CJEM Journal Club

# Critical predictors of pulmonary embolism

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**Clinical question**
Do specific elements of the history and physical examination predict the presence of pulmonary embolism in the emergency department?

**Article chosen**
Courtney DM, Kline JA, Kabrhel C, et al. Clinical features from the history and physical examination that predict the presence or absence of pulmonary embolism in symptomatic emergency department patients: results of a prospective, multicenter study. *Ann Emerg Med* 2010;55:307-15.

**Objective**
To determine whether implicit clinical predictors previously untested predict the presence of pulmonary embolism in the emergency department.

**Keywords:** clinical predictors, pulmonary embolism

## BACKGROUND

Pulmonary embolism (PE) is a significant cause of morbidity and mortality in the emergency department (ED). In recent years, recognition of the high adverse consequences of PE and the advent of highly sensitive D-dimer have led to increased testing with computed tomographic angiography (CTA).[1,2] To promote appropriate use of resources, several groups have validated clinical prediction rules to guide clinicians to either test further or exclude PE as a potential diagnosis.[3–8] However, a survey of emergency clinicians demonstrated that many use implicit, nonvalidated criteria when formulating a pretest probability.[9] The goal of this study was to determine the association of validated (explicit) and nonvalidated (implicit) criteria with the diagnosis of PE.

## STUDY DESIGN

This was a prespecified secondary analysis of a prospective trial of ED patients evaluated for PE. It included 12 EDs in the United States. One site was excluded in this analysis because of incomplete data collection. The EDs included teaching and community hospitals in the urban, suburban, and rural settings. The methodology used was from a previously described report validating the Pulmonary Embolism Rule-out Criteria (PERC) rule, a low-risk PE prediction rule (Table 1).[10]

## POPULATION STUDIED

Patients were enrolled in the ED if the emergency physician deemed a workup for PE necessary. Patients excluded were those already being treated for venous thromboembolism (VTE) who had therapeutic levels of anticoagulation and patients with a diagnostic study that confirmed the presence of a VTE in the preceding 30 days. Patients were also excluded if they were in circulatory shock or respiratory failure or had a comorbid condition predicting the patient's death in the next few days, as well as if their social circumstances predicted a high chance of being lost to follow-up. All patients enrolled required testing with at least a D-dimer, CTA, or ventilation/perfusion ($\dot{V}/Q$) scanning. Patients evaluated only for deep vein thrombosis (DVT) were not enrolled.

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**Table 1. PERC (Pulmonary Embolism Rule-out Criteria) rule**

| |
|---|
| Testing for pulmonary embolism can be avoided if the patient is low risk by clinical gestalt (< 15%) and all the following criteria are met: |
| Age < 50 yr |
| Pulse < 100 beats/min |
| No estrogen use |
| Oxygen saturation ≥ 95% |
| No hemoptysis |
| No surgery or trauma in the last 4 weeks requiring hospitalization |
| No prior venous thromboembolism |
| No unilateral leg swelling |

Adapted from Kline JA et al.[10]

## OUTCOMES MEASURED

The primary outcome was VTE diagnosed during the index ED visit or within the next 45 days. Diagnosis of PE required a CTA read as positive by an attending radiologist, a V̇/Q scan documented as high probability for PE, or PE confirmed at autopsy. Diagnosis of DVT required a positive venous duplex ultrasonographic Doppler examination of the arm or leg. The criterion standard for the diagnosis of VTE required a diagnosis and an intention to treat within 45 days. A significant result was defined as an adjusted odds ratio (OR) with a 95% confidence interval (CI) that did not cross 1.00.

## RESULTS

A total of 7,940 patients underwent testing for PE. This was after a 5% refusal rate and a population excluded for expected loss to follow-up of 3.9%. Testing was ordered by 477 different clinicians. At the end of the 45-day follow-up, 568 patients (OR 7.2%, 95% CI 6.6–7.7%) met the criteria for a diagnosis of VTE, with 552 being diagnosed at the index visit. Twelve implicit variables and 13 validated values were compared. The adjusted ORs are listed in Table 2 (explicit variables) and Table 3 (implicit variables). The implicit predictors positively associated with VTE were a personal history of non–cancer-related thrombophilic conditions, pleuritic chest pain, and a family history of VTE. Of the implicit criteria, female sex, substernal chest pain, and current smoker were negatively associated with VTE. Tachypnea and dyspnea were associated with an increased likelihood of VTE but had a 95% CI at the lower limits, very close to 1.0. The strongest associations for explicit criteria were for patient history of VTE, unilateral leg swelling, surgery within 4 weeks, estrogen use, oxygen saturation less than 95%, active cancer, and immobilization exclusive of travel. The authors concluded that these variables should be incorporated by clinicians when forming a pretest probability for PE and by

**Table 2. Logistic regression model output for the explicit predictor variables**

| Predictor variable | *n* (%) | Adjusted OR | 95% CI |
|---|---|---|---|
| Patient history of VTE | 858 (10.8) | 2.90 | 2.32–3.64 |
| Unilateral leg swelling | 710 (8.9) | 2.60 | 2.05–3.30 |
| Surgery within the previous 4 weeks | 520 (6.6) | 2.27 | 1.70–3.02 |
| Estrogen use currently | 663 (8.4) | 2.31 | 1.63–3.27 |
| Hypoxemia (saturation < 95%) | 1,544 (19.4) | 2.10 | 1.70–2.60 |
| Active or metastatic cancer | 489 (6.2) | 1.92 | 1.43–2.57 |
| Immobilization | 763 (9.6) | 1.72 | 1.34–2.21 |
| Age > 50 yr* | 3,467 (43.7) | 1.35 | 1.10–1.67 |
| Pulse > 94 beats/min† | 3,234 (40.7) | 1.52 | 1.24–1.87 |
| Shock index > 1.0 | 834 (10.5) | 1.26 | 0.96–1.65 |
| Hemoptysis | 227 (2.9) | 0.78 | 0.46–1.32 |
| Trauma within the previous 4 weeks | 90 (1.1) | 0.78 | 0.37–1.65 |

