The Basics Of Pulmonary Embolism: What Is The Role Of The History, Exam, Biomarkers

Raghu Kolluri, MD, MS, RVT, MSVM

System Medical Director – Vascular Medicine & Vascular Labs - OhioHealth Heart and Vascular

President – Syntropic Corelab

Adjunct Clinical Professor – Ohio University HCOM

Columbus, Ohio

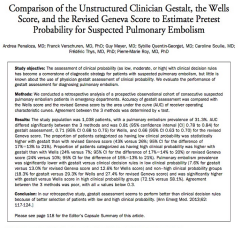
OhioHealth

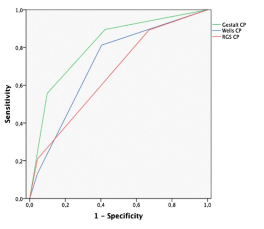
Raghu Kolluri, MD: Disclosures

- **Consultant/Advisor/ DSMB/ CEC -**
  - Abbott, Auxetics, Diachii Sankyo, Koya Medical, Medtronic, Penumbra, Philips, Surmodics, USA Therm, VB Devices
- **Board of Trustee**
  - The VIVA Foundation
  - Intersocietal Accreditation Council | Vascular Testing
- **President**
  - Syntropic Core Lab

OhioHealth

Diagnosis


Comparison of the Unstructured Clinician Gestalt, the Wells Score, and the Revised Geneva Score to Estimate Pretest Probability for Suspected Pulmonary Embolism



ROC: receiver operating characteristic **CP:** clinical probability **RGS:** revised Geneva score

OhioHealth

D - Dimer

- Most appropriate first test
- Highly sensitive (95% sensitive <500 ng/mL).
- Specific (40% to 50%)
- Elevated
  - Elderly (>80 years)
  - Pregnancy (especially in the third trimester)
  - Major trauma or surgery or sickness
  - Sickle cell

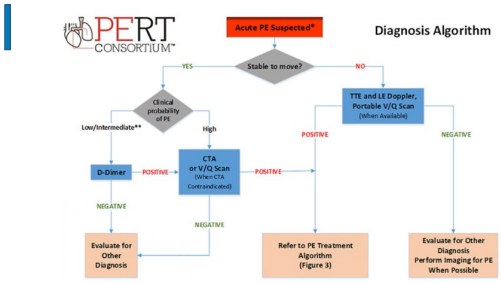
Acad Emerg Med. 2009 Apr; 16(4):325-32.

CT PE

- PIOPED II: sensitivity - 83%; specificity - 96%
  - Difficult to assess since CTA is now the gold standard
- Central thrombus in the main, right or left PA
  - Possibly correlates with 30-day mortality

Hogg et al. Emerg Med J 2006; 23(3):172-178
Vedovati MC et al. J Thromb Haemost 11:2092-2102

OhioHealth



Clin Appl Thromb Hemost. 2019 Jan-Dec;25

OhioHealth

ACCP guidelines – "Stable PE"

- "In patients with low-risk PE and whose home circumstances are adequate, we suggest treatment at home or early discharge over standard discharge (e.g. after first 5 days of treatment) (Grade 2B)."
- "Suggest that patients who satisfy all of the following criteria are suitable for treatment of acute PE out of hospital:
  - Clinically stable with good cardiopulmonary reserve;
  - No contraindications such as recent bleeding, severe renal or liver disease or Severe thrombocytopenia (i.e. < 70,000 /mm^3);
  - Expected to be compliant with treatment
  - Patient feels well enough to be treated at home"

