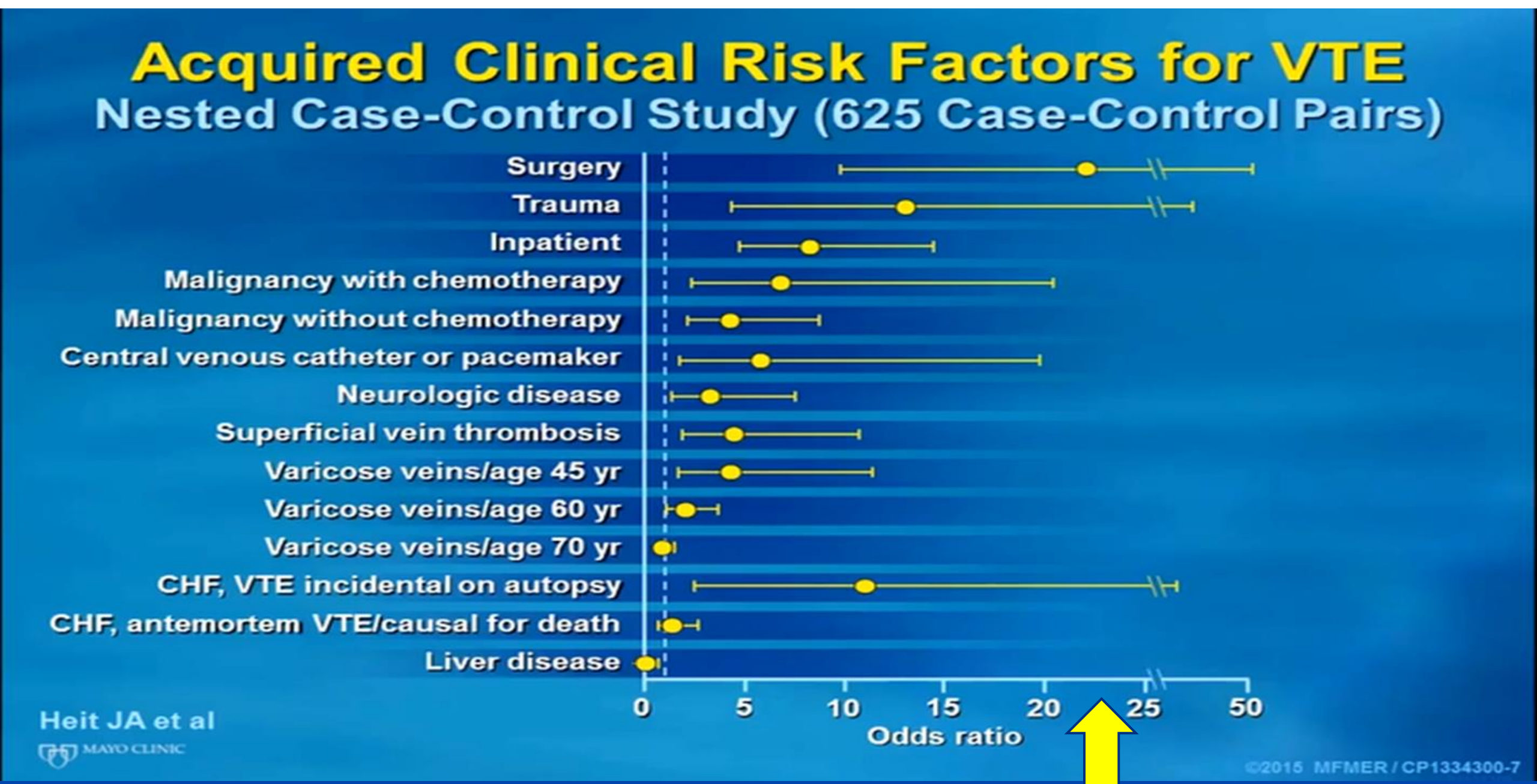
Acquired Clinical Risk Factors for VTE

Nested Case-Control Study (625 Case-Control Pairs)



Our Patient

Treatment vs. Extended Phase

CHEST 2021; 160:e545-e608

Who gets Extended Phase

- In the setting of a ***transient risk factor*** (major or minor), we recommend ***against*** offering extended-phase anticoagulation.

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CHEST 2021; 160:e545-e608

The ASH Choosing Wisely® campaign: five hematologic tests and treatments to question

ASH Recommendations

1. ….transfuse the minimum number of RBCs to relieve symptoms of anemia…
2. ***….do not order thrombophilia testing for VTE occurring in association with a transient risk factor***
3. ….do not routinely insert IVC filters
4. ….do not administer FFP or PCC except in emergency circumstances
5. ….limit surveillance CT scans in asymptomatic patients after curative intent lymphoma treatment…

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Blood 2013;122:3879

75 year old female: DVT following TKA

Will the thrombophilia test results

- explain the thrombosis mechanism? ***No***
- inform management decisions? ***No***
- impact treatment duration? ***No***

75 year old female with left popliteal DVT. ***After 3 months*** of ***apixaban***, what are your recommendations?

1. ***Stop apixaban***
2. Stop apixaban and begin low dose aspirin
3. Continue apixaban at 5 mg twice daily
4. Continue apixaban but reduce dose to 2.5 mg twice daily
5. Stop apixaban and obtain Thrombophilia Testing

Second patient

55 y/o female

One week of exercise intolerance now not able to climb one flight of stairs. This morning, she is not able to take deep breath.

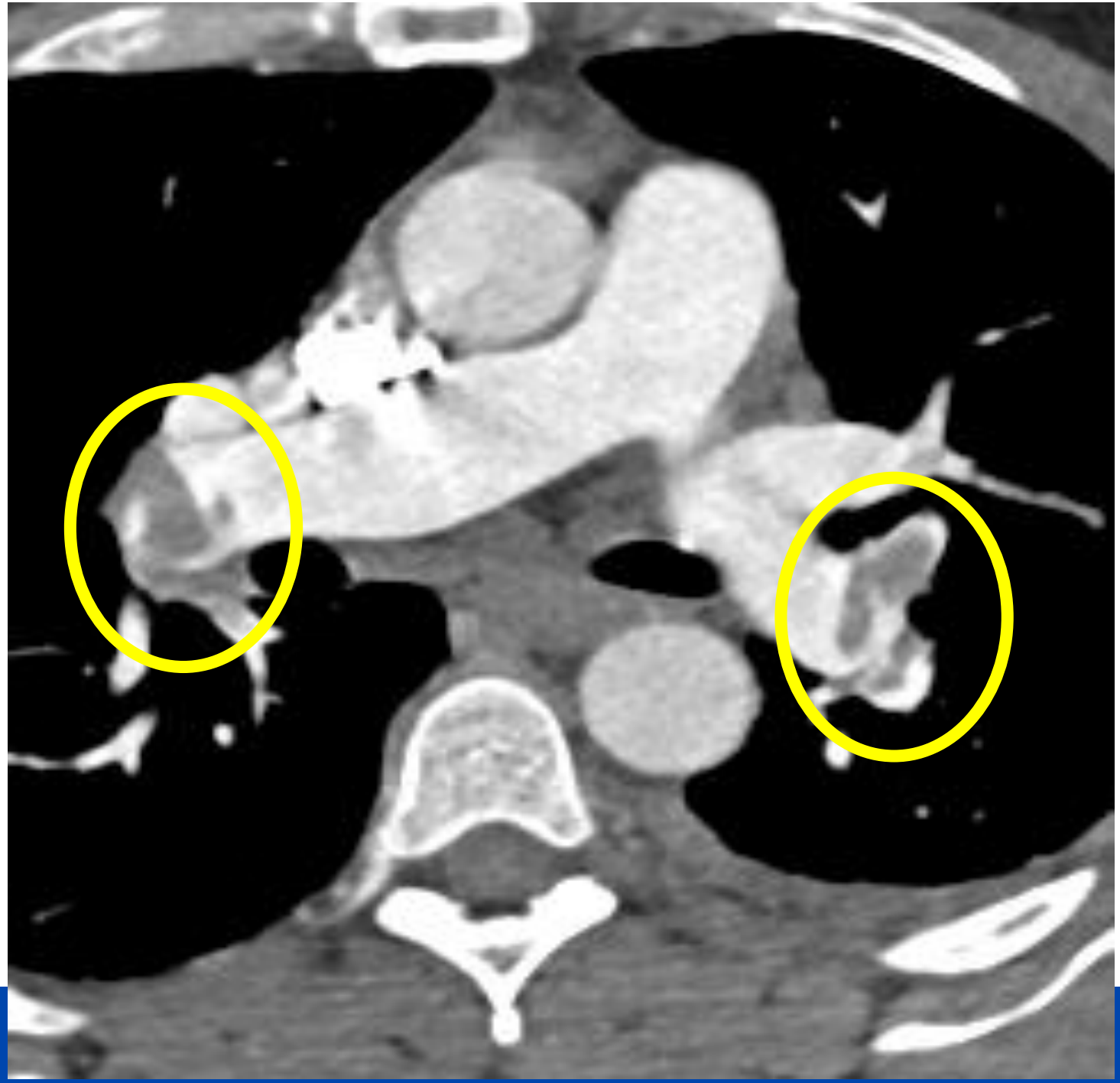
Past history: G4 P4, PCOS (on OCPs)

Examination: Comfortable

BP 150/80 P 77

COR: no JVD or RV lift

Extr: no edema



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55 y/o female

- **Admission Labs:**

Hgb 13.4	(13.2 – 16.6)
WBC 10.0	(3.4 – 9.6)
Platelet 188	(135 – 337)
Creatinine 0.9	
PT INR 1.1	(<1.2)
aPTT 28	(26 – 33)
Ddimer 5730	(<500)

55 year old female treated conservatively and does well and is discharged from the hospital on Xarelto. After 3 months of uneventful AC, what are your recommendations?

1. Repeat CTA for residual thrombus
2. Assess Fibrin D-dimer
3. Stop rivaroxaban
4. Stop rivaroxaban and begin low dose aspirin
5. Continue rivaroxaban at 20 mg
6. Continue rivaroxaban but reduce dose to 10mg
7. Thrombophilia Testing

Who gets Extended Phase

- In the ***absence*** of transient provocation (unprovoked VTE or provoked by persistent risk factor), we recommend offering extended-phase anticoagulation ***with a reduced dose DOAC (apixaban or rivaroxaban)***.

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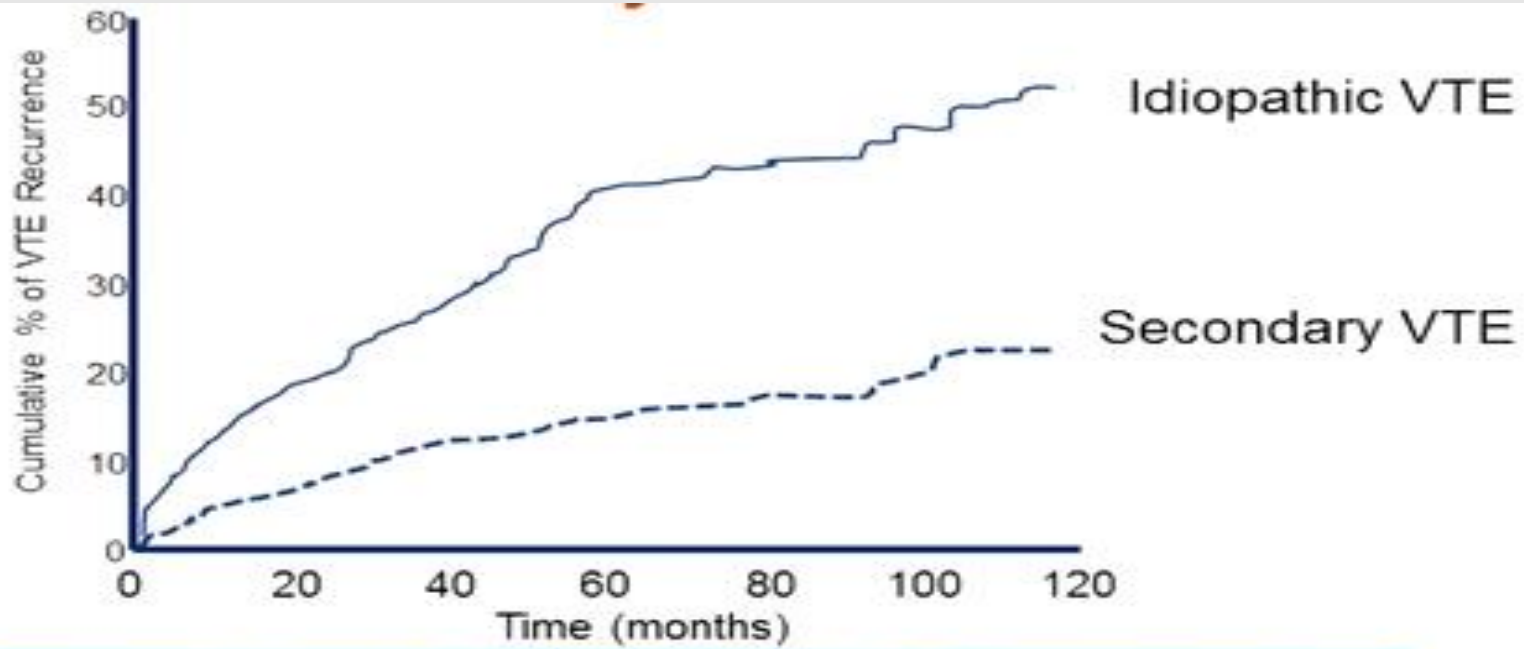
CHEST 2021; 160:e545-e608

Provoked

Unprovoked

Recurrent VTE Rates:

Provoked vs Unprovoked



Cumulative VTE Recurrence	Idiopathic VTE	Secondary VTE
1-year	15%	6.6%
5-year	40.8%	16.1%
10-year	52.6%	22.5%

