CardioVascular Learning Network | CME

VTE FOUNDATIONS

Patient Identification and Risk Stratification

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Faculty Disclosures

- **Trevor Cummings, MD**: Advisory Board—Pfizer, Inari Medical; Speaker—Pfizer, Inari Medical
- **Erin VanDyke, MPAS, PA-C**: Speaker—Inari Medical

Program Information

- This program is provided by HMP Education, an HMP Global company
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Learning Objectives

- Review the current state of VTE patient identification and risk stratification
- Discuss the impact of missed or delayed patient identification and treatment
- Describe the foundational elements of VTE program building
- Review the clinical impact of streamlined DVT and PE referral and treatment pathways

VTE = venous thromboembolism; PE = pulmonary embolism; DVT = deep vein thrombosis.

Overview

- Welcome and Introduction
- VTE Patient Identification and Risk Stratification
- Clinical Impact of Missed or Delayed Identification
- Building the Foundation for a VTE Program
- Streamlining DVT and PE Referral and Treatment Pathways
- Conclusion and Key Takeaways


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Introduction

VTE Is a Highly Prevalent, Major Cause of Hospital Morbidity and Mortality

Over **900,000** patients diagnosed with VTE annually in the U.S.

1 in 5 of these patients will be readmitted within 30 days

VTE kills between **100,000 and 300,000** U.S. patients annually

More than HIV, MVAs, and Breast Cancer combined

$10B Total U.S. Economic Burden

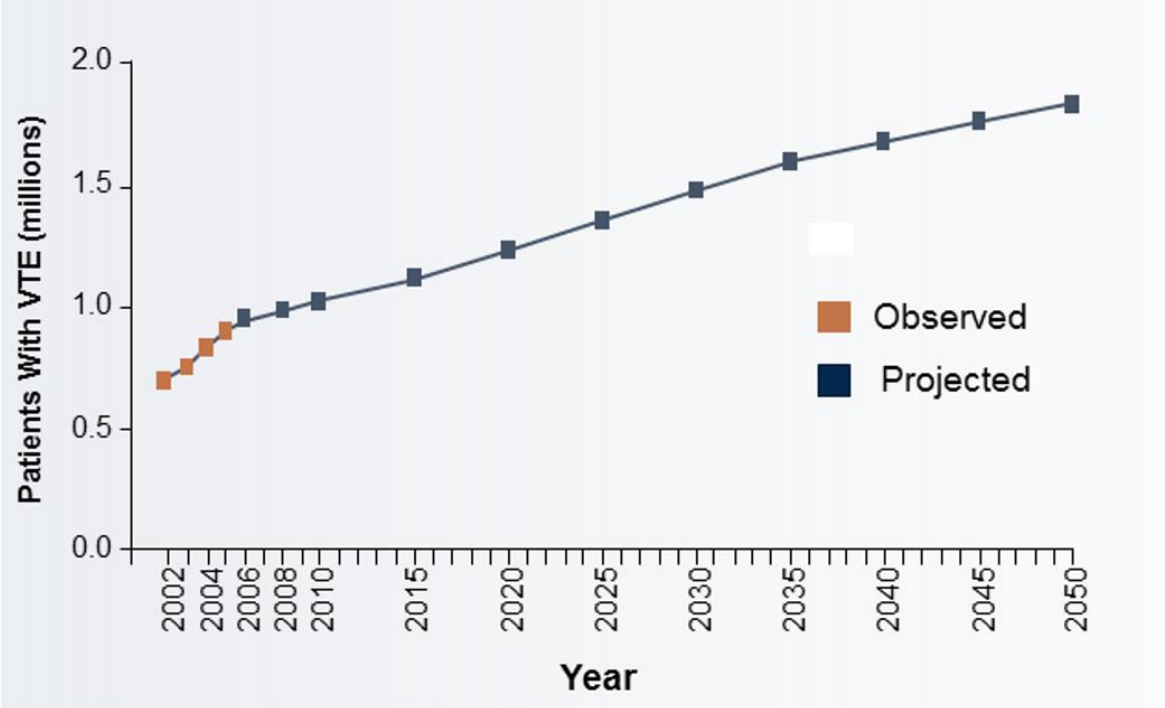
U.S. = United States; HIV = human immunodeficiency virus; MVAs = motor vehicle accidents.

Secemsky, et al. *J Am Heart Assoc*. 2018;7(13):e009047. Centers for Disease Control and Prevention (CDC). Accessed August 25, 205. https://www.cdc.gov/blood-clots/data-research/facts-stats/index.html. Grosse SD, et al. *Thromb Res*. 2016;137:3-10.

Increasing Prevalence of VTE in the U.S.

It is estimated that every year, over 900,000 VTE events* occur in the U.S.

The number of U.S. adults with VTE is projected to almost double.



- In a retrospective analysis of healthcare claims data from **2002 to 2006**, out of **12.7 million study-eligible patients, ~200,000 (1.57%) had VTE events**
  - Data derived from the MarketScan® Commercial and Medicare databases

***Modeling includes incident and recurrent VTE events.**

Roger VL, et al. *Circulation*. 2012;125(1):e2-e220. Deitelzweig SB, et al. *Am J Hematol*. 2011;86:217-220.

VTE Mortality Rate Is Underappreciated

- Exceeds 15% in the first 3 months after diagnosis and approaches 30% if untreated
- In nearly 25% of patients with PE, the initial clinical manifestation is sudden death

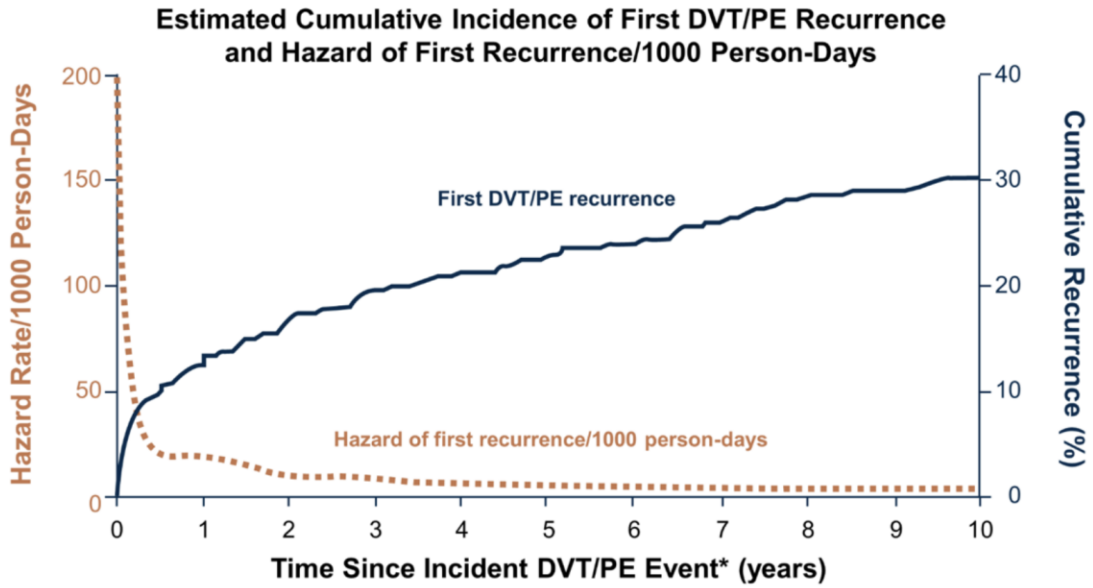
Mortality rate of acute pulmonary embolism according to Czech (2) and European (3) Guidelines

Clinical presentation of acute pulmonary embolism	Mortality rate
Unselected population	11.4% at 2 weeks, 17.4% at 3 months
Massive pulmonary embolism	
Overall	18% to 65%
Treated	Approximately 20%
With cardiogenic shock	25% to 30%
With resuscitation	65%
Submassive pulmonary embolism	5% to 25%
Pulmonary embolism with mobile thrombi in right-heart chambers	As high as 27%
Small pulmonary embolism	Up to 1%

Carson JL, et al. *N Engl J Med*. 1992;326(19):1240-1245. Konstantinides SV, et al. *Eur Heart J*. 2020;41(4):543-603.

It Happens Again...

- Nearly a third of patients with VTE will have had a recurrence at 10 years
- Risk of recurrence is even greater if the event was unprovoked



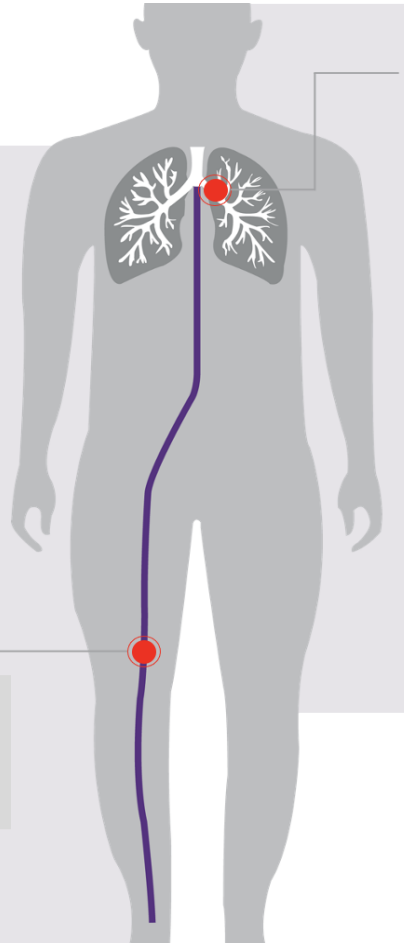
Boutitie F, et al. *BMJ*. 2011;342:d3036.

Overview of Venous Thromboembolism

DEEP VEIN THROMBOSIS (DVT)

Blood clots (aka thrombosis) that form in a deep vein, usually in the lower leg, thigh, or pelvis.

Up to **50%**	expected to develop **Post-thrombotic Syndrome (PTS)**
~90%	**of PTS patients are unable to work** 10 years after diagnosis
>10%	**of PTS patients develop venous leg ulcers.** Patients w/ severe PTS have QoL comparable to congestive heart failure or cancer



PULMONARY EMBOLISM (PE)

Most serious complication of DVT, when part of the clot travels to the lungs, causing a blockage. This is potentially life threatening.

3rd	**leading cause of cardiovascular death** (and a leading cause of preventable deaths in hospital)
Up to **15%**	30-day all-cause **mortality** (**28%** for high-risk PE)
Up to **50%**	**have residual vascular obstruction** , and long-term complications are common

QoL = quality of life.

Kahn SR. *Hematology Am Soc Hematol Educ Program*. 2016;2016(1):413-418. Kahn SR, et al. *Arch Intern Med*. 2004(1);164:17-26. Galanaud JP, et al. *Thromb Haemost*. 2018;118(2):320-328. Office of the Surgeon General (US), National Heart, Lung, and Blood Institute (US). Office of the Surgeon General (US); 2008. Prabhu W, et al. *R I Med J (2013)*. 2017;100(5):27-32. Schultz J, et al. *Pulm Circ*. 2019;9(3):2045894018824563. Chopard R, et al. *Am J Cardiol*. 2017;119(11):1883-1889. Miniati M, et al. *Medicine (Baltimore)*. 2006;85(5):253-262. Mrozek J, et al. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2018;162(2):121-126. Sista AK, et al. *Vasc Med*. 2017;22(1):37-43.

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VTE Patient Identification and Risk Stratification

Variety of Predisposing Risk Factors for VTE

- Clinical conditions
  - Surgery, trauma, cancer
  - Hormonal influences (pregnancy, HRT, birth control)
- Hereditary coagulopathies
  - Factor V Leiden
  - Protein C/S Deficiency
  - Prothrombin gene mutation
  - Antithrombin deficiency
  - Antiphospholipid syndrome (Doac ineligible)
- Acquired coagulopathy
  - Lupus anticoagulant
- Environmental
  - Air travel
  - Smoking
- Age
- Obesity
- Ethnicity
  - Higher rates among Black Americans: 30-60% higher incidence of VTE compared to White Americans

HRT = hormone replacement therapy.