Chest. 2016 Feb;149(2):315-352

No PESI; No biomarker/echo

OhioHealth

Hestia Criteria

Criteria
Hemodynamically instable (e.g. HR > 100 beats/min, systolic BP < 100 mmHg, needs ICU admission)
Thrombolysis or embolectomy necessary
High risk of bleeding (e.g. GI bleed within 14 days, recent stroke (within 4 weeks), recent surgery (within 2 weeks), platelets < 75,000/μL, uncontrolled HTN (systolic BP > 180 mmHg, diastolic BP > 110 mmHg)
Supplemental O_2 needed to keep O_2 saturation > 90 %for > 24 h
Pulmonary embolism during anticoagulation treatment
Intravenous pain medication > 24 h
Medical or social reason for in-hospital treatment > 24 h
Creatinine clearance < 30 mL/min
Severe liver impairment
Pregnant
Documented history of HIT

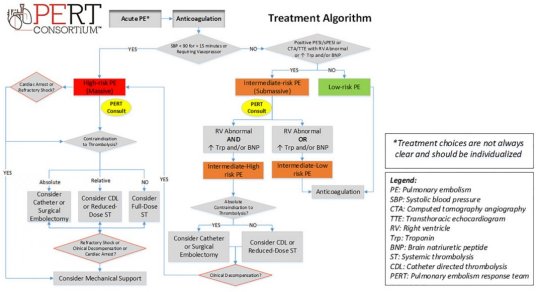
The presence of any criterion precludes outpatient treatment

The presence of any criterion precludes outpatient treatment

J Thromb Thrombolysis (2016) 41:32–67

OhioHealth

Treatment Algorithm



Clin Appl Thromb Hemost. 2019 Jan-Dec;25

OhioHealth

Severity prognostication based on hemodynamics/ Clinical Features

Parameter	Original version[114]	Simplified version[115]
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 stratum*	
	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%)

Thromb Haemost 109(1):47–52

Circulation 124(24):2716–2724

J Thromb Thrombolysis (2016) 41:32–67

OhioHealth

Cardiospecific Biomarkers

Accuracy of Cardiac Biomarkers for the Prediction of In-Hospital Death in Pulmonary Embolism

Reference	n	Biomarker	Assay	Cut-Off Level	Test +, %	NPV, %	PPV, %
Konstantinides et al[11]	106	cTnI	Centaur (Bayer)	0.07 ng/mL	41	98	14
Konstantinides et al[11]	106	cTnT	Elecsys (Roche Pharmaceuticals)	0.04 ng/mL	37	97	12
Giannitsis et al[12]	56	cTnT	TropT (Roche Pharmaceuticals)	0.10 ng/mL	32	97	44
Janata et al[24]	105	cTnT	Elecsys (Roche Pharmaceuticals)	0.09 ng/mL	11	99	34
Pruszczyk et al[13]	64	cTnT	Elecsys (Roche Pharmaceuticals)	0.01 ng/mL	50	100	25
ten Wolde et al[25]	110	BNP	Shionoria (CIS Bio International)	21.7 pmol/L	33	99	17
Kucher et al[14]	73	NT-proBNP	Elecsys (Roche Pharmaceuticals)	500 pg/mL	58	100	12
Kucher et al[17]	73	BNP	Triage (Biosite Technologies)	50 pg/mL	58	100	12
Pruszczyk et al[26]	79	NT-proBNP	Elecsys (Roche Pharmaceuticals)	153 to 334* pg/mL	66	100	23

NPV indicates negative predictive value; PPV, positive predictive value.
*Age and gender adjusted cut-off levels according to the manufacturer.

Circulation 2003;108:2191-4

OhioHealth

Serum Lactate – short term PE complications

Primary end point
- 7-day PE-related death
- Shock/hypotension
- Mechanical ventilation
- CPR

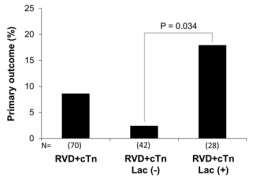
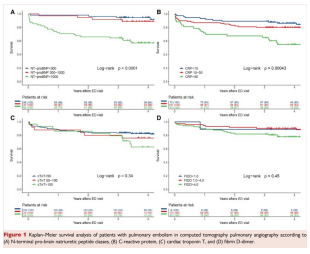


Figure 3 Escalation of PE-related complication rates depending on lactate levels in combination with echocardiography and troponin. cTn, elevated cardiac troponin; Lac (+), lactate ≥2 mmol/L; Lac (−), lactate <2 mmol/L; RVD, right ventricular dysfunction.

