



Brigham and Women's Hospital
Founding Member, Mass General Brigham

CHALLENGES IN VTE MANAGEMENT

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Samuel Z. Goldhaber, MD



- Harvard Medical School
- Medicine Residency @BWH
- CV Medicine Fellowship @BWH
- Director, Thrombosis Research Group
- Professor of Medicine@ HMS
 - Clinical focus: Vascular Medicine, Pulmonary Embolism, DVT, Obesity, Autonomic Dysfunction (e.g., POTS)
 - Research focus: Thrombosis

Disclosures

Research Support:

Bayer, BMS, Boston Scientific, Janssen, NHLBI

Consultant Support:

None

Disclosure: PE Diagnosis at MGB (N=1,712)

	Sensitivity, %	Specificity, %	Positive predictive value, %	Negative predictive value, %
Principal discharge diagnosis	58.30	99.90	92.10	99.10
Secondary discharge diagnosis	24.90	99.70	59.50	98.80

Bikdeli B, et al. JTH 2025; 23: 556-564

Learning Objectives: VTE Update

- 2026 ACC/AHA Guidelines for PE Management
- Pathophysiology
- Rivaroxaban vs Apixaban vs Warfarin
- Optimal duration to anticoagulate provoked VTE:
(HI-PRO Trial NEJM September 2025)
- Management of massive and near-massive PE
- Chronic venous insufficiency
- Future perspectives



American
Heart
Association.



AMERICAN
COLLEGE of
CARDIOLOGY®

JACC 2026; February 19

AHA/ ACC/

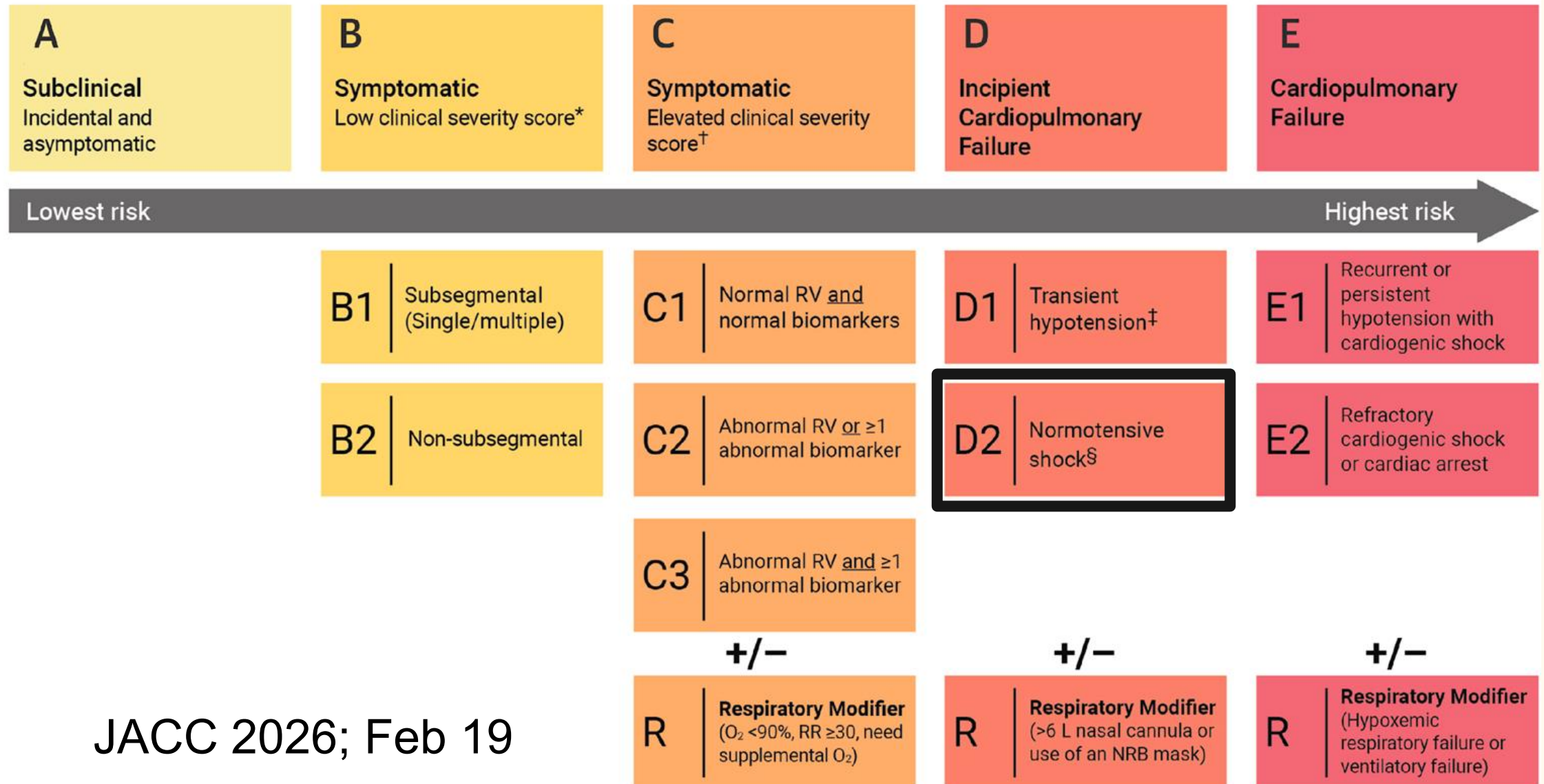
**Guideline for Evaluation and
Management of Acute PE in Adults**

New PE Clinical Categories

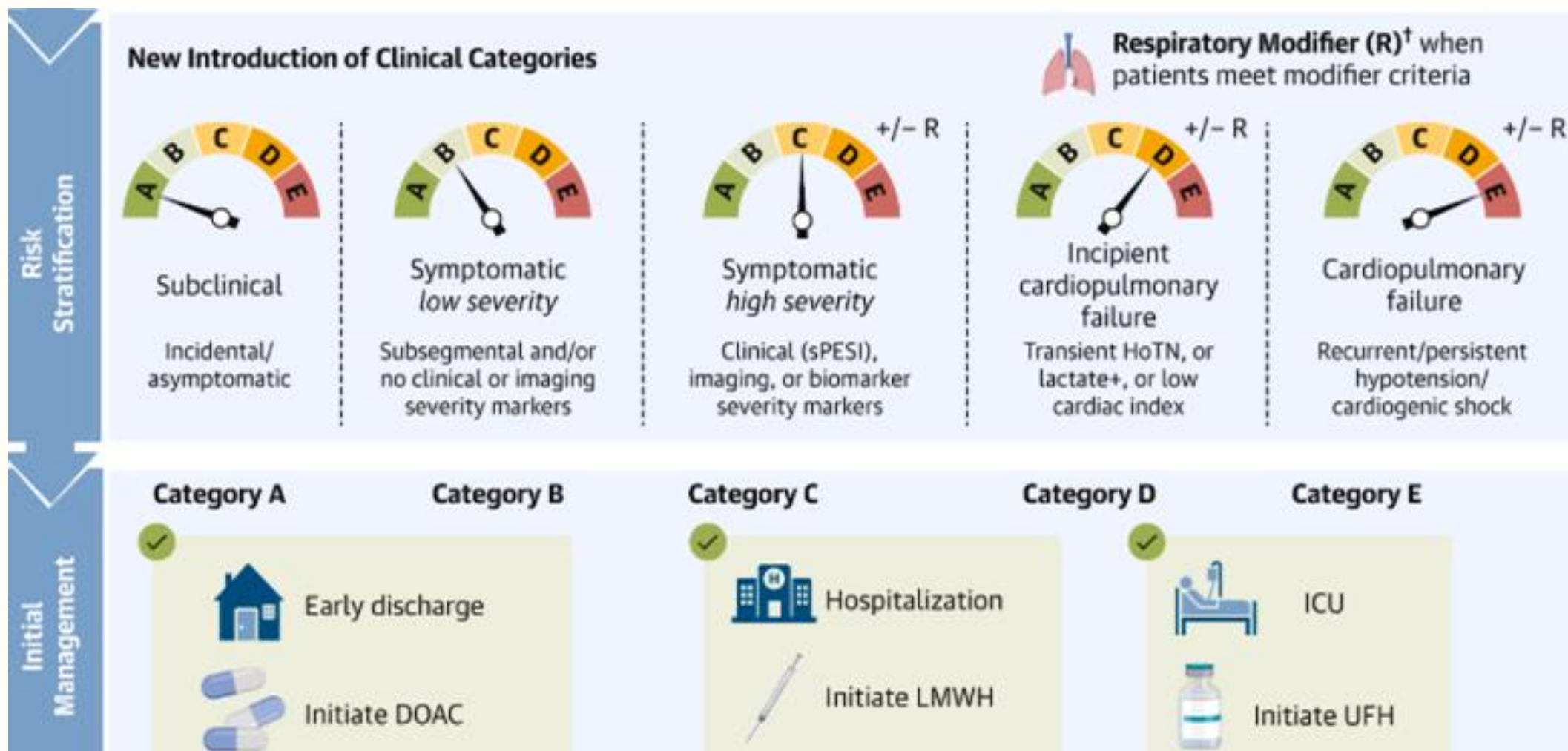
A 2026 widely-endorsed clinical classification scheme has been released: “Acute PE Clinical Categories,” with 5 categories (A-E), ranging from low to high risk for adverse outcomes. It will enhance the precision of severity classification, prognosis assessment, and therapeutic decision-making.

JACC 2026; Feb 19

AHA/ ACC Acute PE Clinical Categories



JACC 2026; Feb 19



Clinical Categories

Asymptomatic

A

Symptomatic

B

Symptomatic

C

Symptomatic

D

Symptomatic

E

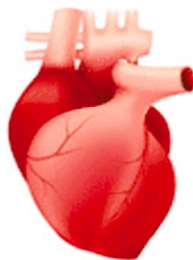
Life-Threatening PE

Comorbidities

Recurrent emboli

Cardiac compromise

Heart rate
Systolic blood pressure
CT RV size
Echocardiographic RV function
Cardiac biomarkers



Respiratory compromise



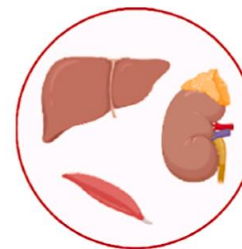
Oxygen saturation
Respiratory rate
Partial pressure of oxygen

R

**Failure to
Detect
Normotensive
Shock can be
Fatal**

Organ hypoperfusion/shock

Lactate
Creatinine
Systolic blood pressure

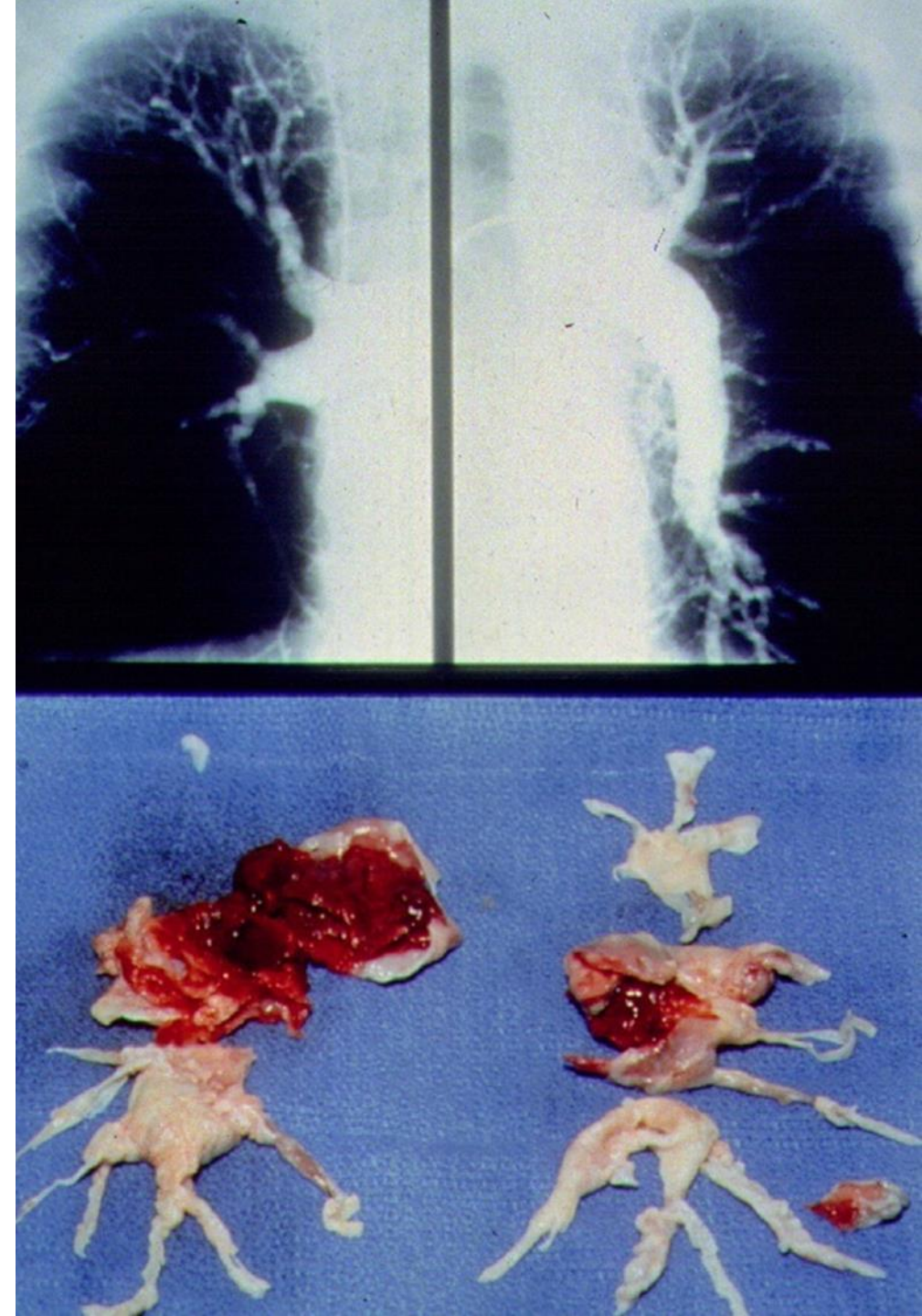


2026 Guidelines for PE Patient Follow-Up

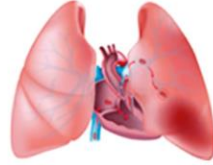
- In patients with a first acute PE without a major reversible risk factor and in those with an enduring risk factor, continue anticoagulation beyond the initial treatment phase (3-6 months), possibly without an end date.
- Ask patients about PE-related symptoms to screen for chronic thromboembolic pulmonary disease or Post-PE Syndrome causing dyspnea, functional limitation, or emotional distress.

Post-PE impairment (PPEI) with persistent dyspnea and incomplete recovery is frequent (16%/2 yrs) and associated with CTEPH, death, re-hospitalization (31%), and decreased quality of life.