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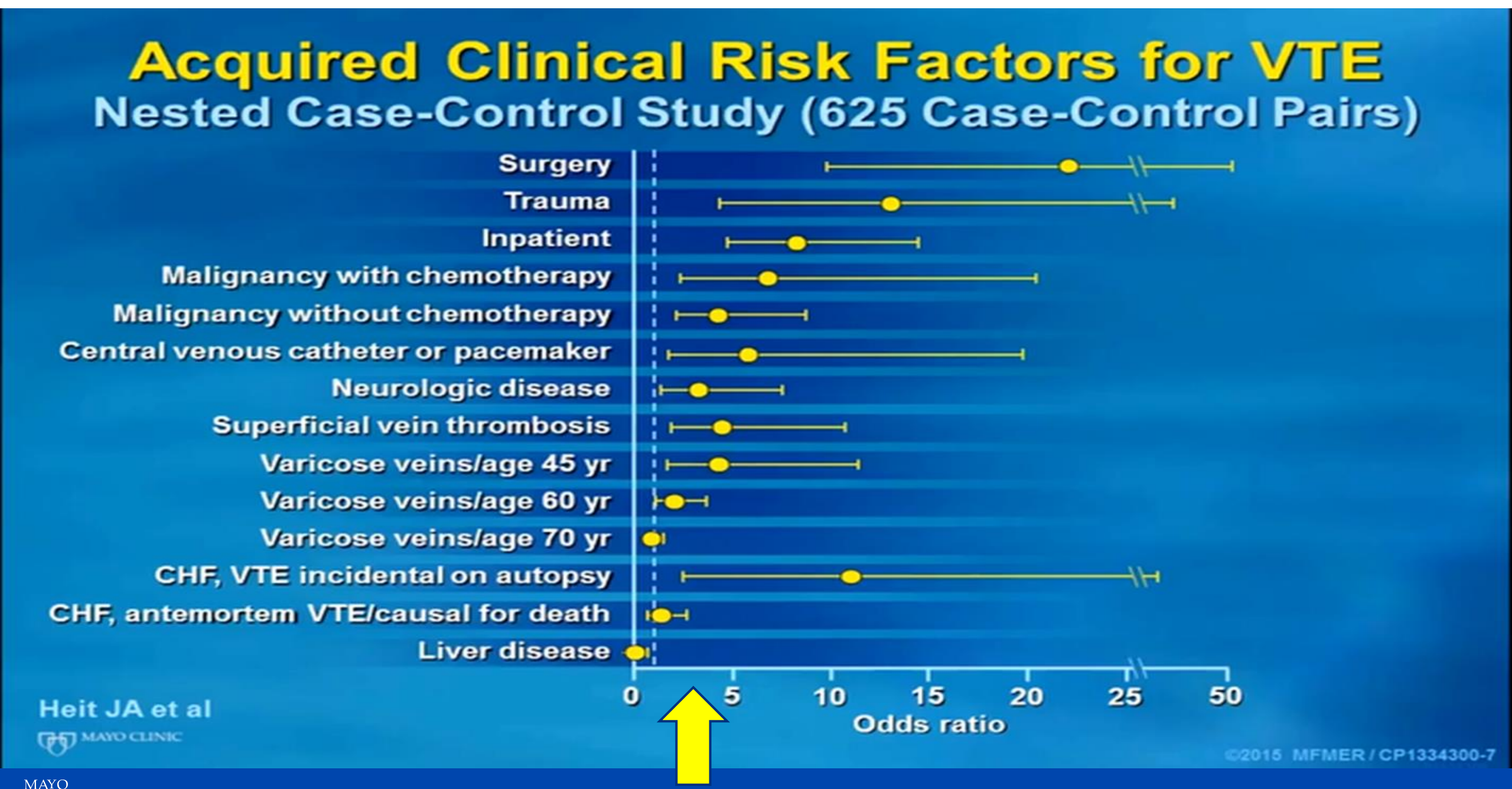
Haematologica 2007;92:199

Acquired Clinical Risk Factors for VTE

Nested Case-Control Study (625 Case-Control Pairs)



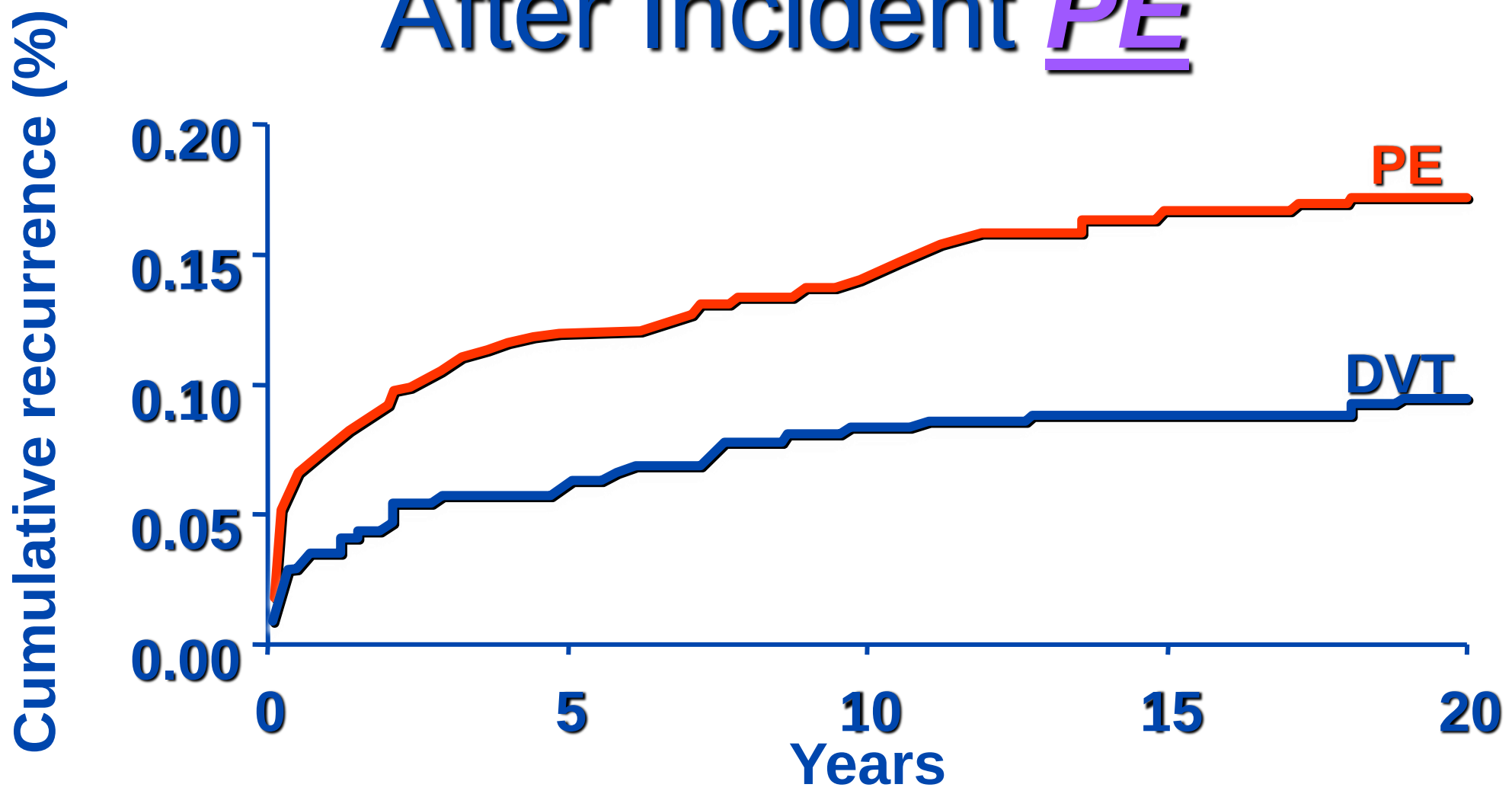
Oral Contraception

Provoked

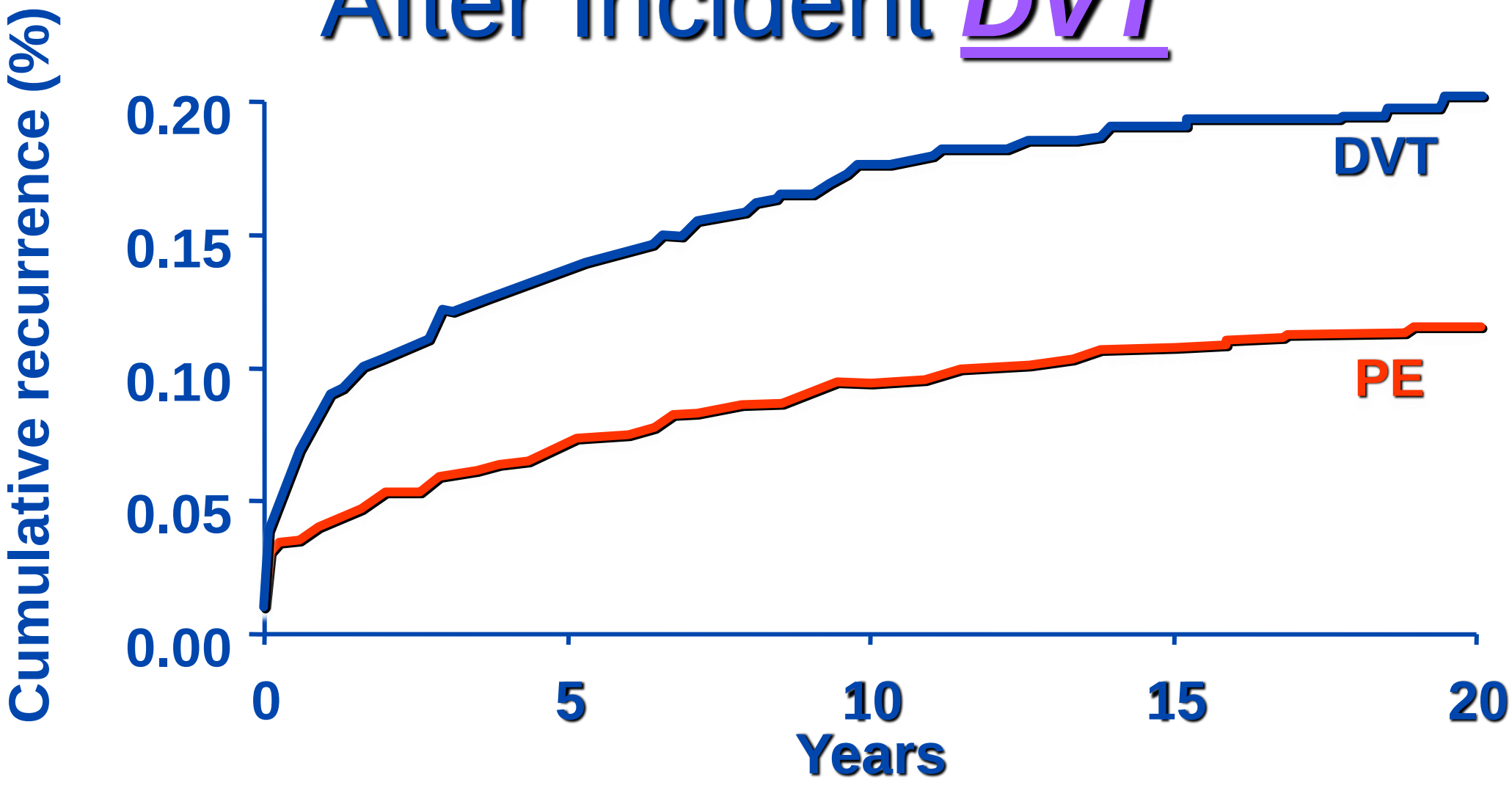
Unprovoked

How do you incorporate the initial ***thrombotic event?***

Cumulative Recurrence of DVT vs PE After Incident ***PE***



Cumulative Recurrence of DVT vs PE After Incident ***DVT***



Recurrence Rates after Anticoagulant Discontinuation

- If ***Calf DVT***, then rates are ***reduced by 50%!***
- If ***Second unprovoked,*** then rates are ***increased by 50%!***

Chest 2016;149;315

And the *Consequences*!!

Recurrent PE

- Case fatality rate ~ 15%

Recurrent DVT

- Case fatality rate ~ 2%

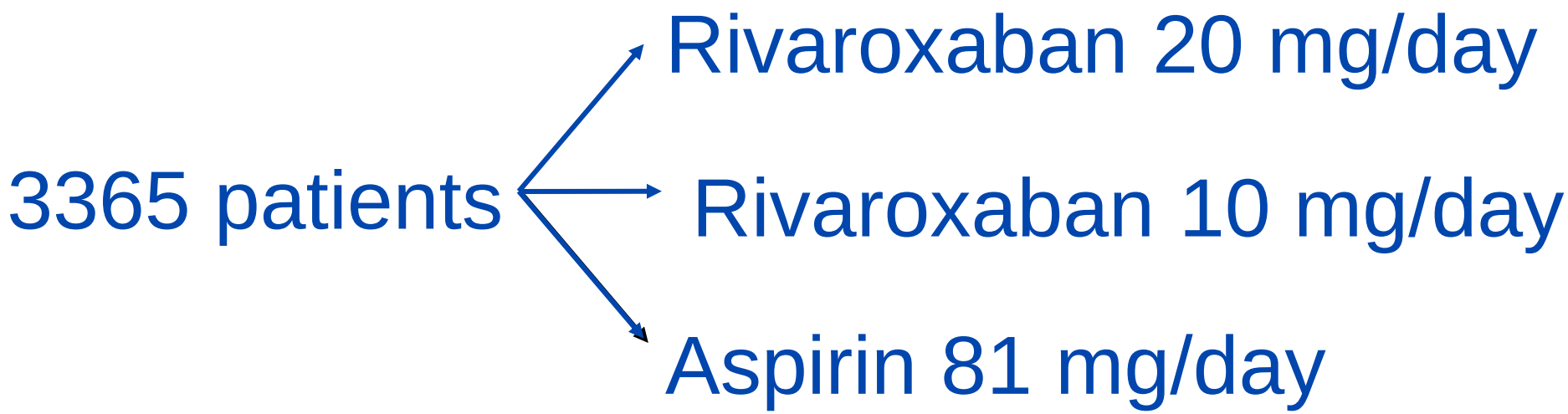
Major Bleeding

- Case fatality rate ~ 9%

Its all about balance!

