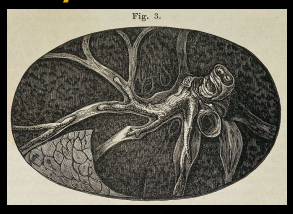
# Evidence Based Approach to Pulmonary Thromboembolism

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***Physician Assistant Program***
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**Thank you to Kristopher R. Maday, MS, PA-C for providing much of the content of this talk.**

# No Financial Disclosures

## Objectives

- Discuss landmark and most recent publications that have led to current recommendations in PTE management
- Evaluate pre-test probability decision tools
- Compare diagnostic modalities
- Appraise current literature regarding treatment
- Develop comprehensive decision algorithm

## Why Do We Care?

- 300,000-600,000 cases per year
  - 1 to 2 cases per 1000 of the population
  - 1/3rd will have recurrence within 10 years
- 30-50% will have chronic post-thrombotic syndromes

Beckman MG. *Am J Prev Med*. 2010;38(4S):S495-S501

## WE ARE SCARED…

- The patient was a male in his late twenties who suffered from obesity, asthma, high blood pressure, and Crohn's disease. He also had a recent history of surgical repair for a femur fracture. The patient visited his regular family medicine practitioner in October and was treated for rhinitis and sinusitis. His pulse oximetry reading at the time was 99 percent.
- A month later, the patient presented to the practice again with complaints of shortness of breath, coughing, and right-sided back pain. At this visit, he saw Dr. M — another family medicine physician in the practice — for the first time. Dr. M ordered a stat chest X-ray, the results of which were negative. The patient's pulse oximetry reading at this visit was 95 percent.
- Dr. M diagnosed the patient with bronchitis and prescribed levofloxacin and guaifenesin; she told the patient to return to the office if his symptoms did not subside. One day later, the patient suffered a massive pulmonary embolism (PE) and died. A malpractice lawsuit was filed against Dr. M, which was ultimately settled with a payment in the high range.

https://www.medpro.com/cs-dxerror-pulmonaryembolism

## Why Are We Scared?

- 10-20% have no identified risk factor
- 10-30% die in 1st 30 days
  - 20-25% as sudden death
- Up to 50% miss rate by clinicians
- 32% of patients with DVT have "Silent" PTE
- Fear of litigation is #1 reason clinicians work-up low-risk patients

Beckman MG. *Am J Prev Med*. 2010;38(4S):S495-S501 Calder KK. *Ann Emerg Med*. 2005;45(3):302-310 Stein PD. *Am J Med*. 2010;123:426-431

## Why Can't We Test Everybody?

Newman DH. *Ann Emerg Med*. 2011;57:622-627

Spyropoulous A. *J Manag Care Pharm*. 2007;13(6):475-486

## Signs and Symptoms

*PIOPED Study*

*EMPEROR Registry*

## Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED II)

| ***Symptoms*** | ***Physical Exam Findings*** |
|---|---|
| Dyspnea *(73%)* | Tachypnea *(57%)* |
| Chest pain *(64%)* | DVT Findings *(47%)* |
| Leg pain/swelling *(44%)* | Abnormal Lung Exam *(37%)* |
| Cough *(43%)* | Tachycardia *(26%)* |
| Wheezing *(21%)* | Abnormal Heart Exam *(22%)* |
| Hemoptysis *(13%)* | |

Stein PD. *Am J Med*. 2007;120:871-879

## Emergency Medicine Pulmonary Embolism in the Real World Registry (EMPEROR)

| ***Symptoms*** | ***Physical Exam Findings*** |
|---|---|
| Dyspnea *(77%)* | Mean HR – *95.7 beats/min* |
| Chest Pain *(55%)* | Mean RR – *20.5 breaths/min* |
| Cough *(31%)* | Mean $O_2$ – *95% on room air* |
| Dizziness *(12%)* | |
| Hemoptysis *(8%)* | DVT Findings *(24%)* |
| Extremity pain *(6%)* | Respiratory Distress *(16%)* |

Pollack CV. *JACC*. 2011;57(6):700-706

## Pre-Test Probability

*Wells Criteria*

*Simplified Geneva Score*

*Pulmonary Embolism Rule-out Criteria (PERC)*

*Clinical Gestalt*

## Wells Criteria for PTE

- Developed in 1998 → 2000 → 2001
- Clinical decision instrument using a point system to grade pre-test probability
  - Applied AFTER history and physical exam
- Risk-assessment grades

Wells PS. *Ann Intern Med*. 1998;129:997-1005

Wells PS. *Thromb Haemost*. 2000;83:416-420

Wells PS. *Ann Intern Med*. 2001;135:98-107

# Wells Criteria for PTE

| History and Physical Exam Findings | Points |
|---|---|
| Clinical Signs and Symptoms of DVT | +3 |
| Heart Rate > 100 beats/min | +1.5 |
| Immobilization ≥ 3 days or Surgery in Previous 4 weeks | +1.5 |
| Previously Diagnosed DVT or PTE | +1.5 |
| Hemoptysis | +1 |
| Malignancy (Active, Treated in last 6 months, or Palliative) | +1 |
| PTE is #1 Diagnosis, or at least as likely | +3 |

| Pre-Test Probability | Points |
|---|---|
| Low-Risk (1.3%) | < 2 |
| Moderate Risk (16.2%) | 3-6 |
| High Risk (40.6%) | > 6 |