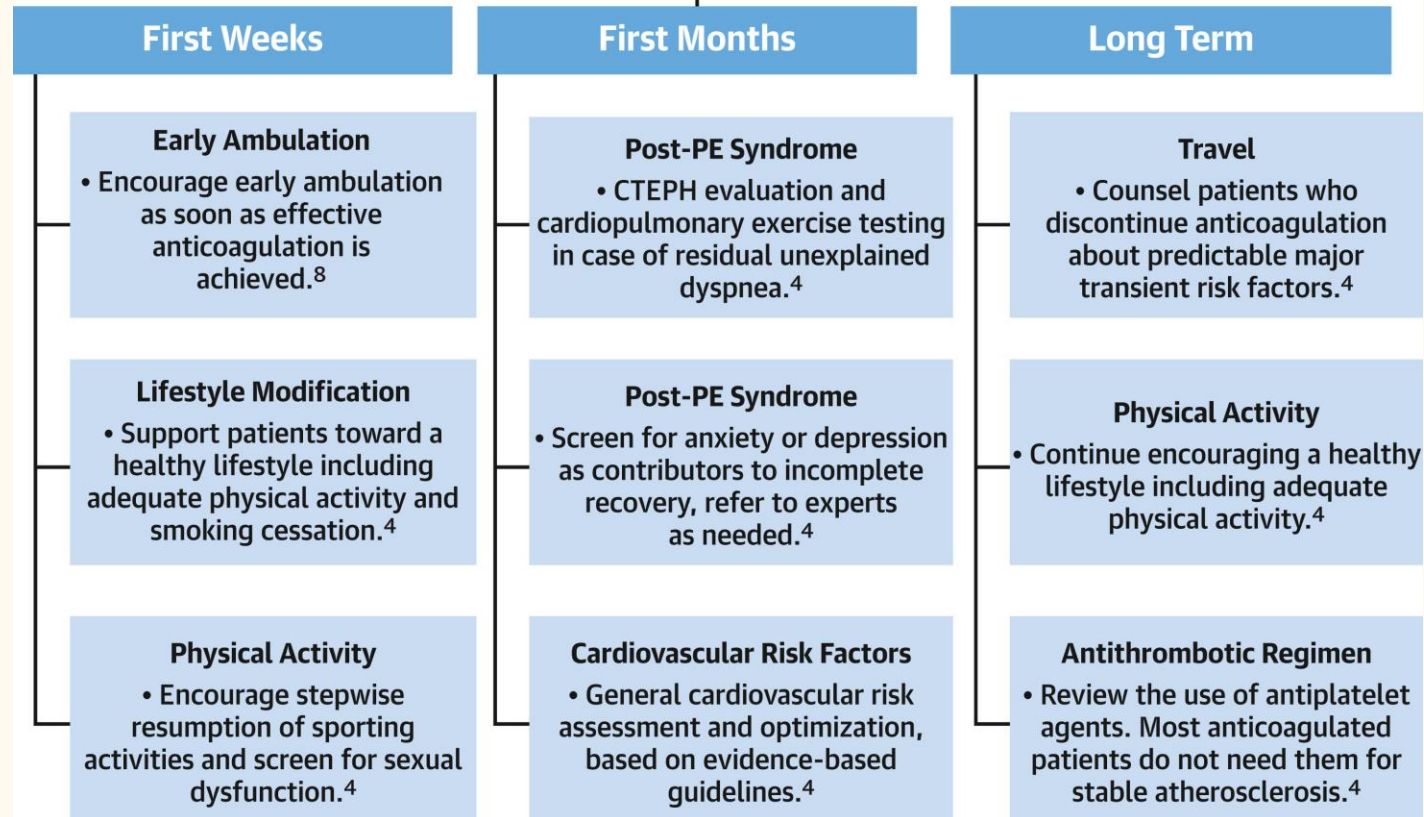
(European Heart Journal 2022; April 7)



Post-PE Lifestyle Recommendations



Post-PE Lifestyle Recommendations

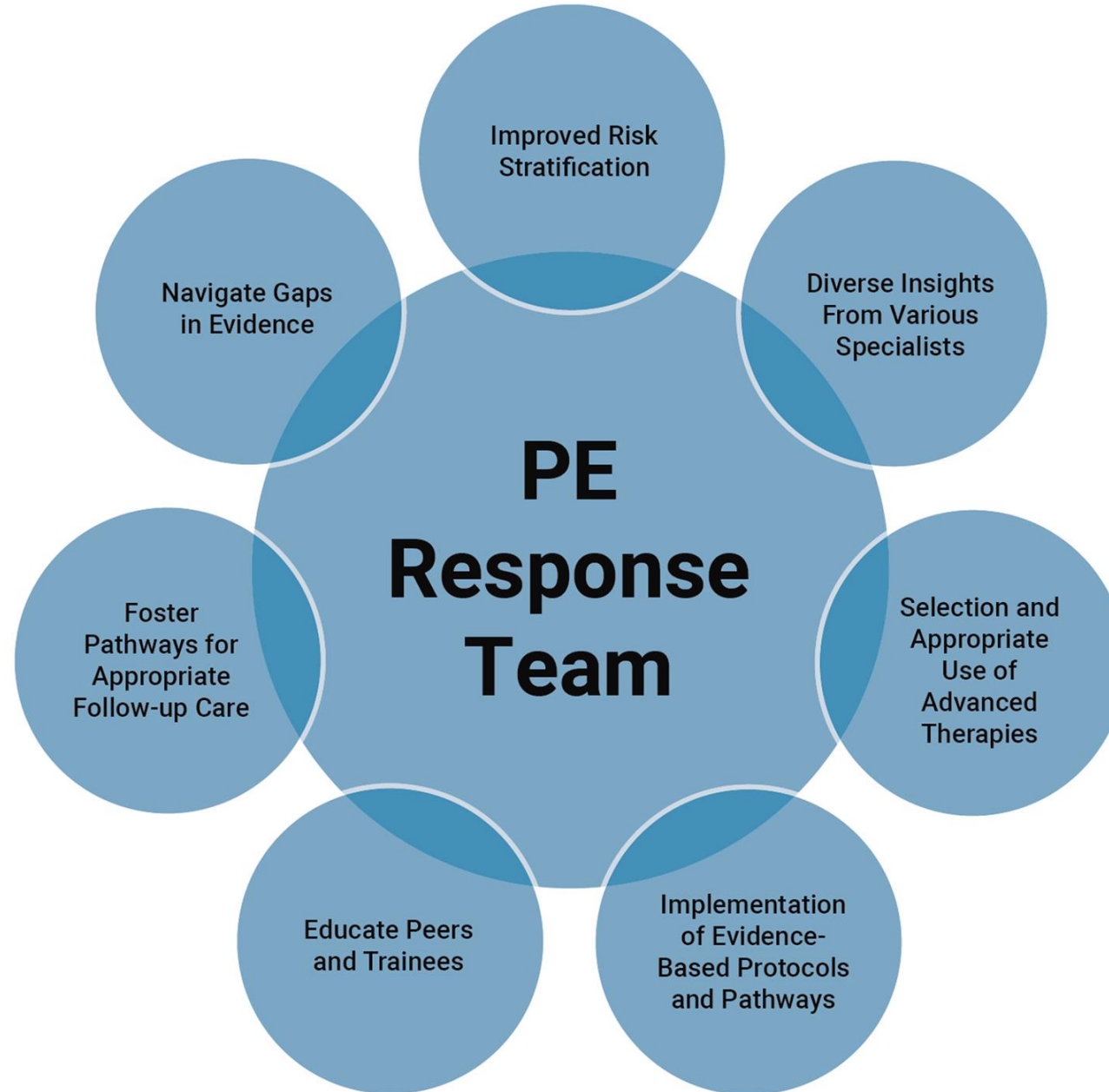


JACC 2024; 84: 1561-1577

2026 ACC/AHA Guidelines: Top Takeaways

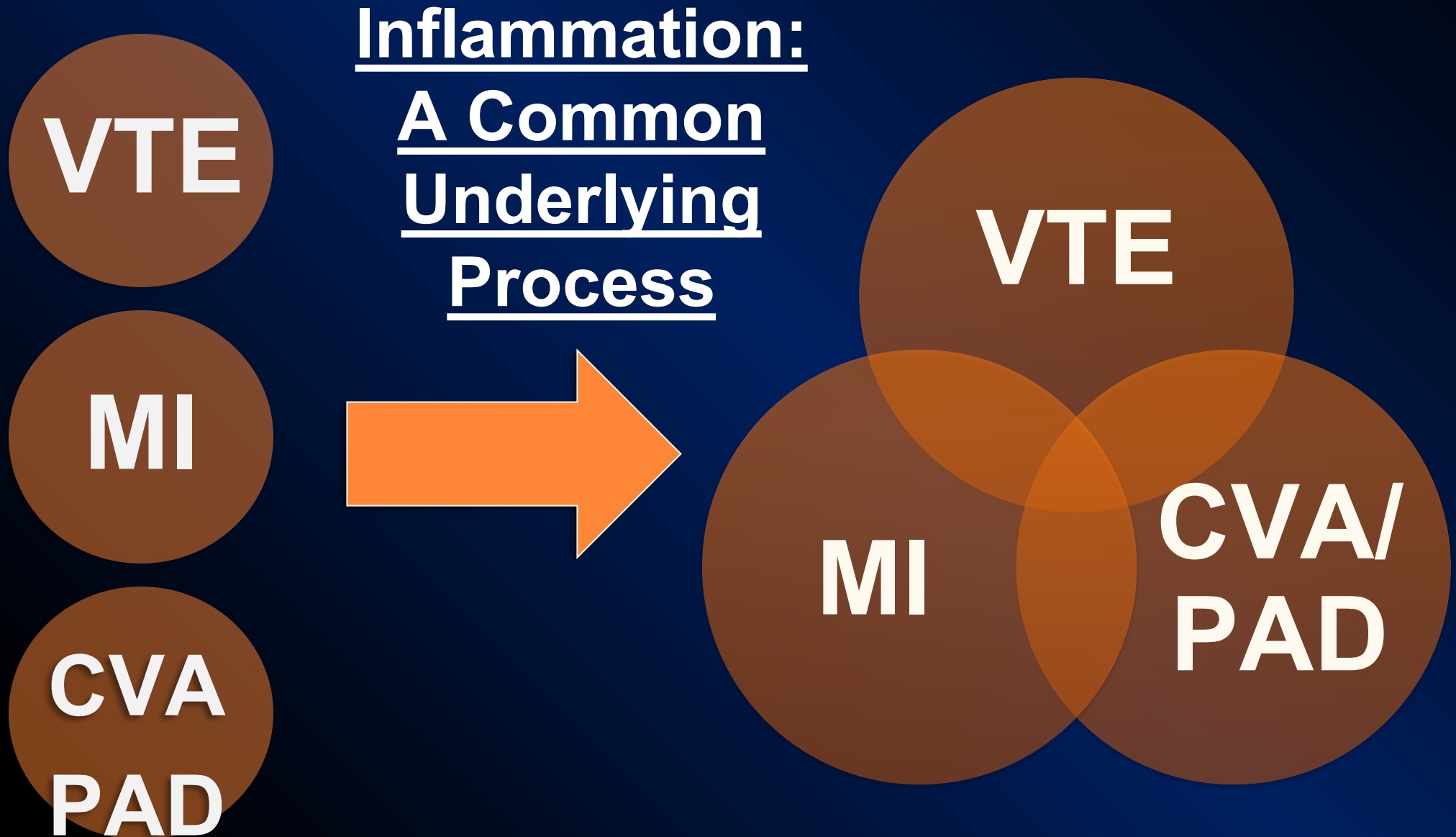
- 1) Incorporate the new detailed PE categories into clinical presentations
- 2) For parenteral therapy, almost always start with LMWH, not UFH
- 3) With weight-based LMWH, monitoring anti-Xa levels is rarely useful.
- 4) High suspicion for normotensive shock; low threshold for ordering lactate levels
- 5) Extend anticoagulation duration in provoked VTE when risk factors persist
- 6) Utilize Pulmonary Embolism Response Teams

Benefits of a PERT Program

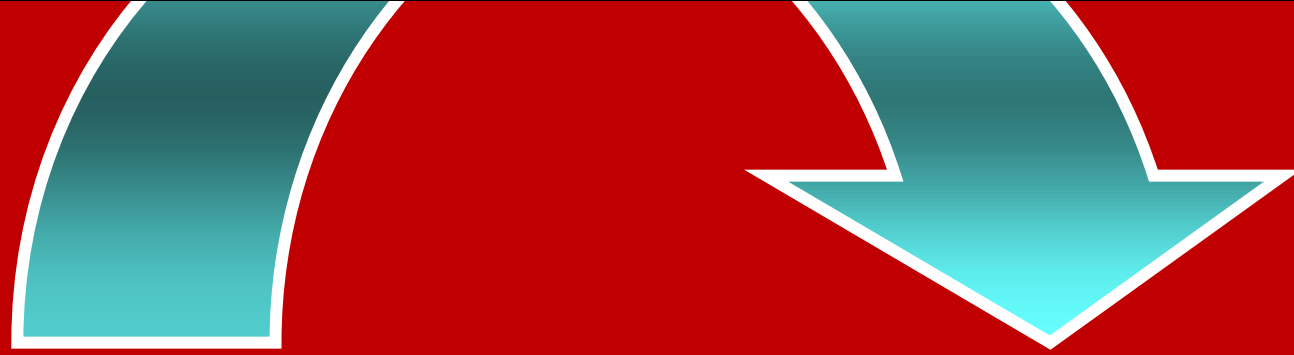


Pathophysiology

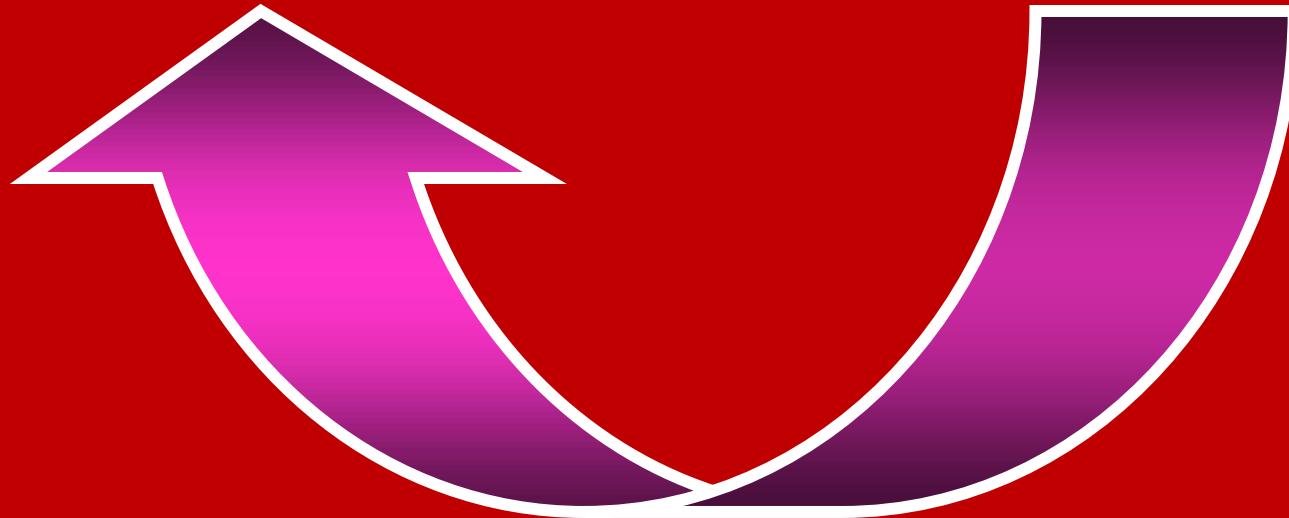
ABANDON “SILO THINKING”



PERSISTENT INFLAMMATION



Inflammation Thrombosis



Inflammation &
Thrombosis:
The Clot
Thickens

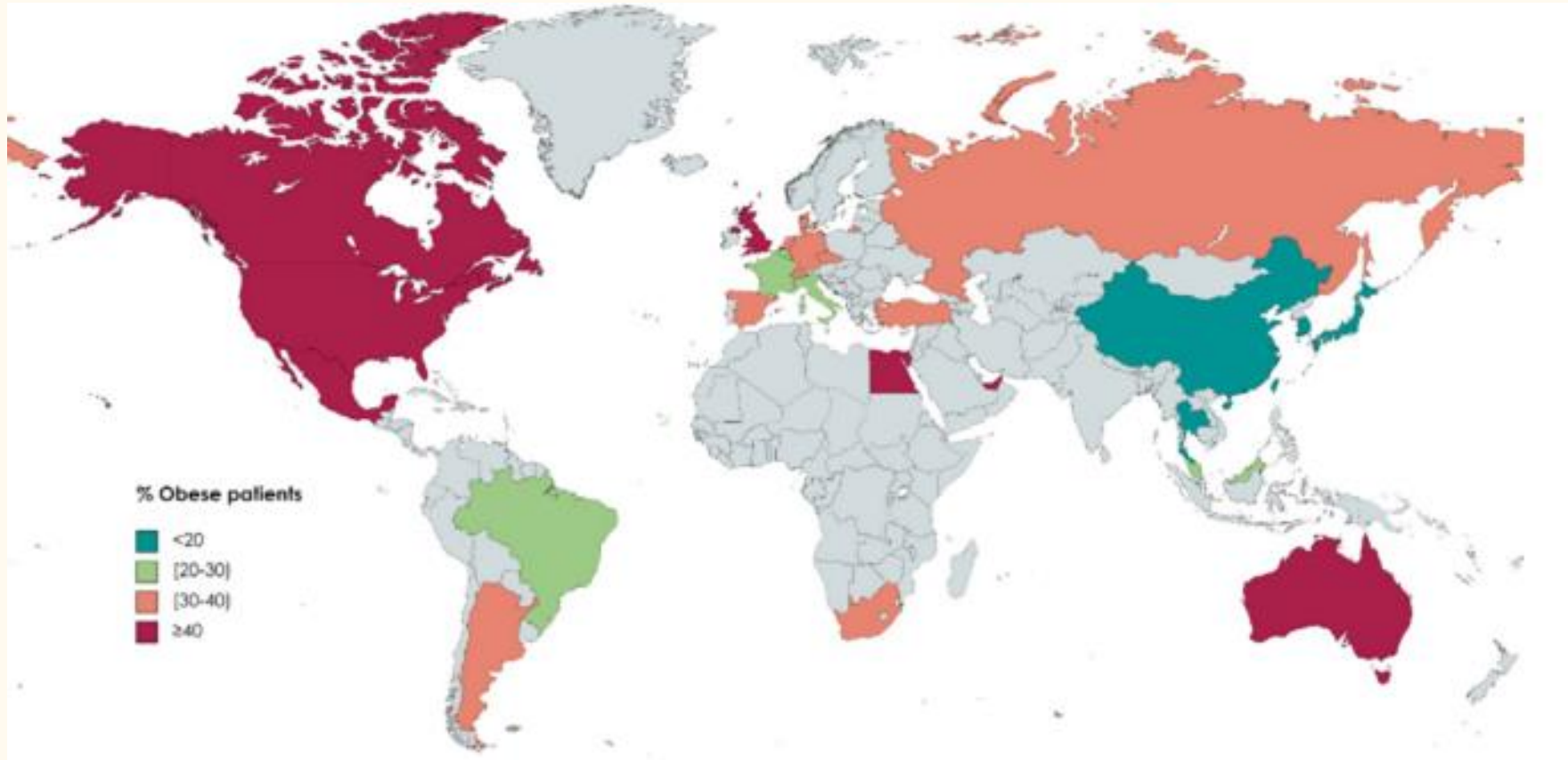
Inflammation-Linked Conditions that Can Trigger PE or DVT