EINSTEIN Choice
Secondary Preventions Trial

Patients: Sympt proximal DVT/PE; completed 6-12 mos AC



1◦ endpoint: composite sympt VTE recurrence or fatal PE

N Engl J Med 2017;376:1211

EINSTEIN Choice
Secondary Prevention Trial

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Rivaroxaban		Aspirin
	20 mg (N = 1107)	10 mg (N = 1127)	100 mg (N = 1131)
Classification of index venous thromboembolism — no. (%)			
Provoked	666 (60.2)	647 (57.4)	663 (58.6)
Unprovoked	441 (39.8)	480 (42.6)	468 (41.4)

EINSTEIN Choice VTE Risk

The following pre-specified risk factors can be entered on the CRF:

Previous episode(s) of VTE

Idiopathic VTE

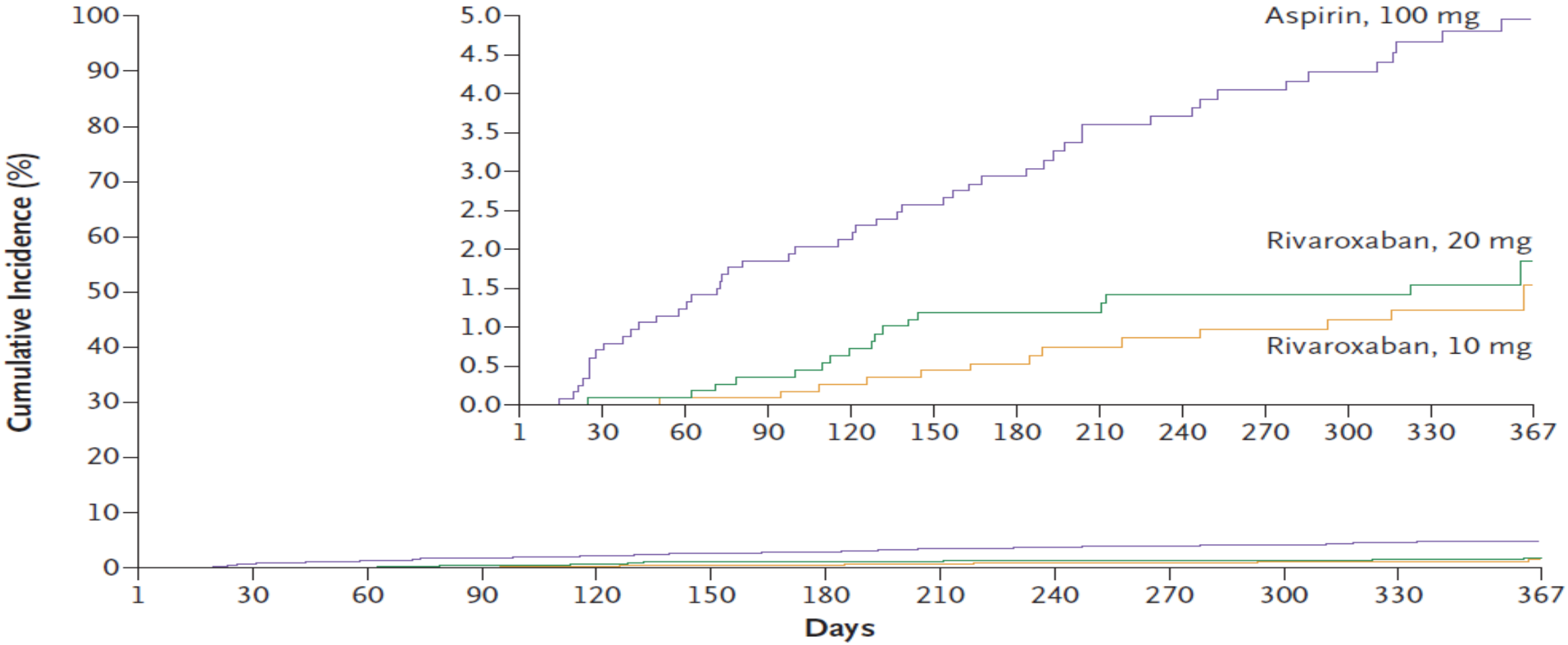
Known risk factor for VTE

If known risk factor:

- Recent surgery or trauma
- Prolonged Immobilization
- Use of estrogen containing drugs
- Puerperium
- Active cancer
- Antithrombin deficiency
- Factor V Leiden gene mutation
- Hyperhomocysteinaemia
- Antiphospholipid antibodies
- Protein C deficiency
- Protein S deficiency
- Prothrombin gene mutation

Other known factors can be specified as free text by the investigators.

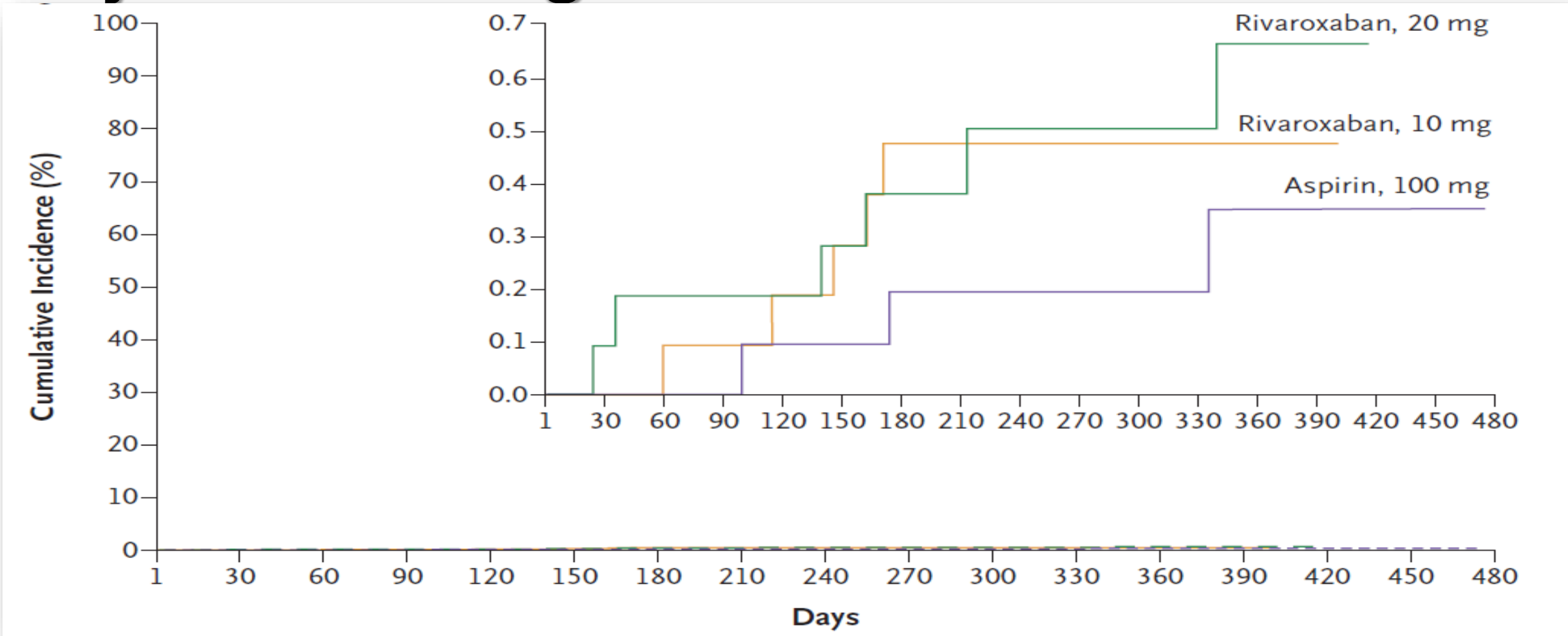
VTE Recurrence *favors Rivaroxaban*



HR (riva 20 vs. asa), 0.34 (0.20 - 0.59) p<0.001
HR (riva 10 vs. asa), 0.26 (0.14 - 0.47) p<0.001

N Engl J Med 2017;376:1211

Major Bleeding Rates *Low* and *Similar*



Major Bleeding Rates:

Riva 20 = 0.5%,
Riva 10 = 0.4%,
ASA = 0.3%

N Engl J Med 2017;376:1211

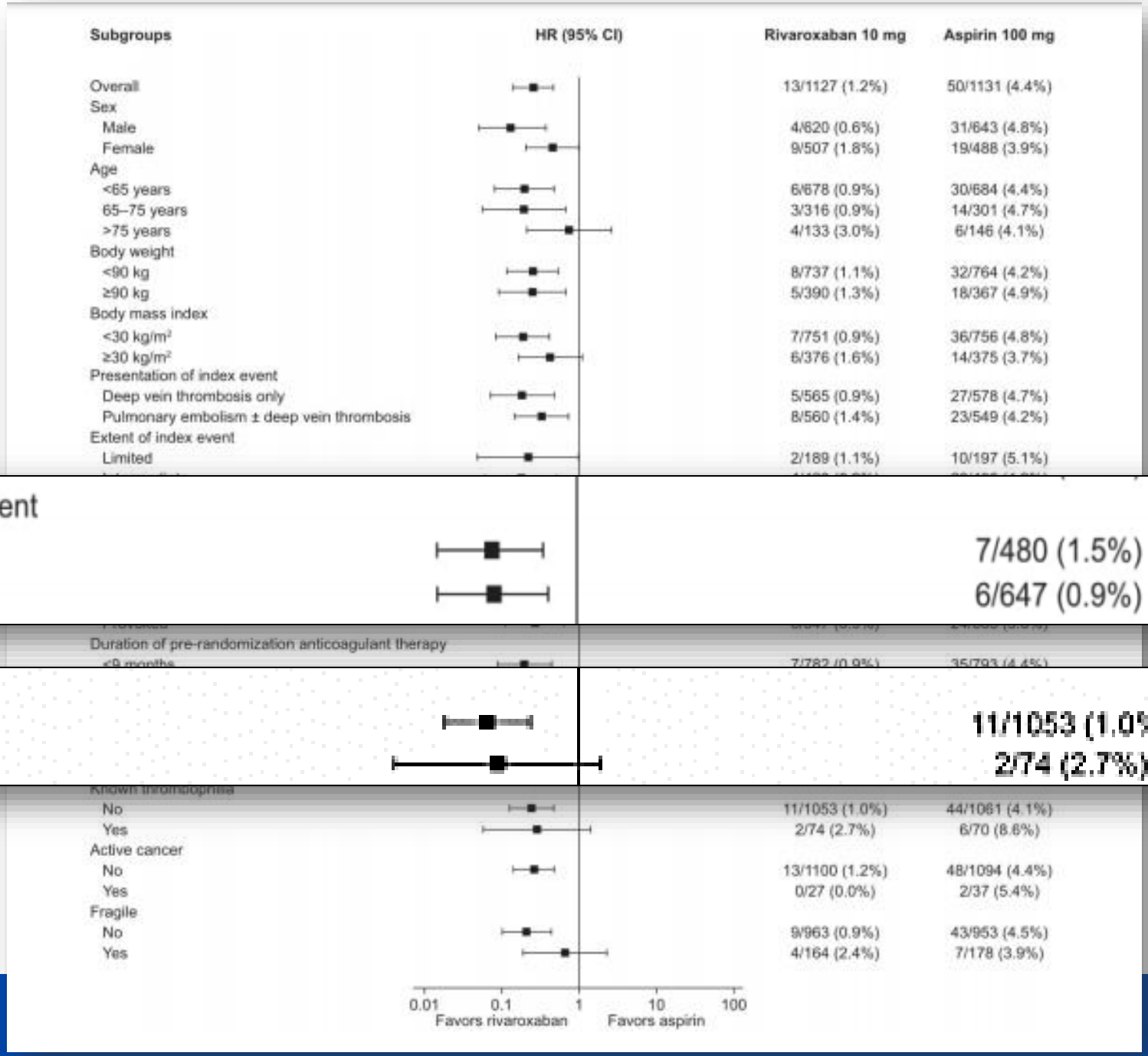
EINSTEIN Choice

Recurrent VTE*

	Provoked	Unprovoked
Riva 20 mg	1.4%	1.8%
Riva 10 mg	0.9%	1.5%
ASA 100 mg	3.6%	5.6%

*Event rates are @ 1 year

N Engl J Med 2017;376:1211



EINSTEIN Choice

Major Bleeding*

	Provoked	Unprovoked
Riva 20 mg	0.3%	0.9%
Riva 10 mg	0.5%	0.4%
ASA 100 mg	0.3%	0.2%

*Event rates are @ 1 year

N Engl J Med 2017;376:1211

55 year old female: Extensive PE

Will the thrombophilia test results

- explain the thrombosis mechanism? ***Maybe***
- inform management decisions? ***No***
- impact treatment duration? ***No***

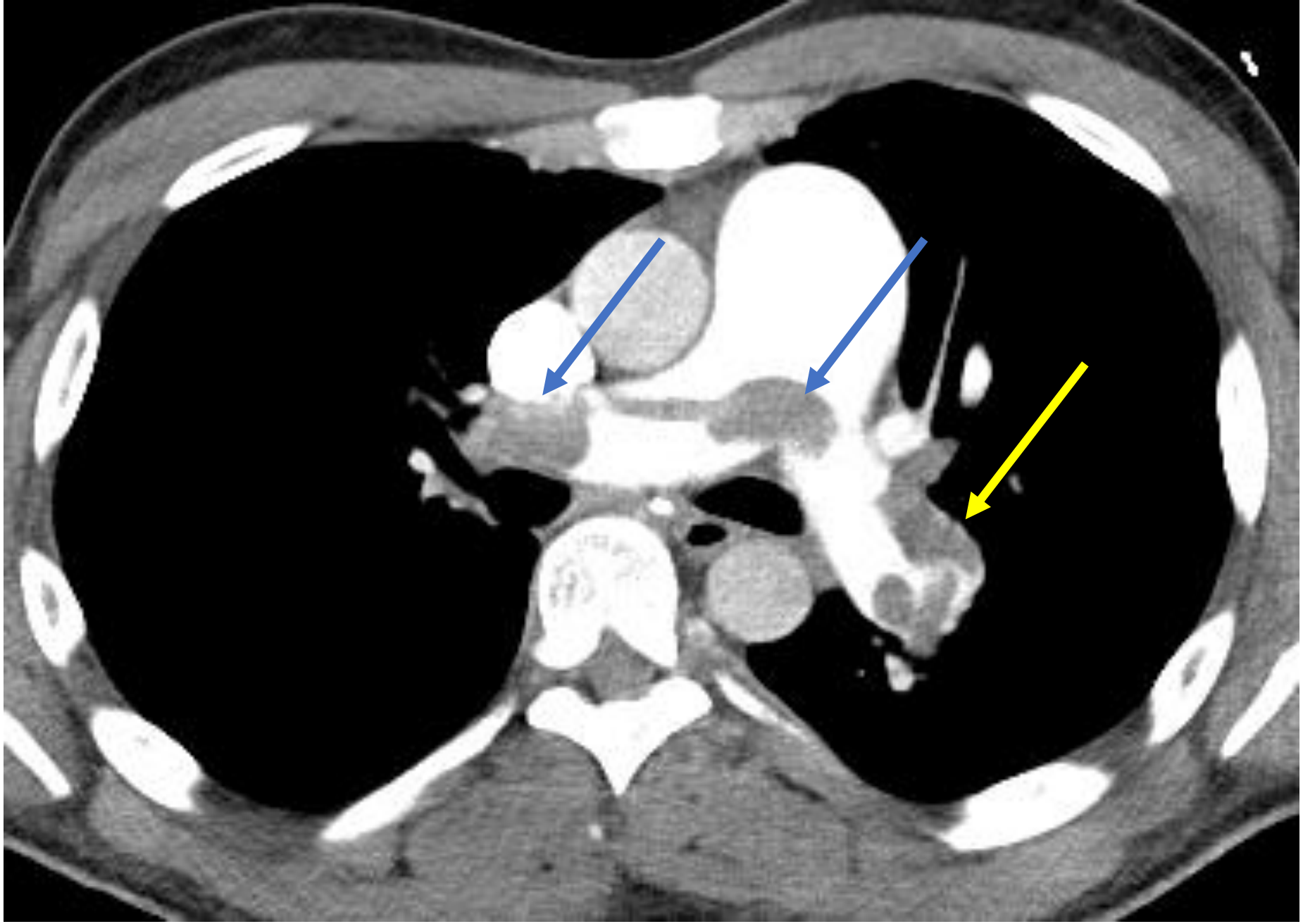
55 year old female treated conservatively and does well and is discharged from the hospital on Xarelto. After 3 months of uneventful AC, what are your recommendations?