Wells PS. *Ann Intern Med.* 2001;135:98-107 van Belle A. *JAMA.* 2006;295(2):172-179

# Geneva Score

*Original Score* **2001**

↓

**2006** *Revised Score*

↓

*Simplified Score* **2008**

Wicki J. *Arch Intern Med.* 2001;161:997-92-97 Le Gal G. *Ann Intern Med.* 2006;144:165-171 Klok FA. *Ann Intern Med.* 2008;168(19):2131-2136

# Simplified Geneva Score

| History and Physical Exam Findings | Points |
|---|---|
| Age 65 years or greater | +1 |
| Previous History of DVT/PTE | +1 |
| Surgery or Fracture within 1 Month | +1 |
| Active Malignant Condition | +1 |
| Unilateral Lower Limb Pain | +1 |
| Hemoptysis | +1 |
| Heart Rate 75-94 beats/min | +1 |
| Heart Rate > 94 beats/min | +2 |
| Unilateral Lower Leg Edema and Pain on Deep Palpation | +1 |

| Pre-Test Probability | Points |
|---|---|
| Low-Risk (7.7%) | < 2 |
| Moderate Risk (29.4%) | 2-4 |
| High Risk (64.3%) | > 4 |

Klok FA. *Ann Intern Med.* 2008;168(19):2131-2136

# Pulmonary Embolism Rule-out Criteria

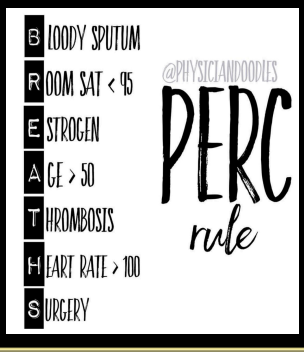
- Developed in 2008
- Rules-out PTE if all criteria (-) ***AND*** pre-test probability is low

Kline JA. *J Thromb Haemost.* 2008;6:772-780

# PERC Criteria

**H**ormone Use
**A**ge (≥50)
**D**VT or PE History
**C**oughing Up Blood
**L**eg Swelling
**$O_2$** Sats < 95%
**T**achycardia (>100)
**S**urgery or Trauma

BoringEM

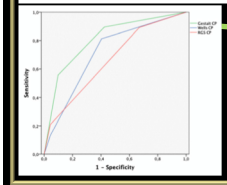



Kline JA. *J Thromb Haemost.* 2008;6:772-780 Thoma B. Tiny Tips: PERC Rule. Boring EM Blog. 2013 July. Available at http://boringem.com/2013/07/07/tiny-tips-perc-rule/

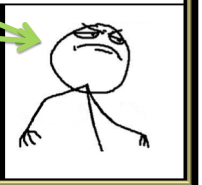
# What About Clinical Gestalt?

| CP Assessment (n=1,038) (%, 95% CI) | Gestalt | Wells Score | RGS |
|---|---|---|---|
| **Number of patients** | | | |
| Low | 445 (43; 40–46) | 486 (47; 44–50) | 270 (26; 23–29) |
| Moderate | 342 (33; 30–36) | 478 (46; 43–49) | 669 (65; 62–67) |
| High | 251 (24; 22–27) | 74 (7; 6–9) | 99 (10; 8–11) |
| **Number of pulmonary embolisms** | | | |
| Low | 34 (7.6; 5.4–10.4) | 61 (12.6; 9.8–15.4) | 35 (13; 9.3–17.4) |
| Moderate | 110 (32.2; 27.4–37.3) | 221 (42.6; 41.8–50.7) | 222 (33.2; 29.7–36.8) |
| High | 181 (72.1; 66.3–77.4) | 43 (58.1; 46.7–68.9) | 68 (68.7; 59.1–77.2) |

*CP*, Clinical probability; *RGS*, revised Geneva score.







Penaloza A. *Ann Emerg Med.* 2013;62(2):117-124

# The Work-Up

*EKG*

*D-Dimer*

*Computed Tomography*

*Ventilation / Perfusion Scan*

## D-Dimer

- High sensitivity, Low specificity
- False Negatives
  - Small clot, impaired fibrinolytic activity
- False Positives
  - Age, smoking, functional impairment

****Should only be used AFTER pre-test probability****

## ADJUST-PE Study

- Multicenter, multinational, prospective study
- 3346 patients
  - Used traditional D-Dimer (> 500 ng/mL) and age-adjusted ( > age x 10 ng/mL)
  - Patients who fell below and had a low pre-test probability were followed for 3 months
    - 0.3% failure rate (1/331)
    - Decrease imaging in patients > 75yo by 29%

Righini M. *NEJM*. 2014;311(11):1117-1124

## Radiographic Imaging

***Computed Tomography***

- Gold Standard
- Higher radiation exposures
- Large contrast bolus

***Ventilation/Perfusion Scan***

- Lower radiation exposure
- 2/3rd are non-diagnostic
- Safer in renal patients

Stein PD. *Am J Med*. 2007;120:871-879

Anderson DR. *Curr Opin Pulm Med*. 2009;15:425–429

# Two Cases

Break into groups, read the cases answer the following…

*What is the Notable History?*
*What are the Notable Signs / Symptoms?*
*List the percentages per PIOPED II and EMPEROR for said signs and symptoms.*
*Determine the Pre-Test Probability using…*
- *-Well's Criteria*
- *-Simplified Geneva Score*
- *-PERC Score*
- *-Clinical Gestalt*

*What is the appropriate Work – Up?*
*What other tests do you want?*

## CASE ONE

- HISTORY
- What is the history?
- SIGNS / SYMPTOMS
- Notable findings?
- List Percentages for each.