White RH, et al. *Thromb Haemost*. 2003;90(3):446-455. Beckman MG, et al. *Am J Prev Med*. 2010;38(4 Suppl):S495-S501.

Risk Factor Profiling across Settings

- Hospitalized
  - Immobility, acute illness, central lines
  - Hospitalization itself increases VTE risk 8-fold compared with the community
- Surgical
  - Orthopedic, abdominal/pelvic, trauma
  - Major orthopedic surgery (hip/knee replacement, hip fracture): 40-60% risk of DVT without prophylaxis
- Ambulatory
  - Cancer, pregnancy, chronic disease
  - Cancer increases VTE risk ~4-7 fold compared with the general population
  - Pregnancy (antepartum): Risk is elevated throughout but highest in the third trimester
    - Postpartum (especially first 6 weeks): Risk is ~20-80 times higher than in non-pregnant women
- Risk varies with setting and patient population, and must be dynamic and repeated over time

Falck-Ytter Y, et al. *Chest*. 2012;141(2 Suppl):e278S-e325S. Heit JA. *Nat Rev Cardiol*. 2015;12(8):464-474. Heit JA, et al. *Arch Intern Med*. 2002;162(11):1245-1248. Heit JA, et al. *Arch Intern Med*. 2000;160:809-815. Khorana AA, et al. *Blood*. 2008;111(10):4902-4907. Pomp ER, et al. *J Thromb Haemost*. 2008;6:632-637.

VTE Identification

- Pulmonary Embolism (PE)
  - Dyspnea (sudden or unexplained)
  - Chest pain (pleuritic or substernal)
  - Tachypnea/tachycardia
  - Hemoptysis (less common)
  - Syncope
  - Hypotension (massive PE)
- Deep Venous Thrombosis (DVT)
  - Less swelling (usually unilateral)
  - Pain/tenderness (often calf or thigh)
  - Warmth, erythema, discoloration
  - Palpable cord

- Symptoms of DVT and PE are often subtle or nonspecific, leading to frequent misdiagnosis
- DVT classically presents with unilateral leg swelling and pain but may be mistaken for muscle strain or cellulitis
- PE often presents with shortness of breath and chest pain but can mimic pneumonia, asthma, or anxiety
- Recognition requires clinical suspicion and risk stratification tools to avoid missed or delayed diagnosis
- Education to patients and providers to recognize red flags early and understand risk

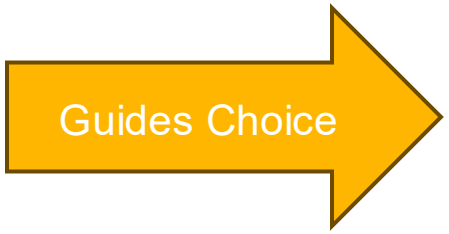
Konstantinides SV, et al. *Eur Heart J*. 2020;41(4):543-603. Kearon C, et al. *Chest*. 2016;149(2):315-352.

Comprehensive VTE Risk Assessment, Evaluation and Treatment Decisions

History and Exam

Clinical Probability

- Low
- Medium
- High



Decision rules, diagnostic studies, and management

VTE Risk: A Whole-Disease State Challenge

- Hospital-Associated VTE (HA-VTE): Up to 60% of all VTEs occur in the setting of hospitalization
- Prophylaxis Gap: Despite guidelines, up to 50% of at-risk hospitalized patients do not receive appropriate prophylaxis
- Up to 70% of hospital-associated VTEs occur after discharge

Spyropoulos AC, et al. *Thromb Haemost*. 2009;102(5):951-957. Amin AN, et al. *J Hosp Med*. 2012;7(3):231-238. Cohen AT, et al. *Thromb Haemost*. 2014;112(2):255-263. Schulman S, et al. *N Engl J Med*. 2013;368(8):709-718. Cohen AT, et al. *N Engl J Med*. 2016;375(6):534-544.

VTE Risk Factors

STOP THE CLOT, **SPREAD THE WORD™**

Checklist for Blood Clot Risk Factors

Listed below are some of the most common risk factors for blood clots.
Put a check in the box next to any risk factors that might apply to you.

- ☐ Hospitalization for illness or surgery
- ☐ Major surgery, particularly of the pelvis, abdomen, hip, knee
- ☐ Severe physical trauma, such as a car accident
- ☐ Injury to a vein that may have been caused by a broken bone or severe muscle injury
- ☐ Hip or knee replacement surgery
- ☐ Cancer and cancer treatments
- ☐ Use of birth control methods that contain estrogen, such as the pill, patch or ring
- ☐ Pregnancy, which includes the six weeks after the baby is born
- ☐ The use of hormone therapy with estrogen
- ☐ Personal or family history of blood clots
- ☐ Overweight
- ☐ Confinement to bed or a wheelchair
- ☐ Sitting too long, especially with legs crossed
- ☐ Smoking
- ☐ Age 55 or older
- ☐ Long-term diseases such as heart and lung conditions, or diabetes

If any of these risk factors apply to you, speak with your doctors about your potential risks for blood clots.
To learn more about blood clots, visit: www.stoptheclot.org.

Risk Stratification Tools for VTE Prophylaxis

Tool	Population	Strengths	Limitations
Caprini Score	Surgical patients (esp. general, oncologic, vascular)	Detailed, widely adopted, identifies very high-risk groups	Time-intensive, complex, not EHR-friendly
Padua Prediction Score	Hospitalized medical patients	Simple, validated for medical inpatients	Limited outside acute care; misses surgical risk
IMPROVEDD Score	Hospitalized medical patients	Incorporates D-dimer, higher sensitivity	Requires lab result, less validated in diverse populations
Khorana Score	Ambulatory cancer patients	Simple, validated in oncology, guides prophylaxis in trials	Low sensitivity—many events occur in “low-risk” patients
Geneva Risk Score	Hospitalized medical patients	Integrates clinical/lab criteria, considered objective	Less widely used in U.S.; moderate complexity

EHR = electronic health record.

Caprini JA. *Curr Opin Pulm Med*. 2010;16(5):448-452. Barbar S, et al. *J Thromb Haemost*. 2010;8(11):2450-2457. Spyropoulos AC, et al. *TH Open*. 2020;4(1):e59-e65. Khorana AA, et al. *Blood*. 2008;111(10):4902-4907. Blondon M, et al. *J Thromb Haemost*. 2020;18(3):676-680.

Wells' Criteria (VTE Identification Risk Scores)

Wells' Criteria for DVT

Calculates risk of DVT based on clinical criteria.

INSTRUCTIONS

- **Note**: The Wells' Score is less useful in hospitalized patients (Silveira PC, 2015).
- There are a few versions of this criteria with minor differences based on the study; this set is the most widely validated, based on Wells 2003.

When to Use | Pearls/Pitfalls | Why Use

Active cancer Treatment or palliation within 6 months	No 0	Yes +1
Bedridden recently >3 days or major surgery within 12 weeks	No 0	Yes +1
Calf swelling >3 cm compared to the other leg Measured 10 cm below tibial tuberosity	No 0	Yes +1
Collateral (nonvaricose) superficial veins present	No 0	Yes +1
Entire leg swollen	No 0	Yes +1
Localized tenderness along the deep venous system	No 0	Yes +1
Pitting edema, confined to symptomatic leg	No 0	Yes +1
Paralysis, paresis, or recent plaster immobilization of the lower extremity	No 0	Yes +1
Previously documented DVT	No 0	Yes +1
Alternative diagnosis to DVT as likely or more likely	No 0	Yes -2

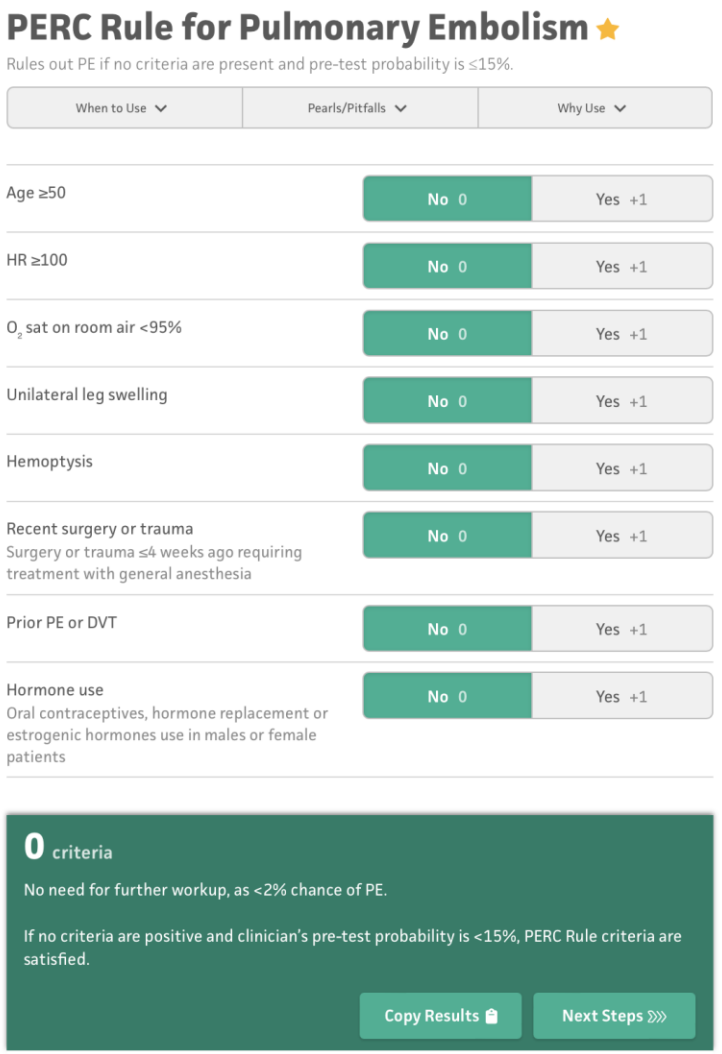
Wells' Criteria for Pulmonary Embolism ★

Objectifies risk of pulmonary embolism.

When to Use | Pearls/Pitfalls | Why Use

Clinical signs and symptoms of DVT	No 0	Yes +3
PE is #1 diagnosis OR equally likely	No 0	Yes +3
Heart rate > 100	No 0	Yes +1.5
Immobilization at least 3 days OR surgery in the previous 4 weeks	No 0	Yes +1.5
Previous, objectively diagnosed PE or DVT	No 0	Yes +1.5
Hemoptysis	No 0	Yes +1
Malignancy w/ treatment within 6 months or palliative	No 0	Yes +1

PERC for PE (Rule-Out Score)



PERC = pulmonary embolism rule-out criteria.

