Pulmonary embolism: simultaneously the most over-tested yet under-diagnosed condition in medicine

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Jeffrey A. Kline, MD

Professor, Department of Emergency Medicine and Indiana University School of Medicine

Indianapolis, IN

@klinelab

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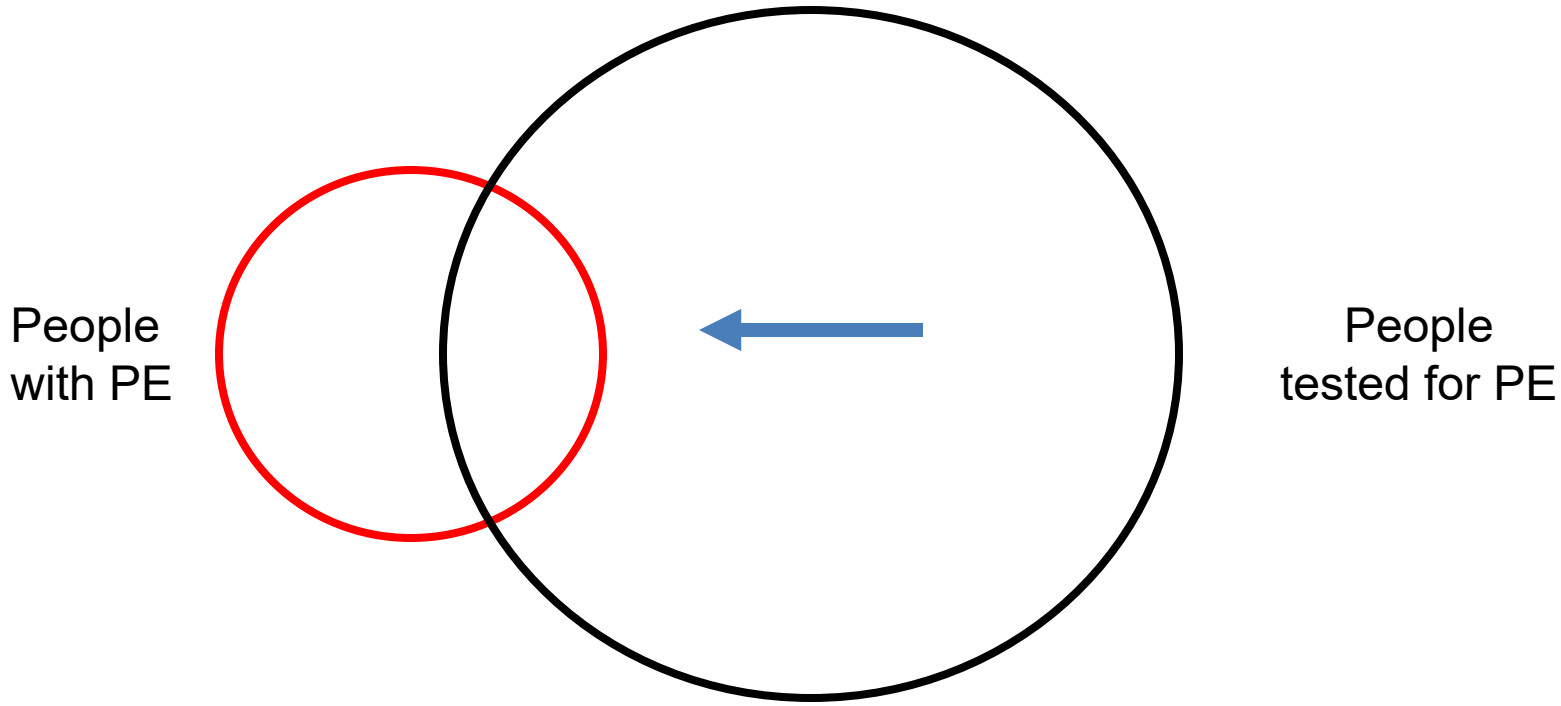

People
with PE
People
tested for PE

Low value testing is rampant

- Prevalence of PE+ decreased to 3-5% *Crichlow, Acad Emerg Med 2012; 19: 1219; Circ Cardiovasc Qual Outcomes. 2020 13(1):e005753.*
- Over 1/3 of CTPA scans in low risk patients had no D-dimer *Venkatesh AK et al. Arch Intern Med 2012;172:1028-3*
- About 5% of CTPA scans called PE+ are reread as false positives *Schissler AJ, et al. PLoS One 2013;8(6):e65669*
- Use of PERC or Wells/D-dimer could have reduced CTPA by 15% *Venkatesh AK et al. Arch Intern Med 2012;172:1028-3; JAMA Intern Med 2014;174(4):509-515*