## CASE ONE

- PRE-TEST PROBABILITY
- Well's Criteria
- Simplified Geneva Score
- PERC
- Clinical Gestalt

- THE WORK UP
- CMP – normal
- CBC – normal
- CT Head – neg
- CXR – clear
- ECG – regular rhythm, Sinus Tachycardia, Q & T waves in lead III and S wave in lead I
- What other tests do you want??

## CASE TWO

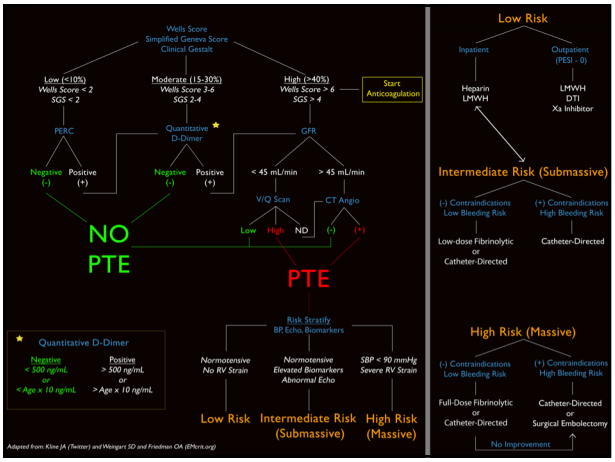
- HISTORY
- What is the history?

- SIGN / SYMPTOMS
- Notable Findings?
- List Percentages for each.

## CASE TWO

- PRE-TEST PROBABILIY
- Well's Criteria
- Simplified Geneva Score
- PERC
- Clinical Gestalt

- THE WORKUP
- UPT is negative
- CXR is clear
- ECG – Sinus Tachycardia at 105 bpm
- What else do you want?




# Risk Assessment

*Echocardiography*

*Biomarkers*

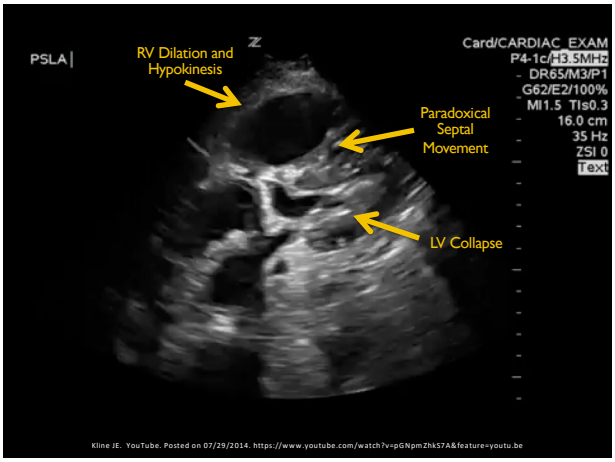
*Pulmonary Embolism Severity Index (PESI)*

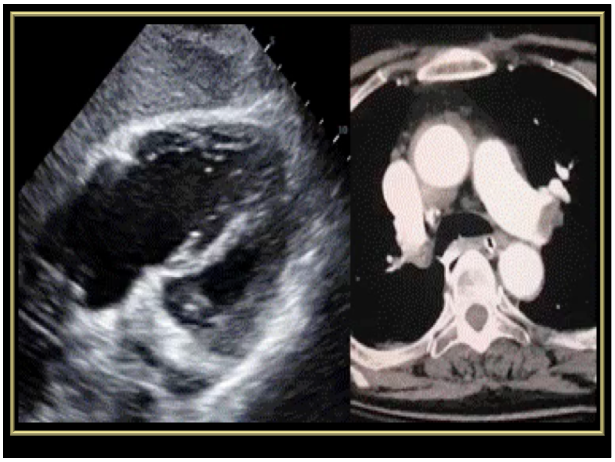
## Echocardiography

- Increasingly utilized at bedside by clinicians
- Helps with determining severity of clot burden
  - RV Strain
    - RV:LV ≥ 1
    - RV hypokinesis
    - Paradoxical septal movement
    - Tricuspid regurgitation

Rudoni RR. *J Emerg Med*. 1998;16(1):5-8

Taylor RA. *J Emerg Med*. 2013;45(3):392-399



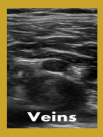
## G.E.L. MULTI-ORGAN US FOR PE

**Question**: Does combining multiple POCUS for PE make for a more accurate exam?

**Scan**:
1. Lung (subpleural consolidation) +
2. Heart (RV dilation or thrombus) +
3. Veins (2 area)

**Study**: prospective ED patients with Wells >4, or +D-dimer n=357, compared to CT pulm ang






| Exam Finding | Sn (%) | Sp (%) | +LR | -LR |
|---|---|---|---|---|
| + Lung | 60.9 | 95.9 | 15 | 0.4 |
| + Heart | 32.7 | 90.9 | 3.6 | 0.7 |
| + DVT | 52.7 | 97.6 | 21.7 | 0.5 |
| + Multiorgan | 90 | 86.2 | 6.5 | 0.1 |