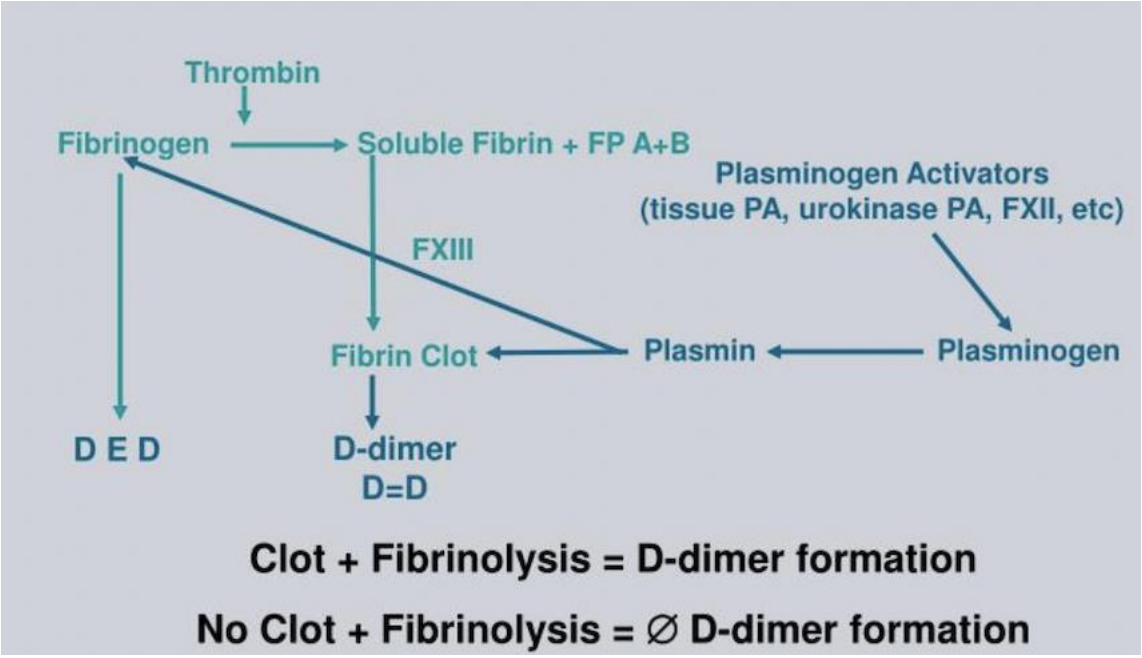
Problems with the Tools

- Limitations
  - Derivation issues
  - Low sensitivity
  - Ease of use challenges
  - High risk of bias
  - Lack of bleeding risk assessment
  - Underrepresentation of certain patient populations
  - Variability in performance
  - Lack of prospective head-to-head comparison
  - Inability to capture all risk factors

Basey AJ, et al. *BMJ Open*. 2012;2(6):e001668.

The D-Dimer

- “The D-dimer is a by-product of the blood clotting and break-down process that can be measured via analysis of a blood sample. D-dimer is released when a blood clot begins to break down.”



Killeen RB, et al. StatPearls [Internet]. StatPearls Publishing; 2025.

Elevated D-Dimer

- DIC
- Fibrinolytic therapy within 7 days
- Malignancies
- Aortic aneurysm, MI
- Sepsis, severe infection, pneumonia
- Trauma, surgery
- Liver cirrhosis
- Pregnancy or obstetric complications
- Age
- Hospitalized patients in general
- Stress
- Excessive exercise
- Lipemic samples
- Hemolyzed samples

Killeen RB, et al. StatPearls [Internet]. StatPearls Publishing; 2025.

False Negative D-Dimer Testing

- Age of thrombus
  - Patients who report greater than 14 days duration of symptoms demonstrate inactive fibrinolysis and D-dimer levels rapidly decrease **FALSE NEGATIVE**
- Size of thrombus
  - Smaller thrombi produce minimal levels of D-dimer **FALSE NEGATIVE**
- Position of thrombus
  - Calf vein thrombi **FALSE NEGATIVE**
  - Sub-segmental PE **FALSE NEGATIVE**
- Anticoagulant therapy
  - Reduces fibrin formation
  - D-dimer levels are reduced **FALSE NEGATIVE**
  - Do not perform D-dimer on these patients!

Bruinstroop E, et al. *Eur J Intern Med*. 2009;20(5):441-446. Gilens JF, et al. *Can Fam Physician*. 2022;68(3):195. Benilde C, et al. *Thromb Res*. 2022;213:163-169. Kraaijenhagen RA, et al. *Thromb Res*. 2003;11(3):155-158.

When to Use D-Dimer?

- Low to moderate risk patients with symptoms less than 14 days (maybe 7?) who are not already on anticoagulation
- Not high enough NPV to rule out VTE in high-risk patients
- Reference adjusted cutoffs in appropriate populations (age adjusted in those over 50 and YEARS Algorithm for pregnancy)
- Develop an elevator speech for patients explaining how it can be used to “rule out” a VTE diagnosis but not “rule in”
- Utility in assisting decision whether to cease or continue anticoagulation in women with unprovoked VTE after acute therapy

NPV = negative predictive value.

Gaps in VTE Screening, Prophylaxis, and Patient Education

- Under-screening: Many hospitalized patients are not assessed for VTE risk at admission or during hospital stay
- Failure to reassess: Risk often changes, yet transitions of care (discharge, unit transfer) rarely trigger re-evaluation
- Prophylaxis gaps
  - Up to 50% of at-risk medical inpatients do not receive guideline-recommended prophylaxis (ENDORSE study)
  - Post-discharge prophylaxis is rarely implemented, despite ongoing HAVTE risk
- Patient education deficits
  - Patients often leave without understanding signs/symptoms of VTE or when to seek care
  - Leads to delayed recognition, readmissions, and preventable complications
- Impact: Missed prophylaxis and poor transitions contribute to preventable morbidity, mortality, and readmissions

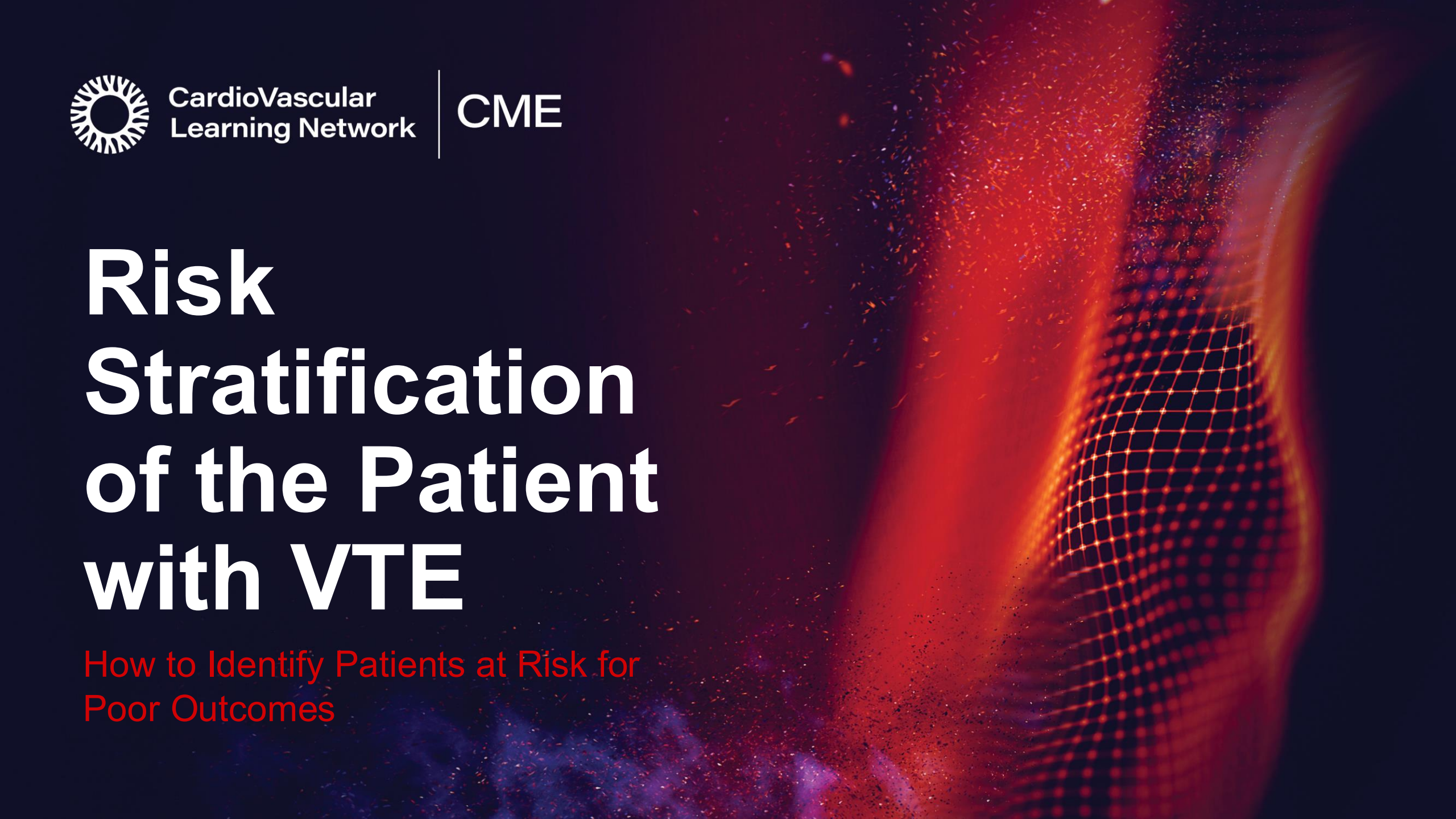
HAVTE = hospital-acquired venous thromboembolism.

Cohen AT, et al. *Lancet*. 2008;371(9610):387-394. Gould MK, et al. *Chest*. 2012;141(2 Suppl):e227S-e277S. Amin AN, et al. *J Hosp Med*. 2012;7(3):231-238. Kahn SR, et al. *Cochrane Database Syst Rev*. 2018;4(4):CD008201.

Recommendations

- When using VTE risk assessment tools, it is crucial to be aware of their limitations and potential biases
- Consider using multiple tools and integrating clinical judgment to assess individual patient risk (apply correct tool for the population)
- Regularly re-evaluate the risk of VTE throughout the patient's hospitalization or course of treatment
- Ensure that data collection and risk assessment are conducted carefully to minimize the risk of information bias
- Be mindful of publication bias and the potential for overestimation of risk in certain populations
- Utilize EMR building tools to enhance data capture and encourage documentation/use

EMR = electronic medical record.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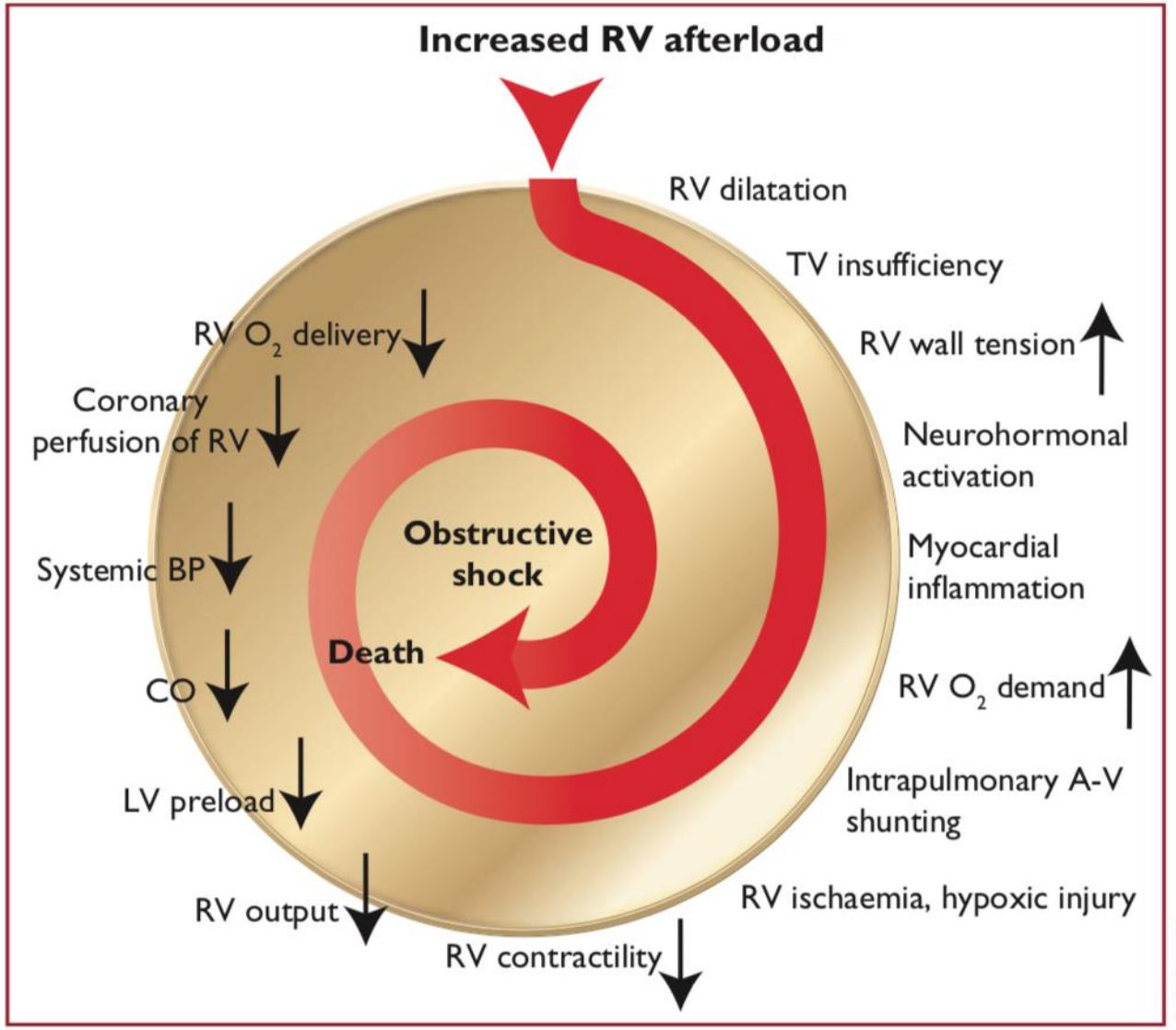
Risk Stratification of the Patient with VTE
How to Identify Patients at Risk for Poor Outcomes