Young women are over-tested

- PE occurs equally between sexes *Clin Chest Med. 2010 Dec;31(4):611-2*
- CT cancer risk highest in young women
- Women comprise 55-65% of those receiving CTPA *Ann Emerg Med. 2010 Apr;55(4):307-315, 2010*
- Yield rate slightly lower in women *Circ CQO 2020 Jan;13(1):e005753*

Young women are over-tested

- PE occurs equally between sexes (Clin Chest Med. 2010 Dec;31(4):611-2)
- CT cancer risk highest in young women
- Women comp… 55-65% of those receiving CTPA (**Ann Eme…** Jan;13(1):e005753)
- Yield rate s… CQO data)

"…for every 10,000 CTPA scans performed in women <40, **35 will develop either breast, thyroid or blood cancer**."
JAMA pediatrics. 2013;167(8):700-707.
Br J Cancer. 2016;114(4):388-394.
Radiation and environmental biophysics. 2015;54(1):1-12.
Radiation and environmental biophysics. 2014;53(1):39-54.
BMJ. 2013;346:f2360.
BMJ. 2012;345:e5660

Underdiagnosis

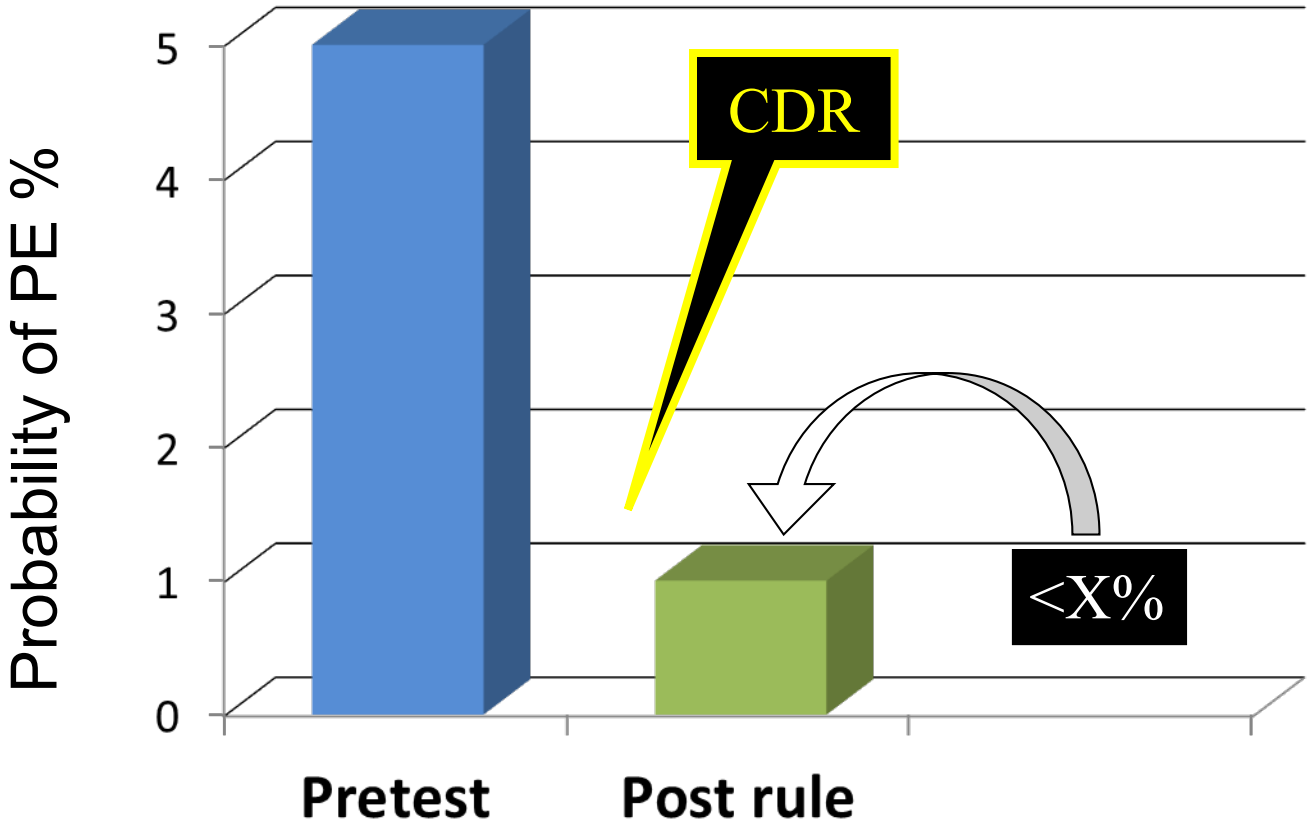
- Every year, at least hundreds of patients with ultimately fatal PE are missed in emergency departments in the US
  - Failure to diagnose PE is approximately 5% of all closed malpractice claims
  - Increased frequency of claims in residents versus non-resident physicians

Acad Emerg Med 2018 Sep;25(9):980-986

Solutions?

