

# Clinical Assessment of the Patient With a Suspected Pulmonary Embolism

## EBEM Commentator Contact

**Richard Sinert, DO**  
**Matthew Foley, MD**

From the Department of Emergency Medicine, SUNY–Downstate Medical Center, Brooklyn, NY.

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## RATIONAL CLINICAL EXAMINATION REVIEW SOURCE

This is a rational clinical examination abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine (EBEM) series. Each features an abstract of a rational clinical examination review from the *Journal of the American Medical Association* and a commentary by an emergency physician knowledgeable in the subject area.

The source for this rational clinical examination review abstract is: Chunilala SD, Eikelbloom JW, Attia J, et al. The rational clinical examination. Does this patient have a pulmonary embolism? *JAMA*. 2003;290:2849-2858.<sup>1</sup> The *Annals'* EBEM editors assisted in the preparation of the abstract of this rational clinical examination review, as well as selection of the Evidence-Based Medicine Teaching Points.

## OBJECTIVE

To summarize the value of the clinical examination, clinical prediction rules, and D-dimer assays in detecting pulmonary embolism in adult patients.

## DATA SOURCES

The authors report a MEDLINE search for English-language articles from 1966 to March 2003 and hand searching of reference lists of identified articles. The search strategy is described in detail.

## STUDY SELECTION

Studies were included that described the operating characteristics of the clinical examination for the diagnosis of pulmonary embolism. The studies selected for inclusion had to satisfy 3 conditions: estimated pretest probability of pulmonary embolism, blinding, and validated methodology for confirming or excluding pulmonary embolism. In addition, each study had to have a minimum number ( $N > 50$ ) of confirmed cases of pulmonary embolism. No selection criteria are reported for the 3 studies cited describing D-dimer operating characteristics. Two of these are medical record review studies on selected populations, whereas a third is a large-scale, multicentered, prospective evaluation.

## DATA EXTRACTION AND ANALYSIS

Potentially eligible articles were reviewed by 3 of the authors, with a senior reviewer resolving disagreements. The operating

characteristics of the clinical prediction rules of pulmonary embolism were summarized with likelihood ratios (LRs) and 95% confidence intervals (CIs), and  $\kappa$  and weighted  $\kappa$  values are reported as measures of precision for clinical prediction rules. Pooled LRs were summarized with random-effects measures.

## MAIN RESULTS

### Performance of Clinical Gestalt

From 1,709 articles identified using the search strategy, 7 studies were found that assessed physicians' clinical gestalt in judging the pretest probability of pulmonary embolism. Of these studies, the physician's clinical gestalt of low, moderate, and high pretest probabilities showed that the actual rates of pulmonary embolism ranged from 8% to 19%, 26% to 47%, and 46% to 91%, respectively. Three of the 7 studies (Prospective Investigation of Pulmonary Embolism Diagnosis,<sup>2</sup> Sanson et al,<sup>3</sup> and Musset et al)<sup>4</sup> used inpatients and outpatients, with the clinical gestalt determined by either the attending physician caring for the patient or the physician in charge of the patient. Perrier et al<sup>5-7</sup> had internal medicine residents working in emergency departments to predict pretest probabilities according to their clinical gestalt. Last, pulmonary specialists in the study completed by Miniati et al<sup>8</sup> determined the clinical gestalt.

### Performance of Clinical Prediction Rules

In derivation studies, the clinical prediction rules divided patients suspected of having pulmonary embolism into low (3% to 10%), moderate (26% to 46%), and high (63% to 98%) pretest probabilities. Pooled LR for each category of predicted risk were low (0.12; 95% CI 0.05 to 0.31), moderate (1.1; 95% CI 0.76 to 1.6), and high (23; 95% CI 7.6 to 69). Table 1 compares the performance of each clinical prediction rule in assigning pretest probabilities in derivation cohorts.

The extended Wells rule<sup>9</sup> was tested for validation by 2 studies. Although the prospective validation study by Kruijff et al<sup>10</sup> confirmed the discriminatory power of the rule to determine pretest probability (low=4%; moderate=28%; high=63%), the validation study by Sanson et al,<sup>3</sup> using a retrospective study design, found lower discriminatory power (28%, 39%, 46%).