PE Death Spiral



Keefe NA, et al. IR Playbook. Springer; 2024.

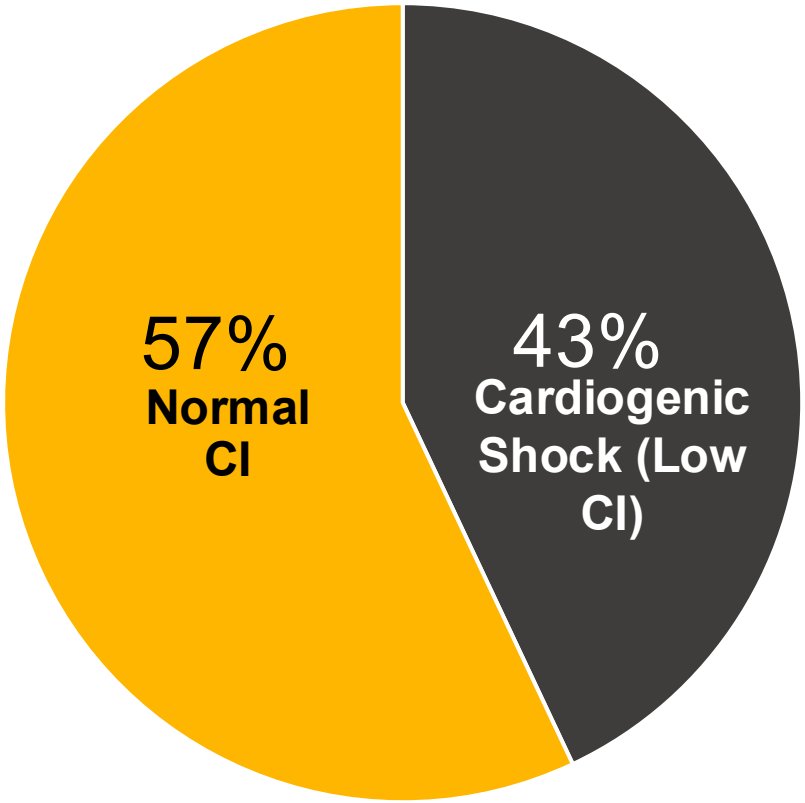
Patients with Normotension Are Often Sicker than They Appear

43%

of normotensive Submassive PE patients have been found to be in cardiogenic shock

"Current risk stratification tools may not be sufficient to identify patients with higher risk Submassive PE who may benefit from more aggressive therapy."

Sub-Massive PE Patients Presenting with Normotension



Porcaro, et al. Presented at: American College of Cardiology's 68th Annual Scientific Sessions (ACC 2019); March 16-18, 2019; New Orleans, Louisiana. Abstract #1007-15. Mehta, et al. Presented at: ACC 2019; March 16-18, 2019; New Orleans, Louisiana. Abstract #1049-03.

Risk Stratification: What Does a Risky Patient Look Like?

History

- Syncope or near-syncope (revealing an absence of hemodynamic reserve)
- Symptom duration is important
  - Having symptoms >10-14 days suggests a more chronic thrombus
  - Having stable symptoms for several days reduces the likelihood of sudden deterioration
  - Recent-onset or accelerating symptoms are worrisome

General Appearance

- "Sense of Doom" (be concerned, patient is often right)
- Diaphoresis (endogenous epinephrine keeping them alive)
- Signs of hypoperfusion or end-organ damage (most concerning)
  - AMS
  - Cool extremities or mottling

AMS = altered mental status.

High Risk Stratification

Bradycardia (may mean an impending brady-asystolic arrest)

Tachycardia (shock index [heart rate/systolic blood pressure] >1 suggests poor hemodynamic reserve and a worse prognosis)

Hypotension (traditionally the main parameter used to define massive PE)

- Systolic blood pressure <90 mm for 15 minutes
- Fall in systolic blood pressure by >40 mm for 15 minutes
- Requiring pressor support

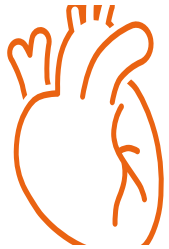
Hypertension (generally reassuring, unless endogenous release of epinephrine leading to hypertension—these patients should look and feel awful)

Tachypnea (excellent predictor of occult critical illness and subsequent deterioration)

>30 breaths/minute has been correlated with worse outcomes

Gökçek K, et al. *Med Clin (Barc)*. 2022;158(8):351-355. Aujesky D, et al. *Am J Respir Crit Care Med*. 2005;172(8):1041-1046.

High Risk Stratification: Labs



Troponin

Elevated troponin correlates with mortality risk (with an odds ratio of ~5)

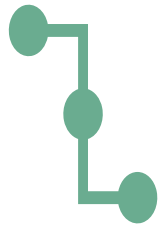
Studies have broad cutoff ranges (also can not compare 5th generations to each other)

4th generation: Troponin I >0.1 ng/mL or troponin T >0.03 ng/mL

Lactate

Underutilized but strong predictor of mortality

Risk of death or hemodynamic collapse rises at levels >2.0



BNP or pro-BNP

Poor predictor of mortality in isolation

Not specific to RV strain

Could help identify patients with benign clinical course

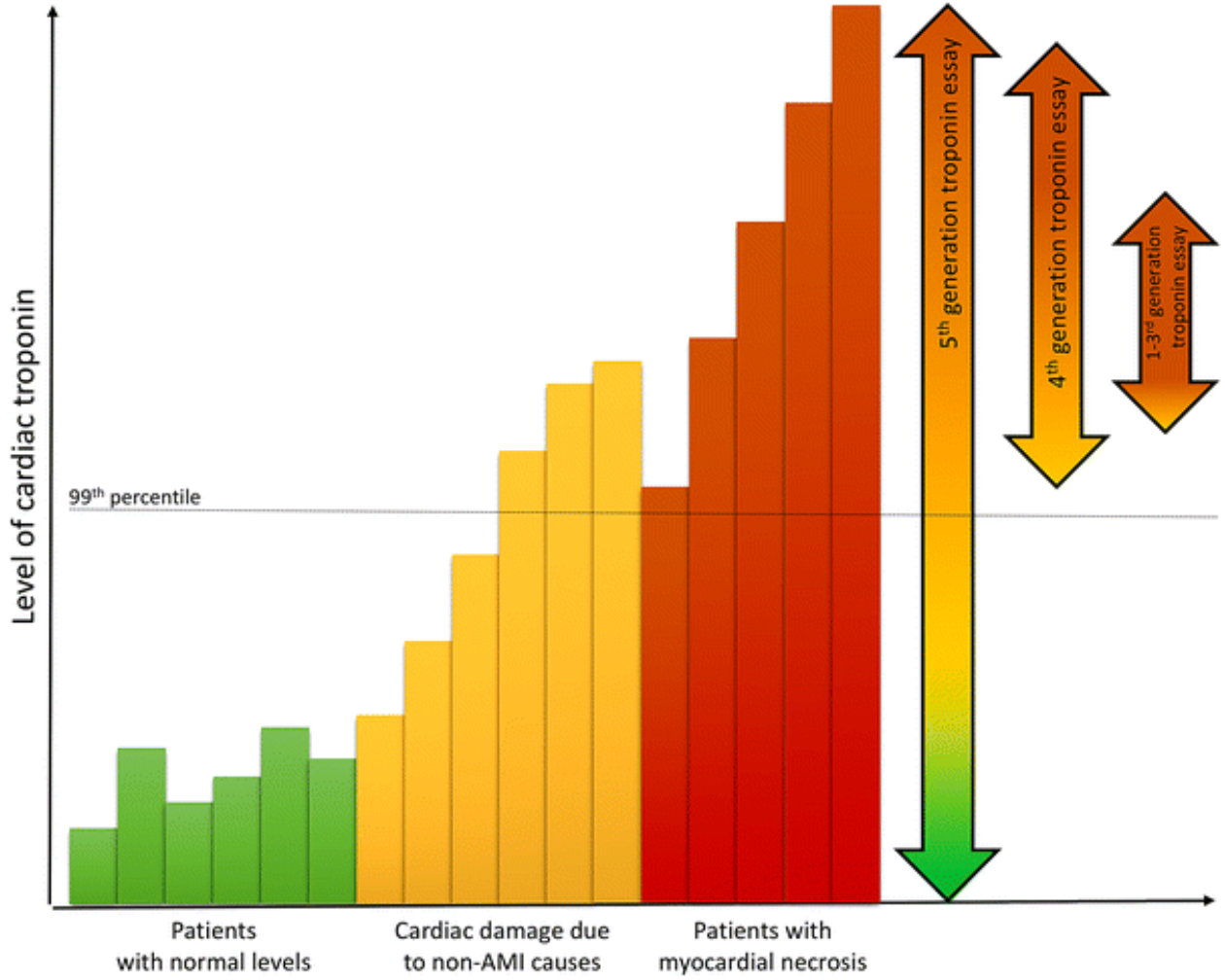
Use in conjunction with other clinical factors

BNP = B-type natriuretic peptide; RV = right ventricular.

Becattini C, et al. *Circulation*. 2007;116(4):427-433. Coutance G, et al. *Crit Care*. 2008;12(4):R109.

Cardiac Biomarkers (Troponin, continued)

- Troponin I (>0.4 ng/mL) or
- Troponin T (>0.1 ng/mL)
- 5th generation troponin
  - Detection at levels not previously possible with prior generations
  - Cutoffs can vary by vendor and sex



AMI = acute myocardial infarction.

Regan B, et al. *Adv Clin Chem*. 2021;104:1-70.

High Risk Stratification: CV Studies and Imaging

ECG Findings

RV Strain

- T-wave inversion in V1 and V2
- T-wave inversion in lead III or precordial lead with deepest T-wave inversion is V1 or V2

RV Injury Pattern

- ST elevation in aVR and ST depression in lead I
- ST elevation in V1-V3 and/or ST depression in V4-V6

CT and/or Echo Findings

RV Dilatation

Bowing of the RV into the LV

Contrast Reflux into the IVC or hepatic veins

RV Systolic Failure

Paradoxical shifting of the inter-ventricular septum (RV pressure overload)

"*Clot-in-transit*" (increases likelihood of PE related death 5-fold)

Past scans/imaging may help differentiate chronic vs acute RV failure

PE with concomitant DVT can lead to a nearly 2-fold increased risk of mortality and is the most common cause of PE.