- More use of what we know works: Exclusion rules and D-dimer
- Computer decision support (CDS) can effect meaningful changes in behavior *during the period of active observation*
  - Implementation science and behavioral economics approach

When am I off the hook?



Test threshold:

Pauker and Kassirer described in 1980

Point estimate of PTP

Mathematical and ethical point of equipoise where:

false negative risk = false positive risk

Test threshold for PE = 2.0%

S. G. Pauker and J. P. Kassirer. *NEJM* 302:1109-1117, 1980.
Lessler AL, et al. *Ann Emerg Med* 2010;55:316-26.

The PERC rule

Gestalt low suspicion and:

1. Age < 50
2. Heart rate < 100
3. No hemoptysis
4. No estrogen use
5. No recent surgery
6. No prior PE or DVT
7. No unilateral leg swelling
8. Room air pulse oximetry ≥ 95%

J Thromb Haemost. 2008 May;6(5):772-80

Clinical practice guidelines

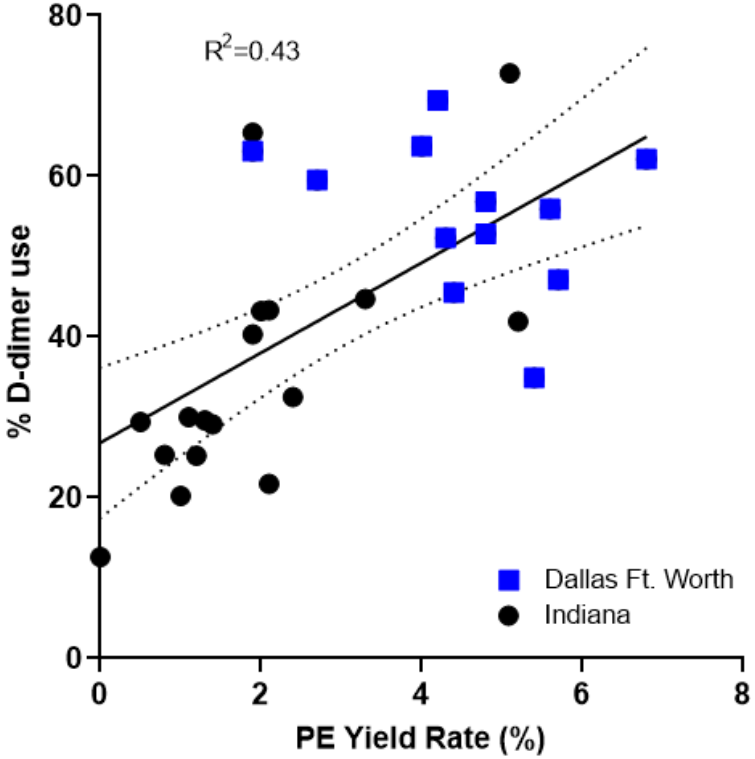
- The ASH CPG (2018) did not cover scoring criteria but nonetheless recommended PERC.

"For patients presenting to an emergency department with a low probability of PE, the Pulmonary Embolism Rule-out Criteria (PERC) may be used to determine whether D-dimer testing is warranted"

- ACP (2015) recommended PERC as "best practice advice".
- ACEP recommended PERC use ("Level B")
- PERC was a "Choose wisely" recommendation

Blood Adv. 2018 Nov 27;2(22):3226-3256
Ann Intern Med. 2015 Nov 3;163(9):701-11
Ann Emerg Med. 2011 Jun;57(6):628-652

Higher D-dimer inversely associated with CTPA use



Circulation: Cardiovascular Quality and Outcomes

ORIGINAL ARTICLE

Over-Testing for Suspected Pulmonary Embolism in American Emergency Departments

The Continuing Epidemic

BACKGROUND: No recent data have investigated rates of diagnostic testing for pulmonary embolism (PE) in US emergency departments (EDs), and no data have examined computed tomographic pulmonary angiography (CTPA) rates in subgroups at high risk for adverse imaging outcomes, including young women and children. We hypothesized that over-testing for PE remains a problem.