Three studies attempted to validate the simplified Wells rule. Sanson et al,<sup>3</sup> again using a retrospective methodology, found a lower (28%, 30%, 38%) discriminatory power than the original

**Table 1.** Pretest probabilities of pulmonary embolism of clinical decision rules.

Source	Patients, No.	Pretest Probability Category	Pretest Probability, %	LR (95% CI)
Wells et al, 1998 (extended)	1,239	Low	3	0.17 (0.12–0.25)
		Moderate	28	1.8 (1.25–2.1)
		High	78	17 (11–27)
Miniati et al, 1999 (PISA-PED)	750	Unlikely	6	0.05 (0.03–0.10)
		Possible	46	0.99 (0.75–1.3)
		Very likely	97	47 (23–98)
		High	63	8.6 (5.7–13)
Wicki et al, 2001 (Geneva Rule)	986	Low	10	0.31 (0.24–0.40)
		Moderate	38	1.7 (1.5–1.9)
		High	81	11 (6.1–21)
Kline et al, 2002	934	Nonhigh	13.3	0.64 (0.56–0.73)
		High	42.1	3.0 (2.4–3.8)
Miniati et al, 2003 (PISA-PED II)	1,100	Low	4	0.07 (0.04–0.11)
		Moderate	26	0.72 (0.6–0.87)
		High	98	66 (31–137)

rule, whereas prospective validation studies were performed by Wells et al<sup>11</sup> (1.3%, 16.2%, 40.6%) and Chagnon et al<sup>12</sup> (12%, 40%, 91%). Chagnon et al<sup>12</sup> also prospectively tested the Wicki (Geneva)<sup>13</sup> clinical prediction rule and found a similar range of pretest probabilities of pulmonary embolism (13%, 38%, 67%).

Table 2 compares the results of prospective validation studies, reported for the extended Wells rule,<sup>9</sup> simplified Wells rule,<sup>14</sup> and Wicki (Geneva).<sup>13</sup> The Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis and Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis II rules developed by Miniati et al<sup>15,16</sup> and the clinical prediction rule by Kline et al<sup>17</sup> did not have prospective validation studies evaluated in this review.

### Precision of Clinical Prediction Rules

Interobserver variability was not measured in any of the studies of clinical gestalt. High agreement for the clinical prediction rules was identified for Wells et al<sup>9</sup> ( $\kappa=0.86$ ) and Kline et al<sup>17</sup> ( $\kappa=0.81$ ).

### D-dimer Assays

Results are reported for 3 individual studies of differing subtypes of D-dimer assays, with positive and negative LRs ranging from 1.7 to 2.7 and 0.09 to 0.22, respectively.

## CONCLUSIONS

Although clinical assessment alone is insufficient to rule in or rule out pulmonary embolism, both the clinical gestalt of experienced clinicians and clinical prediction rules can assign a pretest probability with reasonable accuracy, though given their consistent performance, inexperienced clinicians are encouraged to use clinical prediction rules. Negative D-dimer assays

increasingly appear to be adequate for ruling out pulmonary embolism in low-pretest-probability patients.

### Rational Clinical Examination Author Contact

Jeffrey S. Ginsberg, MD, FRCPC  
 Department of Medicine  
 McMaster University  
 Hamilton, Ontario, Canada  
 E-mail [ginsbrgj@mcmaster.ca](mailto:ginsbrgj@mcmaster.ca)

## COMMENTARY: CLINICAL IMPLICATION

In 2007, the United States can expect almost 100,000 new cases of pulmonary embolism.<sup>18</sup> In addition, the combination of high mortality rate (5%<sup>19</sup> to 25%<sup>20</sup>) and a widely varied presentation often leads to the consideration of pulmonary embolism in the setting of chief complaints from syncope to unexplained fever. The emergency physician's estimation of an individual patient's risk of pulmonary embolism allows for the calculation of posttest probability justifying treatment, further testing, or discharge. Clinical gestalt is central to the practice of emergency medicine, in which high patient turnover leaves little time for extensive testing and consultation. Unfortunately, clinical judgment is extremely variable and depends on training level, local practices, and individual physicians' personal experience. Clinical prediction rules use the experience of many physicians treating diverse patient groups to derive estimates of pretest probability, with the potential for greater precision than any one physician's clinical gestalt.