CV = cardiovascular; aVR = aortic valve replacement; LV = left ventricle; IVC = inferior vena cava.

Predictors of AEs And Long-Term Outcomes OFTEN LEFT IGNORED

1. Right Heart Dysfunction

- Elevated RV/LV ratio ≥0.9, is an independent predictor of death and hemodynamic collapse
- For every 0.1 increase in RV/LV, the odds ratio for death is 1.14

2. Large Clot Burden

- 17.6x risk of mortality at 6 months
- 2.4x risk of adverse events

3. Central Clot Location

- >2x risk of PE related mortality
- 2.4 OR for 30-day adverse events

4. Concomitant DVT

- Over half of acute patients with PE have concomitant DVT
- Mortality: 6.2% with DVT vs 3.8% without DVT
- VTE recurrence: 7.2% with DVT vs 1.7% without DVT

5. Residual Pulmonary Vascular Obstruction (RPVO)

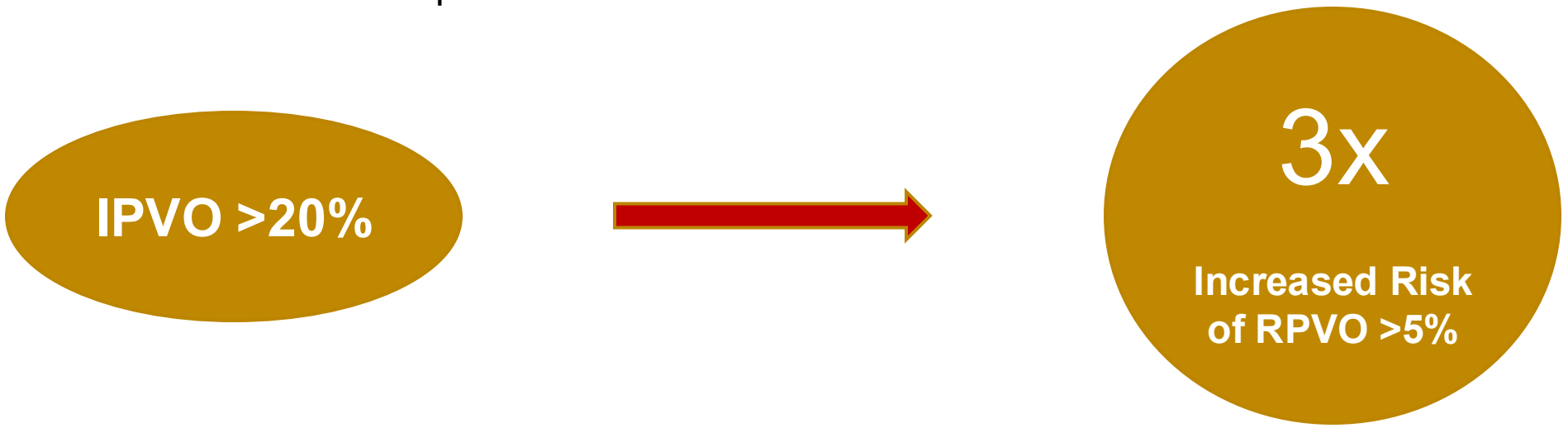
- RVPO is predictive of increased risk of death, pulmonary hypertension, heart failure or worsening dyspnea, and decreased QOL

AE = adverse event; OR = odds ratio.

Porcaro, et al. Presented at: ACC 2019; March 16-18, 2019; New Orleans, Louisiana. Abstract #1007-15. Mehta, et al. Presented at: ACC 2019; March 16-18, 2019; New Orleans, Louisiana. Abstract #1049-03. Martinez JLA, et al. *N Am J Med Sci.* 2016;8(3):134-142. Meinell FG, et al. *Am J Med*. 2015;128(7):747-59.e2. Jimenez D, et al. *Am J Respir Crit Care Med*. 2010;181(9):983-991.

Large Clot Burden Is Predictive of Residual Obstruction

N = 256 with V/Q scanning at diagnosis and 3–24-month follow-up



Initial Pulmonary Vascular Obstruction (IPVO) >20% is predictive of Residual Pulmonary Vascular Obstruction (RPVO) at follow up.

Picart G, et al. *Thromb Res*. 2020;194:1-7.

Classification of PE Severity and Risk of 30-Day Death

ESC 2019

Early mortality risk		Indicators of risk			
		Haemodynamic instability	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥I	RV dysfunction on TTE or CTPA	Elevated cardiac troponin levels
High		+	(+)	+	(+)
Intermediate	Intermediate-high	–	+	+	+
	Intermediate-low	–	+	One (or none) positive	
Low		–	–	–	Assessment optional; if assessed, negative

High Risk 25-50% **Intermediate-High 17-20%** **Intermediate-Low ~10%** **Low ~1% or less**

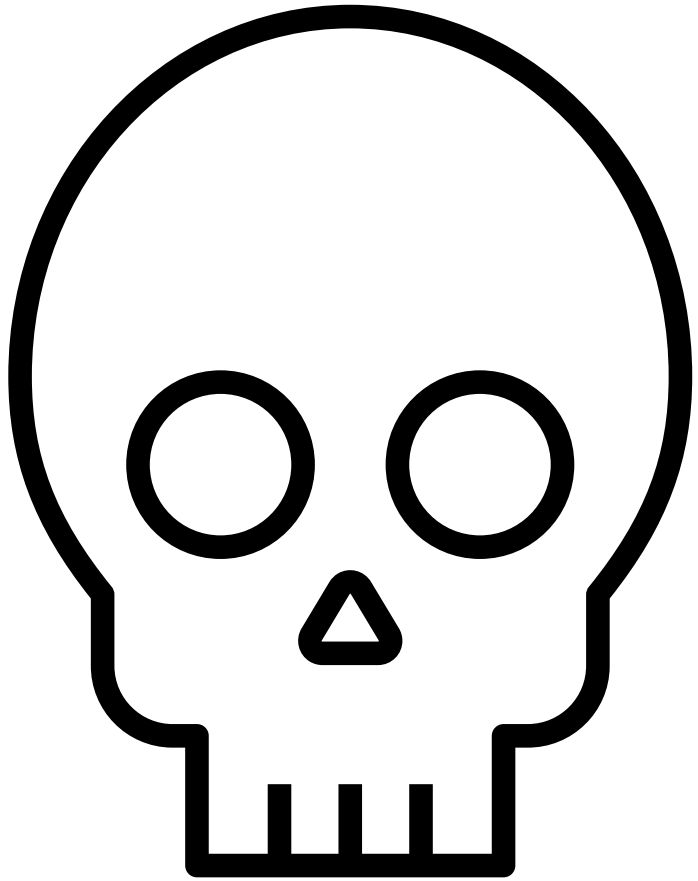
ESC = European Society of Cardiology; CTPA = CT pulmonary angiogram.
Konstantinides SV, et al. *Eur Heart J*. 2020;41(4):543-603.

Massive/High-Risk PE

Acute PE with shock

- Systolic blood pressure <90 mm for 15 minutes
- Fall in systolic blood pressure by >40 mm for 15 minutes
- Requiring pressor support

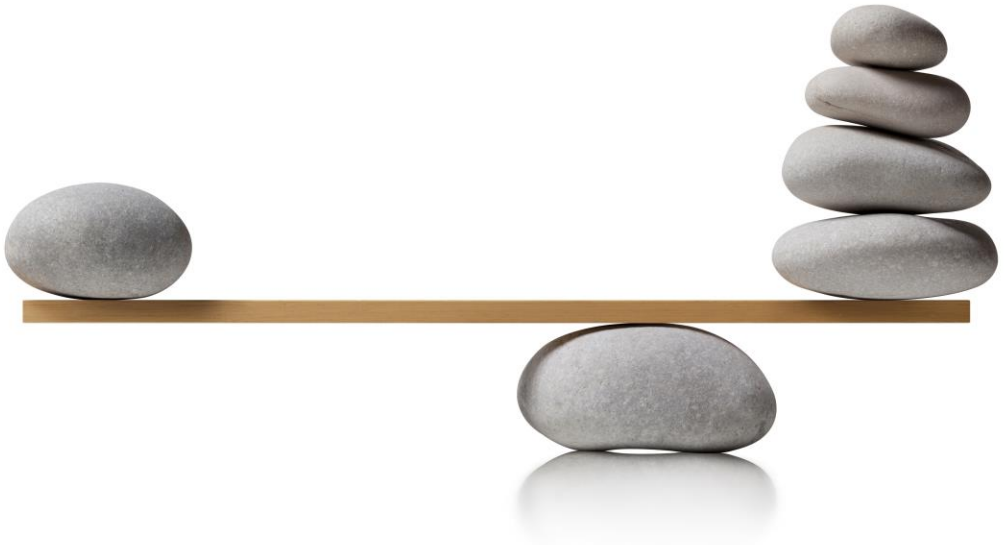
- **High Risk Mortality 25-50%**



Sekhri V, et al. *Arch Med Sci*. 2012;8(6):957-969. Bělohlávek J, et al. *Exp Clin Cardiol*. 2013;18(2):129-138.

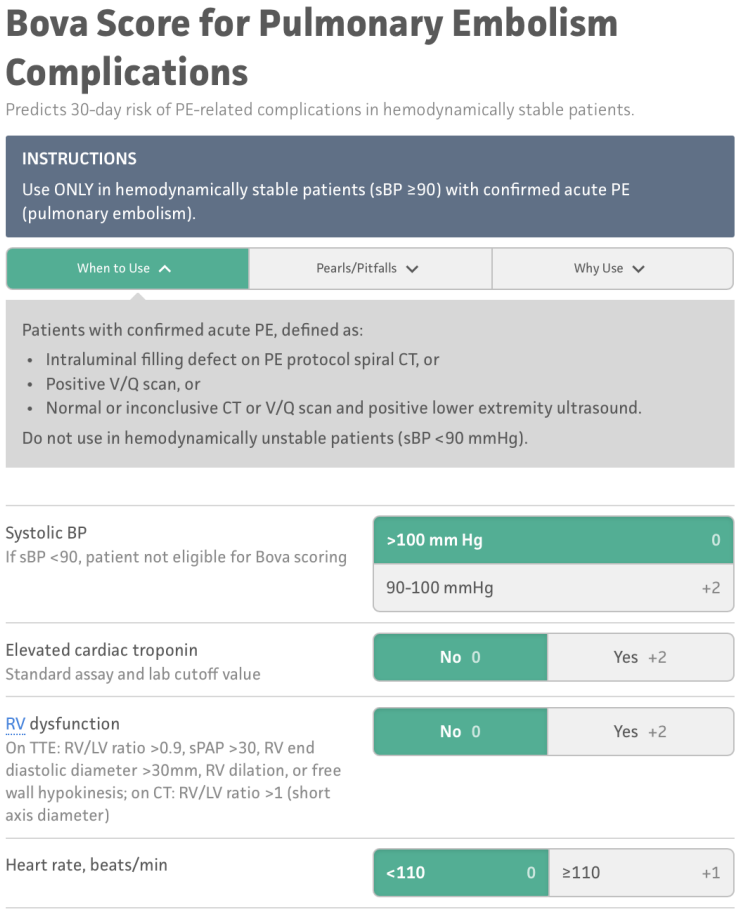
Sub-Massive PE: Intermediate Risk

- Patients with acute PE and without systemic hypotension
- With
  - Evidence of either RV dysfunction or myocardial necrosis
    - Changes on imaging
    - Abnormal cardiac biomarkers



Bova Score for Pulmonary Embolism

Predicts 30-day risk of PE-related complications in hemodynamically stable patients.