- **Ulcerative colitis/ Crohn's disease**
- **Rheumatoid arthritis/ psoriasis**
- **Obstructive sleep apnea; obesity**
- **Elevated LDL cholesterol or LP(a)**

Acute coronary syndrome/ stroke

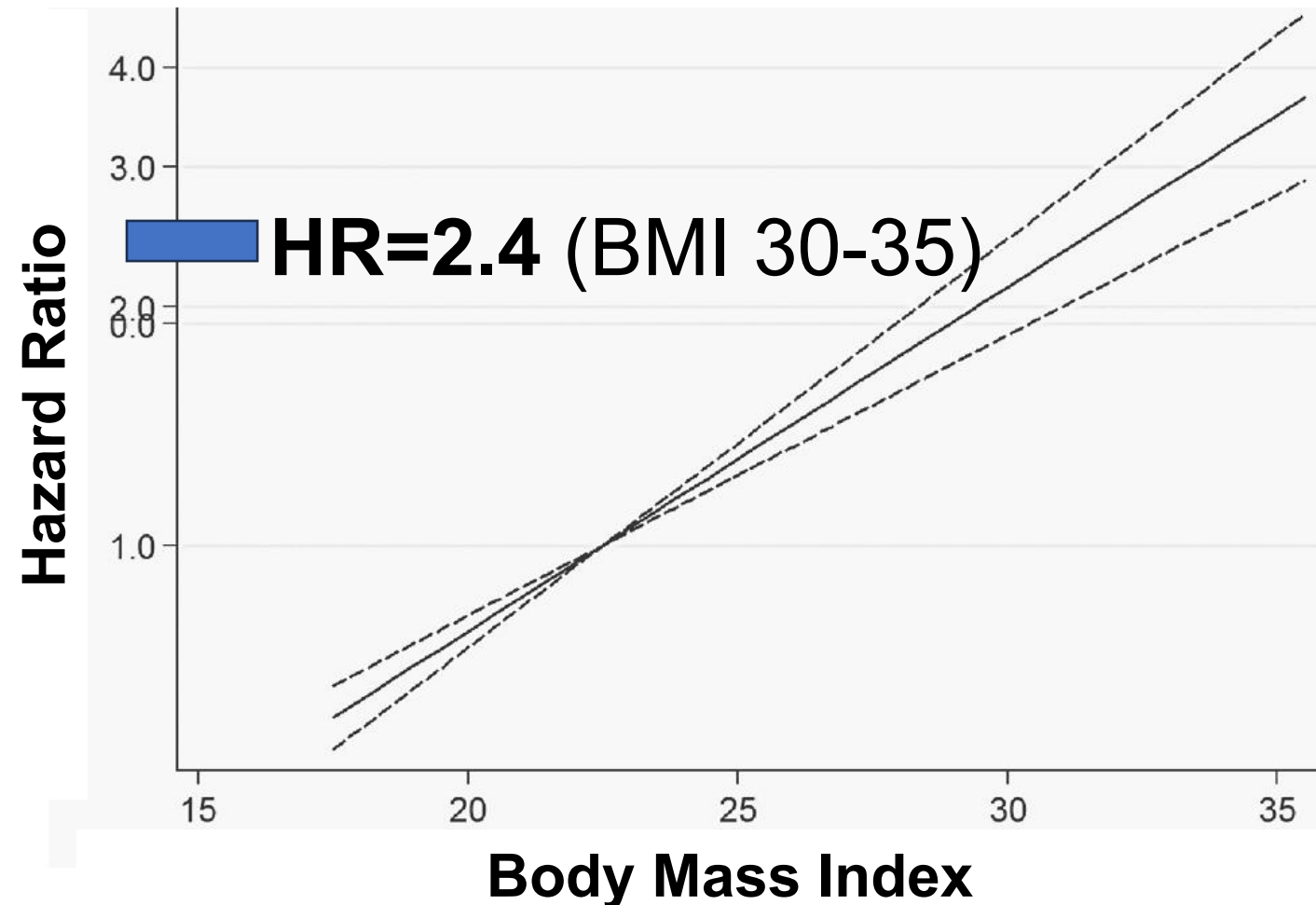
Pneumonia/ COPD/ cigarette smoking

Distribution of Obese Patients According to Country



J Thromb Haemost 2021; 19: 3031–3043.

Hazard Ratio=2.4 for PE in those with Obesity (N=3,910,747—UK Biobank)



Thrombosis Research 2020; 192: 64-72

Lab Tests of Hypercoagulability

- Genetic: Factor V Leiden; PT Gene Mutation
- Acquired: Lupus Anticoagulant; Anticardiolipin Antibodies; Antiphospholipid Syndrome
- Genetic or Acquired: Deficiencies of antithrombin III, protein C, protein S

VTE Management Strategy

1) Apixaban vs Rivaroxaban vs Warfarin

**2) Optimal Duration of Anticoagulation
for Provoked PE and DVT**

(HI-PRO Trial NEJM September 2025)

DOACS: SITES OF ACTION

Steps in Coagulation

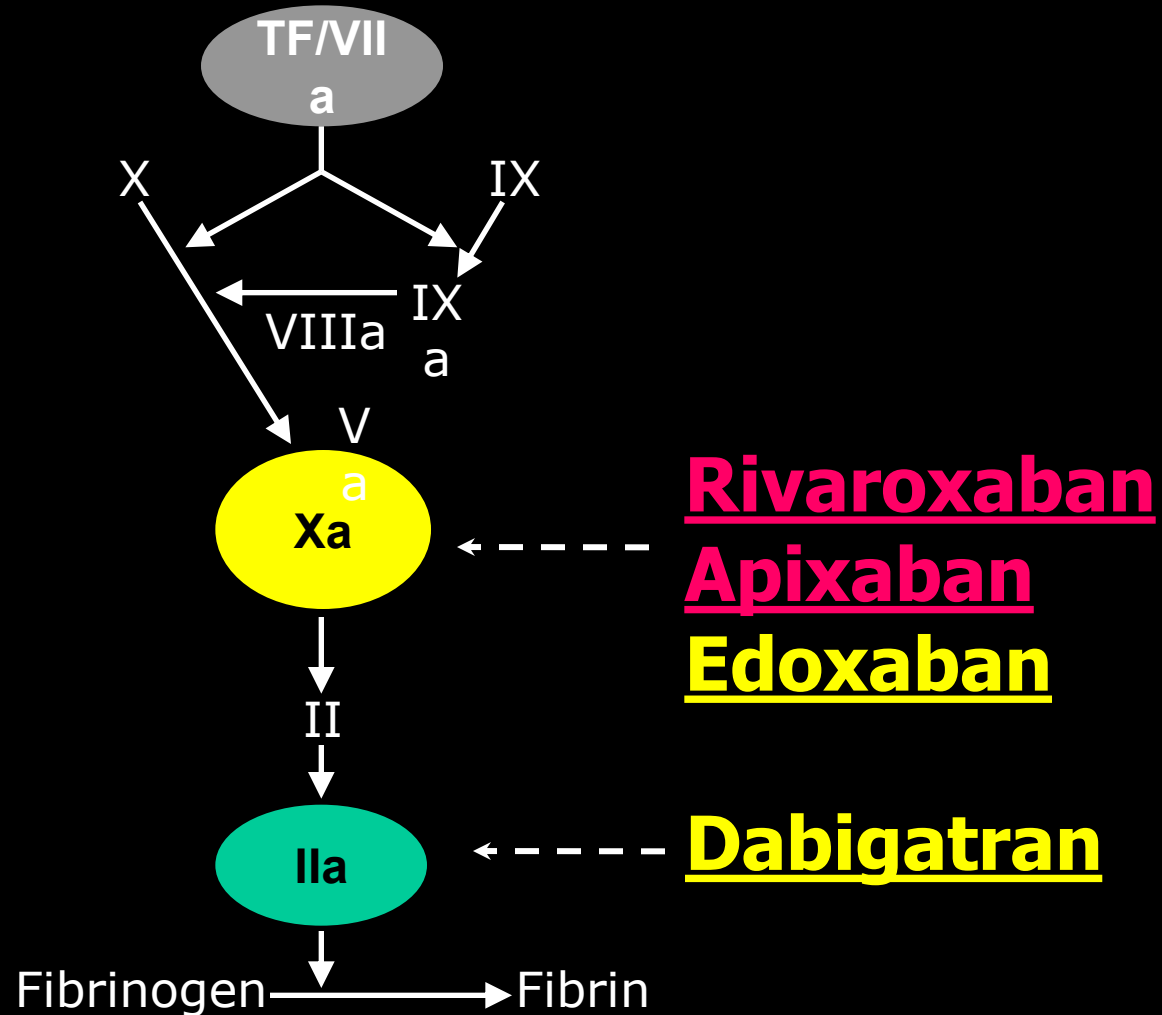
Initiation

Coagulation Pathway

Drugs

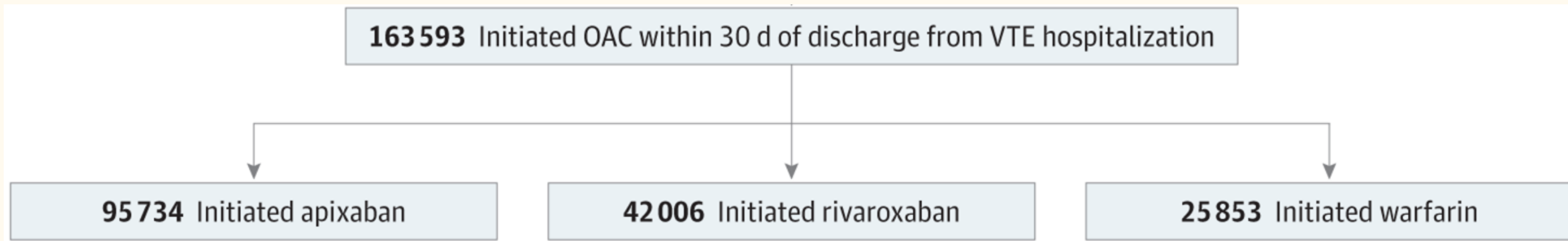
Propagation

Fibrin formation



(Circulation 2011;123:1436-1450)

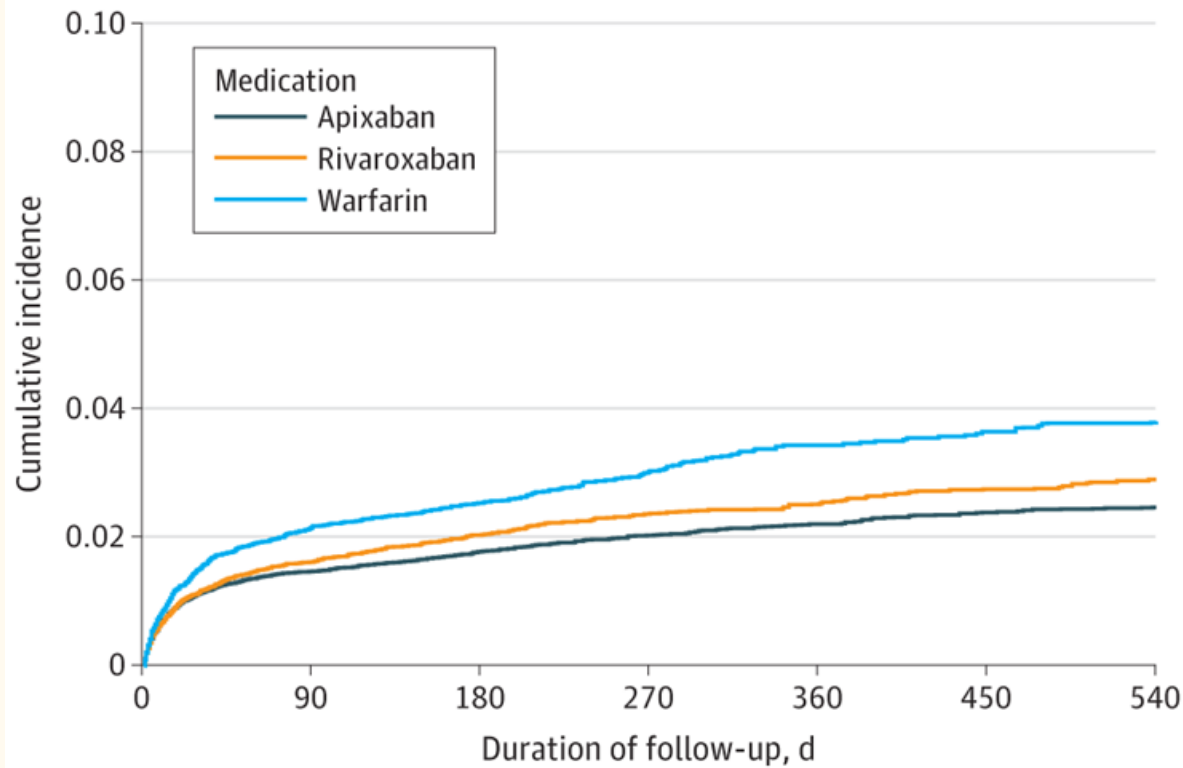
Recurrent VTE and Major Bleeding: Apixaban vs Rivaroxaban vs Warfarin (N=163,593)



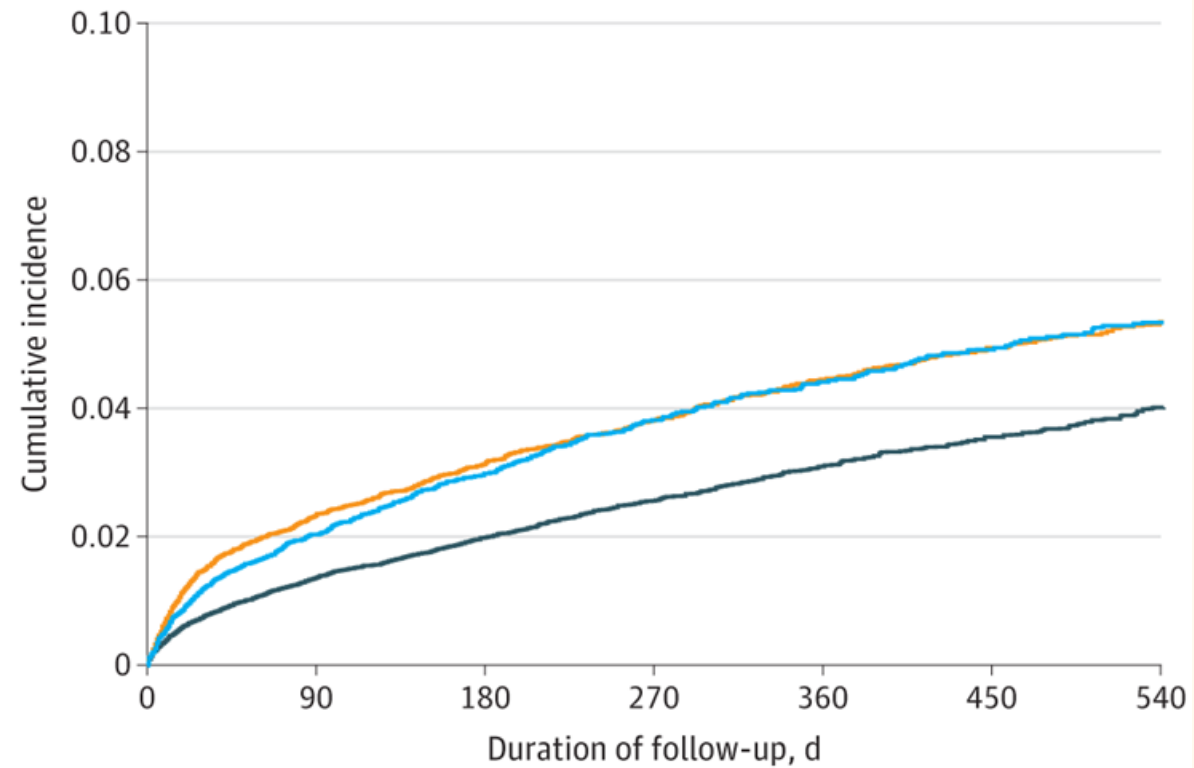
JAMA Internal Medicine 2025; May 12

Recurrent VTE and Major Bleeding: Apixaban vs Rivaroxaban vs Warfarin (N=163,593)