Nazerian P, Vanni S, Volpicelli G. Accuracy of point-of-care multiorgan ultrasonography for the diagnosis of pulmonary embolism. Chest. 145(5):950-7. 2014

Nazerian P, et al. *CHEST*. 2014;145(5):950-957

## Biomarkers

***Hemodynamically stable patients***

- Brain Natriuretic Peptide (BNP)
  - > 90 pg/mL associated with increased mortality
- Troponin I
  - > 0.01 ng/mL suggests RV dysfunction

Kiely DG. *Resp Med*. 2005;99:1286-1291 Jaff MR. *Circulation*. 2011;123:1788-1830 Keller K. *Neth Heart J*. 2015;23:55-61

## Pulmonary Embolism Severity Index

- Originally developed in 2005 to prognosticate 30-day mortality
  - 11 variables with 5 risk categories
- Simplified in 2010
  - 5 variables with 2 risk categories
  - 96% sensitivity, 99% negative predictive value, and 0.12 negative likelihood ratio

Aujesky D. *Am J Respir Crit Care Med*. 2005;172:1041-1046 Jimenez D. *Arch Intern Med*. 2010;170(15):1383-1389

## Simplified PESI Score

| Variable |
|---|
| Age > 80 |
| History of Cancer |
| History of Chronic Cardiopulmonary Disease |
| Heart Rate > 110 beats/min |
| Systolic BP < 100 mmHg |
| $O_2$ Saturation < 90% on Room Air |

| Risk Assessment | Score |
|---|---|
| Low Risk (1.1% risk of death) | 0 |
| High Risk (8.9% risk of death) | ≥ 1 |

**Adverse Event Rate for Low Risk PTE**
13.0% (inpatient) vs 3.3% (outpatient)

Roy PM. *JTH*. 2017;15(4):685-694
Jimenez D. *Arch Intern Med*. 2010;170(15):1383-1389

# Definitions

*Low-Risk*

*Intermediate (Submassive)*

*High Risk (Massive)*


# Treatment

*Anticoagulation*

*Fibrinolytic Therapy*

*Catheter-Directed Therapy*

*Surgical Embolectomy*

## Anticoagulation

- Should be started with:
  - Confirmation of acute PTE
    or
  - High pre-test probability during work-up
- Options
  - Low-molecular weight heparin (LMWH)
  - Unfractionated heparin
  - Direct Thrombin Inhibitors (DTI)
  - Factor Xa Inhibitors

Jaff MR. *Circulation*. 2011;123:1788-1830 Tapson VF. *Crit Care Clin*. 2011;27:825-839

## Fibrinolytic Therapy

**Table 6. Mortality Rates for Acute PE From Published Results of Registries and a Publicly Available Database (HCUP-NIS)**

| | | | | Mortality Rate, % | | | |
|---|---|---|---|---|---|---|---|
| Source | Year | N | Follow-Up | Massive PE | Submassive PE | Massive PE Given Lytic | Submassive PE Given Lytic |
| MAPPET[138] | 1997 | 719 | 30 | NA | 9.6 | NA | 4.7 |
| ICOPER[9] | 1999 | 2284 | 90 | 52.4 | 14.7 | 46.3 | 21 |
| RIETE[71,139] | 2007 | 6264 | 90 | 9.3 | 3.0 | 1.3 | 7.7 |
| EMPEROR[140] | 2008 | 1840 | In-hospital | 14.6 | 3.0 | 0 | 9.5 |
| HCUP-2007 NIS[141] | 2007 | 146 323 | In-hospital | 3.5 | | NA | |

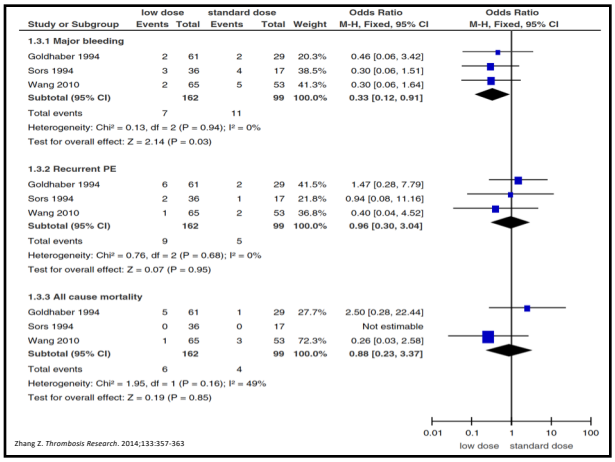
PE indicates pulmonary embolism; HCUP-NIS, Healthcare Cost and Utilization Program Nationwide Inpatient Sample; MAPPET, Management strategy And Prognosis of Pulmonary Embolism regisTry; NA, not available; ICOPER, International COoperative Pulmonary Embolism Registry; RIETE, Registro Informatizado de la Enfermedad TromboEmbólica; and EMPEROR, Emergency Medicine Pulmonary Embolism in the Real-wOrld Registry.