Bova Score for Pulmonary Embolism Complications

Predicts 30-day risk of PE-related complications in hemodynamically stable patients.

INSTRUCTIONS

Use ONLY in hemodynamically stable patients (sBP ≥90) with confirmed acute PE (pulmonary embolism).

When to Use | Pearls/Pitfalls | Why Use

Patients with confirmed acute PE, defined as:

- Intraluminal filling defect on PE protocol spiral CT, or
- Positive V/Q scan, or
- Normal or inconclusive CT or V/Q scan and positive lower extremity ultrasound.

Do not use in hemodynamically unstable patients (sBP <90 mmHg).

Systolic BP If sBP <90, patient not eligible for Bova scoring	>100 mm Hg 0	90-100 mmHg +2
Elevated cardiac troponin Standard assay and lab cutoff value	No 0	Yes +2
RV dysfunction On TTE: RV/LV ratio >0.9, sPAP >30, RV end diastolic diameter >30mm, RV dilation, or free wall hypokinesis; on CT: RV/LV ratio >1 (short axis diameter)	No 0	Yes +2
Heart rate, beats/min	<110 0	≥110 +1

sBP = systolic blood pressure; CT = computed tomography; TTE = transthoracic echocardiogram.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How Do We Identify Those at Lower Risk?
PESI and Hestia Predictive Models

PESI and sPESI

- PESI: Predicts 30-day outcome of patients with pulmonary embolism
- sPESI: Predicts 30-day outcome of patients with PE, with fewer criteria than the original PESI
- Most extensively validated of available scores

Table 7 Original and simplified PESI

Parameter	Original version	Simplified version
Age	Age in years	1 point (if age >80 years)
Male sex	+10 points	–
Cancer	+30 points	1 point
Chronic heart failure	+10 points	1 point
Chronic pulmonary disease	+10 points	
Pulse rate ≥110 b.p.m.	+20 points	1 point
Systolic blood pressure <100 mm Hg	+30 points	1 point
Respiratory rate >30 breaths per minute	+20 points	–
Temperature <36 °C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1 point
	Risk strata[a]	
	Class I:≤65 points very low 30-day mortality risk (0–1.6%) **Class II: 66–85 points** low mortality risk (1.7–3.5%) **Class III: 86–105 points** moderate mortality risk (3.2–7.1%) **Class IV: 106–125 points** high mortality risk (4.0–11.4%) **Class V: >125 points** very high mortality risk (10.0–24.5%)	**0 points**= 30-day mortality risk 1.0% (95% CI 0.0%–2.1%) **≥1 point(s)**= 30-day mortality risk 10.9% (95% CI 8.5%–13.2%)

[a]Based on the sum of points.
PESI = pulmonary embolism severity index; s = simplified; CI = confidence interval.
Konstantinides SV, et al. *Eur Heart J*. 2014;35(43):3033-3073.

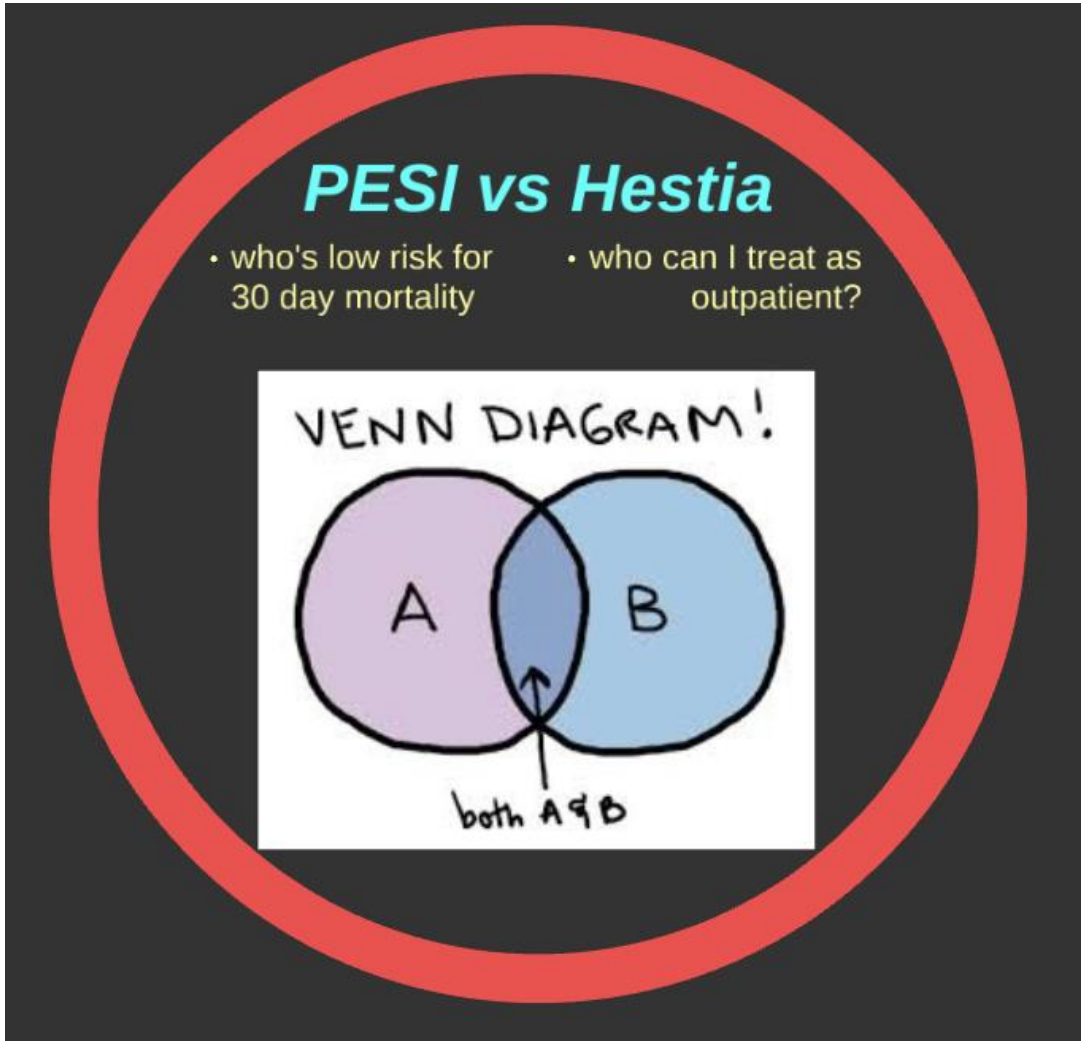
Hestia Criteria

- Looks to identify who is appropriate for outpatient treatment
  - No increase in the risk of VTE recurrence, mortality or major bleeding as compared to established inpatient rates

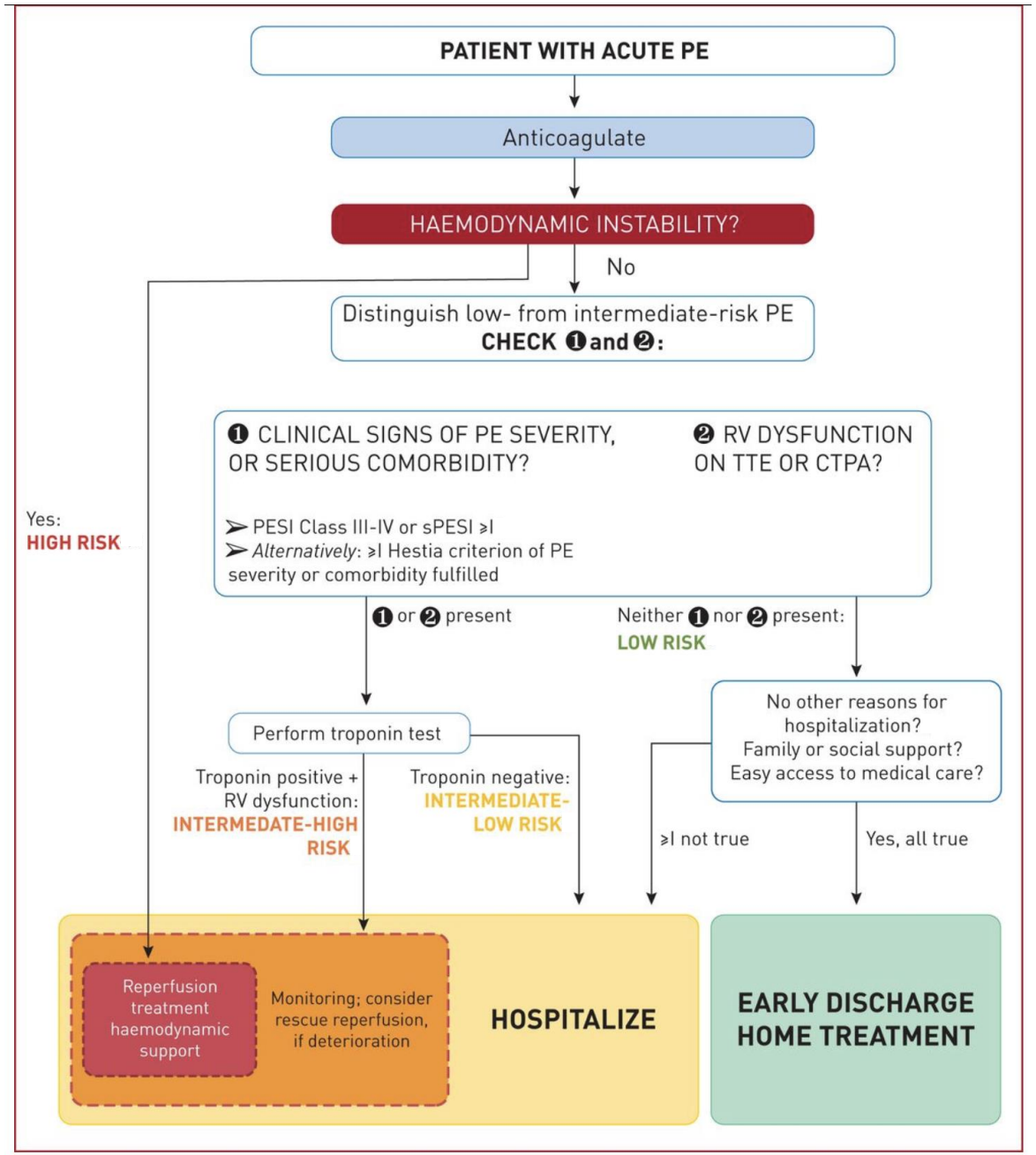
Is the patient hemodynamically unstable?	Yes	No
Is thrombolysis or embolectomy necessary?	Yes	No
Active bleeding or high risk of bleeding?	Yes	No
More than 24 h of oxygen supply to maintain oxygen saturation > 90%?	Yes	No
Is pulmonary embolism diagnosed during anticoagulant treatment?	Yes	No
Severe pain needing intravenous pain medication for more than 24 h?	Yes	No
Medical or social reason for treatment in the hospital for more than 24 h (infection, malignancy, no support system)?	Yes	No
Does the patient have a creatinine clearance of < 30 mL min^{-1}?	Yes	No
Does the patient have severe liver impairment?	Yes	No
Is the patient pregnant?	Yes	No
Does the patient have a documented history of heparin-induced thrombocytopenia?	Yes	No

Hestia vs PESI

- Current available evidence shows
  - Hestia rule and the PESI or sPESI appear capable of reliably identifying patients who are 1) at low PE-related risk, and 2) free of serious comorbidity
  - Either may be used for clinical triage according to local experience and preference
  - If a PESI or sPESI is chosen, it must be combined with assessment of the feasibility of early discharge and home treatment
  - This assessment is already integrated into the Hestia criteria



Palas M, et al. *TH Open*. 2022;6(4):e347-e353.



