Critical Review Form
Clinical Practice Guidelines

Clinical Policy: Critical Issues in the Evaluation and management of Adult Patients Presenting with Suspected Pulmonary Embolism, *Ann Emerg Med* 2003; 41:257-270

Objectives: **To revise the 1995 ACEP "Clinical Policy for the Initial Approach to Adults Presenting with a Chief Complaint of Chest Pain, with No History of Trauma" as it relates to the initial approach to patients with signs and symptoms of PE.**

Methods: **A MEDLINE search was conducted from Jan 1995 through April 2001 using the keyword "pulmonary embolism". In addition, practice guidelines were reviewed from the American Heart Association, British Thoracic Society, American College of Chest Physicians, American Thoracic Society, and European Heart Association (the last of which was updated in 2008). After the PE subcommittee reviewed the available evidence four topics were selected for this guideline:**

1) **Diagnostic utility of D-dimer for PE;**
2) **Diagnostic utility of ventilation-perfusion scanning for PE;**
3) **Diagnostic utility of spiral computed tomography for PE;**
4) **Therapeutic implications for fibrinolytic agents in PE.**

Each manuscript was graded for quality by at least two sub-committee members based on study design. Design 1 represents the strongest evidence and design 3 the weakest evidence

*Literature classification schema.**

Design/ Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analyses of randomized trials	Prospective cohort using a criterion standard	Population prospective cohort
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing ≥2 interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome including mortality and morbidity.

Next, subcommittee members graded the evidence on 6 dimensions felt to be most important for guideline development: blinding of outcome assessment, blinded/randomized allocation, direct or indirect outcome measures, bias (selection, detection, transfer), external validity and sample size. The recommendations generated were then classified as Level A, B, or C.

Approach to downgrading strength of evidence.

	Design/Class		
Downgrading	1	2	3
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

Level A – high degree of clinical certainty based on Class 1 strength of evidence or preponderance of Class II studies.
Level B – moderate clinical certainty based on Class II studies or strong consensus of Class III studies.
Level C – preliminary or inconclusive evidence or panel consensus.

This guideline excluded studies of pregnant patients.

Guide		Comments
I.	**Are the Recommendations Valid?**	Answer questions IA-D below
A.	**Did the recommendations consider all relevant patient groups, management options, and possible outcomes?**	No. This guideline development process excluded pregnant patients (and asymptomatic patients) (p.260)
B.	**If necessary, was an explicit, systematic, and reliable process used to tap expert opinion?** *You should look for a clear description of how the panel was assembled along with the members' specialties and any organizations they are representing.*	Uncertain. The process used to select ACEP Guideline Committee or PE Subcommittee members was not explained. Also, no conflicts of interest are explained. The authors did seek guidance from pertinent shareholders such as ATS, BTS, AHA, etc.

C.	**Is there an explicit, systematic specification of values or preferences?** *Panelists' ratings presumably reflect the risk-benefit trade-offs of specific interventions, but whether other physicians or patients themselves would make the same decisions remains uncertain. Whether given options are value or preference related should be clearly stated in the guideline.*	No. The authors do not provide any description of clinician risk aversion variability, policy-maker, medico-legal or cost implications, or mechanisms to incorporate unique patient preferences into the diagnostic and therapeutic decision making for PE.
D.	**If the quality of the evidence used in originally framing the criteria was weak, have the criteria themselves been correlated with patient outcomes?** *When the studies utilized to produce guidelines are less than randomized-controlled trials, conclusions can be strengthened by noting how outcomes can be correlated with adherence to the guidelines.*	In some instances the guideline authors provide outcomes-based trial evidence to support recommendations. Examples: 1) "In a retrospective study, Rajendran and Jacobson investigated 536 patients with a low probability V/Q scan and found no evidence of PE on 6-month follow-up" (p. 263) 2) "In the largest study to date, Swensen et al retrospectively studied 1512 consecutive patients undergoing CT angiography for suspected PE for 3-month outcome. The incidence of DVT or PE on follow-up was 0.5% and fatal PE 0.3% in the 1,010 patients with negative findings on a spiral CT." (p. 264)

II.	What are the recommendations?	Answer questions II A-B below
A.	**Are practical, clinically important recommendations made?**	Yes, within the limitations of the pre-2001 search strategy being applied in 2011. **Question 1:** *Can a negative D-dimer exclude PE?* Level A Recommendations: None Level B Recommendations: In patients with a low pretest probability of PE, use the following tests to exclude PE: 1) A negative quantitative D-dimer assay (turbidimetric or ELISA). 2) A negative whole blood cell qualitative D-dimer assay in conjunction with wells score of 2 or less. Level C Recommendations: In patients with a low pretest probability of PE, negative findings on a whole blood D-dimer assay (when not used with well's scoring system) or immunofiltration D-dimer assay can be used to exclude PE. Guideline authors offer the following evidence to support those recommendations. • The qualitative whole blood assay requires 5-minutes to administer and when used with Well' criteria has a NPV of 99.5%. • Two rapid (~ 2 hours) quantitative D-dimer tests are available (ELISA, turbidimetric) with negative LR 0.07 at cutoff 0.05 ng/mL. **Question 2:** *Can V/Q scan alone or in combination with venous Doppler or D-dimer exclude PE?*