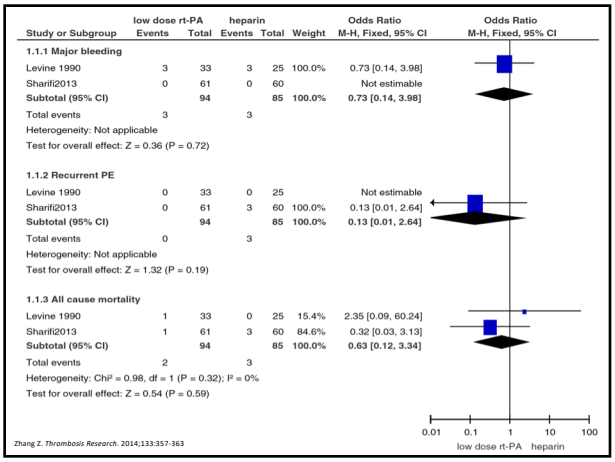
Jaff MR. *Circulation*. 2011;123:1788-1830

## **MO**derate **P**ulmonary **E**mbolism **T**reated with **T**hrombolysis

- Reduction in pulmonary hypertension
- No significant difference in recurrent PTE
- Reduction in total mortality
- Reduction in hospital stay
- No difference in bleeding complications

Sharifi M. *Am J Cardiol*. 2013;111:273-277

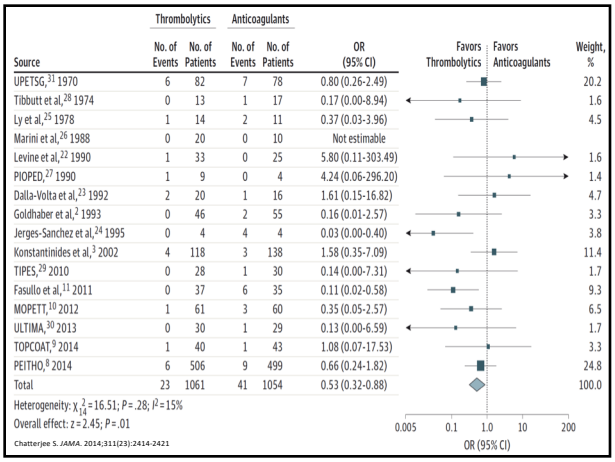


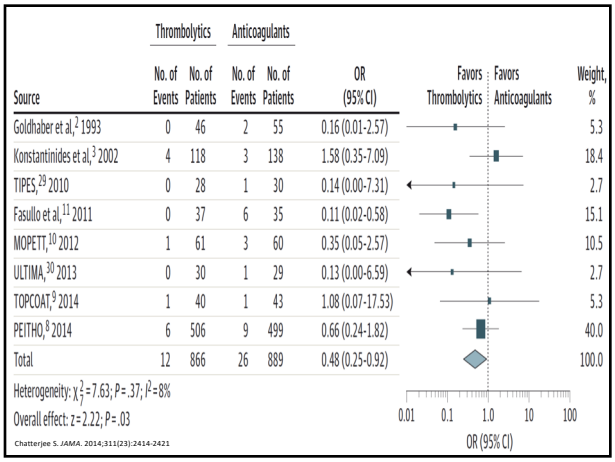




# Pulmonary EmbolIsm THrombOlysis

- No significant overall mortality benefit
- 3-fold reduction of hemodynamic compromise
- 10-fold increase in intracranial hemorrhage
- 5-fold increase in major bleeding

Meyer GM. *NEJM*. 2014;370(15):1402-1411




| Outcome of Interest (No. of Studies Reporting) | No. of Events/No. of Patients, Absolute Event Rate (%) | | No. Needed to Treat or Harm | *P* Value |
|---|---|---|---|---|
| | Thrombolytic Group | Anticoagulant Group | | |
| All-cause mortality (16) | 23/1061 (2.17) | 41/1054 (3.89) | NNT = 59 | .01 |
| Major bleeding (16)[a] | 98/1061 (9.24) | 36/1054 (3.42) | NNH = 18 | <.001 |
| ICH (15) | 15/1024 (1.46) | 2/1019 (0.19) | NNH = 78 | .002 |
| Recurrent PE (15) | 12/1024 (1.17) | 31/1019 (3.04) | NNT = 54 | .003 |
| Age >65 y | | | | |
| All-cause mortality (5) | 14/673 (2.08) | 24/658 (3.65) | NNT = 64 | .07 |
| Major bleeding (5)[a] | 87/673 (12.93) | 27/658 (4.10) | NNH = 11 | <.001 |
| Age ≤65 y | | | | |
| All-cause mortality (11) | 9/388 (2.32) | 17/396 (4.29) | NNT = 51 | .09 |
| Major bleeding (11)[a] | 11/388 (2.84) | 9/396 (2.27) | NNH = 176 | .89 |
| Intermediate-risk PE | | | | |
| All-cause mortality (8) | 12/866 (1.39) | 26/889 (2.92) | NNT = 65 | .03 |
| Major bleeding (8)[a] | 67/866 (7.74) | 20/889 (2.25) | NNH = 18 | <.001 |

# Contraindications For Fibrinolysis

| ***Absolute*** | ***Relative*** |
|---|---|
| • Any history of ICH | • Age > 75 years |
| • Structural intracranial malformation | • Current anticoagulation use |
| • Known intracranial neoplasm | • Pregnancy |
| • Ischemic CVA in last 3 months | • Non-compressible puncture |
| • Suspected aortic dissection | • Prolonged CPR > 10 minutes |
| • Active bleeding | • History of internal bleeding < 1 month |
| • History of bleeding dyscrasias | • SBP > 180 or DBP > 110 |
| • Recent CNS surgery | • Dementia |
| • Recent history of facial/head trauma | • Surgery < 3 weeks |
| | • Ischemic CVA > 3 months |