Konstantinides SV, et al. *Eur Heart J*. 2020;41(4):543-603.

Identifying the Patient at Risk of Clot-Throwing Death

Proximal DVT is an independent risk factor for poor outcomes	Meta-analysis confirms that DVT doubles 30-day mortality
Patients at greatest risk for sudden death are those with	Large proximal DVT (significant residual clot burden) Sub-massive PE concomitant Established pulmonary hypertension, eg, pre-existing right heart failure
Consider risk of concomitant DVT whenever you find a PE	Anticoagulation alone stops clot from expanding Embolic risk remains

Dubois-Silva Á, et al. *Eur J Intern Med*. 2023;108:43-51.

DVT Identification and Management

- Discrepancies in treatment for DVT exist in several key areas
  - When to use advanced interventions beyond anticoagulation
  - Appropriate duration of anticoagulation therapy
- Clinical guidelines and practice are still evolving, leading to debates on the best approach for individual patients
- For most patients with DVT, standard treatment involves anticoagulation to prevent the clot from growing and to reduce the risk of PE
- For certain patients with proximal, large clot burden, more aggressive interventions may be considered
  - It is an evolving topic with the introduction of new techniques such as mechanical thrombectomy

Recommendations

- Incorporate an evidence-based approach for population management and individual workups
  - Prophylaxis, diagnosis, and treatment (which includes long-term management)
- Develop EMR tools allowing for easy access, reference, and use (automate)
- Develop education and escalation pathways for clinical teams
- Quality assessments for tracking compliance to pathway and prophylaxis standards

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Clinical Impact of Missed or Delayed Identification

Patient Voices: Gaps in VTE Diagnosis and Care

From an international online survey of **1050 blood clot patients** conducted in May-June 2023

- A majority (**65%**) said the diagnosis discussion lasted **less than 10 minutes**, and only **55%** felt the explanation of their diagnosis was satisfactory
- Only **16%** received printed or electronic educational materials at diagnosis
- While **97%** were treated with anticoagulation, just **48%** recalled receiving detailed information about their medication's risks and benefits
- **35%** weren't diagnosed correctly on their first visit
  - 50% needed 3+ visits before accurate diagnosis
  - 32% of inpatients returned because symptoms persisted
  - Only 55% felt adequately informed; just 16% received educational materials

Mahajan A, et al. *Blood*. 2025:100081. [Epub ahead of print].

DVT Facts (Common Symptoms)

- Pain
- Tenderness
- Sudden onset swelling of extremity
- Discoloration or large visible veins
- Skin that is warm to the touch

DVT Facts (Less Commonly Known)

- May occur without obvious symptoms (making it difficult to diagnose)
- Up to 50% of incident DVTs may produce minimal symptoms or are completely “silent”
- 85% are in the proximal venous system, and 15% are limited to the calf
- 20-30% of calf thrombi extend proximally

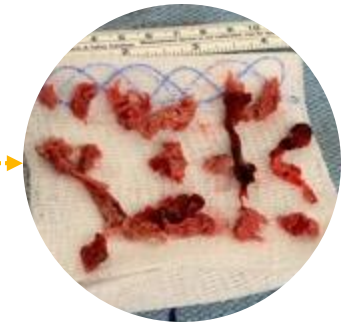
Waheed SM, et al. StatPearls [Internet]. StatPearls Publishing; 2025.

Venous Clot Becomes Chronic Quickly, Complicating Management

>70% of clot removed at **time of treatment** is resistant to lytics (non-fibrin)

Clot formation

Day 3	Day 7	Day 15	Day 21
Fibrin-rich matrix	~20% collagen	>50% collagen	~80% collagen



Silver MJ, et al. *Catheter Cardiovasc Interv.* 2021;97(7):1422-1429. Czaplicki, et al. *Cardiovasc Diagn Ther.* 2017;7(Suppl 3):S186-S196.

Residual Clot Can Lead to Increased Mortality and Long-Term Complications

DVT

~50% of patients have residual clot despite treatment with anticoagulants (AC)

Patients with residual clot have **3x increased** risk of death

Patients with residual clot have **3x greater severity** of post-thrombotic syndrome (PTS)

PE

Up to 50% of patients have residual clot after acute PE despite treatment with AC

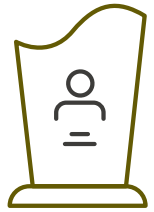
Patients with residual clot have **3x increased** risk of death

Patients with residual clot are **significantly more likely** to develop chronic thromboembolic pulmonary hypertension (CTEPH)

Donadini MP, et al. *Thromb Haemost*. 2014;111(1):172-179. Young L, et al. *J Thromb Haemost*. 2006;4:1919-1924. Bonnefoy PB, et al. *Thromb Res*. 2019;184:67-76. Meneveau N, et al. *Eur Heart J*. 2013;34(9):693-701. Chopard R, et al. *Am J Cardiol*. 2017;119(11):1883-1889.

DVT Adverse Events

Residual venous obstruction (RVO) is common. Clinical studies show **RVO is associated with adverse events.**



3x

Higher risk of **death** with RVO

>3x

Higher risk of **recurrent DVT**

3x

Greater risk of developing **PTS** (by Villalta score)

Higher risk of venous **stent failure**

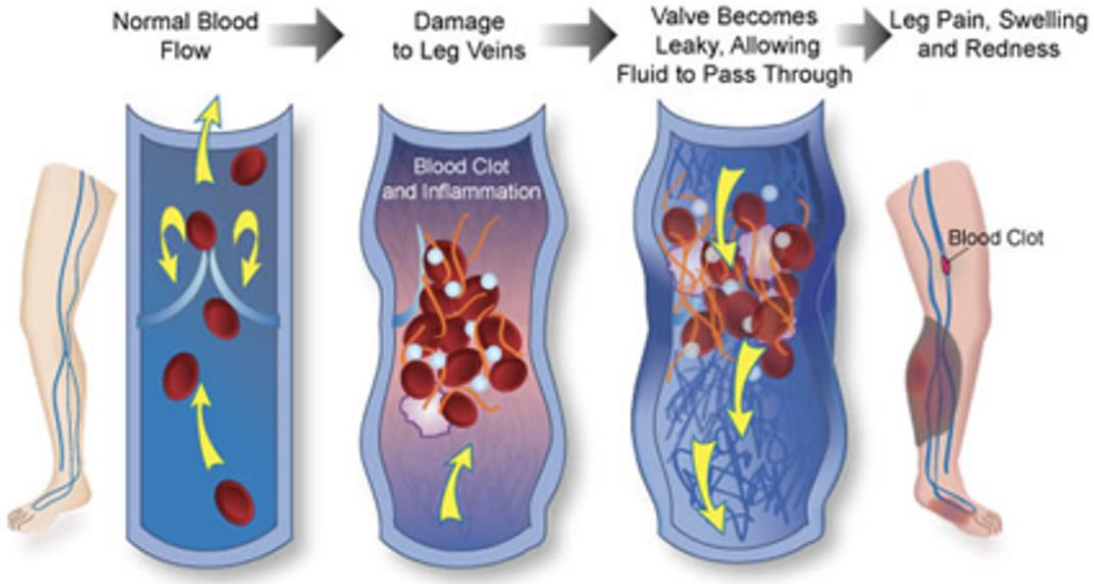
Removing clot burden in DVT **may improve longer-term outcomes.**

Young L, et al. *J Thromb Haemost*. 2006;4:1919-1924. Yoo T, et al. *J Vasc Surg Venous Lymphat Disord*. 2018;6(5):575-583.e1. Dronkers CEA, et al. *Thromb Haemost*. 2018;118(8):1428-1438. Avgerinos ED, et al. *J Vasc Surg Venous Lymphat Disord*. 2019;7(2):153-161.

Why Treat DVT with Intervention?

- Early restoration of vein patency
- Preserve valvular function to limit long-term complications
- Prevent pulmonary embolism
- Limit recurrent DVT and PTS

Follow-up	Recurrent DVT	PTS	Survival Rate
2 years	17%	25%	80%
5 years	24%	30%	74%
8 years	30%	30%	69%



Prandoni P, et al. *Ann Intern Med.* 1996;125(1):1-7. Prandoni P, et al. *Vasc Med.* 1998;3(1):57-60. Prandoni P, et al. *Haemotalogica.* 1997;82(4):423-428. Vazquez SR, et al. *Circulation*. 2010;121:e217-e219.

Pulmonary Embolism Mortality over the Last 20 Years

ICOPER 1999

90-Day Follow-Up

Mortality: **17.4%** overall

- **52.4%** high-risk (massive)
- **14.7%** intermediate-risk (sub-massive)
- **45.1%** of deaths ascribed to PE

Major bleeding: **10.5%**

ICH: **0.6%** overall

2018 MGH PERT Data

30-Day Follow-Up

Mortality

- **34.8%** high-risk (massive)
- **8.2%** intermediate-risk (submassive)

Major bleeding: **11.5%**

ICH: **4.3%** high-risk, **0.4%** intermediate-risk

90-Day Follow-Up

Mortality: **16.3%** overall

- **41.3%** high-risk
- **12.3%** intermediate-risk
- **37%** of deaths directly attributed to PE

Major bleeding: **14.2%**

ICH: **4.3%** high-risk, **0.8%** intermediate-risk

2/3 of intermediate-risk deaths were post-discharge

2020 PERT Consortium Data

30-Day Follow-Up

Mortality

- **25.9%** high-risk (massive)
- **6.1%** intermediate-risk (sub-massive)

In-hospital major bleeding: **5%**

In-hospital death: **5%**

30-day all-cause mortality by risk level

6-15%

in **sub-massive** PE patients

25-50%

in **massive** PE patients

PERT = PE response teams; ICH = intracerebral hemorrhage.

Kucher N, et al. *Circulation*. 2006;113(4):577-582. Secemsky E, et al. *Am J Med.* 2018;131(12):1506-1514.e0. PERT Consortium Registry Data. Presented at: PERT Consortium 6th Annual Scientific Symposium; October 23-24, 2020; Virtual.

Long-Term Consequences of PE: "Post-PE Syndrome"

Meta-analysis including **nearly 3,700** PE patients (18-month median follow-up):

18%
ongoing RV dysfunction

11%
moderate or severe functional impairment (NYHA III-IV)

5th percentile
6-minute walk test scores (vs. population norms)

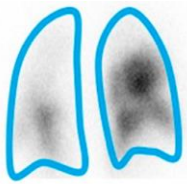
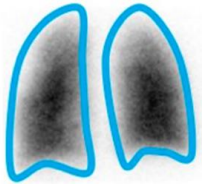
PERT Consortium 2020 data

24%
30-day all-cause readmission

"Mechanistically, rapid unloading of the right ventricle and **increased thrombus clearance may prevent maladaptive cardiopulmonary remodeling**."

Sista AK, et al. *Vasc Med*. 2017;22(1):37-43. PERT Consortium Registry Data. Presented at: PERT Consortium 6th Annual Scientific Symposium; October 23-24, 2020; Virtual.