1. Repeat CTA for residual thrombus
2. Assess Fibrin D-dimer
3. Stop rivaroxaban
4. Stop rivaroxaban and begin low dose aspirin
5. Continue rivaroxaban at 20 mg
6. ***Continue rivaroxaban but reduce dose to 10mg***
7. Thrombophilia Testing

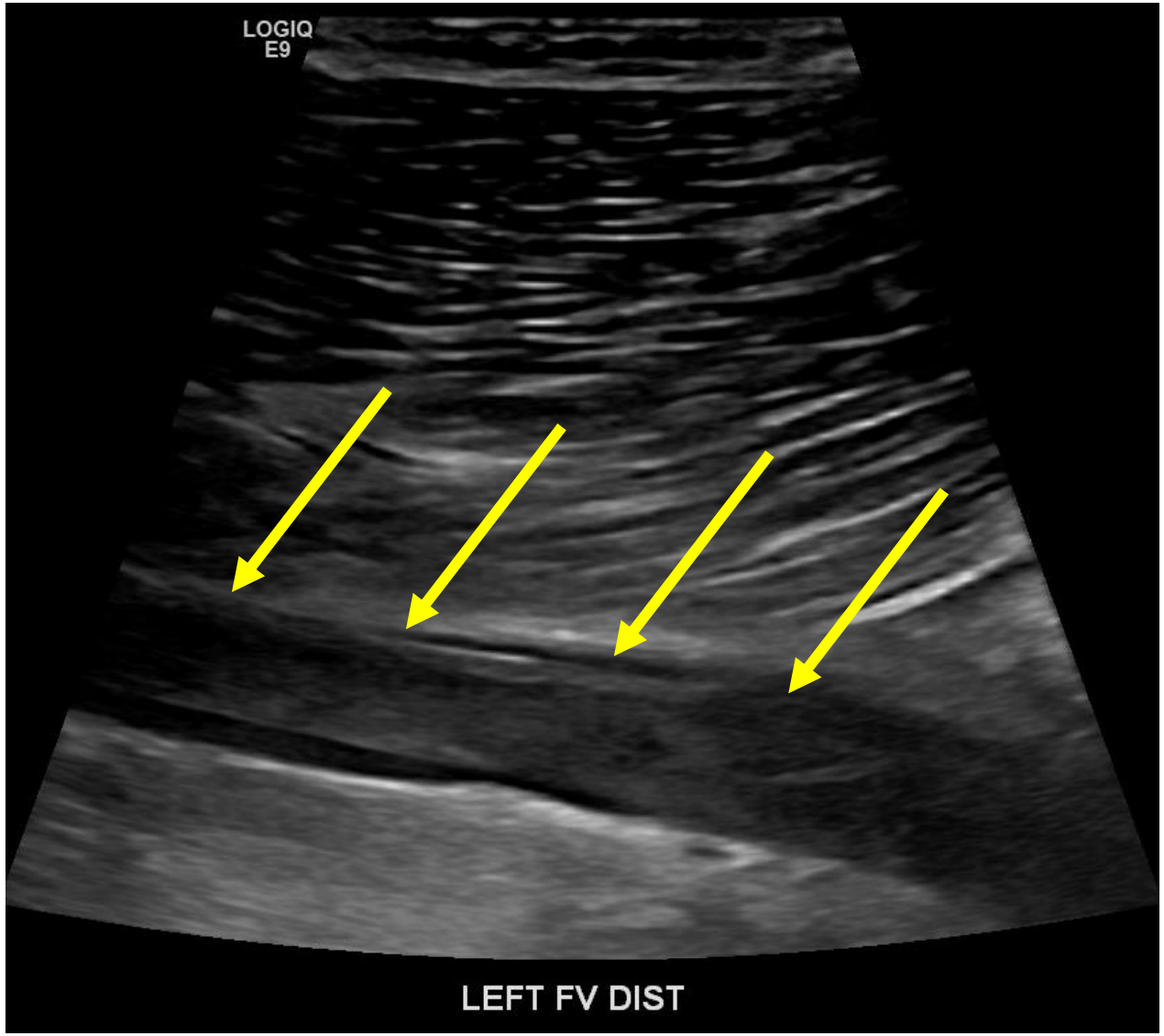
Third patient

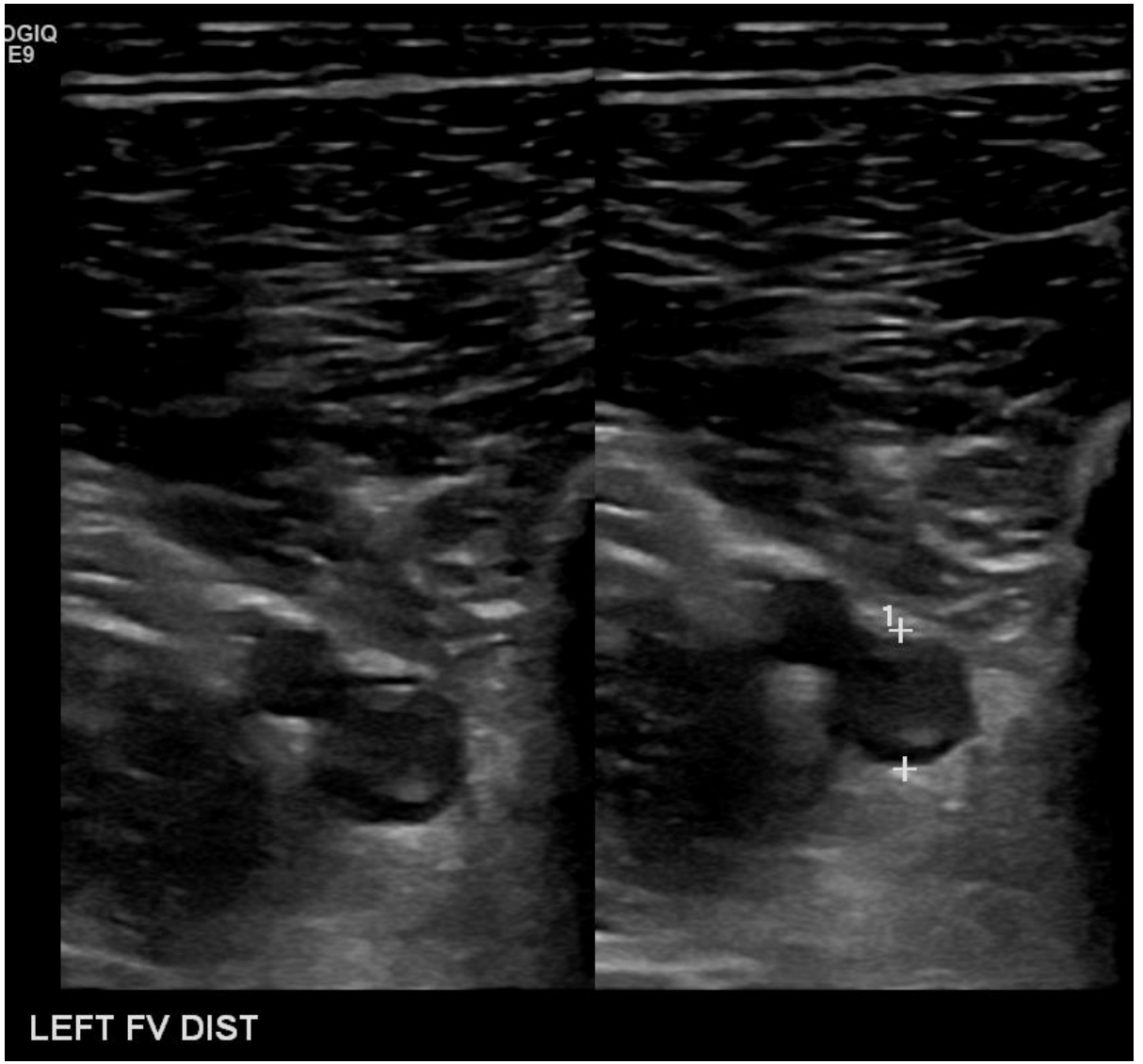
23 year-old D1 College Basketball Player

- June 2021 — COVID 19 Loss of smell/taste, malaise and fatigue for 1 – 2 weeks. Afterwards, he noted difficulty resuming athletics.
- Jan 2022 — Progressive exertional dyspnea. Not able to play more than 2 - 3 minutes at a time.
- April 2022 — “Exercise induced asthma”; treated with inhalers and steroids
- June 2022 — No longer able to walk across the room.



June 2022





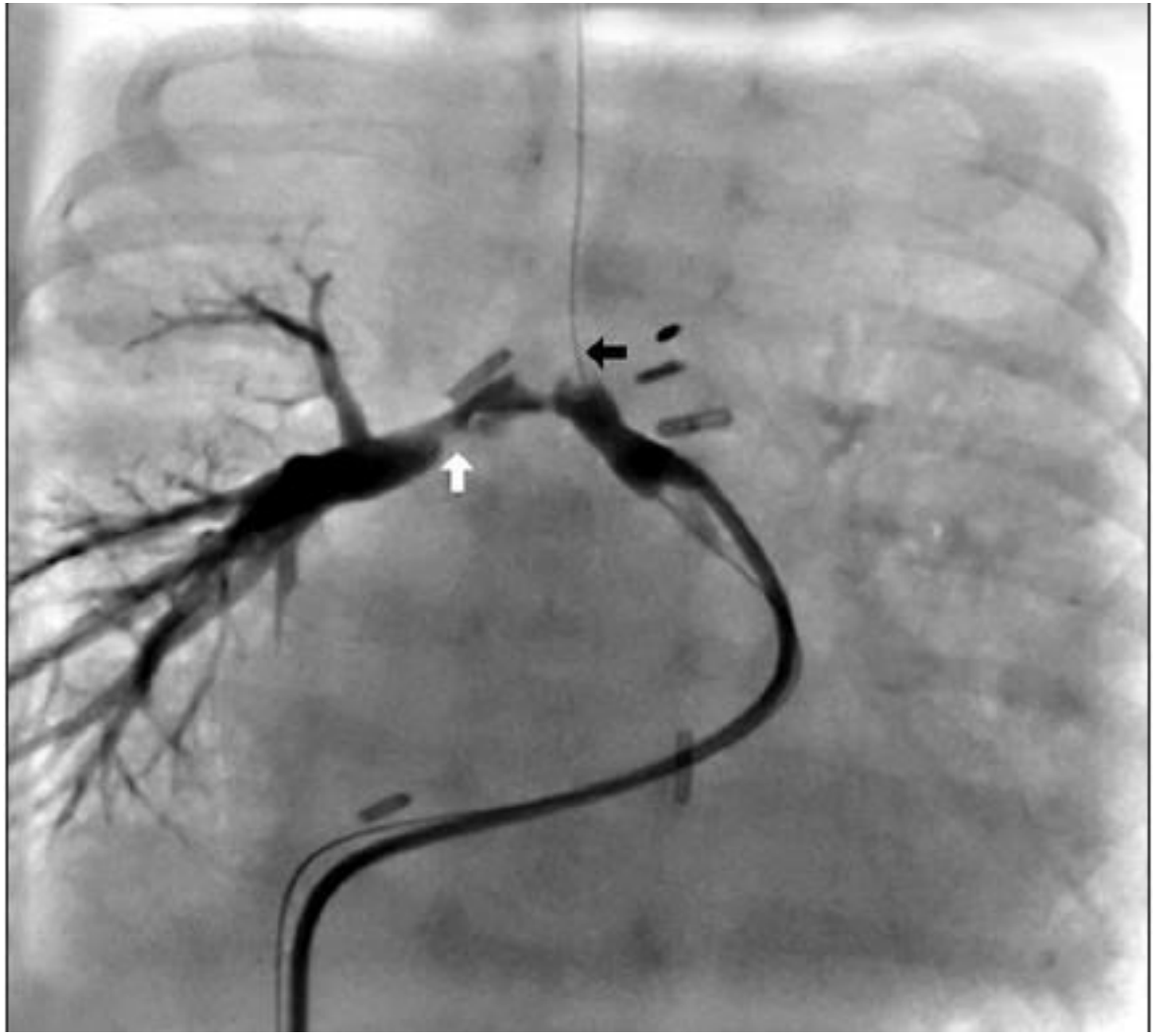
Left Femoral Vein

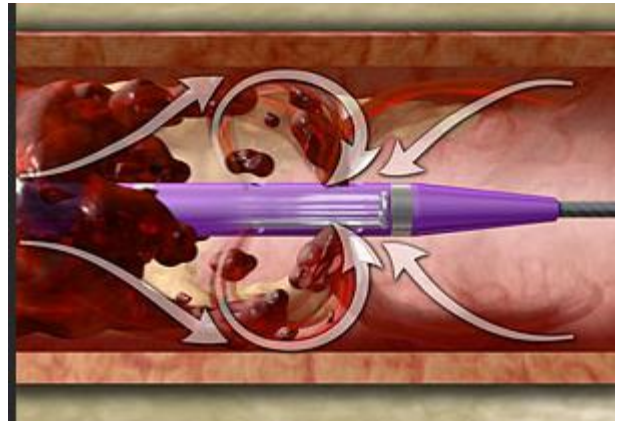
23 year-old male

- **Admission Labs:**

Hgb 15.4	(13.2 – 16.6)
WBC 11.0	(3.4 – 9.6)
Platelet 103	***(135 – 337)***
Creatinine 0.9	
PT INR 1.1	(<1.2)
aPTT 37	***(26 – 33)***
Ddimer 7650	***(<500)***