Vanni S, Jiménez D, Nazerian P, et al. Thorax 2015;70:333–338.

OhioHealth

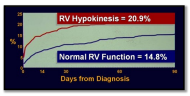
Prognosis in patients with PE diagnosis and positive biomarkers

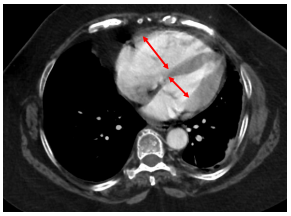


FIDD = fibrin D-dimer

Physiologic surrogate for RA and PA

- RV:LV > 1.0 on axial, or
- RV:LV >0.9 on 4 chamber view
- PA diameter should be less than Ascending Aorta

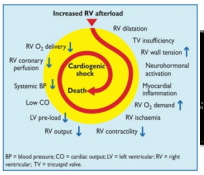




Hogg et al. Emerg Med J 2006; 23(3):172-178

OhioHealth

Echo/ POCUS/RV dysfunction



European Heart Journal (2014) 35, 3033–3080

OhioHealth

CLOT-5 Score – 30 Day Mortality

Table 2. Components of the CLOT-5 Score as Predictors of 30-day Mortality.

Variable	Beta	P value	Odds Ratio	95% Confidence Interval
Cancer	1.867	0.000	6.5	2.6–15.6
Pressor requirements	2.96	0.000	19.1	8.1–21.2
Oxygen saturation < 90%	1.59	0.034	4.8	1.2–18.1
Tachycardia > 120	1.32	0.05	3.74	1.01–14.5
Lactate > 2	1.6	0.02	5.1	1.5–22.1
NLR >5.46	1	0.05	2.03	1.01–4.39
RDW >15	2.17	0.006	8.7	1.86–31.00
RVILV > 1.4	0.79	0.04	2.1	1.02–4.4
RVOT VTI <9.5 cm	0.855	0.015	2.35	1.78–4.7

Nine explanatory variables identified by a multivariable logistic regression analysis to correlate with 30-day mortality, and which were used to compile the CLOT-5 score. NLR (neutrophils to lymphocyte ratio), RDW (red blood cell distribution width), RVILV (right to left ventricular diameter ratio), RVOT VTI (right ventricular outflow tract velocity time integral). A p-value of <0.05 implied significance. Values are reported as odds ratios and 95% confidence interval.

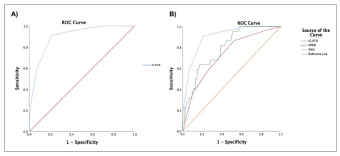


Figure 1. Comparison of receiver operator curves for the CLOT-5, PESI, and sPESI scores. (A) The receiver operator curve for the CLOT-5 Score as calculated based on the patient population included in the study. (B) A comparison of the CLOT-5, PESI, and sPESI receiver operator curves calculated for the patient population included in the study.

Clin Appl Thromb Hemost. 2024 Jan-Dec;30:10760296241278353. doi: 10.1177/10760296241278353. PMID: 39183532

OhioHealth

ACP American College of Physicians — Clinical Guideline

Appropriate Use of Point-of-Care Ultrasonography in Patients With Acute Dyspnea in Emergency Department or Inpatient Settings: A Clinical Guideline From the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Islair Etxeandia-Ikobaltzeta, PharmD, PhD; Reem A. Mustafa, MD, MPH, PhD; Devan Kansagara, MD, MCR; Nick Fitterman, MD; and Timothy J. Wilt, MD, MPH; for the Clinical Guidelines Committee of the American College of Physicians*