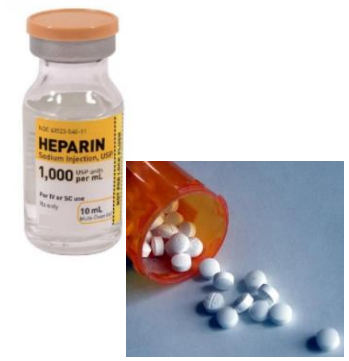
RPVO Is Associated with Increased Adverse Events

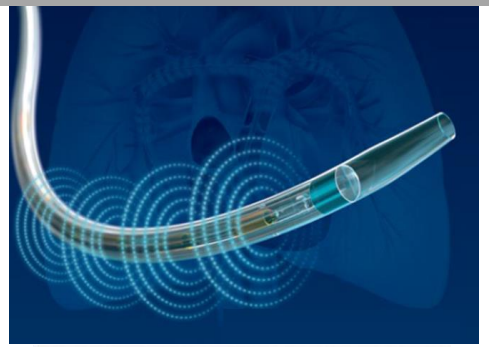
	Mortality		Recurrent VTE		Heart Failure and Dyspnea		CTEPH
	6 mos	5 yrs	6 mos	4 yrs	6 mos	5 yrs	3 mos
 Patients **with RPVO**	**6.8%**	**31%** *increased relative risk*	**7.8%**	**21.2%**	**9.8%**	**41%**	**7.1%**
 Patients with **NO RPVO**	**1.6%**	–	**1.9%**	**7.0%**	**0.6%**	**27%**	**0%**

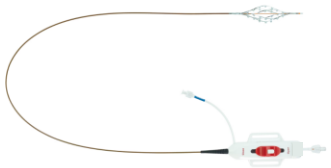
Meneveau N, et al. *Eur Heart J*. 2013;4(9):693-701. Meneveau N, et al. *Eur Heart J*. 2003;24(15):1447-1454. Wan T, et al. *Thromb Res*. 2018;162:104-109. Chopard R, et al. *Am J Cardiol*. 2017;119(11):1883-1889.

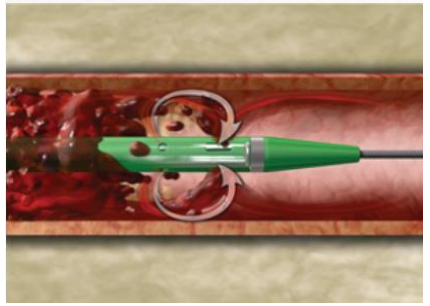
There Is Now a Broader Spectrum of Treatment Strategies for Patients with VTE

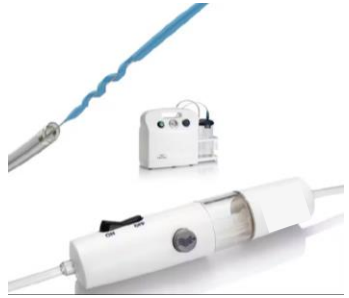
Anticoagulation (AC)	Systemic Thrombolysis	Catheter-Directed Thrombolysis	Mechanical Thrombectomy
Medical Therapy	Lytic-based intervention		Thrombectomy





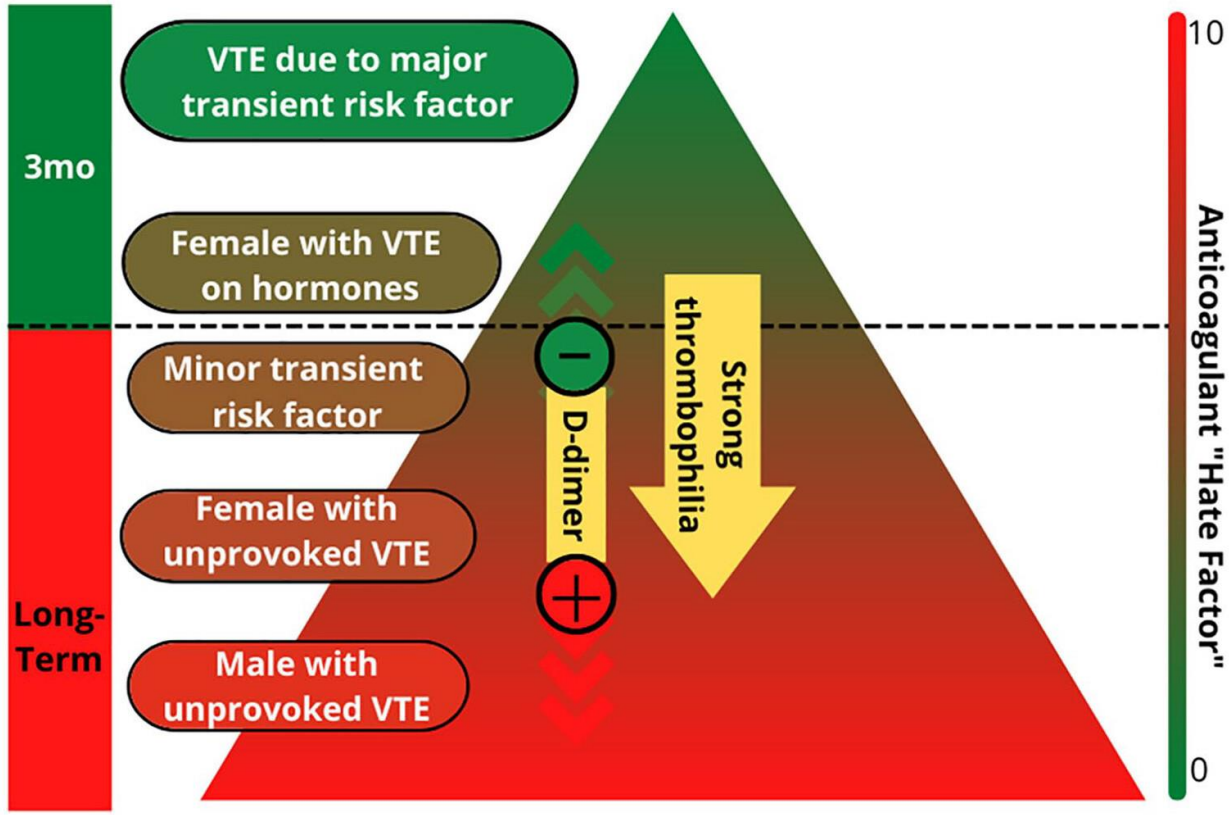






The Risk of VTE Recurrence

- Duration of anticoagulation is determined by many factors
  - Clot location (for acute management)
    - Superficial or distal clot
    - Proximal PE
  - Decision to continue anticoagulation depends on risk of recurrence
    - Transient versus persistent risk factors
    - Provoked vs unprovoked events



Frank C, et al. *Vasc Med*. 2023;28(5):481-486.

Recommendations

- Evolving treatment strategies and pathways should focus on improving short-term outcomes as mortality remains high for this diagnosis
- Further studies/updated guidelines that help identify therapies that best improve long-term outcomes (decreased incidence of RVO and RPVO) are needed
- Utilization of treatment strategies that account for both the long-term risk of recurrence and bleeding is also needed
- Opportunities exist in both obtaining the correct diagnosis and improving education provided to patients around their diagnosis and treatment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CME
Building the
Foundation
for a VTE
Program

Where Do We Start?

Everyone has an opinion

Core Components of a VTE Program

- Leadership and institutional buy-in
  - Executive sponsorship and clinical champions
- Standardized diagnostic/management protocols and pathways
  - Consistency is key across specialties and departments
  - Pathways are not programs
- Dedicated VTE resources
- VTE governance
  - Representatives to help champion program evolution in the institution
  - Quality review and program expansion
- Data collection and quality monitoring
  - Outcomes tracking, feedback loops, barriers, optimization opportunities

Nicolaides AN, et al. *Int Angiol.* 2024;43(1):1-222. Stevens SM, et al. *Chest*. 2021;160(6):e545-e608. Vedantham S, et al. *J Vasc Interv Radiol*. 2023;34(2):284-299.

Multidisciplinary Collaboration

- Abolish the silo
- Outline barriers and obstacles
- Education
- In-reach and outreach
- Interdisciplinary collaboration/coordination
- Frontline champions
- Process mapping
- COMMUNICATION COMMUNICATION COMMUNICATION

Nicholson M, et al. *J Clin Med.* 2020;9(8):2467. Lyman GH, et al. *Blood Adv.* 2021;5(4):927-974.

Developing Pathways and Protocols

- Local adaptation of national guidelines
  - Framework and understanding local resources
- Pathways and protocols must define
  - Imaging
  - Anticoagulation initiation
  - Escalation to specialists
  - Follow up
  - Patient education

Konstantinides SV, et al. *Eur Heart J*. 2020;41(4):543-603. Kearon C, et al. *Chest*. 2016;149(2):315-352. PERT Consortium Registry Data. Presented at: PERT Consortium 6th Annual Scientific Symposium; October 23-24, 2020; Virtual.

Lessons from Implementation

- Engage champions early
- VTE governance structure adaptability
  - Condense by attrition, not exclusion
- Continuous feedback
  - Implementation is a cycle, not an event
  - Collect feedback, refine, relaunch, repeat
- Celebrate every win
  - Quick wins from low-hanging fruit are still wins
  - Support challenges and maintain engagement


CardioVascular
Learning Network
CME
Streamlining
DVT and PE
Pathways

Why Streamlined Pathways Matter

- VTE remains underdiagnosed and inconsistently managed without structured pathways
- Improvement in care metrics
  - Time-to-diagnosis
  - Reduction of unnecessary testing
  - Support early treatment and risk stratification
- Reduces variability and bias and improves safety
- Consistent follow-up and safe outpatient management

Konstantinides SV, et al. *Eur Heart J*. 2020;41(4):543-603. Barnes GD, et al. *Am J Med*. 2015;128(12):1300-1305.e2.

Standardized Workflows

- Diagnostic algorithms
  - Validated tools, notification process for early identification and treatment
- Anticoagulation initiation
  - Early treatment improves survival
  - Ensure protocols cover ED/inpatient/outpatient management
- Inpatient vs outpatient criteria
  - Outpatient: Hemodynamically stable, low bleeding risk, and good support at home
    - Look for additional risk factors, ensure follow-up, and low threshold for expert opinion

ED = emergency department.

Kearon C, et al. *Chest*. 2016;149(2):315-352. Zondag W, et al. *J Thromb Haemost*. 2011;9(8):1500-1507.

PE Response Teams (PERT)

- Multidisciplinary team
  - IR, cardiology, pulmonology, critical care, hematology, surgery as needed/available
- Purpose: Rapid triage, coordinated decision making, escalation of therapies
- Evidence
  - Faster treatment decisions
  - Increased interdisciplinary collaboration and education
- Challenges
  - Resource-intensive
  - No universal model

IR = interventional radiology.

Rosovsky R, et al. *Res Pract Thromb Haemost.* 2019;3(3):315-330.

Outcome Improvement

- Early anticoagulation: Reduces recurrence and mortality; delays increase risk
- Pathway-based care: Ensures consistent, guideline-concordant management across providers/departments
- Ongoing data need: Registries and COE participation critical for demonstrating long-term benefit
- Institutions adopting structured pathways report
  - ↓ LOS
  - ↑ appropriate outpatient care
  - ↑ adherence to guidelines

COE = cycle of engagement; LOS = length of stay.

Jiménez D, et al. *Chest*. 2007;132(1):24-30. Smith SB, et al. *Chest*. 2010;137(6):1382-1390.

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Conclusion and Key Takeaways

Recap of Core Topics

- Burden of VTE
  - Population management, morbidity, mortality, cost of care, and more
- Building the Foundation
  - Leadership buy-in, standardized protocols, multidisciplinary collaboration → programs make a difference
- Streamline Pathways
  - Diagnostic algorithms, anticoagulation initiation, VTE/PERT models
- Continuous Improvement
  - Learn lessons after you implement
  - Start small, engage champions, refine processes and program

Closing Reflections

"A center of excellence is a program within a healthcare institution which is assembled to supply an exceptionally high concentration of expertise and related resources centered on a particular discipline of medicine, delivering associated care in comprehensive, interdisciplinary fashion to afford the best patient outcomes possible."

- Elrod and Fortenberry, 2017

Call to Action

- Apply foundational principles
  - Start with achievable wins and build momentum
- Foster collaboration
  - Engage champions and all aspects of clinical support
- Measure and share outcomes
  - Collect data to demonstrate progress and areas for optimization
- Center of Excellence
  - Support clinicians, patients, and the community/public
  - Opportunity to lead VTE care nationally

Thank you

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