Jaff MR. *Circulation*. 2011;123(16):1788-1830

# HAS BLED Score

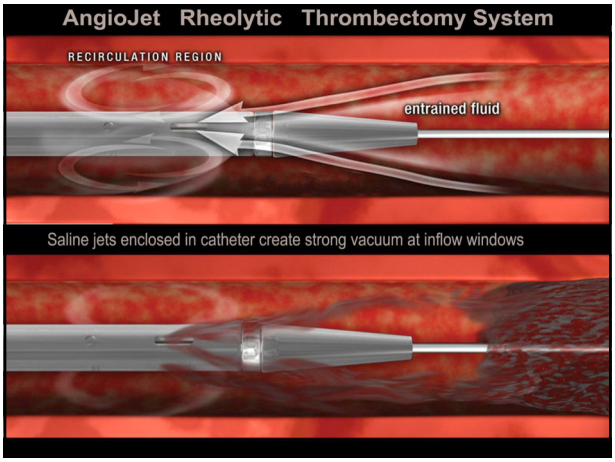
| | | |
|---|---|---|
| Hypertension<br>Uncontrolled, >160 mmHg systolic | No 0 | Yes +1 |
| Renal disease<br>Dialysis, transplant, Cr >2.26 mg/dL or >200 µmol/L | No 0 | Yes +1 |
| Liver disease<br>Cirrhosis or bilirubin >2x normal with AST/ALT/AP >3x normal | No 0 | Yes +1 |
| Stroke history | No 0 | Yes +1 |
| Prior major bleeding or predisposition to bleeding | No 0 | Yes +1 |
| Labile INR<br>Unstable/high INRs, time in therapeutic range <60% | No 0 | Yes +1 |
| Age >65 | No 0 | Yes +1 |
| Medication usage predisposing to bleeding<br>Aspirin, clopidogrel, NSAIDs | No 0 | Yes +1 |
| Alcohol use<br>≥8 drinks/week | No 0 | Yes +1 |

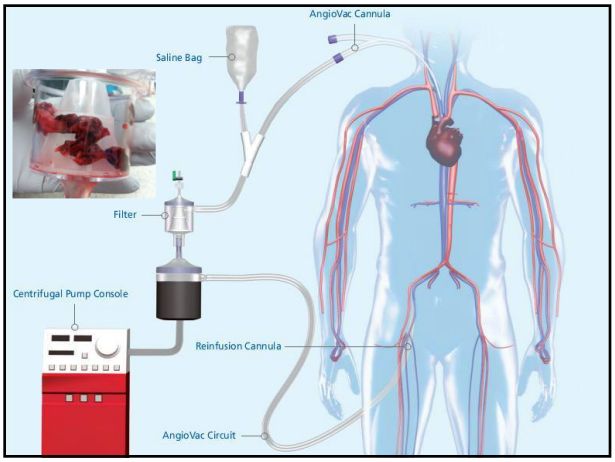
0-1 = Low Risk

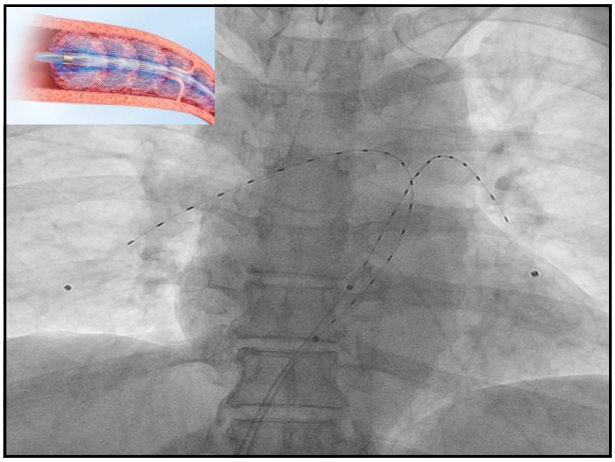
2 = Moderate Risk

> 2 = High Risk

Pisters R. *CHEST*. 2010;138(5):1093-1100



# ULTIMA Trial

- Prospective, Randomized Control Trial
- SUBMASSIVE PTE ONLY!!!
- 59 patients
- Primary Outcome
  - Difference of RV/LV at 24°
- Safety Outcome
  - Death, bleeding, and recurrent VTE at 90-days

Kucher N. *Circulation*. 2014;129:479-486

# ULTIMA Trial

- Results
  - Primary End Point
    - USAT = RV/LV reduced by mean 0.29
    - Heparin = RV/LV reduced by mean 0.03
  - Safety End point
    - No episodes of hemodynamic decompensation or recurrent VTE in either group
    - Bleeding
      - USAT = 3 minor bleeding complications
      - Heparin = 1 minor bleeding complication

Kennedy RJ. *J Vasc Interv Radiol*. 2013;24:841-848

# SEATLE-II Study

- Submassive and Massive PTE
- 150 patients
- Intervention
  - Full dose IV heparin AND ultrasound-facilitated, low-dose, catheter-directed fibrinolytic therapy
- Outcome
  - Primary – change in RV/LV diameter ratio at 48°
  - Safety – Major bleeding at 72°
- Results
  - Primary – -0.42 in RV/LV ratio
  - Safety – 1 severe hematoma episode