Mechanical Thrombectomy (without Lytic therapy)





Post procedural:
Enoxaparin 1 mg/kg BID

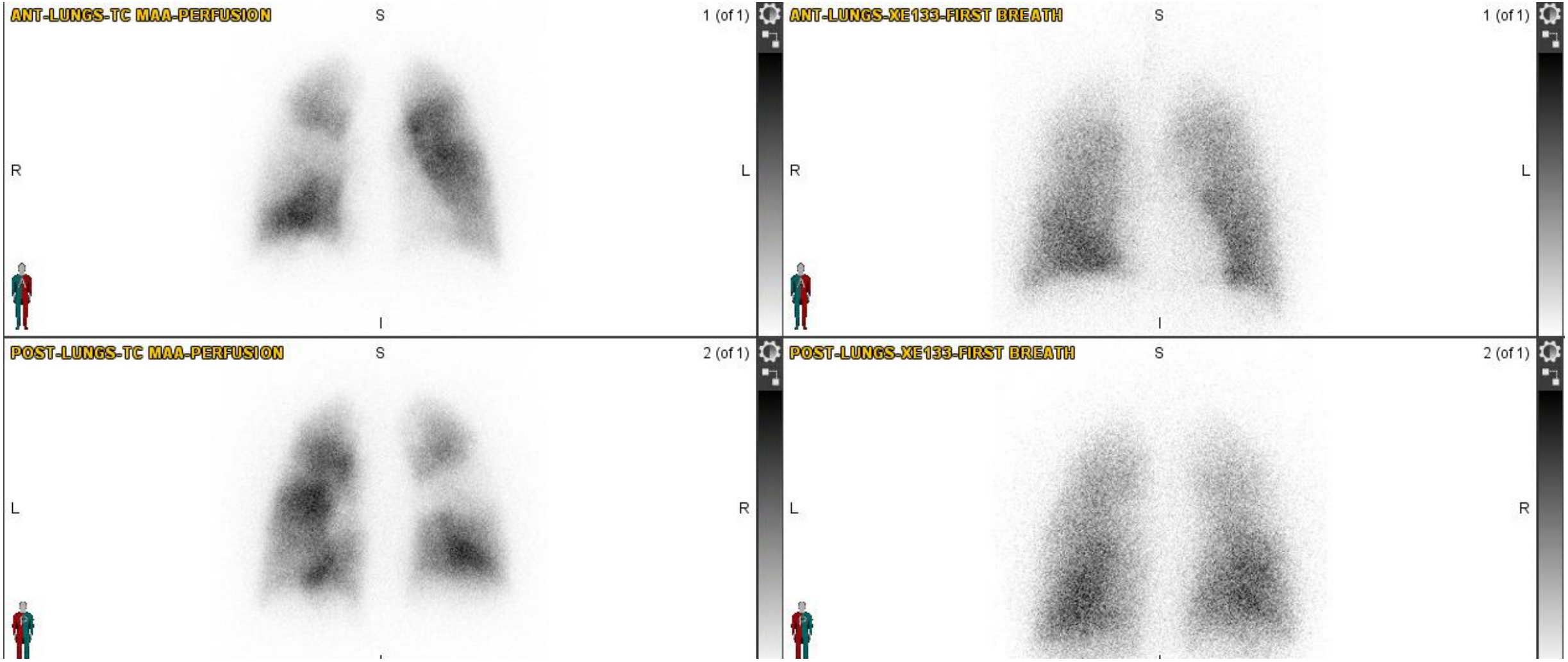
23 year-old D1 College Basketball Player

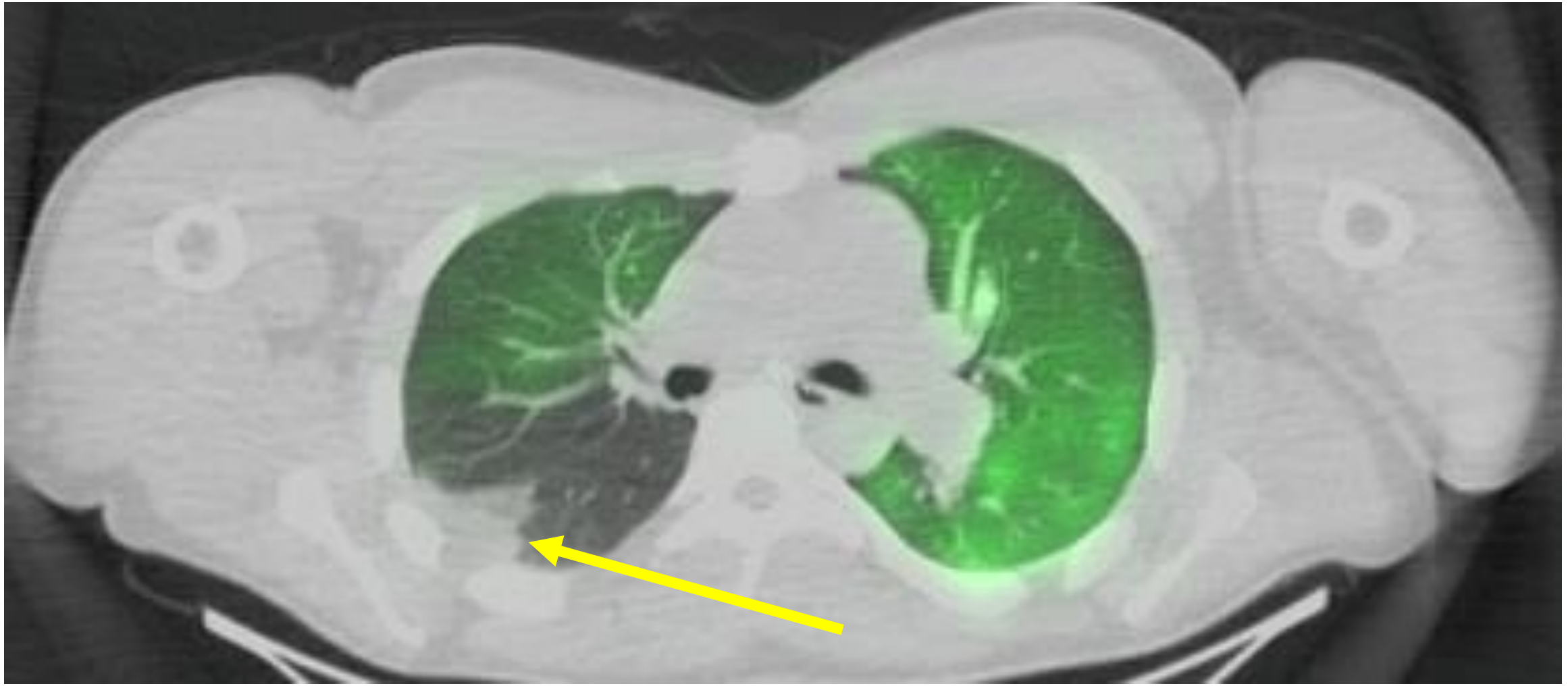
- July 2022 Discharged from hospital on ***Eliquis***
- Oct 2022 He can walk/jog for 30 minutes, leisurely pace.
  Mayo Clinic Evaluation.

VQ Spect CT October 2022

Perfusion imaging

Ventilation imaging





"Multiple bilateral perfusion defects
"New" peripheral wedge-shaped pulmonary infarction"

Transthoracic Echo

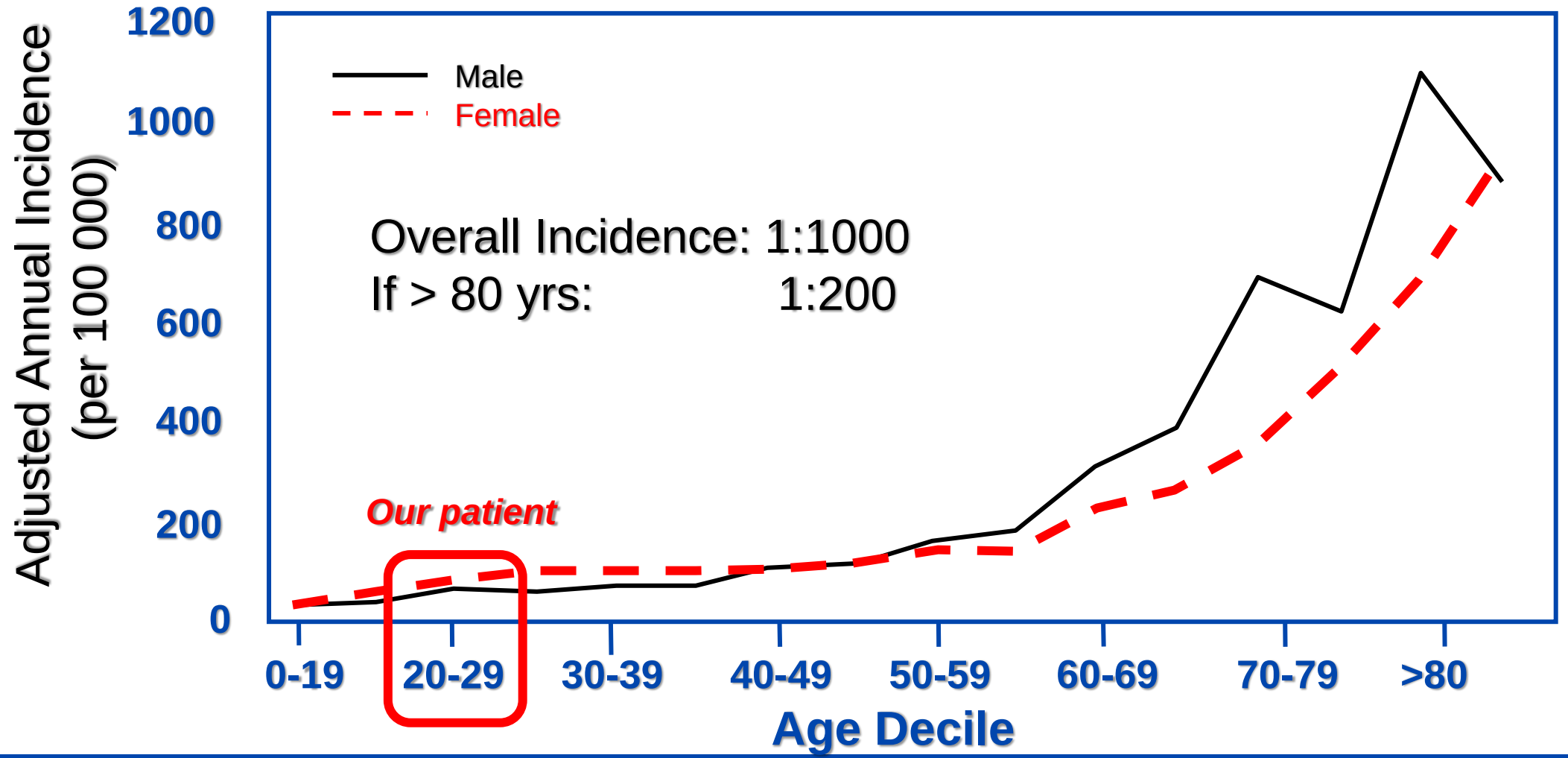
- Moderately enlarged right ventricle
- Moderately reduced right ventricular systolic function
- Estimated RVSP 32 mmHg (systolic BP 150 mmHg).

23 year old male

Will the thrombophilia test results

- explain the thrombosis mechanism?
- inform management decisions?
- impact treatment duration?

Venous thromboembolism: Disease of the Elderly



Arch Int Med 1998:585

Is this simply COVID 19?

Thrombosis Research 207 (2021) 150–157

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Timing of venous thromboembolism diagnosis in hospitalized and non-hospitalized patients with COVID-19

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ARTICLE INFO

Keywords:
SARS-CoV-2
COVID-19
Venous thromboembolism
Deep vein thrombosis
Pulmonary embolism

ABSTRACT

Background: The reported incidence of venous thromboembolism (VTE) in COVID-19 patients varies widely depending on patient populations sampled and has been predominately studied in hospitalized patients. The goal of this study was to assess the evolving burden of COVID-19 and the timing of associated VTE events in a systems-wide cohort.

Methods: COVID-19 PCR positive hospitalized and non-hospitalized patients ≥18 years of age tested between 1/1/2020 through 12/31/2020 were retrospectively analyzed using electronic medical records from multiple states across the Mayo Clinic enterprise.

Radiology reports within 90 days before and after confirmed COVID-19 diagnosis were examined for VTE outcomes using validated Natural Language Processing (NLP) algorithms.

Results: A 29-fold increased rate of VTE compared to the pre-COVID-19 period was noted during the first week following the first positive COVID-19 test (RR: 29.39; 95% CI 21.77-40.03). The rate of VTE steadily decreased and returned to baseline by the 6th week. Among 366 VTE events, most occurred during (n = 243, 66.3%) or after (n = 111, 30.3%) initial hospitalization. Only 11 VTE events were identified in patients who did not require hospitalization (3.0% of total VTE events). VTE and mortality increased with advancing age with a pronounced increased each decade in older patients.

Conclusion: We observed a profoundly increased risk of VTE within the first week after positive testing for COVID-19 that returned to baseline levels after 6 weeks. VTE events occurred almost exclusively in patients who were hospitalized, with the majority of VTE events identified within the first days of hospitalization.