Jeffrey A. Kline, MD
John S. Garrett, MD
Elisa J. Sarmiento, MS
Christian C. Strachan, MD
D. Mark Courtney, MD

N=27 hospitals. Blue squares represent hospitals with monitored-feedback QA methodology to increase D-dimer use in low pretest probability patients

Adoption of D-dimer is slow

- Physicians perceive the D-dimer as a waste of time
- Fewer than ¼ use age adjustment
- Physicians “game” the system to order CT
- Value of desire for alternative diagnoses on CT underestimated in understanding behavior

Acad Emerg Med. 2017 Jul;24(7):839-845
Acad Emerg Med 2020 Jun;27(6):447-456

Age adjustment increases specificity

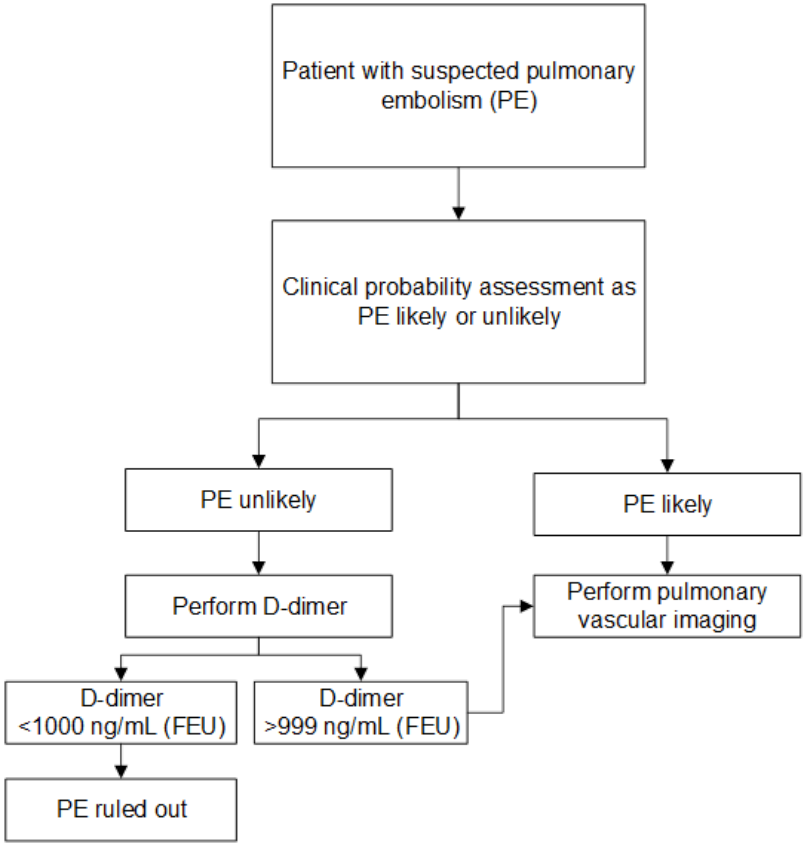
Table 2. Summary of results of studies informing sensitivity and specificity of tests for diagnosis of PE

Test	No. of participants (studies)	Sensitivity (95% CI)	Specificity (95% CI)	Quality of evidence
CTPA	3 929 (15)	0.93 (0.88-0.96)	0.98 (0.96-0.99)	Moderate*,†,‡
D-dimer	20 568 (30)	0.97 (0.96-0.98)	0.39 (0.36-0.43)	Moderate*,†,§
Age-adjusted D-dimer	2 885 (1)	0.99 (0.98-1.00)	0.47 (0.45-0.49)	High‖
Proximal ultrasound	1 715 (7)	0.49 (0.31-0.66)	0.96 (0.95-0.98)	Low*,¶,#
VQ 1	3 994 (13)	0.58 (0.50-0.66)	0.98 (0.96-0.99)	Moderate*,†,**
VQ 2	3 994 (13)	0.98 (0.95-0.99)	0.36 (0.27-0.45)	Moderate*,†,††
VQ 3	3 994 (13)	0.96 (0.91-0.98)	0.95 (0.89-0.98)	High*,†,‡,‡

Blood Adv. 2018 27;2(22):3226-3256.

Other D-dimer threshold adjustments

- Pretest probability: Double the standard cutoff (1000 ng/mL) for low pretest probability (i.e., Wells <5), which increases net exclusion rate by 10%
- Or use gestalt low (<15%)
- Pregnancy



Lancet. 2017 Jul 15;390(10091):289-297

N Engl J Med 2019 Nov 28;381(22):2125-2134

What works?

What works?

- Combined approach: electronic + human supervision
  - A champion; cultural buy-in
  - Tied to compensation with comparative data
  - Hawthorne effect probably important
- Baylor-Scott White system in Dallas
  - **Persistent reduction** in Chest CT scanning from 6 to 2%, head CT scanning from 13% to 9%

Summary

- The 2021 solution to over-testing and undertesting for PE is more use of existing knowledge, namely the PERC rule and D-dimer

- Whether or not clinical/computer decision support can make a long-term impact probably depends upon system commitment