A Hospitalization for recurrent VTE



B Hospitalization for major bleeding



JAMA Internal Medicine 2025; May 12

Warfarin: Multiple VTE Indications

- Monitor medication adherence
- Frail and obese patients
- APLAS
- Recurrent VTE despite DOAC
- Major bleeding despite DOAC
- Titrate intensity of anticoagulation
 - INR 3.0-4.0—High intensity
 - INR 2.0-3.0—Standard intensity
 - INR 1.5-2.0—Low intensity

Management of Warfarin Dosing: Tricks of the Trade

- Don't check INR more than twice per week
- Make small, subtle changes in dosing
- Remember to ask about adherence to warfarin
- Caution re: alcohol, NSAIDs, fish oil capsules, turmeric
- Humidify the bedroom at night to prevent nosebleeds
- Prescribe warfarin for 8:00 p.m. nightly
- Low-dose vitamin K to increase INR (counterintuitive)
- BID warfarin dose if total dose exceeds 12 mg

Optimal Duration of Anticoagulation: **An Example of Clinical Equipoise**

- Is Classifying DVT as “Provoked” versus “Unprovoked” relevant?
ASH: Yes ESC: No
- Does evidence support this classification to determine optimal duration of Rx?
ASH: Yes ESC: No



The NEW ENGLAND
JOURNAL of MEDICINE

Apixaban for Extended Treatment of Provoked Venous Thromboembolism

Gregory Piazza, M.D.,^{1,2} Behnood Bikdeli, M.D.,^{1,3} Arvind K. Pandey, M.D.,²
Darsiya Krishnathasan, M.S.,¹ Candrika D. Khairani, M.D.,¹
Antoine Bejjani, M.D.,^{1,4} Ruth H. Morrison, R.N., B.S.N.,¹
Heather Hogan, R.N., B.S.N.,¹ Sina Rashedi, M.D., M.P.H.,¹
Mariana Pfeferman, M.D.,¹ Junyang Lou, M.D., Ph.D.,^{1,2} John Fanikos, R.P.H.,^{1,5}
Nicole Porio, B.A.,¹ Lisa Rosenbaum, M.D.,⁶ Piotr Sobieszczyk, M.D.,²
Zhou Lan, Ph.D.,^{1,7} Marie Gerhard-Herman, M.D.,² Umberto Campia, M.D.,^{1,2}
and Samuel Z. Goldhaber, M.D.,^{1,2} for the HI-PRO Trial Investigators*

September 25, 2025

Hypothesis: Provoked VTE with Enduring Risk Factors

Extended-duration thromboprophylaxis with apixaban 2.5 mg orally twice daily:

1. Will reduce the incidence of symptomatic recurrent venous thromboembolism (VTE)
2. Will not increase the incidence of major bleeding

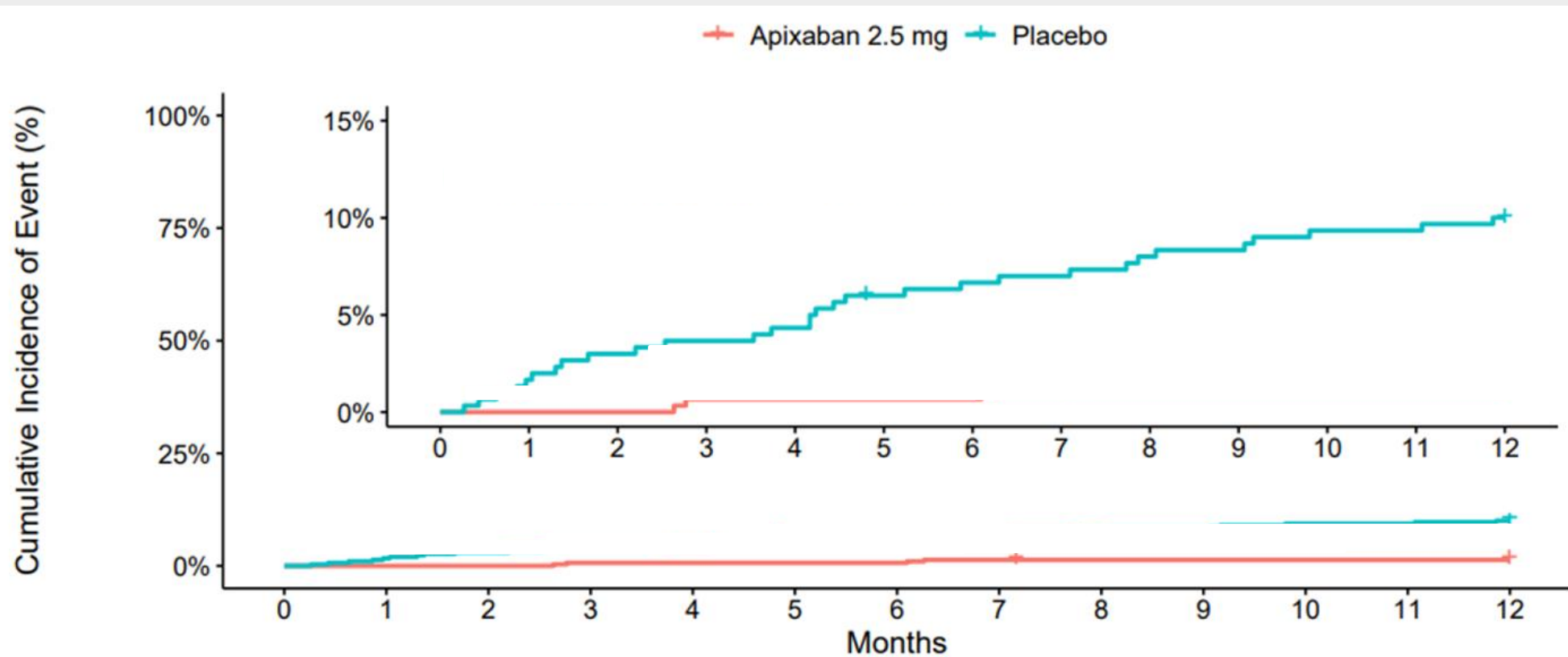


Efficacy and Safety Outcomes at 12 months

- **Primary Efficacy Outcome:** time-to-first symptomatic, recurrent, objectively-confirmed VTE, defined as a composite of DVT and/or PE.
- **Principal Safety Outcome:** time-to-first occurrence of major bleeding



Primary Efficacy Outcome: Symptomatic Recurrent VTE

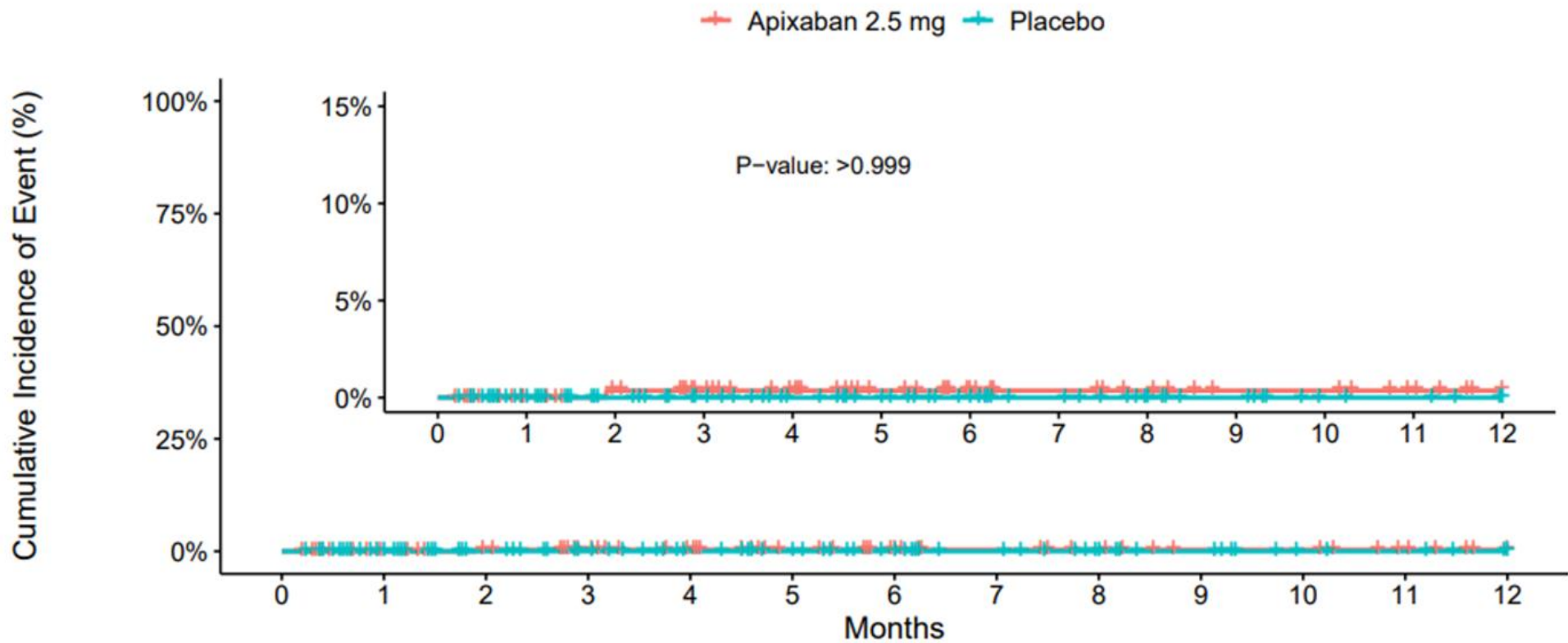


No. at Risk

Apixaban 2.5 mg	300	298	298	295	295
Placebo	300	289	279	274	269



Principal Safety Outcome: Major Bleeding



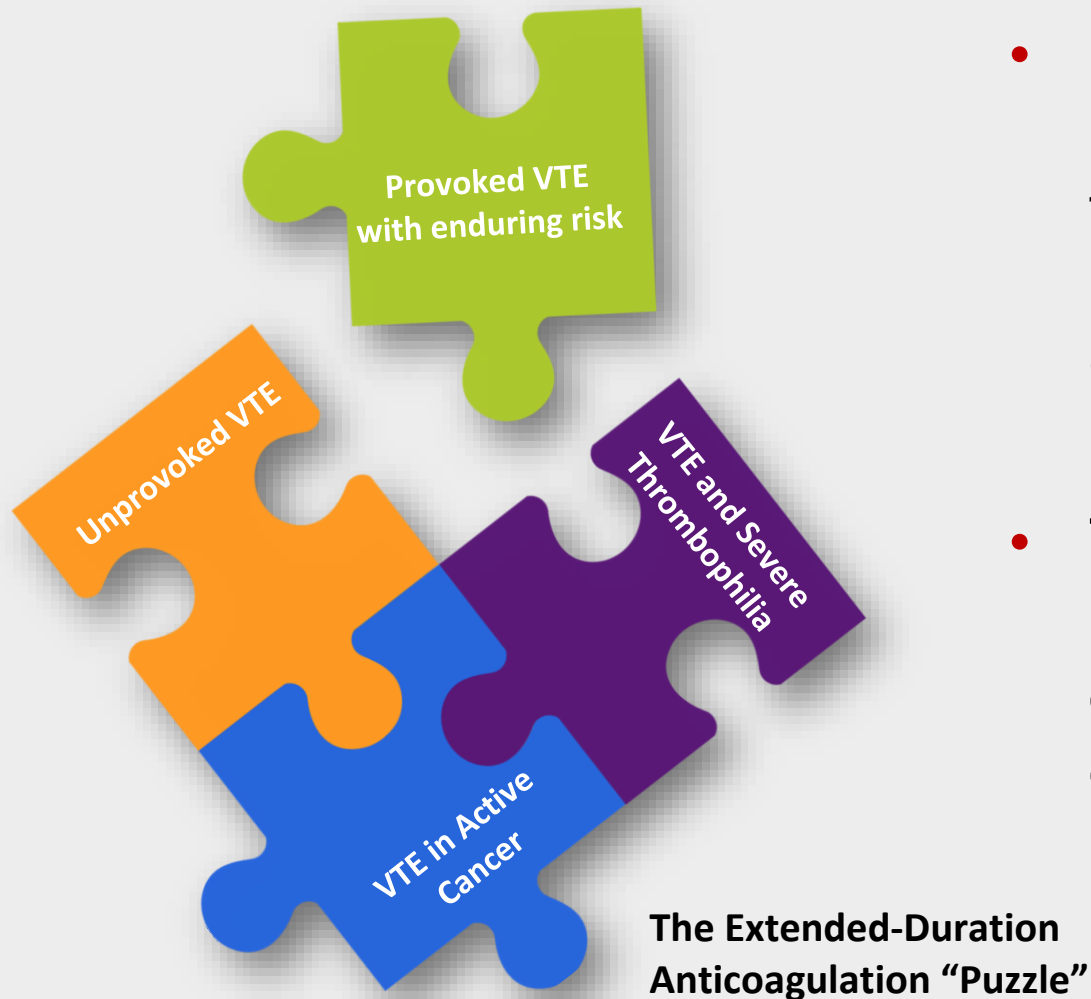
No. at Risk

Apixaban 2.5 mg	294	271	248	235	227
Placebo	294	259	233	216	203





HI-PRO: In Context



- HI-PRO highlights a population with provoked VTE and enduring risk in which the risk of recurrence off anticoagulation is high enough to warrant consideration of continued anticoagulation.
- The hazard of clinically-relevant non-major bleeding highlights the importance of bleeding risk assessment and shared decision-making.

Weitz JI, et al. N Engl J Med. 2017;376:1211
Iorio A, et al. Arch Intern Med. 2010;170:1710
Agnelli G, et al. N Engl J Med. 2013;368:699
Couturaud F, et al. Lancet. 2025;405:725
Schulman A, et al. N Engl J Med. 2013;368:709





HI-PRO Trial Conclusions

- Compared with placebo, apixaban 2.5 mg orally twice daily reduced the risk of symptomatic recurrence over 12 months in patients with provoked VTE and ≥ 1 enduring risk factor for recurrent events.
- The benefits for the prevention of recurrent VTE with extended-duration apixaban were observed with a low risk of major bleeding.
- The frequency of clinically relevant non-major bleeding was numerically greater in patients receiving apixaban.



My Approach to Duration of VTE Anticoagulation: Queries Prior to Setting an “End Date”

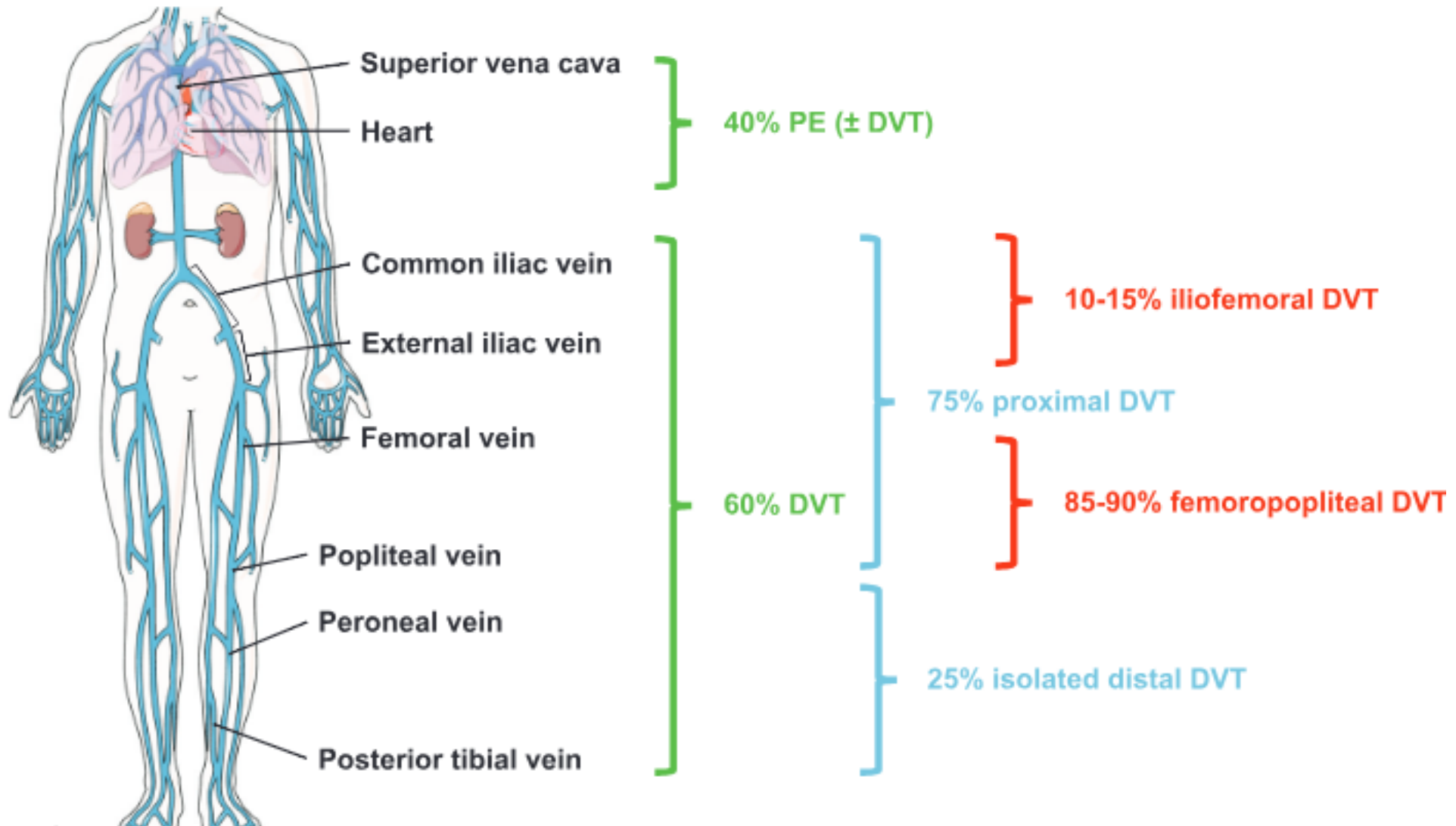
- 1) Is VTE a surrogate for high risk of MI, stroke, or DM2? Check LDL-C, A1C, APLAS, and Lp(a)?
- 2) Is there a PMHx or family history of PE or DVT?
- 3) Is there active cancer, possibly occult?
- 4) Are there enduring CV risk factors that can be reversed: obesity, sedentary lifestyle, obstructive sleep apnea, cigarette smoking?