1. Introduction

Severe acute respiratory syndrome (SARS) Coronavirus 2 (SARS-CoV-2), also known as COVID-19, has spread around the world causing significant morbidity and mortality [1] and has created significant challenges for health care systems and staff [2,3]. COVID-19 daily mortality rates have exceeded those from cardiovascular disease and cancer [4] with a unique and alarming association with thrombosis [5]. Hematologic derangements that constitute a form of coagulopathy often manifest in the form of venous thromboembolism (VTE) [6–8]. Numerous reports from various countries have demonstrated a high incidence of VTE in COVID-19 patients [9–11], however, there is a lot of heterogeneity reported in the risk of VTE [12]. Furthermore, the precise timing of VTE events as they relate to the diagnosis of COVID-19 has not been well studied. Much of the published data shows a high incidence of VTE in critically ill hospitalized patients, the group with the most severe presentations and most comorbidities. While managing VTE risk in hospitalized patients is essential, an exclusive focus on this setting limits

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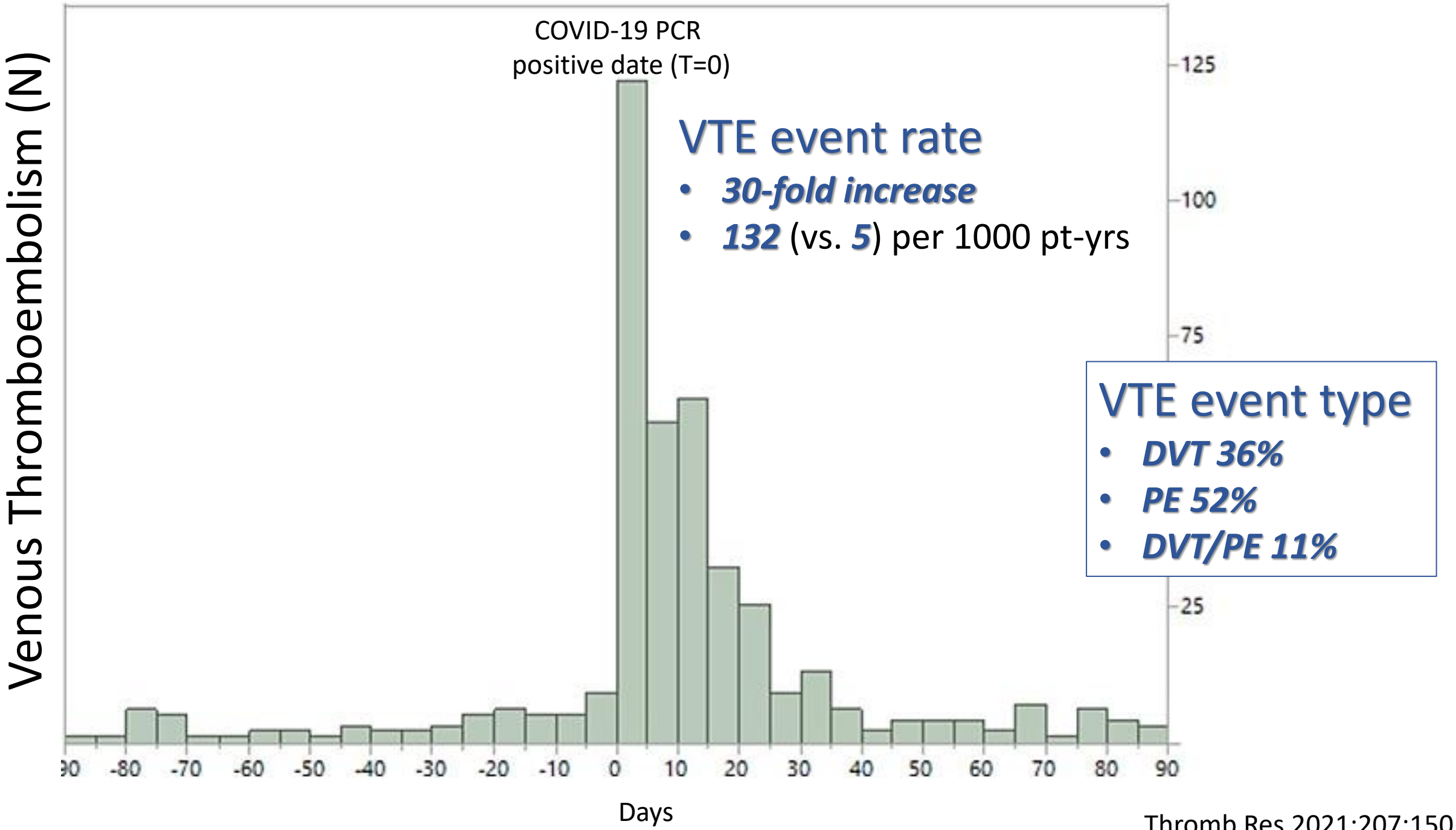
https://doi.org/10.1016/j.thromres.2021.09.021
Received 2 July 2021; Received in revised form 13 September 2021; Accepted 15 September 2021
Available online 7 October 2021

Mayo Clinic Enterprise Data

- 54,354 COVID-19 PCR confirmed patients
- 1/1/2020 – 12/31/2020
- 8% hospitalized (92% outpatient)

Thromb Res 2021;207:150

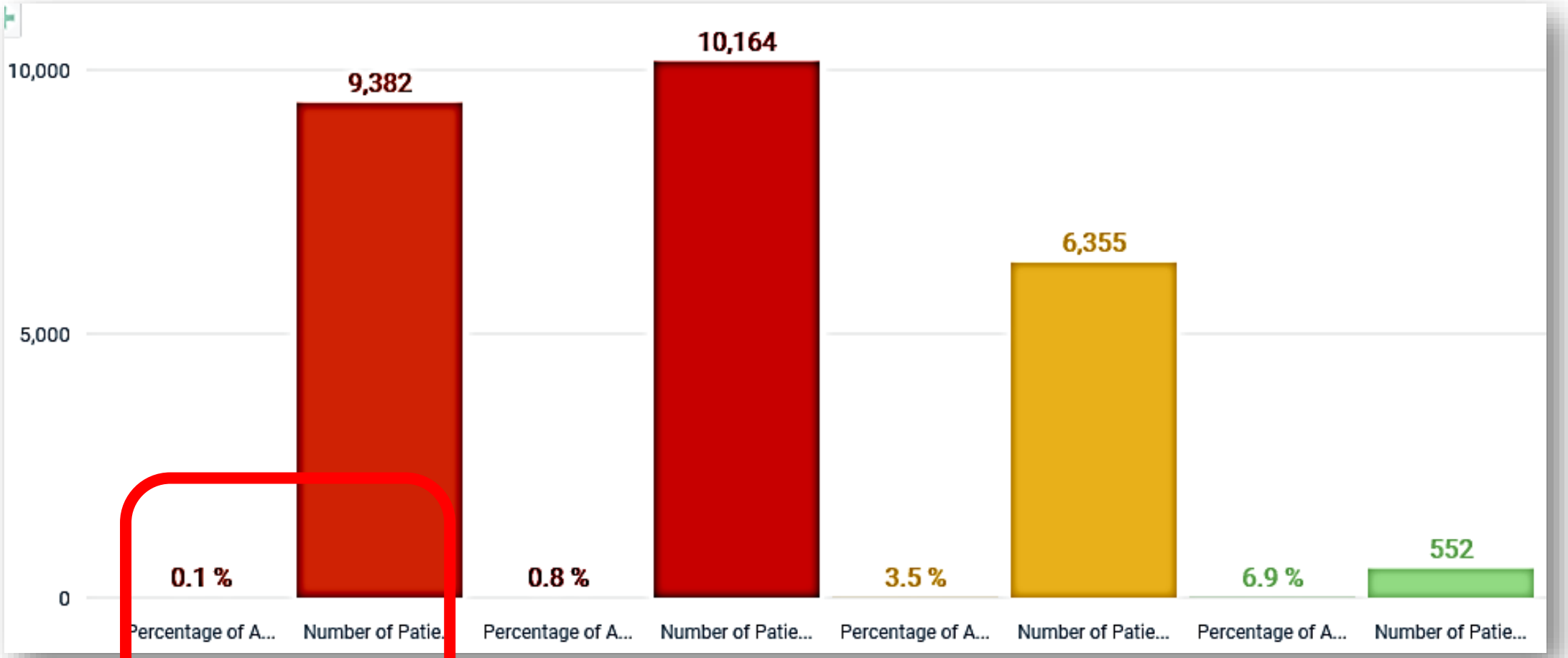


Thromb Res 2021;207:150

Mayo Enterprise Numbers

VTE stratified by Age Quartile

COVID 19 Case number



VTE Rate (%)

< 27 yrs | 27- 54 yrs | 54-82 yrs | > 82 yrs

Our Patient

Age Quartiles

Thromb Res 2021;207:150

VTE following COVID 19 Infection

- Hospitalized Patients
  - 5.6% developed VTE while hospitalized
  - 2.6% had VTE following dismissal
- Ambulatory patients
  - VTE rate 0.02%

Our Patient

Thromb Res 2021;207:150

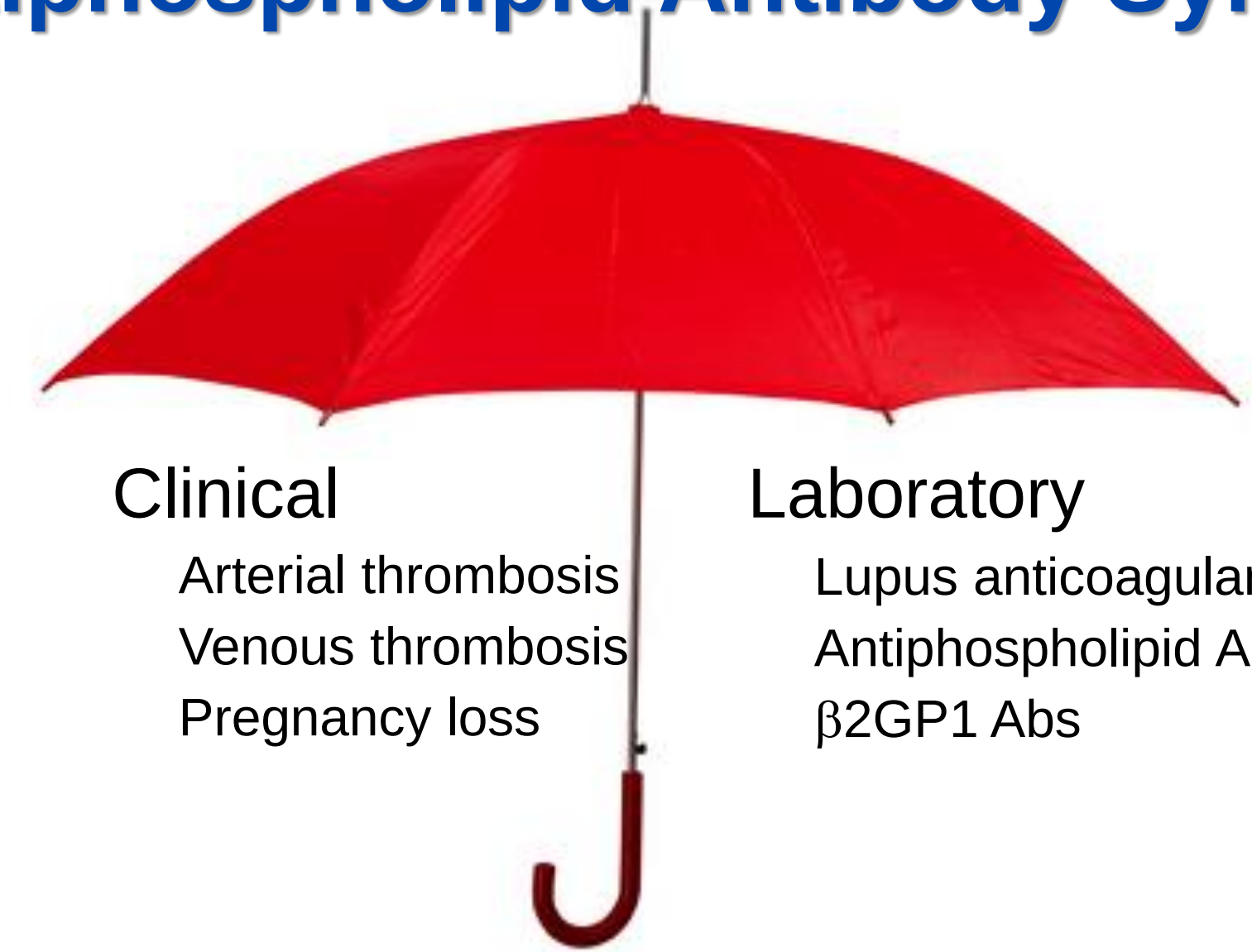
23 year-old male

- **Admission Lab:**

Hgb 15.4	(13.2 – 16.6)
WBC 11.0	(3.4 – 9.6)
Platelet 103	(150 – 337)
Creatinine 0.9	
PT INR 1.1	(<1.2)
aPTT 37	(26 – 33)
Ddimer 7650	(<500)

Lupus Anticoagulant and APS

Antiphospholipid Antibody Syndrome



Clinical

- Arterial thrombosis
- Venous thrombosis
- Pregnancy loss

Laboratory

- Lupus anticoagulant
- Antiphospholipid Abs
- β2GP1 Abs

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J Thromb Haemost 2006;4:295

Look for Clues!