		Level A Recommendations: In patients with a low-to-moderate pretest probability of PE, a normal perfusion scan reliably excludes clinically significant PE. Level B Recommendations: In patients with a low-to-moderate pretest probability of PE and a non-diagnostic V/Q scan, the following tests can be used instead of a pulmonary arteriogram to exclude PE. 1) A negative quantitative D-dimer assay. 2) A negative whole blood qualitative D-dimer in conjunction with a Well's score ≤4. 3) For low-probability patients, a single negative bilateral venous ultrasonographic scan. 4) For moderate probability patients, serial (repeat at day 3-7) bilateral venous ultrasonographic scan. Level C Recommendations: In patients with a low-to-moderate pretest probability of PE and a nondiagnostic V/Q scan, use a negative whole blood D-dimer assay (When not used with Well's score) or immunofiltration D-dimer assay to exclude PE. Guideline authors offer the following evidence to support these recommendations. • In the initial PIOPED analysis, PE rates for V/Q results of high, intermediate, low, and normal were 87%, 30%, 14%, and 4% with LR^+ for "high" 18.3 and LR^- for normal 0.1. • Unfortunately, 60% of PIOPED patients were non-diagnostic (intermediate or low probability V/Q scans).

		• In patients with low probability V/Q scans, PE rates for low, intermediate, or high clinical probability patients were 4%, 16%, and 40% respectively. • In one retrospective study, Rajendran and Jacobson investigated 536 patients with low probability V/Q scans and found no patient with evidence of PE at 6-month follow-up. • Sensitivity of LE Duplex for patients with a nondiagnostic V/Q is 50%. **Question 3:** *Can spiral CT replace V/Q scanning in the diagnostic evaluation of PE?* Level A Recommendations: None Level B Recommendations: Thin collimation spiral CT scan of the thorax with 1- or 2-mm image reconstruction may be used as an alternative to V/Q in evaluating patients with suspected PE. Level C Recommendations: Spiral CT scan of the thorax with delayed CT venography may be used for increased detection of patients with significant thromboembolic disease. Guideline authors offer the following evidence to support these recommendations: • Meta-analysis of 9 prospective spiral CT trials indicates pooled sensitivity 77%, specificity 89% with increased sensitivity (95%), for segmental (or larger) PE's and lower for subsegmental PE (under 75%). • Goodman et al evaluated 198 patients with negative CT and

		188 with a normal or low prob V/Q and 3% in those with low probability V/Q. • Swenson et al retrospectively evaluated 1512 consecutive patients with CT angiography for suspected PE with an incidence of PE or DVT 0.5% and fatal PE 0.3% in the 1010 patients with negative findings on spiral CT. **Question 4:** What are the indications for fibrinolytic therapy in patients with PE? See the July 2010 Journal Club.
B.	**How strong are the recommendations?**	See the Level A, B or C of recommendations above.
III.	**How Can I Apply the Criteria to Patient Care?**	
A.	**Are the criteria relevant to your practice setting?** *Medical practice is shaped by an amalgam of evidence, values and circumstances; clinicians should consider their local medical culture and practice circumstances before importing a particular set of audit criteria.*	Yes. However, "recommendations offered in this policy are not intended to represent the only diagnostic and management options that the emergency physician should consider. ACEP clearly recognizes the importance of the individual clinician's judgment. Rather, they define for the clinician those strategies for which medical literature exists to provide strong support for their utility in answering the crucial questions addressed in this policy." (p. 258)
B.	**Have the criteria been field-tested for feasibility of use in diverse settings, include settings similar to yours?**	No, these recommendations (and guideline development methods) have not been field tested for feasibility in heterogeneous settings.

Limitations

1) **Outdated guideline – update pending which should incorporate concern below.**

2) **Failure to address frequent diagnostic and therapeutic issues such as the work-up threshold for symptomatic patients with known PE, indications for vena cava filter placement, and emergency physician Doppler ultrasound for DVT as part of PE work-up when V/Q is non-diagnostic.**

3) **Exclusion of pregnant patients.**

4) **Pre-dated PERC criteria.**

Bottom Line

Well's criteria (below) or similar validated decision aids like the Wicki criteria or Kline criteria should be used prior to test-ordering to risk stratify ED patients with suspected PE. Once PE probability stratification is deduced, use of quantitative D-dimer (ELISA or turbidimetric) can exclude patients with low pre-test probability. In low to moderate pretest probability patients, a normal V/Q scan excludes clinically significant PE. The 3-month risk of DVT or PE in patients with a negative spiral CT is 0.5%.

Well's Criteria

Risk Factor	Points
Suspected DVT	3
Alternative Diagnosis Less Likely than PE	3
Heart Rate > 100	1.5
Immobilization or surgery previous 4 weeks	1.5
Previous DVT or PE	1.5
Hemoptysis	1
Malignancy (last 6 months or palliative)	1

Score	Mean Probability PE (%)	% with this Score	Risk Interpretation
0-2 points	3.6	40	Low
3-6 points	20.5	53	Moderate
>6 points	66.7	7	High