Chronic Venous Insufficiency

(Post-Phlebitic Syndrome)

(Post-Thrombotic Syndrome)

Anatomical Distribution of VTE



Vasa 2024; 53: 298-307

Post Thrombotic Syndrome

- Diagnosed clinically in patients with chronic venous insufficiency and a DVT $\geq$ 3 months previously
- Within two years after a DVT, 20–40% of patients will develop post thrombotic syndrome
- Annual costs of billions of dollars to treat
- PTS: extracts a progressive toll on physical function, psychological well-being, and social participation

Post Thrombotic Syndrome (PTS)

<u>SYMPTOMS</u>	<u>SIGNS</u>
Pain	Edema
Swelling	Telangiectasias
Cramps	Venous Dilatation
Heaviness	Varicose Veins
Fatigue	Redness
Itching	Cyanosis
Paresthesia	Hyperpigmentation

(Kahn SR. Circulation 2014; 130: 1636-1661)

Post Thrombotic Chronic Venous Ulcers: Decrease Quality of Life



Progression of Chronic Venous Insufficiency



**Stasis
Dermatitis—
skin oozing**

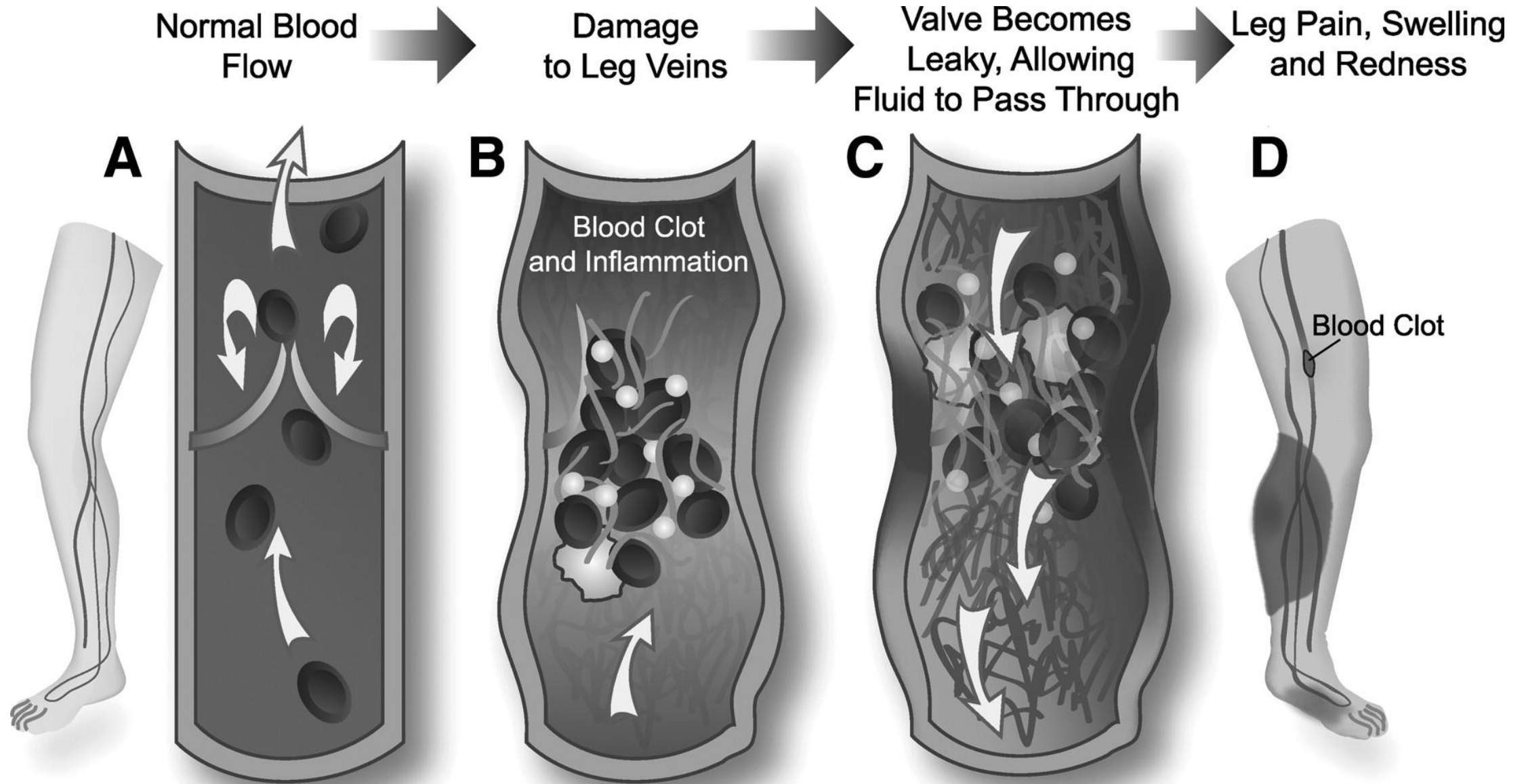


**Chronic Edema/
Advanced
Pigment
Changes**



**Venous Stasis
Ulcer**

PTS: Valves in the leg veins become leaky



Sara R. Vazquez and Susan R. Kahn *Circulation* 2010; 121: e217-e219

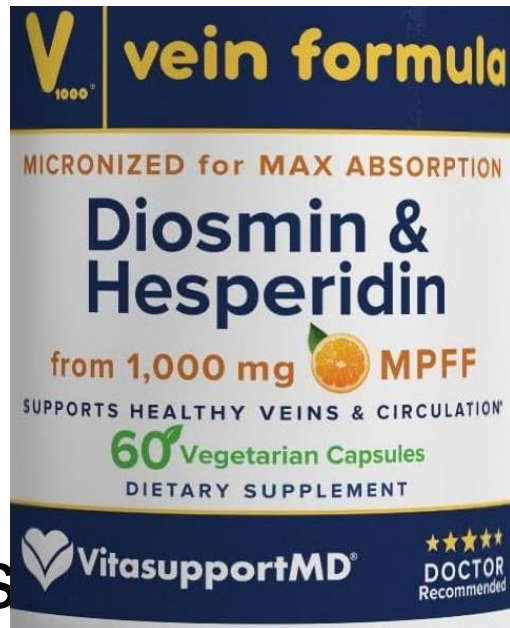
CVI Guideline Recommendations

- Ultrasound is the test of choice to diagnose venous reflux in a patient with CVI
- Compression therapy is the primary treatment option: stockings or CircAid



Guideline Recommendations for CVI

- Intervene surgically if venous reflux extends from above to below the knee
- If surgery isn't feasible, relieve CVI-related leg pain, leg heaviness, night cramps, swelling with: Micronized Purified Flavonoid Fraction (MPFF)



A venotonic and plant-based antioxidant. It improves blood circulation, reduces inflammation, and strengthens blood

vessels

NEJM 2024; 391: 2350

Mechanisms: Micronized Purified Flavonoid Fraction (MPFF)

- Over-the-counter medication. Order on Amazon.
- Protects the microcirculation from oxidative stress
- Modulates microvalve function
- Reduces transient venous reflux
- Promotes better valve competence
- These mechanisms collectively reduce leg pain, heaviness, swelling, and improve quality of life

Home Exercises for Leg Swelling

- Ankle Pumps: Perform plantar/ dorsiflexion of the ankle. Curl toes forward in plantar flexion; flex toes toward you in dorsiflexion.
- Ankle Rotations: Perform large ankle circles in both directions.
- Toe Gripping: Curl toes forward; make a fist with your toes in sitting position. Toe-grab a towel on the floor
- Toe Spreading: Spread the toes as much as possible. Alternate with toe gripping,
- Calf Squeezing: Contract the calf muscles.
- Leg Elevation: Keep legs elevated during prolonged sitting. (NEJM 2024; 391: 2350-2359)

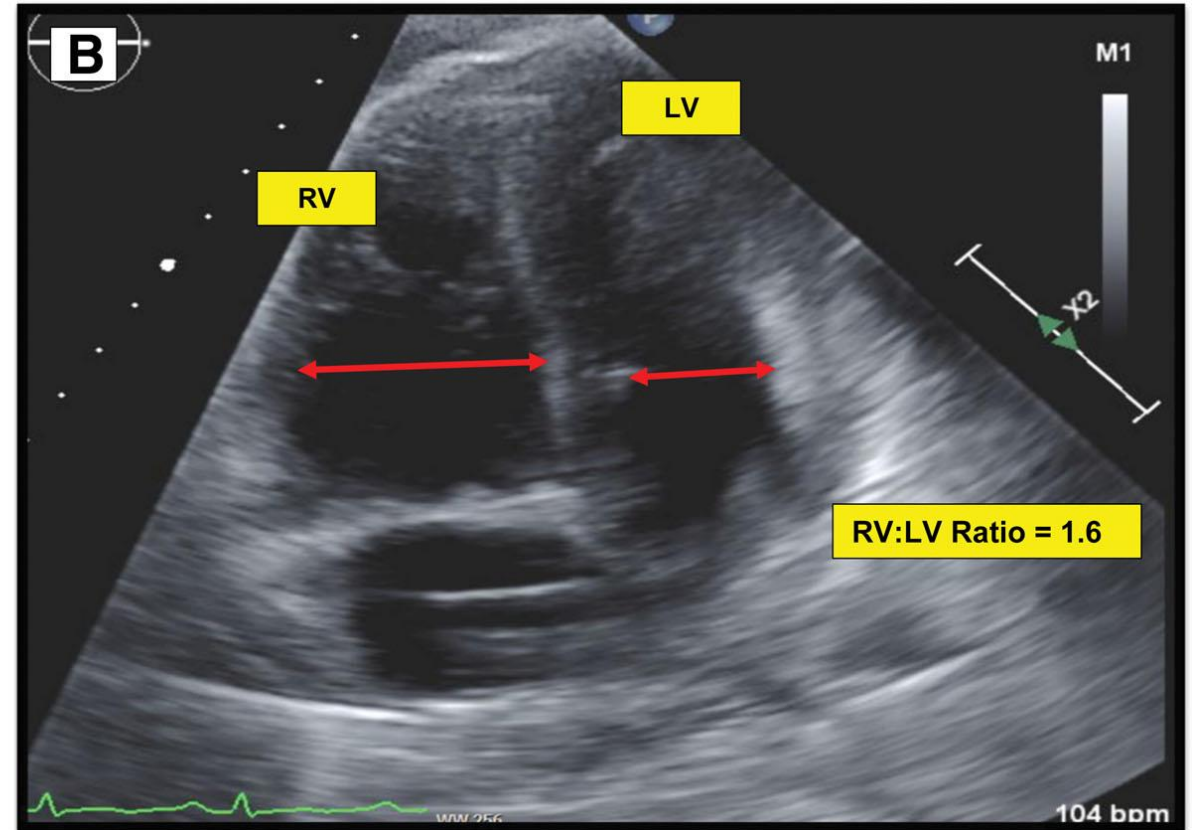
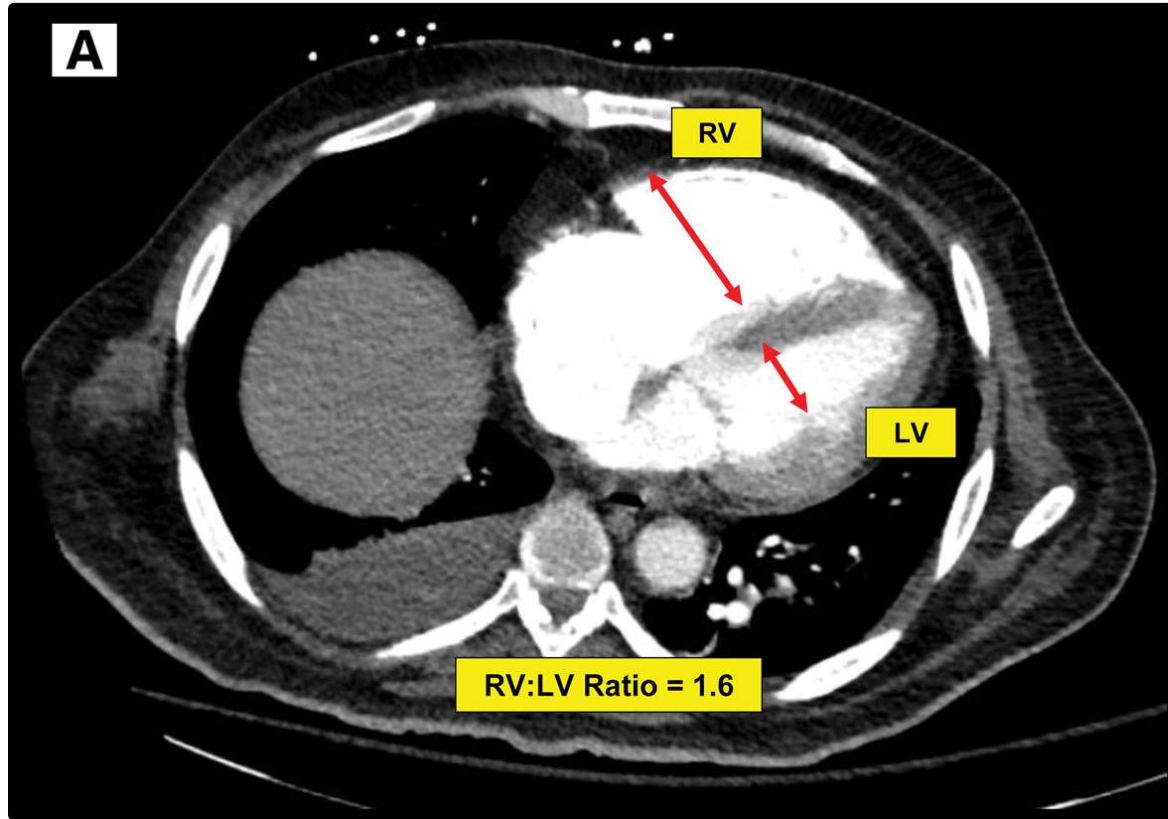
Management of Massive and Near-Massive PE

**Our Options for Treating PE
When Anticoagulation Alone
Does Not Suffice**

Background

- Hemodynamically unstable PE has an 8-fold higher mortality rate than stable PE.
- In patients with hemodynamically unstable PE, systemic thrombolysis decreases the death rate by 35-50%, but it causes a 2-3% rate of intracranial hemorrhage.
- In 1990, the FDA approved systemic TPA to treat massive PE in a dose of 100 mg as a continuous infusion over 2 hours.