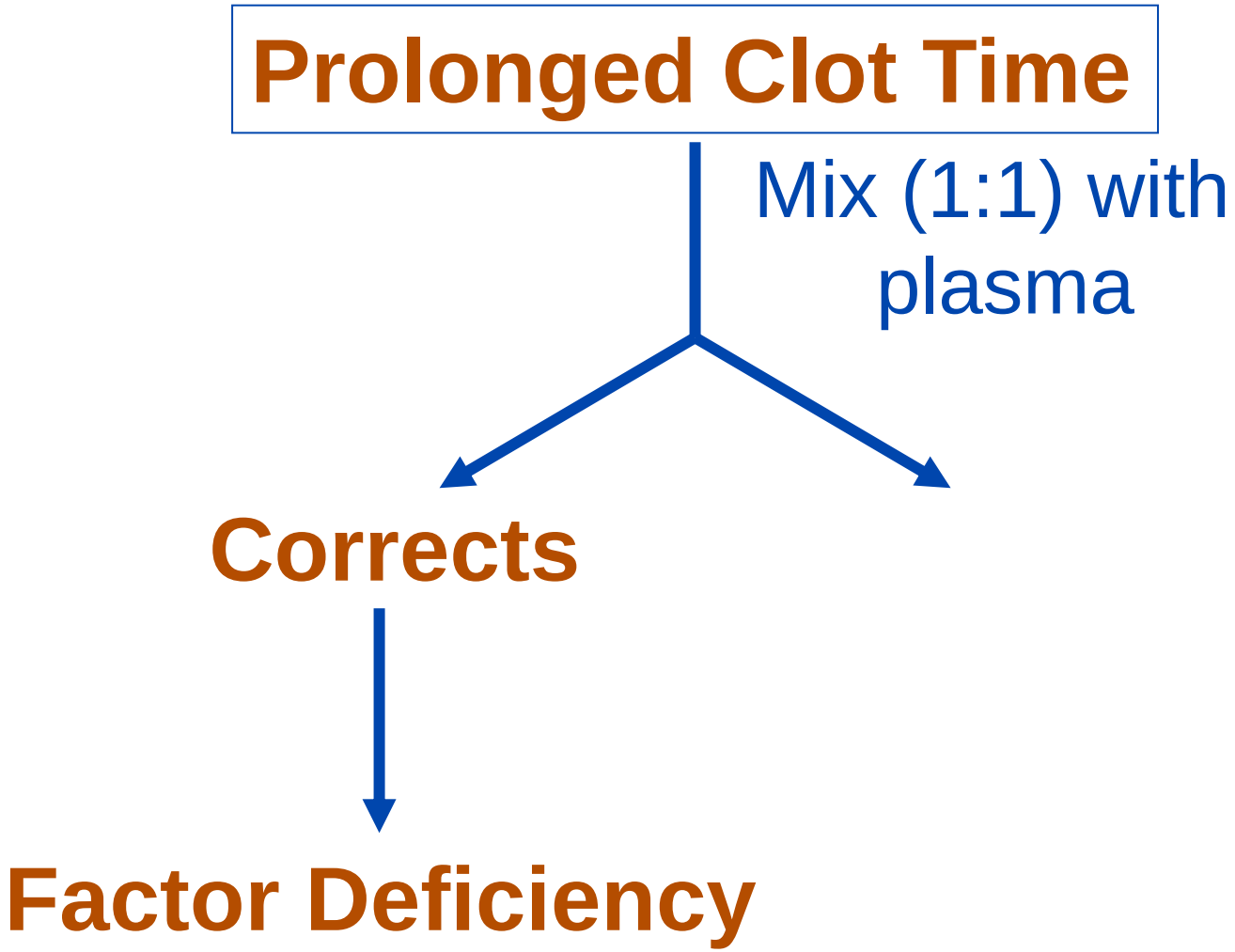
- Baseline prolongation of clotting assays
- Thrombocytopenia
- Recurrent fetal demise
- Unexplained arterial thrombosis
- Valvular vegetations (nonbacterial thrombotic endocarditis)
- DOAC treatment failure
- Note! ***Do not screen*** for APS on all patients prior to starting DOAC therapy

How do you test/interpret testing for a ***lupus anticoagulant***?

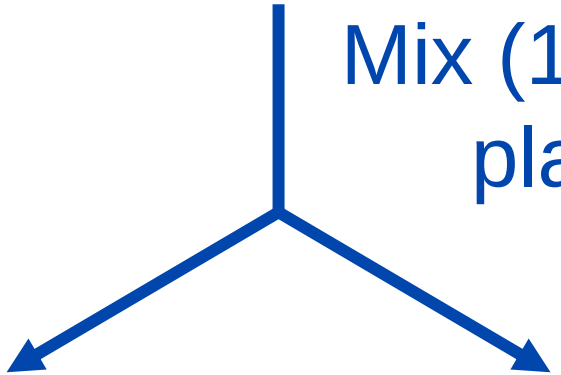
4 easy steps

Step 1.

Is the clotting time (***PT, aPTT, DRVVT, TT***) prolonged?



Prolonged Clot Time



Does not Correct…

"inhibited"

Step 2.

Is there heparin or DTI present?

DTI: direct thrombin inhibitor

Heparin or DTI present?

aPTT	37 sec (23-33 s)
mix	35 sec
Thrombin Time	22 sec (18-25 s)

Interpretation: No anticoagulant present

DTI: direct thrombin inhibitor

Step 3.

Is the inhibited assay phospholipid dependent?

Prolonged Clot Time

Mix (1:1) with plasma

Doesn't correct

Add excess phospholipid

"Improves"

Lupus anticoagulant

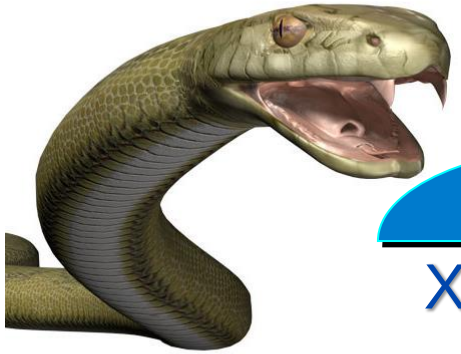
Our Patient

aPTT	37 sec (23-33 s)
mix	35 sec
Phospholipid	30 sec
Saline control	45 sec

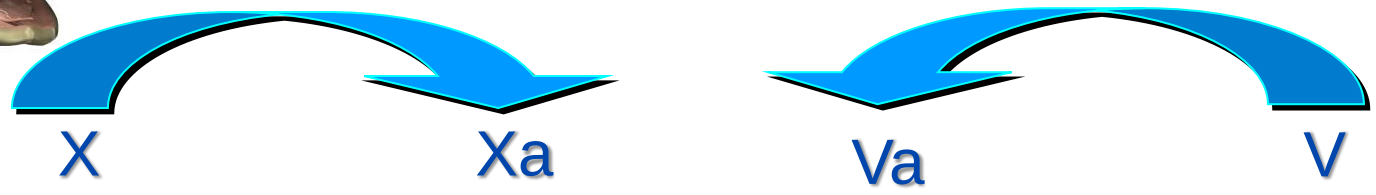
Interpretation: Lupus Anticoagulant

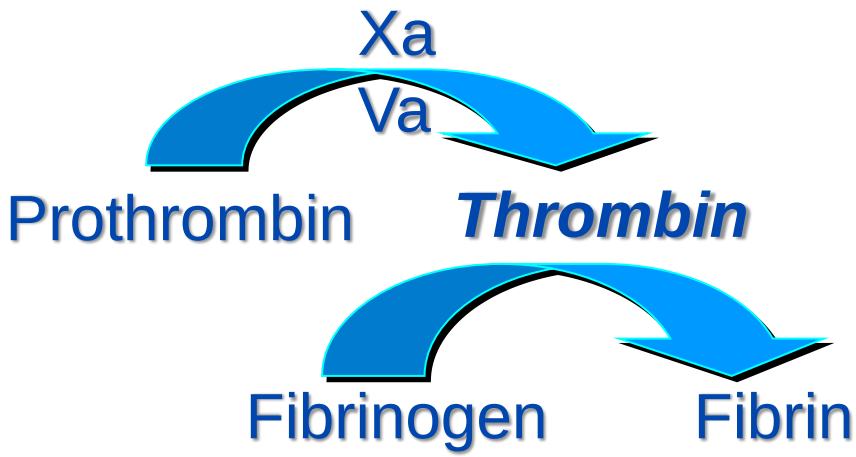
DTI: direct thrombin inhibitor

Dilute Russel Viper Venom Time (DRVVT)



Russel viper





Confounders:

DOAC Xa inhibitor (apixaban, rivaroxaban)
DOAC thrombin inhibitor (dabigatran)
Warfarin

Our Patient

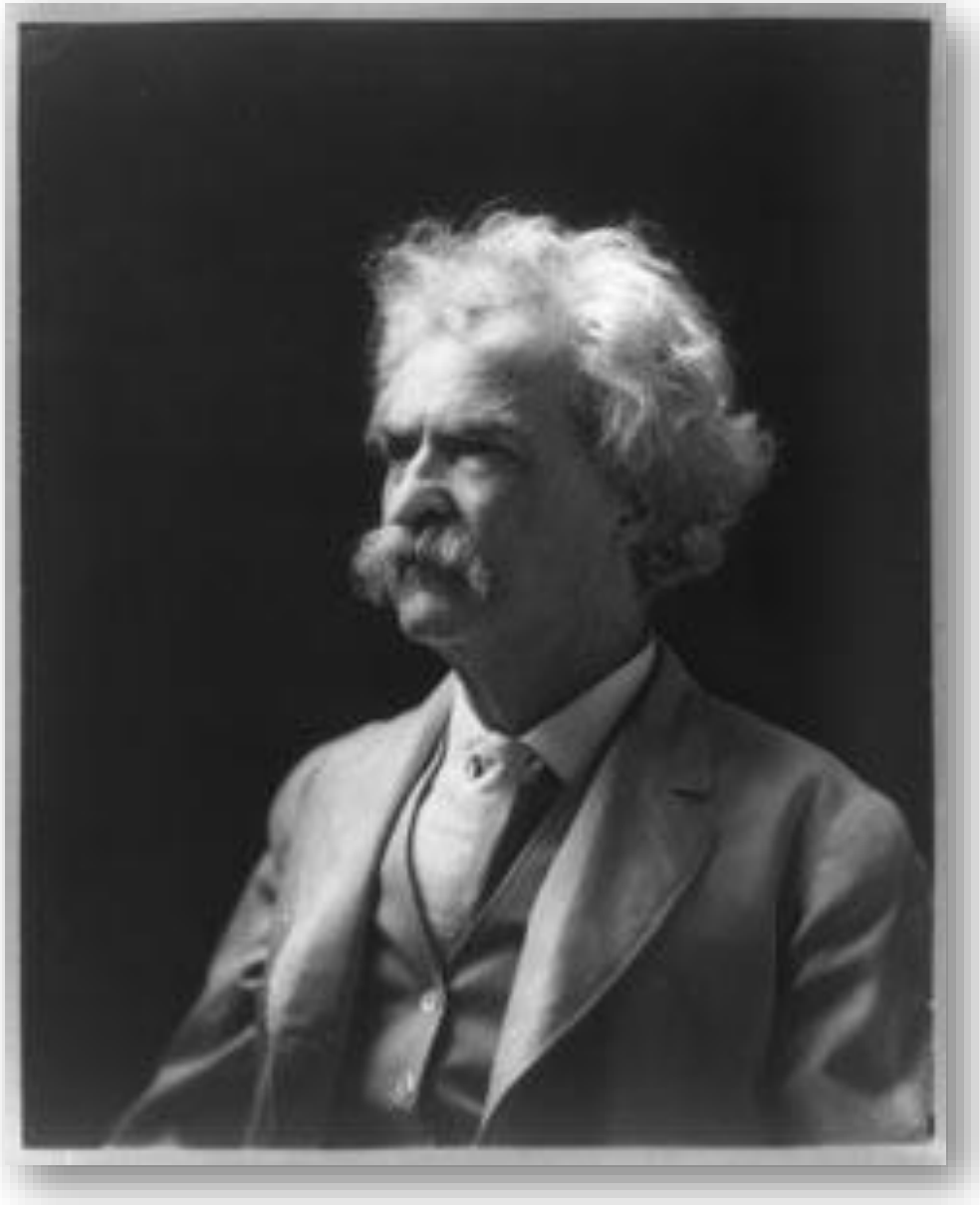
DRVVT	(normal < 1.2)
Screen ratio	3.1
Mix ratio	2.8
Confirm ratio	2.7

Interpretation: Lupus Anticoagulant

DTI: direct thrombin inhibitor

The more you explain it,

the more I don't understand it.



Impact of Anticoagulant Therapy on Lupus Anticoagulant Testing

Assay	Heparin	Warfarin	Dabigatran	Riva/Apixa
• **PT***	-	++	+	+
• **aPTT**	+++	High dose	++	+
• **DRVVT***	High dose	+	++	+
• **Thrombin Time**	+++	-	+++	-
• **Staclot Test***	High dose	-	±	±
• **ELISA**	-	-	-	-

*reagents neutralize up to 1 IU/ml of heparin

Antiphospholipid Antibody Syndrome

Diagnosis

- LAC: Phospholipid-dependent clotting assays

- aCL Abs: ≥ 40 GPL or MPL units
- β_2GP1 Abs: ≥ 40 units

- **Persistently positive for at least 12 weeks**

AJR 1998:170:285

23 year old male

Will the thrombophilia test results

- explain the thrombosis mechanism? ***Yes***
- inform management decisions?
- impact treatment duration?

23 year old male

Will the thrombophilia test results

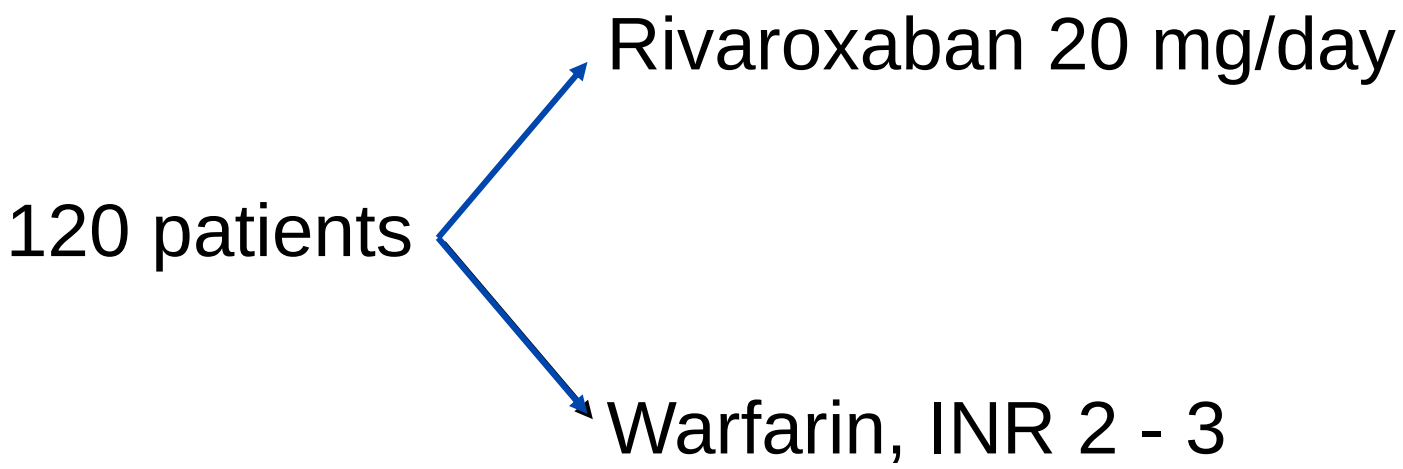
- explain the thrombosis mechanism? ***Yes***
- inform management decisions?
- impact treatment duration?