Piazza G. *JACC*. 2015;8(10):1382-1392

# PERFECT Study

- Submassive and Massive PTE
- 101 patients
- Intervention
  - Immediate catheter-directed mechanical or pharmacomechanical thrombectomy and/or catheter-directed thrombolysis with low-dose fibrinolytic infusion
- Outcome
  - Primary
    1. stabilization of hemodynamics
    2. improvement in pulmonary hypertension and/or improved RV strain
    3. Survival to hospital D/C
  - Safety – major procedure related complications and major bleeding events
- Results
  - Primary – 86% in massive and 97% in submassive
  - Safety – no complications or major bleeding event

Kuo WT. *CHEST*. 2015;148:667-673

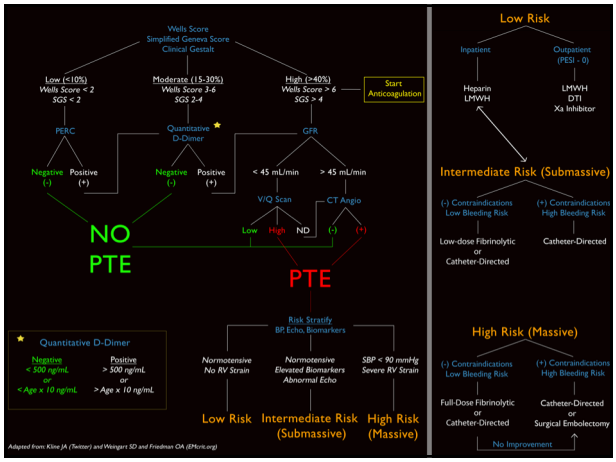
# Surgical Embolectomy

- Old and Busted
  - 1960s (**57%**) → 1990s (**26%**)

Twitter - @FToranMD - 04/01/2015

- New Hotness
  - 2005 (**6%**)

Cross FS. *Circulation*. 1967;35:186-191 Stulz P. *Eur J Cardio-thorac Surg*. 1994;8:188-193 Leacche M. *J Thorac Cardiovasc Surg*. 2005;129:1018-1023




# Break Into Groups

*Determine Risk Assessment and Treatment for each case.*

Answer the three questions as a group.

## CASE ONE

- RISK ASSESSMENT
- ECHO RESULTS
- BNP
- TROPONIN
- PESI SCORE
- Low, Intermediate or High Risk??
- TREATMENT
- WHAT DO YOU RECOMMEND??

## CASE TWO

- RISK ASSESSMENT
- Low, Intermediate or High Risk??
- TREATMENT
- WHAT DO YOU RECOMMEND??

## Question #1

Which of the following clinical decision instruments, when negative, can be used to rule-out pulmonary thromboembolism?

A. Wells Criteria
B. Revised Geneva Score
C. PERC Criteria
D. PEITHO

## Question #2

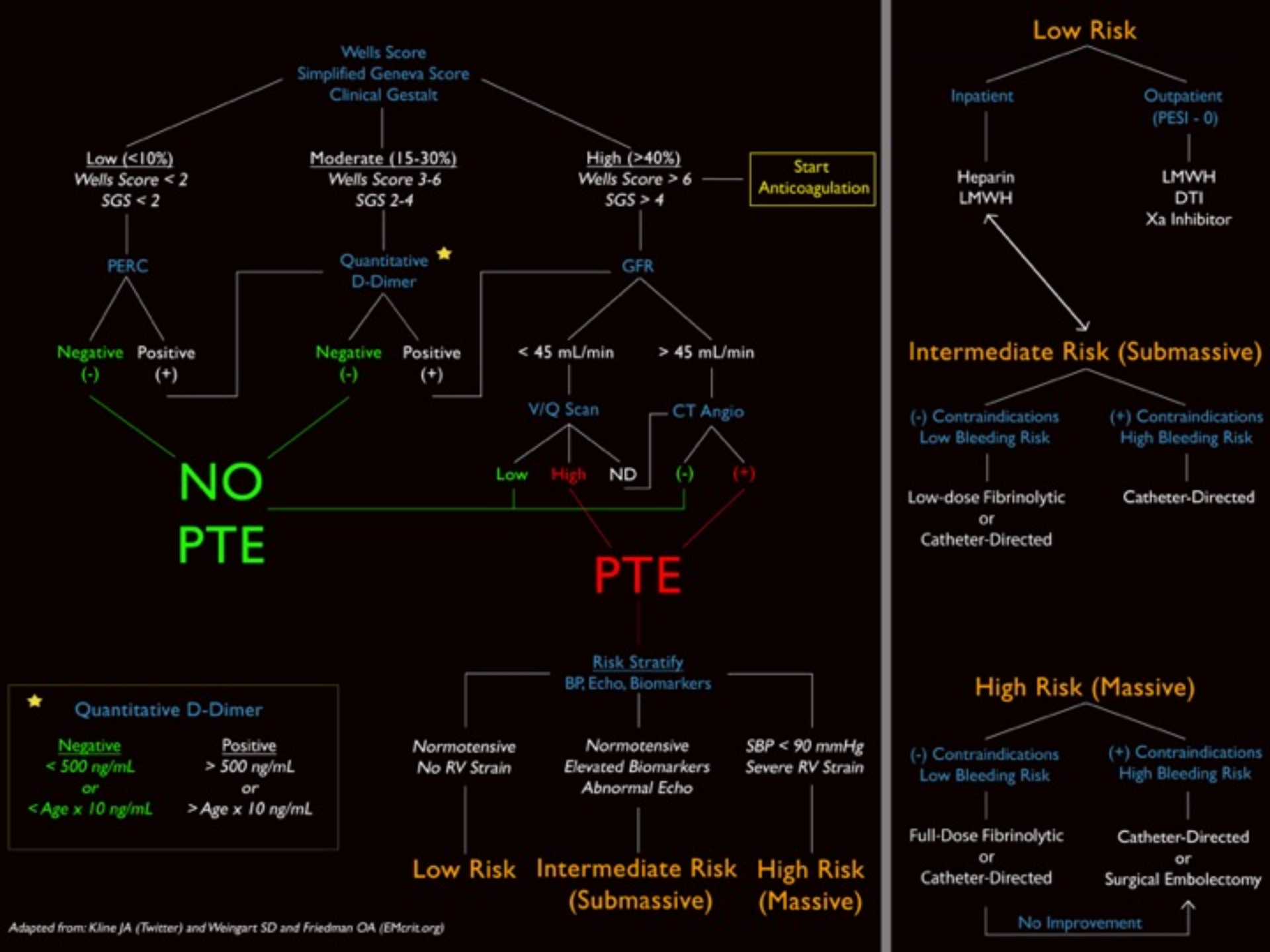
What is the most common abnormality seen on electrocardiogram in pulmonary thromboembolism?