Acute RV Dilation with PE: CT and TTE



Circulation 2023; Jan 23. 147: e628–e647. AHA Scientific Statement

Adjunctive Therapy for Massive PE

- Ensure excellent oxygenation and intensive anticoagulation
- Do not volume load the fragile RV with more than 500 ml to raise the BP
- Low threshold to begin pressors
 - 1) Norepinephrine
 - 2) Dobutamine

HI-PEITHO

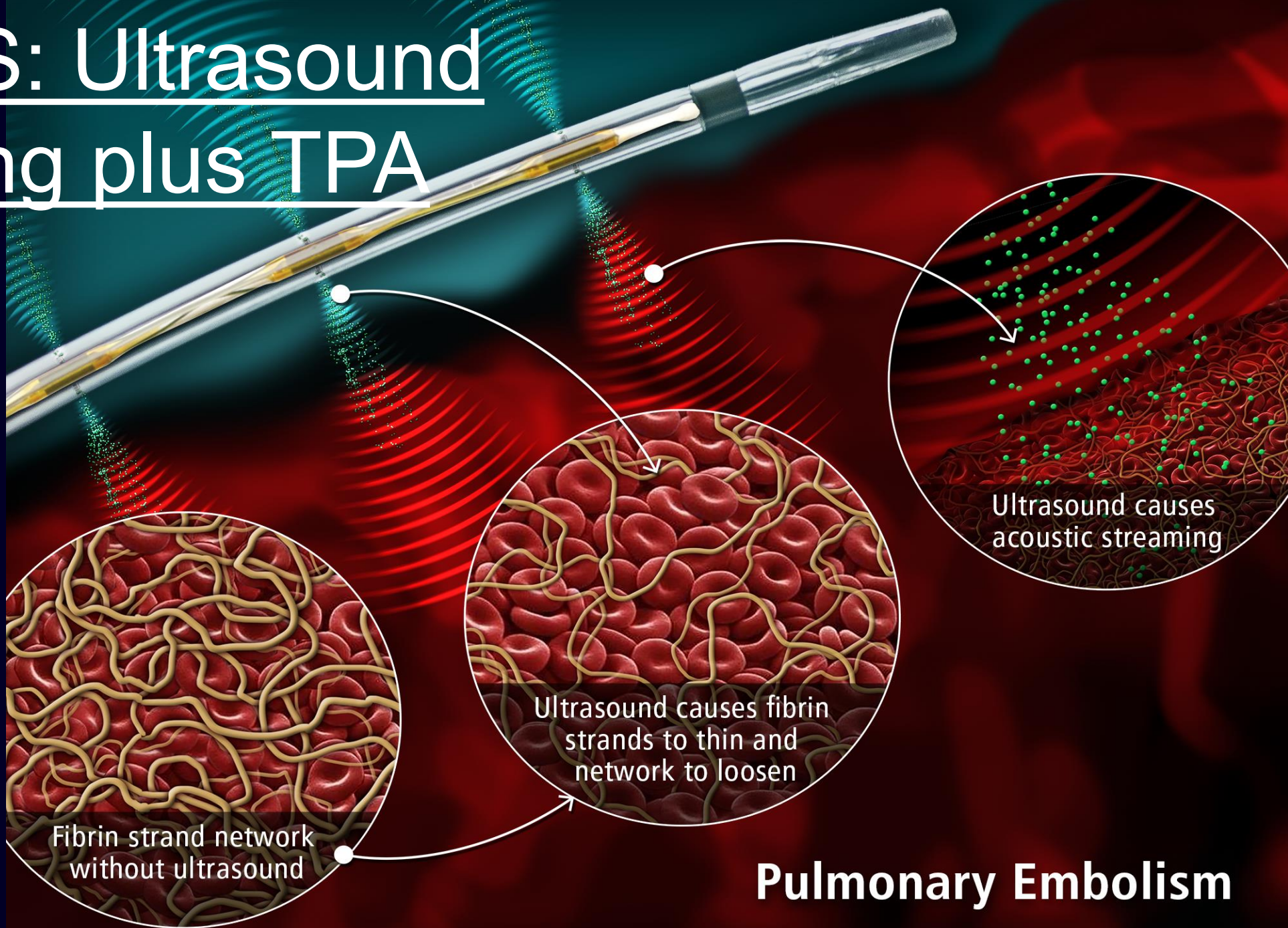
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ultrasound-Facilitated, Catheter-Directed Fibrinolysis for Acute Pulmonary Embolism

K. Rosenfield,¹ F.A. Klok,^{2,3} G. Piazza,^{4,5} A.S.P. Sharp,^{6,7} F. Ní Áinle,⁶ M.R. Jaff,⁸ S. Barco,^{3,9} S.Z. Goldhaber,^{4,5} N. Kucher,⁹ I.M. Lang,¹⁰ I. Schmidtman,¹¹ K.M. Sterling,⁸ A. Araszkievicz,¹² V. Arora,¹³ R. Cires-Drouet,¹⁴ J. Coghlan,¹⁵ L. Hobohm,^{3,16} W.D. Ito,¹⁷ K. Jacobson,¹⁸ C. Kaiser,¹⁹ G. Kopec,^{20,21} K. Marx,²² S. McElwee,²³ N. Meneveau,²⁴⁻²⁶ P. Monteleone,²⁷ J.M. Montero-Cabezas,²⁸ C.B. Olivier,^{29,30} J. Park,³¹ M. Roik,³² R. Sakhuja,¹ A. Tego,²² M. Theurl,³³ G. Visveswaran,³⁴ J.A. Vos,³⁵ M.N. Young,^{36,37} F.M. Asch,³⁸ and S.V. Konstantinides,^{3,39} for the HI-PEITHO Investigators*

EKOS: Ultrasound Pulsing plus TPA



Pulmonary Embolism

PEITHO: Greek Goddess of Persuasion



HI-PEITHO: Design

 **544** patients

 **65** centres U.S. & Europe



Inclusion Criteria:

Intermediate-high risk PE patients

Confirmed acute PE $RV/LV \geq 1.0$ & elevated troponin

Risk of early death/haemodynamic collapse (≥ 2 criteria)



RANDOMISED 1:1

EKOS™ + Anticoagulation

Ultrasound-facilitated, catheter-directed thrombolysis + unfractionated heparin or low molecular weight heparin

7-Days



Primary Endpoint:

7-day composite of
PE-related mortality

PE recurrence

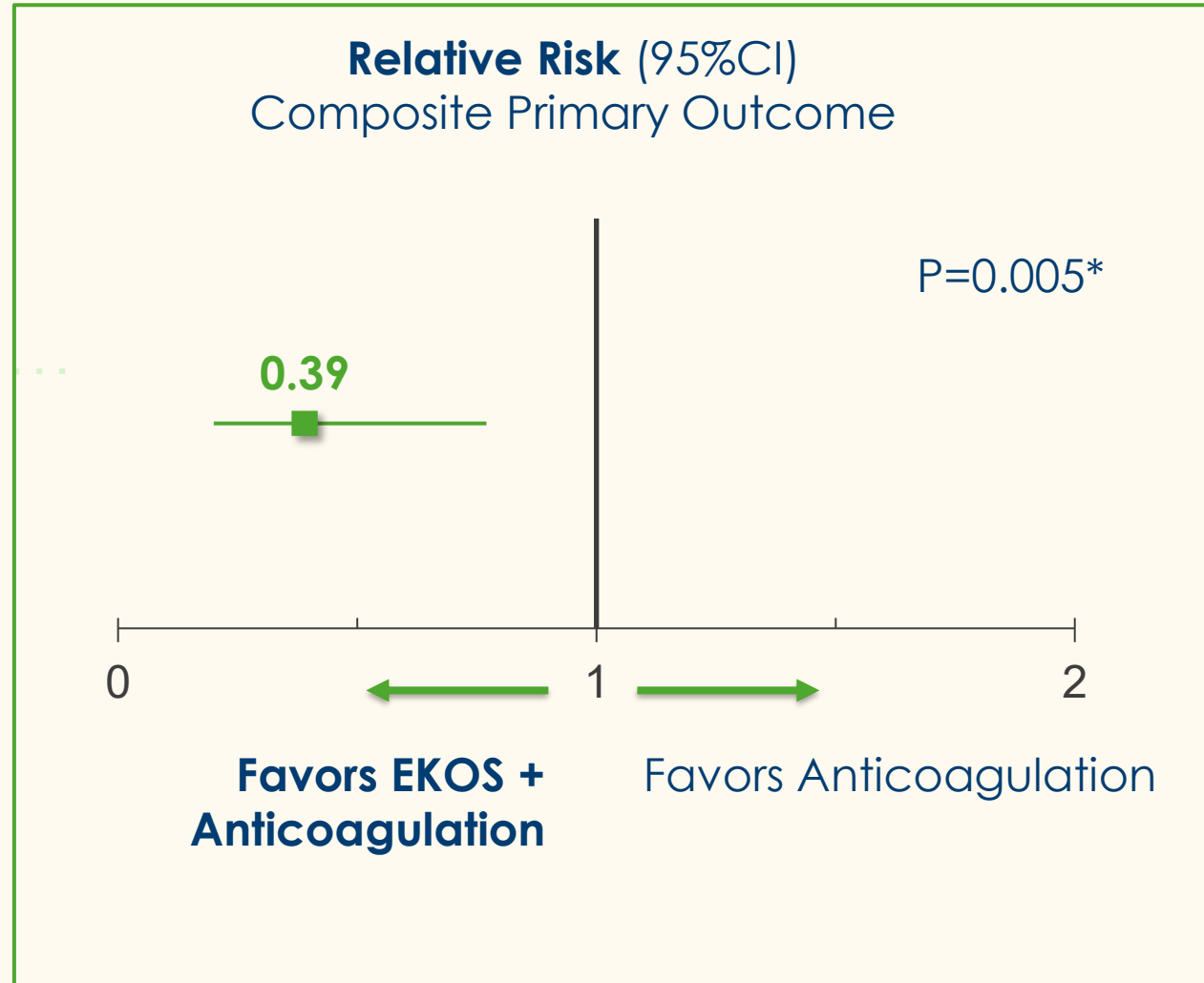
Cardiorespiratory
decompensation or collapse

Anticoagulation (Control)

Unfractionated heparin or low
molecular weight heparin

7-Days

HI-PEITHO: Primary Efficacy Outcome



Rosenfield K, et al. N Engl J Med. 2026

HI-PEITHO Conclusions

In patients with **acute intermediate-risk pulmonary embolism**:

- EKOS reduced the composite outcome of PE-related mortality, cardiopulmonary decompensation, or PE recurrence within 7 days compared to anticoagulation alone.
- No significant differences in major bleeding complications between the two treatment arms; no intracranial bleeding occurred in either group.

Mechanical **Thrombectomy**

Case Presentation: Saddle PE with Cor Pulmonale

45 y.o. woman on OC presented with sudden-onset acute SOB, pleuritic chest pain, and nausea.

Trop 276 -> 264, D-dimer >7k. WBC 13.4; BMI=25

CT PE: saddle PE, clot burden in the distal right and main left pulmonary arteries extending into lobar, segmental, and subsegmental branches.

RV/LV ratio greater than 3!

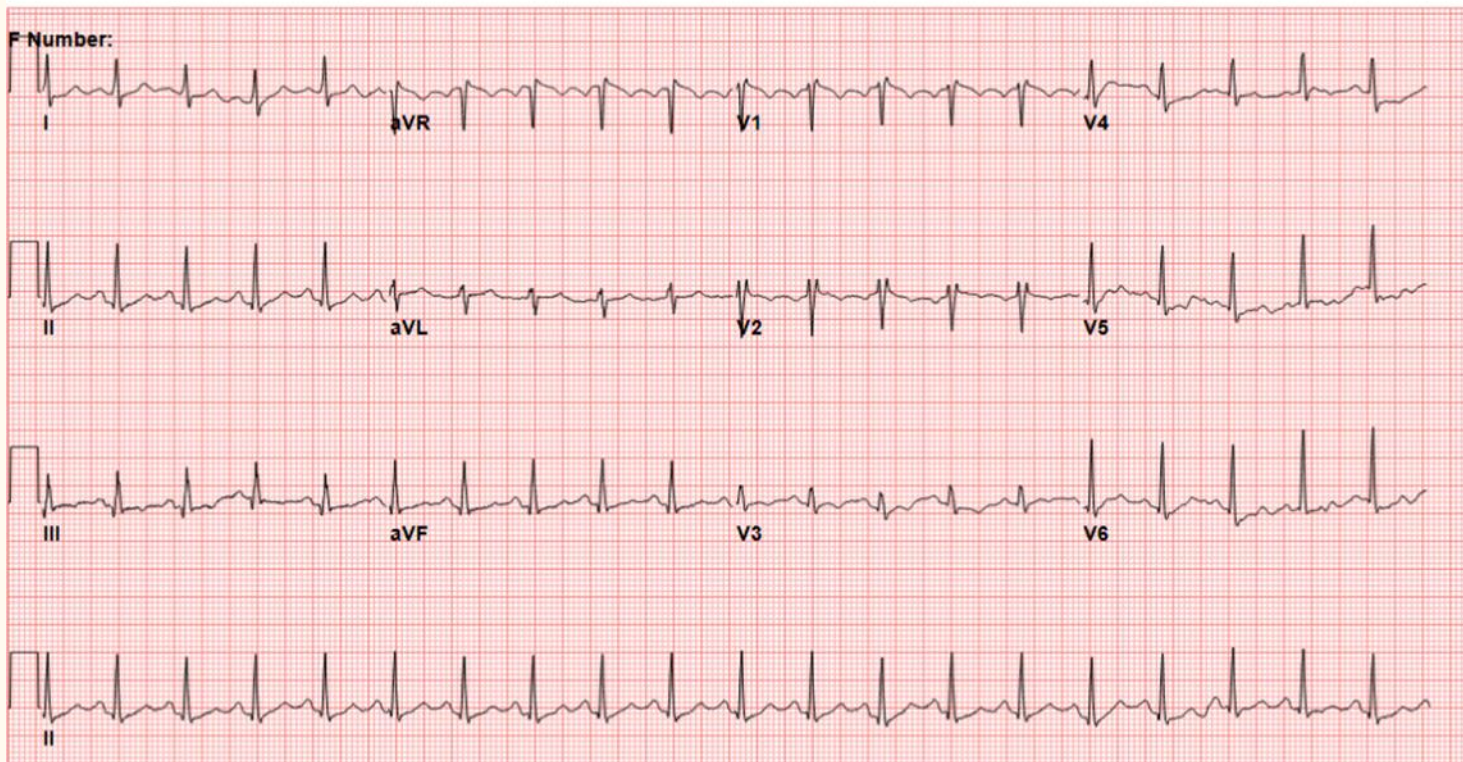
R leg LENI: popliteal and calf DVT

ECG and R Heart Cath

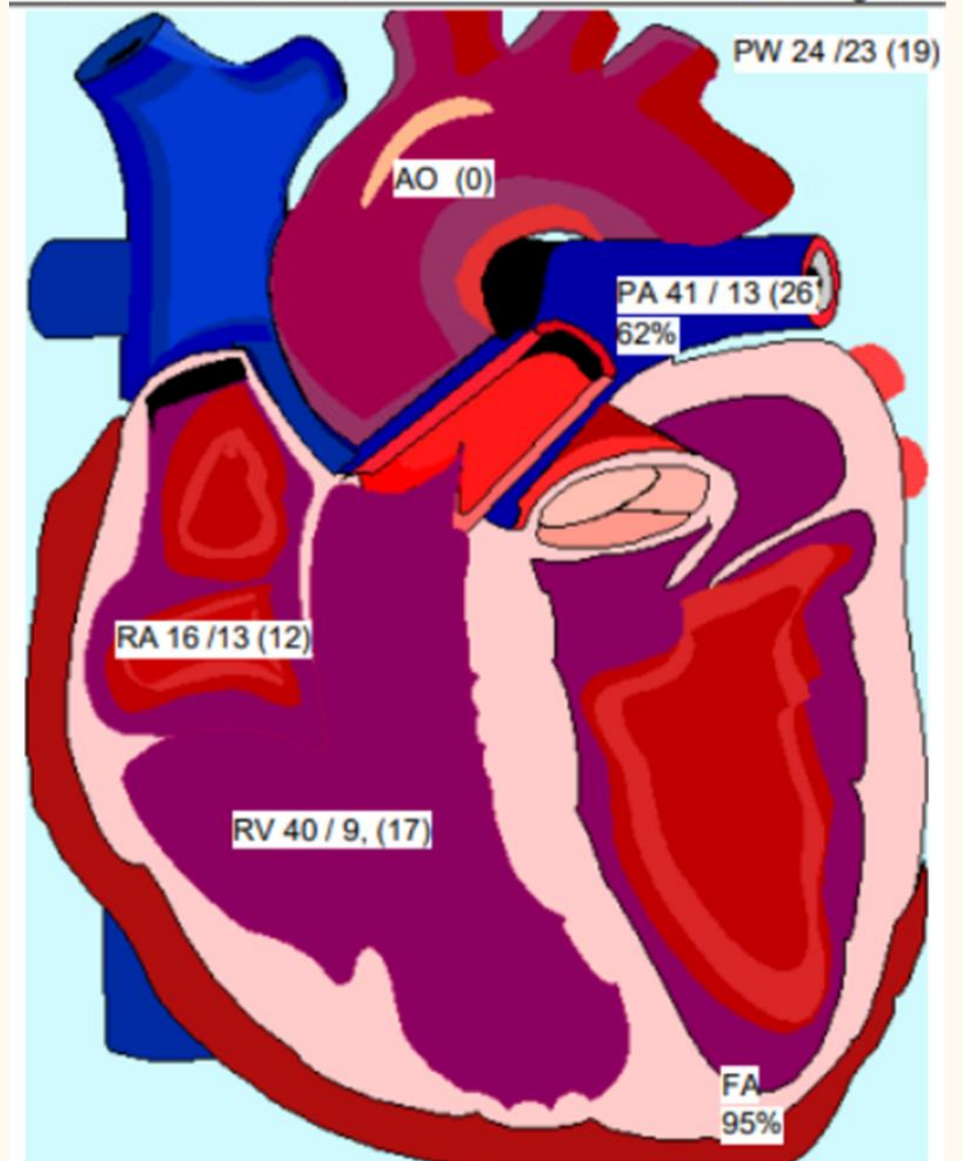
Vent. rate 119 BPM
PR interval 144 ms
QRS duration 90 ms
QT/QTcB 308/433 ms
P-R-T axes 69 63 27