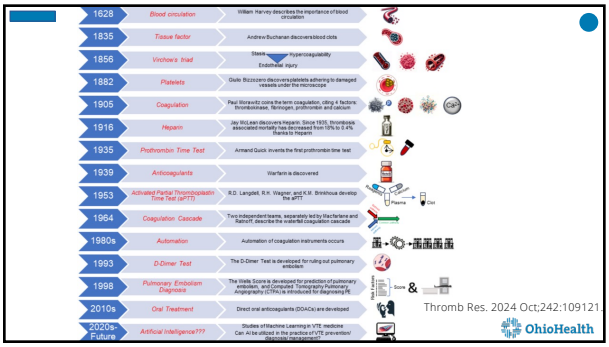
Pulmonary Embolism. Low-certainty evidence showed that POCUS (lung, heart, inferior vena cava, and deep veins) in addition to the standard diagnostic pathway correctly identified 89% to 100% of patients with unspecified dyspnea who had pulmonary embolism and 95% to 100% of patients who did not have pulmonary embolism (7, 17, 20).

Recommendation: ACP suggests that clinicians may use point-of-care ultrasonography in addition to the standard diagnostic pathway when there is diagnostic uncertainty in patients with acute dyspnea in emergency department or inpatient settings (conditional recommendation; low-certainty evidence).

Considerations:
- Scanning included lung, heart, IVC & deep veins
- DO NOT apply to handheld devices

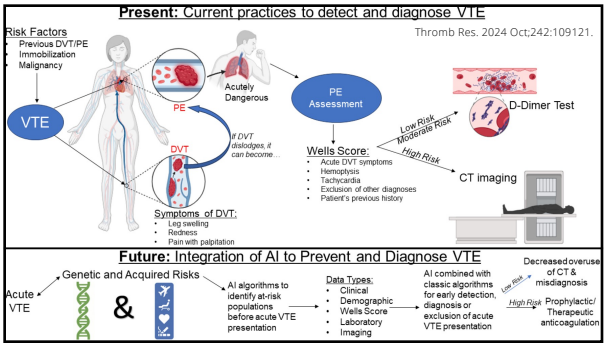
Ann Intern Med. 2021 Jul;174(7):985-993.

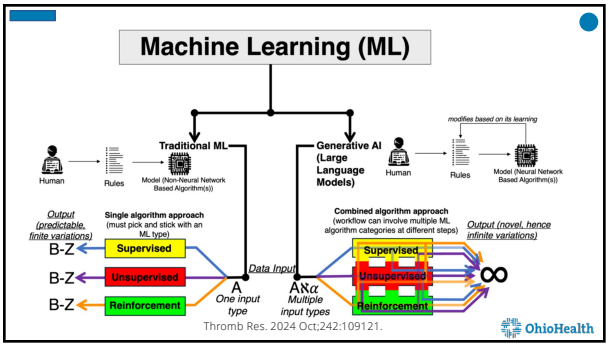
OhioHealth



Thromb Res. 2024 Oct;242:109121.

OhioHealth





History and PE Care Pathway issue

- EMR Parroting
  - "Covid Induced"/ "Vaccine-induced"
  - "Provoked PE" – "Because I was on a 2-hour flight/3-hour car ride", "Because I am a software professional, I sit at my desk."
  - First things first - Cancer, family history
- Care Pathway issues
  - Inadequate or Inappropriate Treatment → recurrence
    - Baseline PTT – heparin gtt dosing erroneous! ? APS?
    - Platelet monitoring while on heparin gtt– HIT?
    - Duplex not done when diagnosed with PE. 3 months later there are "post thrombotic changes" in the DUS. If these were there at the time of PE = 2 VTE events Vs 1!
  - Repeat ED visits due to chest pain, but multiple negative work ups.
    - Post PE anxiety, panic attacks, nightmares!!

OhioHealth

Summary

- PE care
  - Good history + Clinical gestalt + Imaging + biomarkers + individual tailored therapy

OhioHealth