A. S1Q3T3
B. Sinus Tachycardia
C. Left Axis Deviation
D. Poor R-Wave Progression

## Question #3

Which of the following is an indication for fibrinolysis of a pulmonary thromboembolism?

A. Systolic BP of 75 mmHg
B. Heart rate of 110 bpm
C. PaO2 of 75 mmHg
D. Respiratory Rate of 22 bpm




*Adapted from: Kline JA (Twitter) and Weingart SD and Friedman OA (EMcrit.org)*

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***CASE ONE***

A 26-year-old man with no history of disease was admitted to Gazi University Emergency Department after he had a syncopal episode in his home. The patient was in his usual good state of health until he suddenly collapsed while standing and lost consciousness for approximately five minutes. He recovered spontaneously but was extremely weak and dyspneic. He was also diaphoretic and tachypneic, but denied any associated chest pain or palpitations. No tonic-clonic activity was witnessed, and he experienced no incontinence.

The patient was a computer programmer and he had been working 18 hours a day without rest periods for a month. On admission, physical examination revealed a diaphoretic and dyspneic patient without focal neurologic findings. His heart rate was regular but tachycardic at 128 beats/minute, his blood pressure was 126/72 mmHg without orthostatic changes, and his respiratory rate was 32 breaths/minute. The room air oxygen saturation was 90%, and arterial blood gas analysis in room air revealed hypoxemia ($PO_2$ = 58 mmHg) with an elevated alveolo-arterial oxygen gradient (A-a $O_2$ gradient). Examination of his head and neck was normal. The results of chest wall examination revealed reduced breath sounds bilaterally at the lung bases. The findings of heart and abdominal examinations were unremarkable, but on examination of his legs, deep venous thrombosis (DVT) was noted in his left leg, with a positive Homans' sign in the left leg and the left calf measured 3 cm more than the right one.

Levels of serum electrolytes, glucose, blood urea and creatinine, and complete blood counts were normal. Results of a computed tomographic scan of his head were negative for bleeding, aneurysm or an embolic event. Chest X-ray was clear. An electrocardiogram showed a regular rhythm consistent with sinus tachycardia; there were Q and T waves in lead III and an S wave in lead I. A ventilation-perfusion scan demonstrated an unmatched segmental perfusion defect, indicating a high probability of the presence of a pulmonary thromboembolism (PTE). A transthoracic echocardiogram revealed normal left ventricle function without a patent foramen ovale, an atrial septal defect or a ventricular septal defect, but with mild pulmonary hypertension (42 mmHg). A Doppler scan of the legs revealed an acute DVT in the patient's left leg, in the popliteal vein. Thrombolytic treatment was not given - the patient received standard anticoagulation treatment with unfractionated heparin and an oral anticoagulant. Before treatment, a blood sample was taken to examine the thrombophilia panel. After a 12-day course of hospital treatment, he was discharged on oral warfarin therapy. The patient's long-term follow-up was performed by the Department of Pulmonary Disease, and we learned that the patient was well for four months after that episode without any evidence of recurrent syncope or pulmonary embolism.

***CASE TWO***

A 40-year-old female with no past medical history presents to Urgent Care on Friday afternoon at 5pm complaining of a non-productive cough x 3 days. She has no other complaints. She has no diaphoresis, chest pain or palpitations. She denies any known sick contacts. She denies any aggravating or alleviating factors. She works as a Nanny for three children and is on the go all day. She does not smoke, drink, nor does she take any medications.

On physical examination patient is well appearing and in no distress. There is no diaphoresis and dyspnea. Her heart rate is regular at 98 beats/minute; blood pressure is 126/72 mmHg without orthostatic changes, and her respiratory rate is 20 breaths/minute. The room air oxygen saturation is 94%. Examination of her head and neck is normal. The results of chest wall examination reveals wheezes bilaterally at the lung bases. The findings of heart, abdominal, and lower extremity examinations were unremarkable.

No labs are able to be obtained at urgent care but her urine pregnancy test is negative. Chest X-ray is clear. An electrocardiogram shows a regular rhythm consistent with sinus tachycardia at a rate of 105.

What other tests do you desire?

What treatment do you recommend?