This rational clinical examination installment addresses the value of clinical gestalt and clinical prediction rules in estimating the pretest probability of pulmonary embolism and attempts to address the value of D-dimer for detection of pulmonary embolism. Clinical gestalt of experienced internal medicine and chest physicians had similar results to clinical decision rules; for example, from the Prospective Investigation of Pulmonary Embolism Diagnosis study, the calculated LRs for high (5.3; 95% CI 4.0 to 8.0) intermediate (1.1; 95% CI 1.0 to 1.2), and low (0.3; 95% CI 0.2 to 0.4) risk.<sup>2</sup> Of the 7 studies of clinical gestalt for pulmonary embolism, none tested implementation of the decision rules using emergency physicians. In addition, for the 5 clinical decision rules covered, only the extended Wells rule<sup>9</sup> and simplified Wells rule<sup>14</sup> had more than 1 validation study, and these demonstrated widely varying results, making conclusions difficult and reliability and accuracy difficult to predict (Table 2). In particular, the Wells group (using their own rule) was able to successfully demonstrate both accuracy and high sensitivity with an internally validated decision rule although there remains a need for external validation.

The utility of D-dimer testing to diagnose pulmonary emboli was also briefly discussed. The author chose 3 studies evaluating D-dimer assays to review, each an example of a separate assay type (latex agglutination, enzyme-linked immunosorbent assay, and whole-blood agglutination tests). Because of the limited nature of

**Table 2.** Comparisons of clinical decision rules with their validation studies.

Clinical Prediction Rule	Validation Study	Posttest Probability, %			LR (95% CI)		
		Low	Moderate	High	Low	Moderate	High
Simplified Wells	Wells et al	1.3	16.2	40.6	0.13 (0.06–0.26)	1.9 (1.6–2.3)	5.9 (3.7–9.3)
	Chagnon et al	12	40	91	0.39 (0.26–0.58)	2.0 (1.5–2.6)	29 (3.8–223)
Extended Wells	Kruij et al	4	28	63	0.15 (0.07–0.33)	1.5 (1.01–2.2)	5.85 (3.51–9.74)
	Chagnon et al	13	38	67	0.44 (0.30–0.65)	1.8 (1.4–2.3)	5.8 (1.8–19.0)

these data (2 medical record reviews and a single prospective investigation), firm conclusions cannot be drawn from this review. For a more detailed review of D-dimer testing for pulmonary emboli, high-quality systematic reviews are available.<sup>21,22</sup>

Given the high stakes and variability in presentation of the disease, emergency physicians await prospective external validation of clinical gestalt and decision rules in multiple ED settings. Until then, emergency physicians will have to continue to use a combination of clinical judgment and the selective and cautious application of decision rules for their patients in whom pulmonary embolism is suspected.

### TAKE-HOME MESSAGE

When suspecting a patient with pulmonary embolism, clinical gestalt should be buttressed with any of these clinical decision rules to improve the accuracy and precision of estimating pretest probability of disease. Combining this with an algorithm approach using D-dimer testing in low-risk patients in the ED has been shown to result in excellent outcomes.

### EBEM Commentator Contact

Richard Sinert, DO

Matthew Foley, MD

Department of Emergency Medicine

SUNY-Downstate Medical Center

Brooklyn, NY

### EBEM TEACHING POINT

*The hierarchy and utility of clinical decision rules.* The Evidence-Based Medicine Working Group in 2000 set forth a users guide to assessing the utility of clinical decision rules.<sup>23</sup> The authors defined a hierarchy of evidence for clinical decision rules. Level 4, the lowest assessment, is for rules that have yet to be externally validated and thus should not be applied clinically. Level 3 includes rules that have been prospectively validated in only a narrow range of patients. These rules may be used clinically if the patient population is similar to the validation group. Level 2 denotes clinical rules prospectively validated in a variety of clinical settings. This level of confidence allows level 2 rules to be used in a broad spectrum of patients. Finally, level 1 refers to rules that have been prospectively validated as in the level 2 group, with the addition of an impact analysis that demonstrates both a change in physician behavior and a clear clinical benefit.

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#### CORRECTION NOTICE

In the April 2008 issue, in abstract 192 by Sende, Bongrand, Campos-Richard, et al ("Who Reads the Electrocardiograms in Emergency Departments in France"; page 529), on page 478, there was a translation error. In all instances where the word "reads" is used, (ie, "who mainly reads ECGs") the correct term should have been "performs." We apologize for this error.