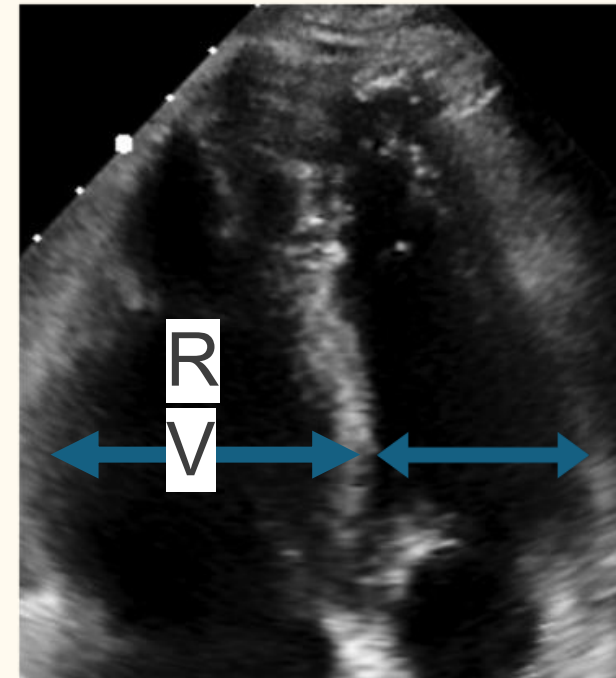
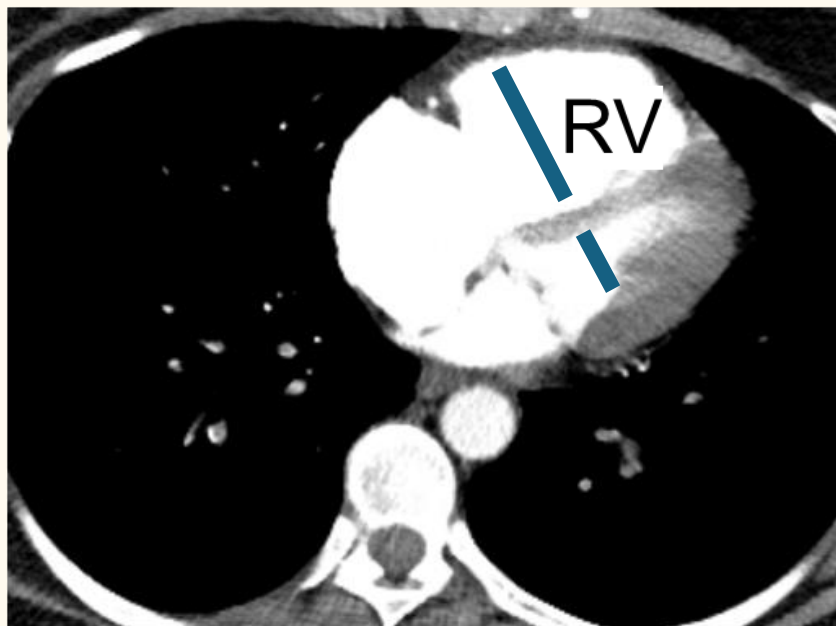
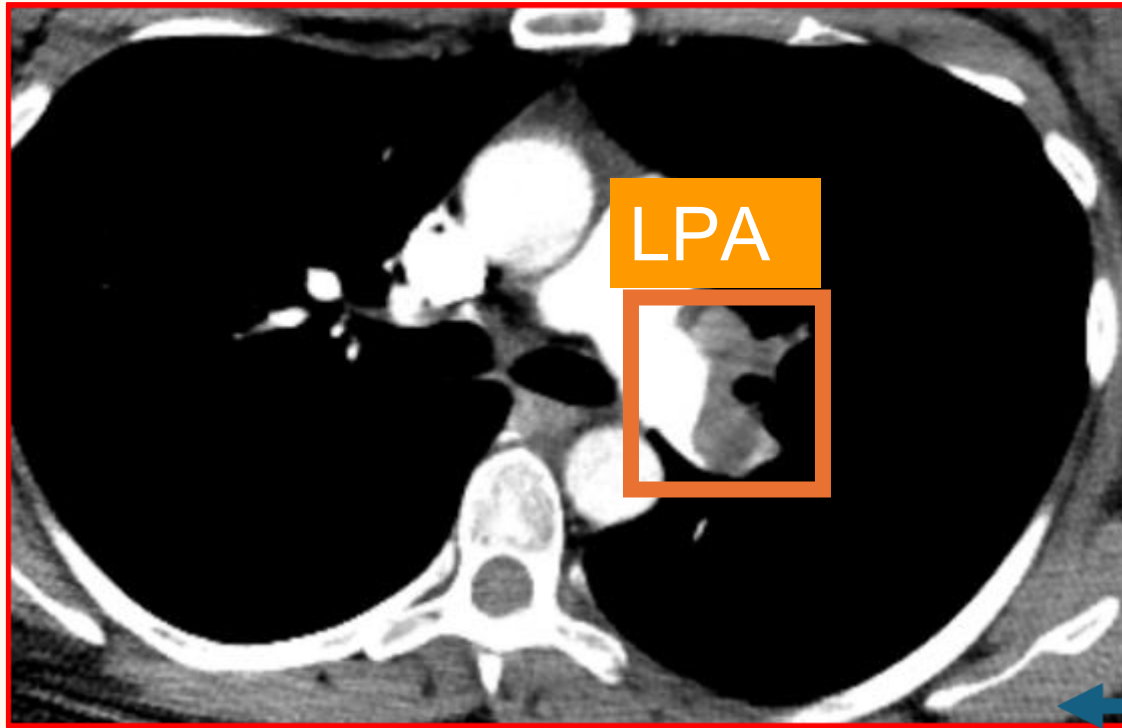
SINUS TACHYCARDIA
NONSPECIFIC ST AND T WAVE ABNORMALITY
NO PREVIOUS ECGS AVAILABLE

Technician: AJC67
Test ind: 786.50, 413.9



Proc: PULMONARY ANGIOGRAM
Cond: AIR REST BSA: 1.84 m² Hgb: 13.

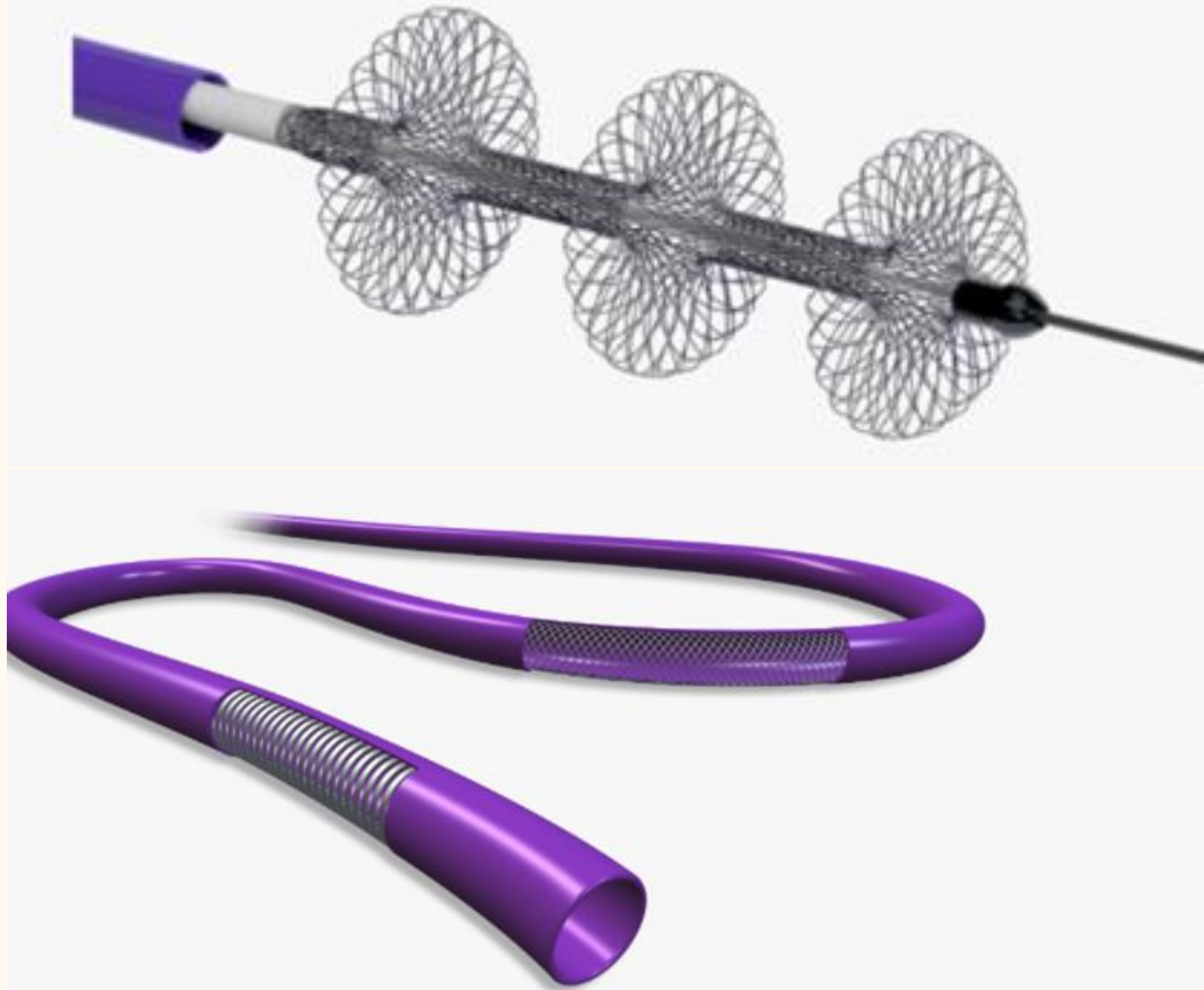




ECHO: Interventricular Septal Bowing



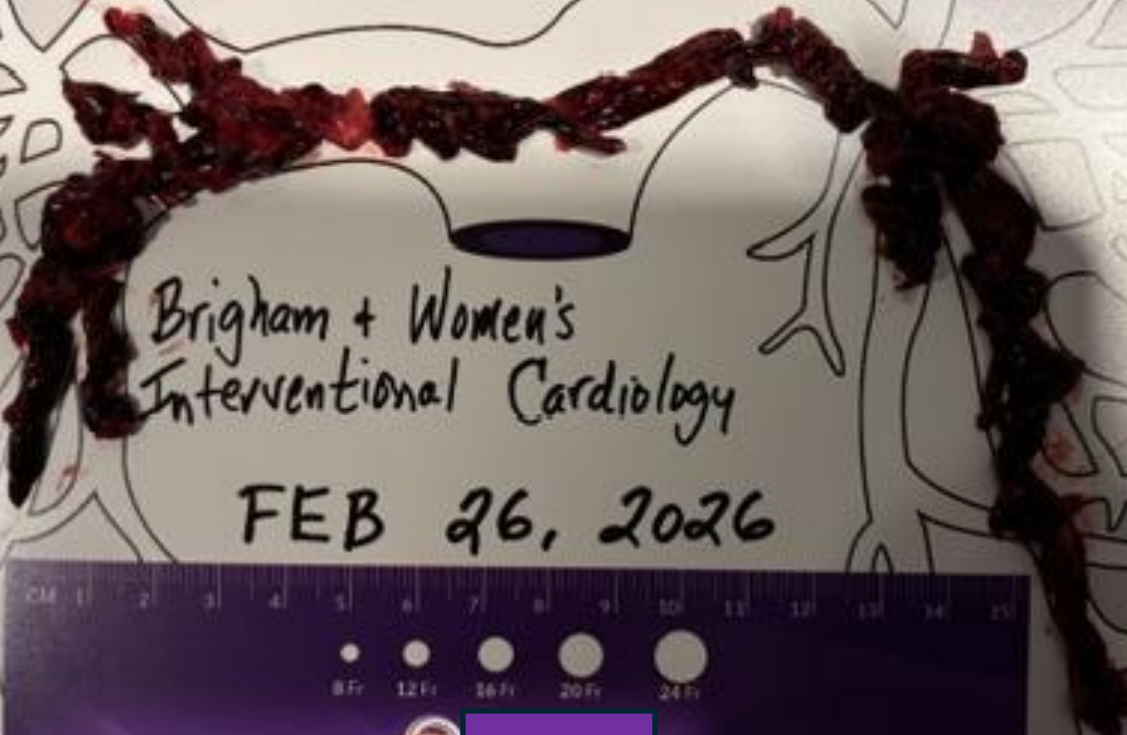
FlowTrieve:
20F—No tPA





PRE	POST
HR- 80	HR- 74
BP- 106/73	BP- 102/67
O2- 96%	O2- 95%
PAP- 41/18/26	PAP-

FlowTrievery®



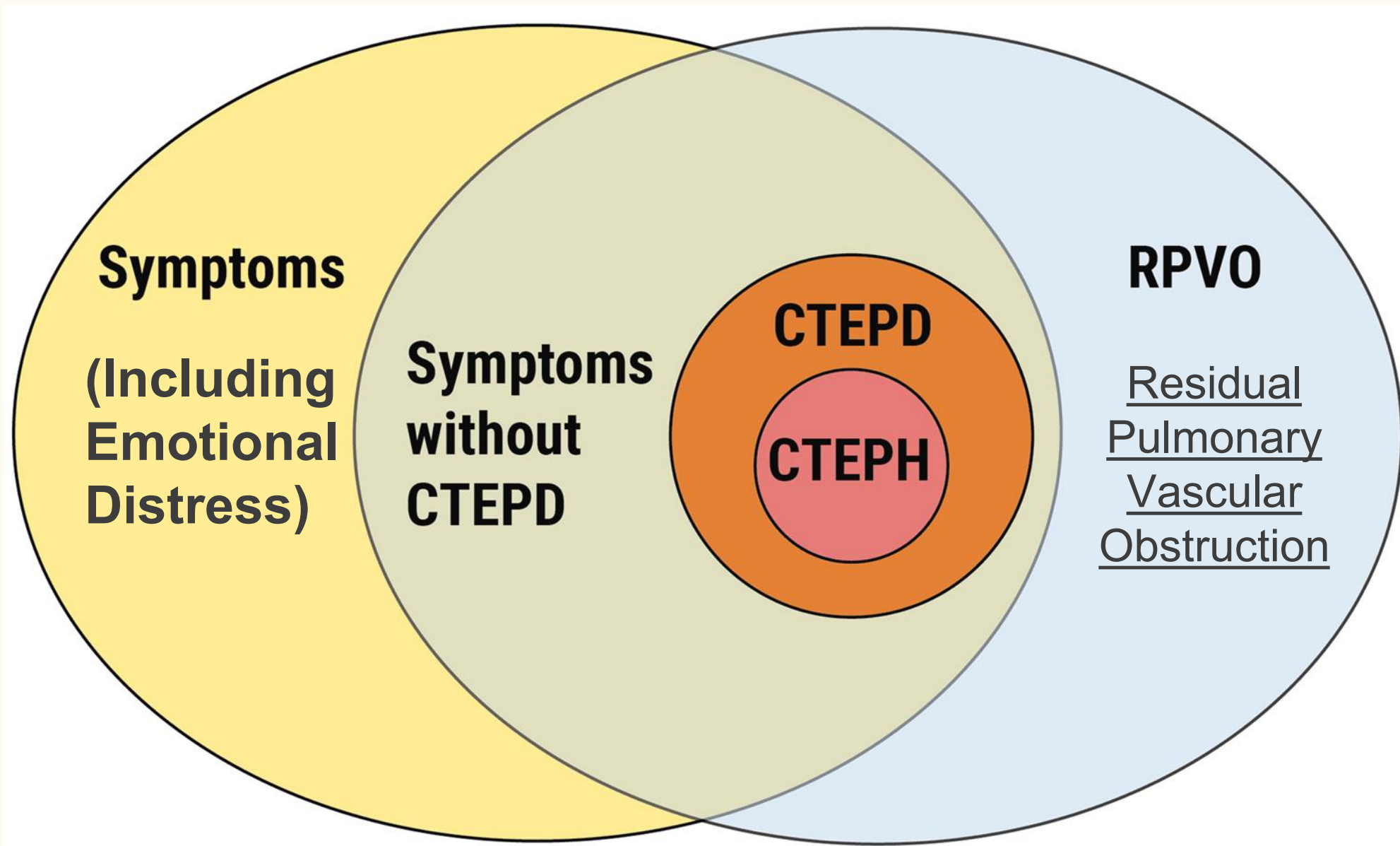
Brigham + Women's
Interventional Cardiology