VTE = venous thromboembolism.
*Age greater than 65 years from the revised Geneva score was alternatively used in the multivariate model but resulted in no qualitative difference in the adjusted OR (data not shown).
†Pulse greater than 100 beats/min from the Wells score and pulse 75 to 94 beats/min from the revised Geneva score were used in the multivariate model sequentially and resulted in no qualitative difference in the adjusted OR. Pulse greater than 94 beats/min is reported here in the final model because it resulted in the largest pseudo-$R^2$ (data not shown).

**Table 3. Logistic regression model output for the implicit predictor variables**

| Predictor variable | *n* (%) | Adjusted OR | 95% CI |
|---|---|---|---|
| Personal history of non–cancer-related thrombophilia | 149 (1.9) | 1.99 | 1.21–3.3 |
| Pleuritic chest pain | 3,660 (46.1) | 1.53 | 1.26–1.86 |
| Family history of VTE | 820 (10.3) | 1.51 | 1.14–2.00 |
| Female sex | 5,328 (67.1) | 0.57 | 0.47–0.69 |
| Smoking tobacco currently | 1,839 (23.2) | 0.59 | 0.46–0.76 |
| Substernal chest pain | 2,909 (36.6) | 0.58 | 0.46–0.72 |
| Pregnancy or postpartum state* | 285 (3.6) | 0.60 | 0.29–1.26 |
| Sudden onset of symptoms | 4,407 (55.5) | 0.88 | 0.73–1.06 |
| Obesity (body mass index ≥ 30 kg/m²) | 2,885 (36.3) | 1.13 | 0.93–1.38 |
| Tachypnea (RR > 24) | 1,667 (21.0) | 1.26 | 1.02–1.56 |
| Dyspnea | 5,587 (70.4) | 1.26 | 1.00–1.58 |
| History of malignancy, now inactive | 512 (6.4) | 0.82 | 0.56–1.18 |
| Fever (temperature ≥ 38.0°C [100.4°F]) | 292 (3.7) | 1.13 | 0.76–1.69 |

RR = Respiratory Rate; VTE = venous thromboembolism.
*Postpartum included pregnancy within past 4 weeks.

researchers when developing new clinical prediction tools.

## COMMENTARY

Although clinical predictors and clinician gestalt have been extensively studied, this is the first study that looked at a large number of variables that make up a clinical gestalt in aggregate and quantified them as predictors of PE. The researchers included all varieties of disease severity other than those in shock. The heterogeneity of their sample represents the heterogeneity of ED patients presenting with clinical manifestations suspicious for PE. The exclusion criteria are similar to those of the PERC study group[10] and exclude fewer patients than the Wells and colleagues PE prediction model.[7]

The data were prospectively collected and included many variables pertaining to the diagnosis of VTE. The investigators used a computer-based data collecting system, ensuring that all important data points were collected. The clinician needed to input all the appropriate data before proceeding to testing for VTE. However, this did not eliminate the possibility of recall bias in patients who had an episode of VTE in their personal or family history. Clinical manifestations were appropriately described and easily dichotomized into yes/no answers. However, one of the variables, abrupt onset of dyspnea, could lend itself to variable interpretations by patients and clinicians. The authors themselves noted that in a previous study, "sudden onset" had a low kappa value.

The authors considered patients as having PE if PE was suspected by the treating physician, but the patients only had objective confirmation of a DVT and were treated for PE. We can only presume that these patients could not undergo further testing. This was a small percentage (0.9%) of the population studied and therefore would unlikely change the results.

The authors explained the negative correlation of women by noting that the study enrolled twice as many women; therefore, women were more likely to be tested. They explained the negative correlation of smokers and PE by noting the high prevalence of smokers in the ED and that symptoms of smoking related to lung disease are also suggestive of PE. They are therefore subjected to increased testing. These negative correlations are not supported by previous literature. However, these results cannot be dismissed, and further studies on these populations are needed. Pregnancy or postpartum state and sudden onset of

symptoms, often used to justify testing, were not statistically significant. This is contrary to previous reports in the literature.[11–13] It is possible that this is due to an unperceived confounding factor. As there were few pregnant women in this sample, this subpopulation will need further study to determine the association with VTE.

Hemoptysis, shock index > 1.0, and trauma within 4 weeks, previously validated as predictors for VTE, did not reach statistical significance. Given that patients in shock were excluded, the study was likely underpowered in patients with a shock index > 1.0 and hemoptysis. The authors noted that "trauma in the last 4 weeks requiring hospitalization" was not appropriately defined, accounting for the wide confidence interval. These factors should not be ignored based on this study.

## CONCLUSION

Clinical manifestations not previously used in prediction rules, such as pleuritic chest pain, thrombophilia, and a family history of VTE, were significantly associated with VTE. Previously validated criteria such as a history of VTE, unilateral leg swelling, surgery within the past 4 weeks, estrogen use, oxygen saturation less than 95%, and active malignancy were also validated in this study. Criteria commonly thought of as predictors, such as pregnancy or postpartum state, sudden onset, and obesity, were not significant predictors. ED clinicians may consider including these evidence-based implicit criteria when formulating a pretest probability for further testing for VTE.

**Competing interests:** None declared.

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