TRAPS

Rivaroxaban vs. Warfarin in APS

Patients: "***Triple*** positive" APS (ACLA > 40 U, β2GP1 > 40 U, Lupus Anticoagulant)

*(Non-inferiority design, **Sample size 536,** assuming 6% annual event rate)*



1◦ endpoint composite: Thromboembolism, Major bleed, Vascular Death

Blood. 2018;132:1365

Early trial termination!

Outcome, n	"As treated" analysis			
	Rivaroxaban (n = 59)	Warfarin (n = 61)	HR (95% CI)	*P*
Thromboembolic events, major bleeding, and vascular death	11 (19)	2 (3)	6.7 (1.5-30.5)	.01
Arterial thrombosis	7 (12)	0	—	—
Ischemic stroke	4 (7)	0		
Myocardial infarction	3 (5)	0		
Venous thromboembolism	0	0		
Major bleeding	4 (7)	2 (3)	2.5 (0.5-13.6)	.3
Death	0	0	—	—

Blood. 2018;132:1365

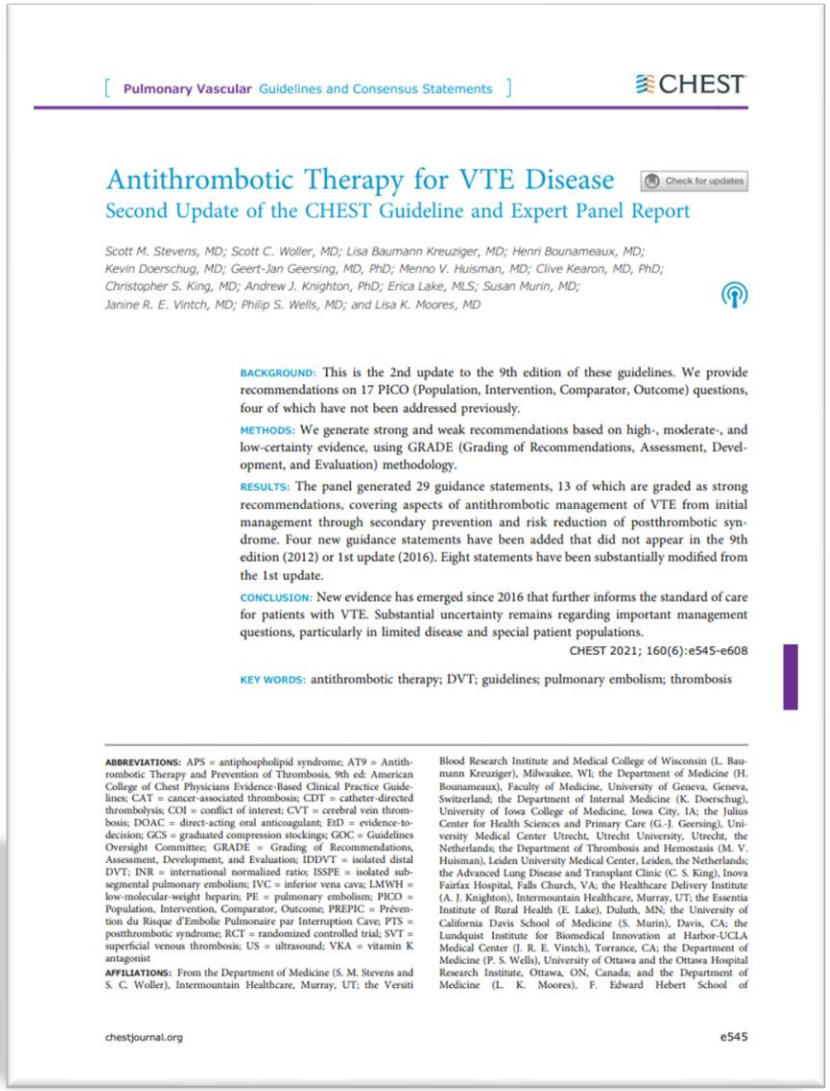
Rivaroxaban vs Warfarin in APS

Spanish Trial

Intension to treat	Rivaroxaban (n=95)	Warfarin (n=95)	P-value
All events	12.6%	6.3%	0.150
Arterial	***11.6%***	***3.2%***	***0.04***
Venous	2.1%	3.2%	0.65
Stroke	10.5%	0%	0.001

MAYO CLINIC

Ann Intern Med 2019; 171:685-694.



[Pulmonary Vascular Guidelines and Consensus Statements]

CHEST

Antithrombotic Therapy for VTE Disease

Second Update of the CHEST Guideline and Expert Panel Report

Scott M. Stevens, MD; Scott C. Woller, MD; Lisa Baumann Kreuziger, MD; Henri Bounameaux, MD; Kevin Doerschug, MD; Geert-Jan Geersing, MD, PhD; Menno V. Huisman, MD; Clive Kearon, MD, PhD; Christopher S. King, MD; Andrew J. Knighton, PhD; Erica Lake, MLS; Susan Murin, MD; Janine R. E. Vintch, MD; Philip S. Wells, MD; and Lisa K. Moores, MD

BACKGROUND: This is the 2nd update to the 9th edition of these guidelines. We provide recommendations on 17 PICO (Population, Intervention, Comparator, Outcome) questions, four of which have not been addressed previously.

METHODS: We generate strong and weak recommendations based on high-, moderate-, and low-certainty evidence, using GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) methodology.

RESULTS: The panel generated 29 guidance statements, 13 of which are graded as strong recommendations, covering aspects of antithrombotic management of VTE from initial management through secondary prevention and risk reduction of postthrombotic syndrome. Four new guidance statements have been added that did not appear in the 9th edition (2012) or 1st update (2016). Eight statements have been substantially modified from the 1st update.

CONCLUSION: New evidence has emerged since 2016 that further informs the standard of care for patients with VTE. Substantial uncertainty remains regarding important management questions, particularly in limited disease and special patient populations.

CHEST 2021; 160(6):e545-e608

KEY WORDS: antithrombotic therapy; DVT; guidelines; pulmonary embolism; thrombosis

ABBREVIATIONS: APS = antiphospholipid syndrome; AT9 = Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines; CAT = cancer-associated thrombosis; CDT = catheter-directed thrombolysis; COI = conflict of interest; CVT = cerebral vein thrombosis; DOAC = direct-acting oral anticoagulant; EtD = evidence-to-decision; GCS = graduated compression stockings; GOC = Guidelines Oversight Committee; GRADE = Grading of Recommendations, Assessment, Development, and Evaluation; IDDVT = isolated distal DVT; INR = international normalized ratio; ISSPE = isolated subsegmental pulmonary embolism; IVC = inferior vena cava; LMWH = low-molecular-weight heparin; PE = pulmonary embolism; PICO = Population, Intervention, Comparator, Outcome; PREPIC = Prévention du Risque d'Embolie Pulmonaire par Interruption Cave; PTS = postthrombotic syndrome; RCT = randomized controlled trial; SVT = superficial venous thrombosis; US = ultrasound; VKA = vitamin K antagonist

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In patients with antiphospholipid syndrome, we suggest ***warfarin*** (Target INR 2.5)

DOACs should be avoided especially if positive for ***lupus anticoagulant***

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CHEST 2021; 160:e545

23 year old male

Will the thrombophilia test results

- explain the thrombosis mechanism? ***Yes***
- inform management decisions? ***Yes***
- impact treatment duration? ***Yes***

If you do test, ***how often*** will you ***find something***?

- Special Coagulation Laboratory database
- 3621 Mayo Clinic patients (1995 – 2005) with ***leg DVT ± PE***

- *Percent positive test results* *25%*
- ***"Strong" thrombophilia*** ***10%***

J Gastroenterol. 2013;48:1111

What will you find?

• Antiphospholipid syndrome	5.2%
• Lupus anticoagulant	3.8%
• Factor V Leiden	15.8%
• Heterozygous	15.1%
• Prothrombin G20210A	5.2%
• Heterozygous	4.9%
• Protein C deficiency	0.2%
• Protein S deficiency	0.9%
• Antithrombin deficiency	1.3%

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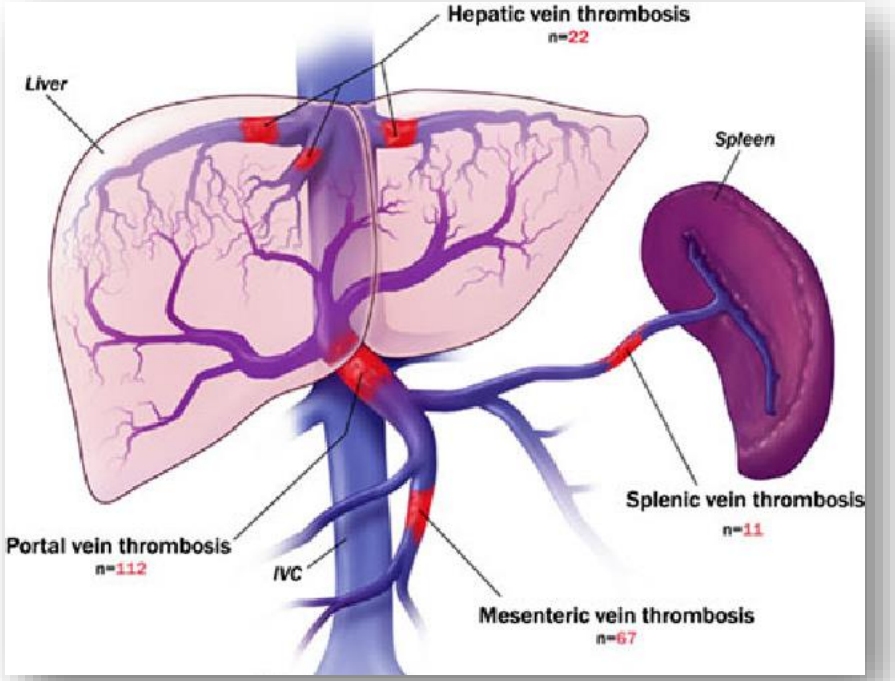
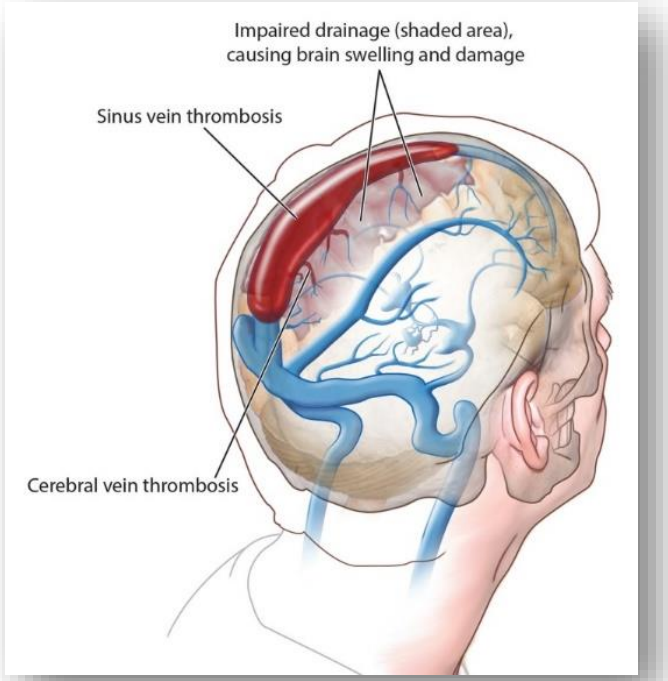
J Gastroenterol. 2013;48:1111

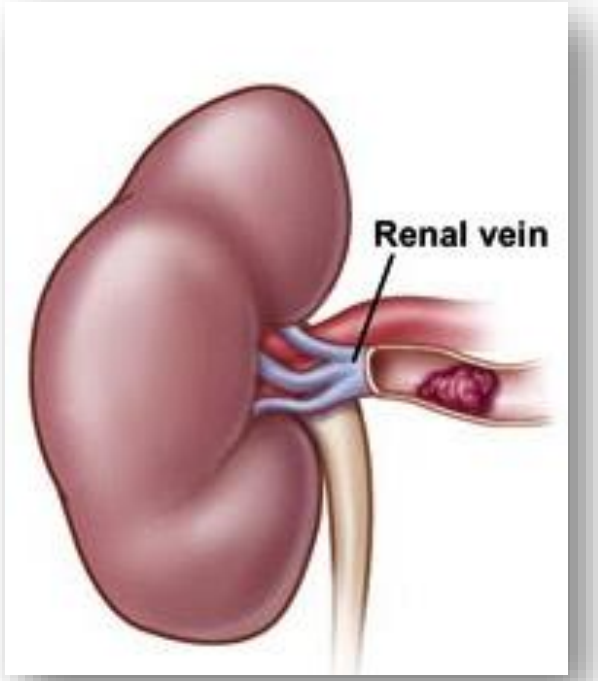
Atypical Thrombus Locations



Splanchnic Veins



Cerebral Veins/Sinuses



Renal Veins

Atypical DVT: what's wrong with organ?

- Cerebral — Cancer, trauma, infection, surgery
- Portal — Cancer, cirrhosis, surgery
- Splenic — Cancer (MPN), pancreatitis, surgery
- Mesenteric — Cancer, IBD, surgery, infection
- Renal — Cancer, nephrotic/nephritic syndrome
- Gonadal — Cancer, PID
- Retinal — Atherosclerosis risk factors

Atypical DVT; What will you find?

		Leg DVT
• Antiphospholipid syndrome	5.9%	5.2%
• Lupus anticoagulant	3.8%	3.8%
• Factor V Leiden	10.9%	15.8%
• Heterozygous	10.3%	15.1%
• Prothrombin G20210A	5.0%	5.2%
• Heterozygous	4.3%	4.9%
• Protein C deficiency	0.3%	0.2%
• Protein S deficiency	3.5%	0.9%
• Antithrombin deficiency	1.5%	1.3%

MAYO CLINIC

J Gastroenterol. 2013;48:1111

Just One More Question!!!

Last Quick Questions

- When should you test?
- How much is testing?

Test Interpretation Caveats

If you see this….	Watch for….
Antithrombin Deficiency	***Heparin*** consumption Nephrotic syndrome Liver disease
Protein C Deficiency	***Warfarin*** effect Liver disease
Protein S Deficiency	Warfarin effect ***Hormonal*** effect (pregnancy, OCPs, HRT)

“Thrombophilia” Testing: Bottom Line

- ***Choose carefully*** who you offer testing to
- Do ***not obtain*** for patients with a ***provoked event***
- Yield is ***relatively low (25%)***
- 1 in 10 will have a ***severe thrombophilia*** (10%)
- Results ***may*** or ***may not*** change management