FEB 26, 2026

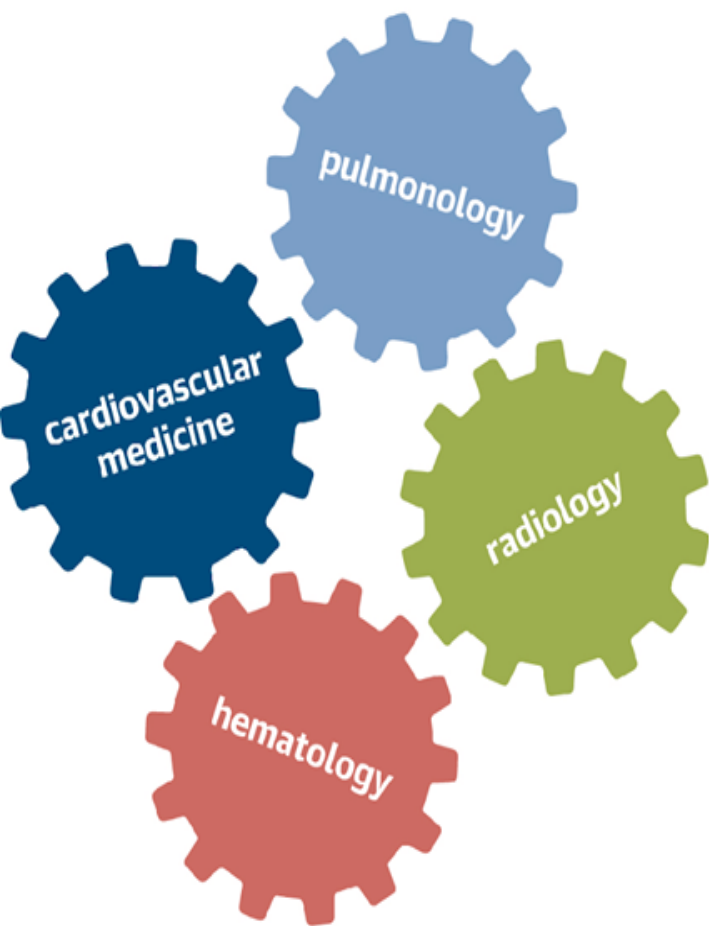


Future Perspectives

PE's Physical, Psychological, and Emotional Toll

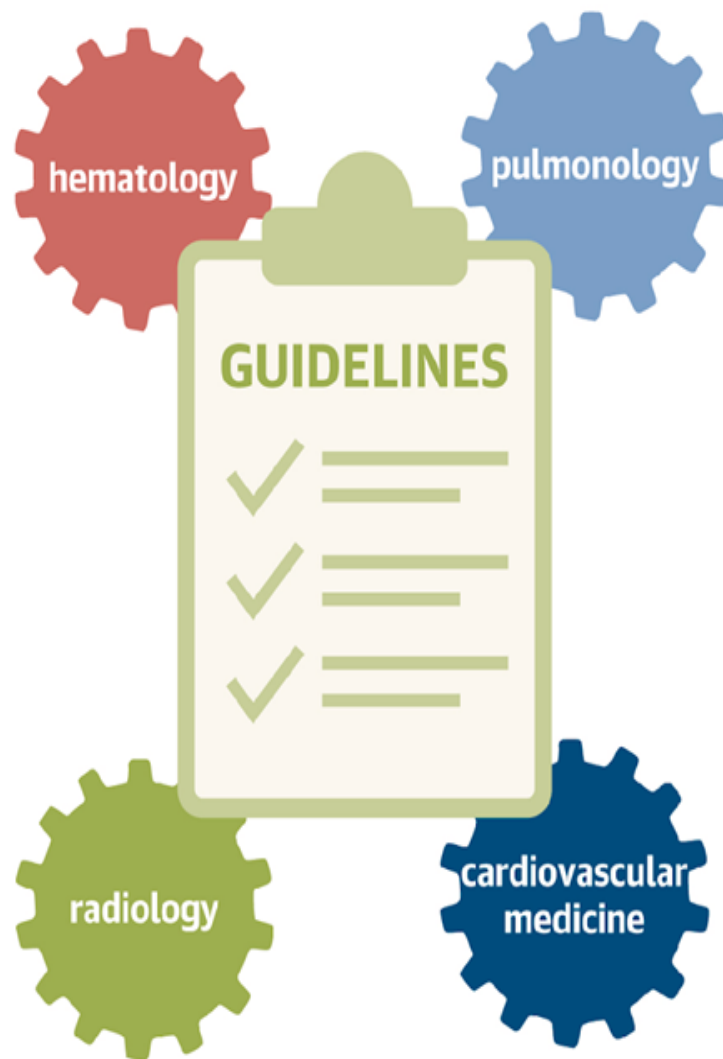


Fragmented PE Training



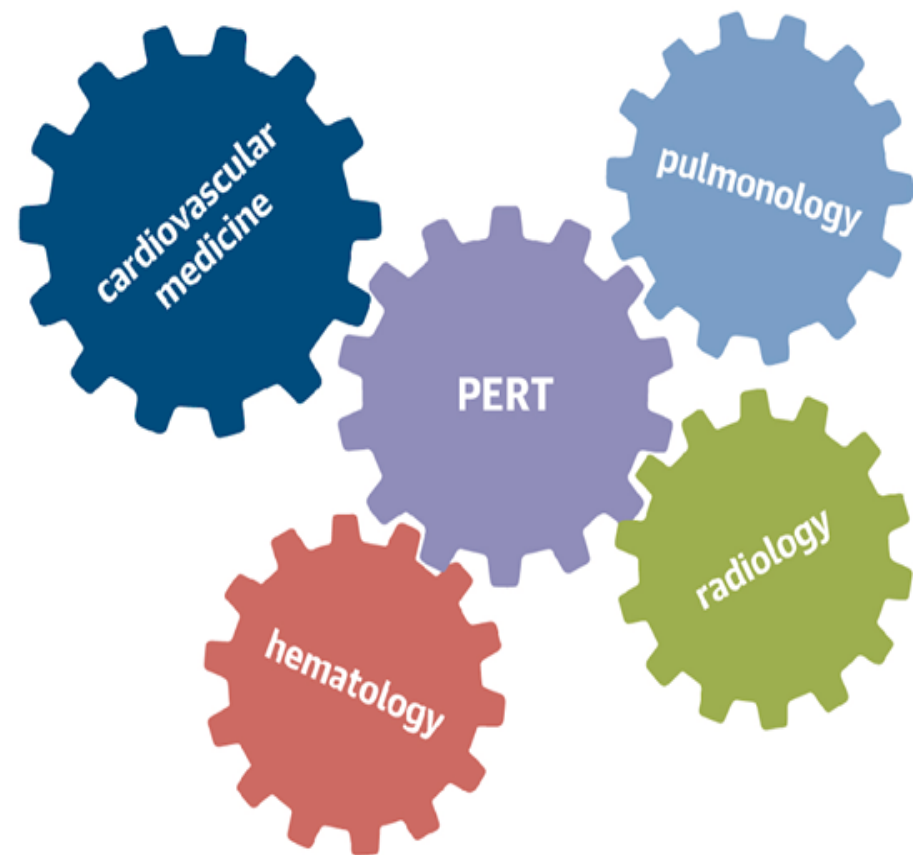
Lacks a coherent, longitudinal curriculum and is siloed across multiple specialties

AHA/ACC Guidelines: A Unified Foundation



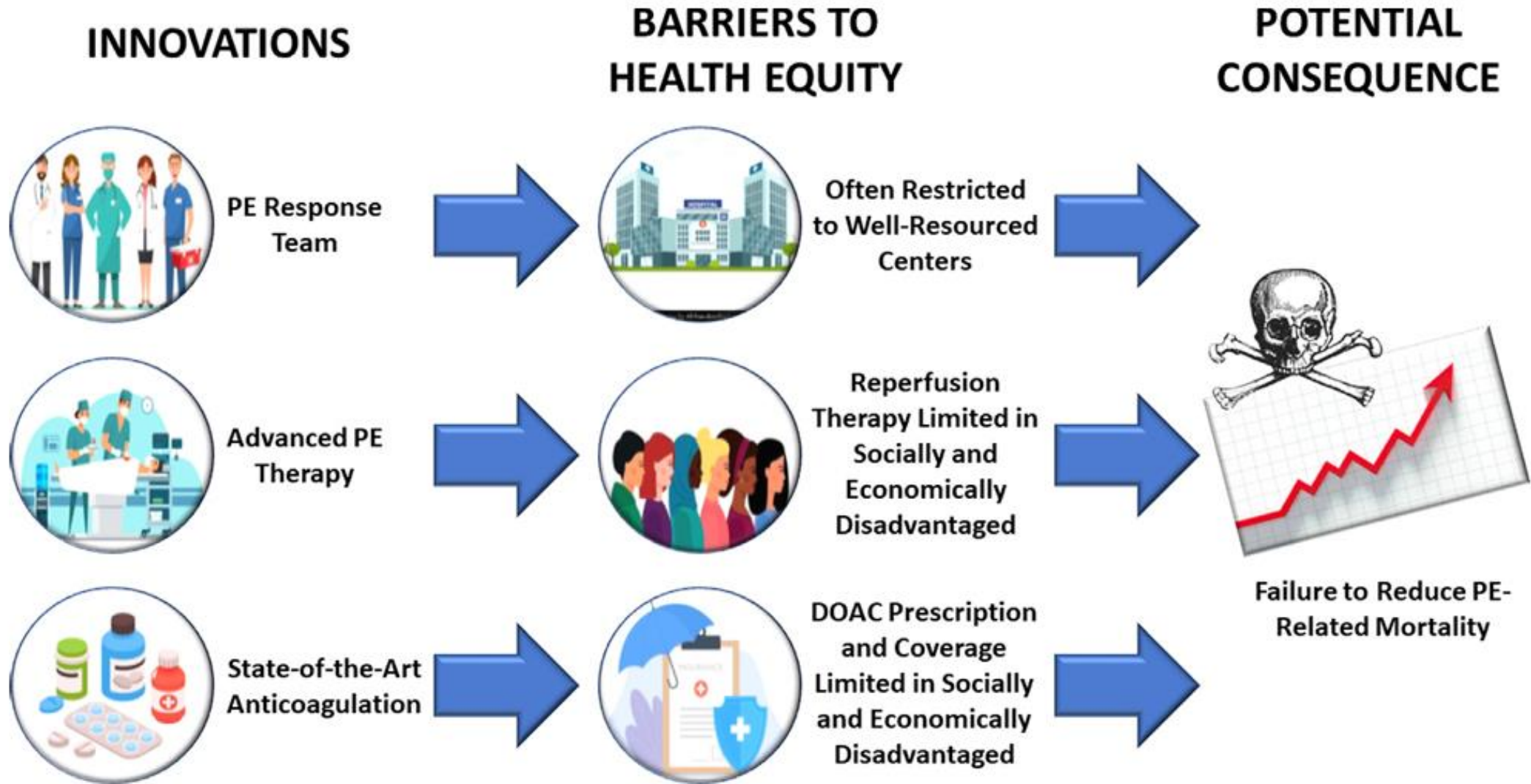
The inaugural AHA/ACC PE guidelines provide the missing foundation for a deliberate, comprehensive curriculum

Leadership in Multidisciplinary PERT

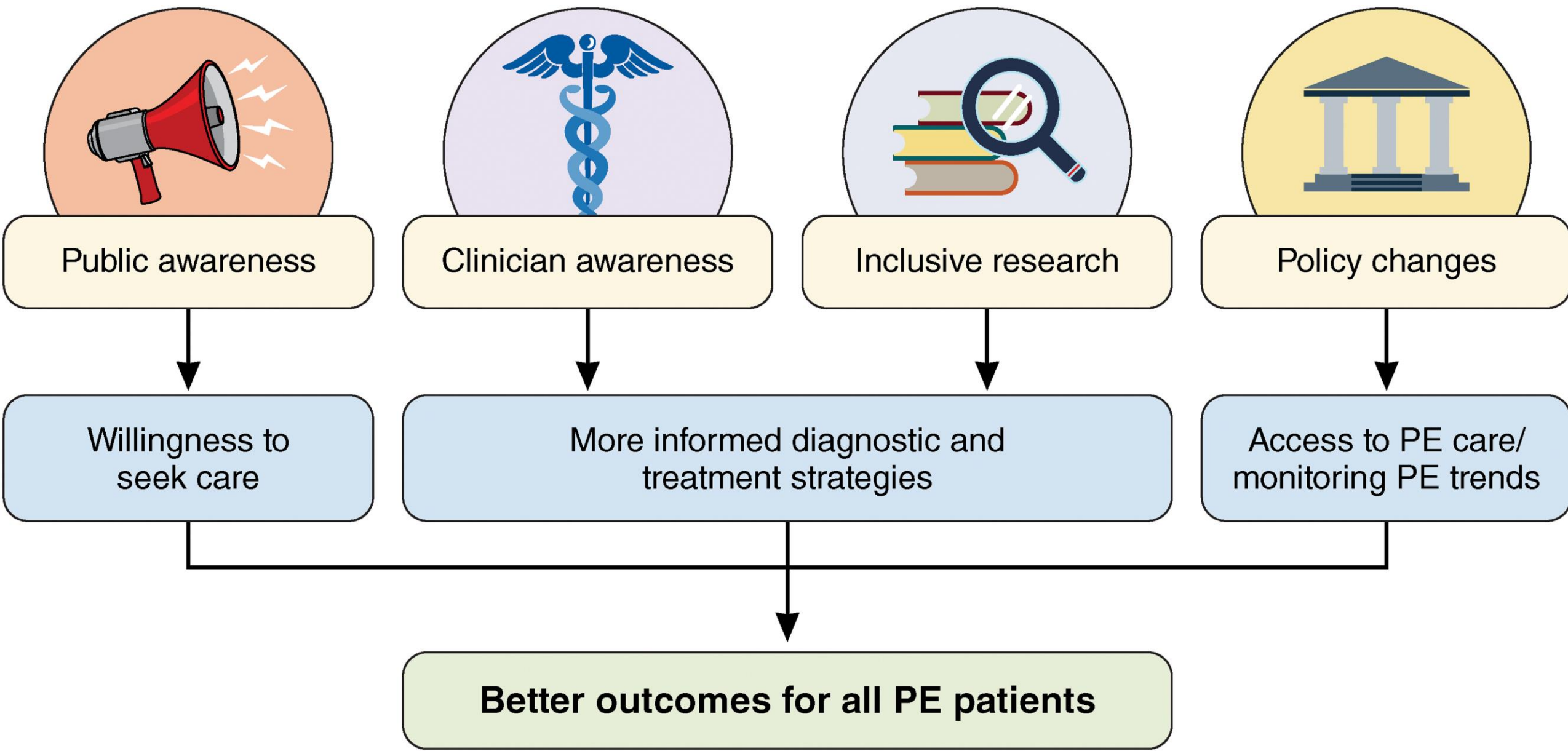


Graduating fellows must possess the collaborative skills and judgment to lead multidisciplinary PE care

Health Equity Barriers in PE



Piazza G. JTH 2024; 22: 1838-1840



Circulation 2025 Apr 15;151: e944-e955

Take-Home Points

- The ACC/ AHA's new 5-category PE classification system facilitates precision, prediction of prognosis, and clinical management.
- Anticoagulate with LMWH rather than UFH.
- Monitoring anti-Xa levels is rarely useful.
- With provoked VTE, consider extended duration anticoagulation if enduring risk factors persist.
- Pulmonary Embolism Response Teams enhance teamwork and family communication

References

- Guideline for the Evaluation and Management of Acute PE in Adults 2026; JACC Feb 19
- Dudzinski DM, Cibotti-Sun M, Moore MM. Acute PE Guideline-at-a-Glance 2026; JACC Feb 23
- Farmakis IT, Sagoschen I, Barco S, et al. ECMO and reperfusion strategies in high-risk PE. Crit Care Med. 2024; 52:e512–e521
- Jaber WA, Gonsalves CF, Stortecky S, et al. The PEERLESS RCT. Circulation 2025; 151: 260–273

Additional Tools and Resources

Scan here for VascuLearn VTE Communication Clinician Toolkit:



Scan here for VascuLearn Anticoagulation Chart: A Quick Guide for Prescribers:

