

Predictors of Pulmonary Embolism

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.

Study Overview

Objective. To validate and study 12 clinical factors found in 4 published prediction rules (explicit) and 13 factors not a part of existing prediction models but commonly used in routine care (implicit) as an indication to test for pulmonary embolism (PE).

Design. Prospective, multicenter observational cohort study.

Setting and participants. Participating sites included 12 centers throughout the United States (9 teaching hospitals: 4 urban, 4 suburban, 1 rural) and 3 community hospitals (all suburban) that enrolled subjects from 1 Jul 2003 through 30 Nov 2006. Subjects were enrolled by research personnel during randomly assigned shifts or with consecutive enrollment while in the emergency department (ED) with informed consent. Inclusion criteria were having signs or symptoms the treating clinician interpreted as sufficient to warrant testing for PE (at least 1 of the following: D-dimer blood test, CT angiography of the pulmonary arteries, or ventilation-perfusion (V/Q) scan). Subjects were excluded if they were already being treated for venous thromboembolism (VTE) with therapeutic levels of anticoagulation, if they had CT, V/Q, or duplex Doppler testing in the 30 days prior that was diagnostic of PE or deep venous thrombosis (DVT), or if there were social circumstances highly predictive of loss to follow-up (ie, homelessness or imprisonment).

Study protocol. All eligible subjects had a structured interview by either the clinician or research assistant while in the ED with support from the medical record. All clinical data, including signs and symptoms, and variables of interest were entered while the subject was in the ED before results of the final PE testing were available.

Methods of measurement. The 12 explicit predefined predictive factors validated were (1) unilateral leg swelling, (2) surgery, (3) trauma, (4) immobilization, (5) hemoptysis, (6) patient history of VTE, (7) pulse > 94, (8) active malignancy,

(9) shock index > 1.0, (10) age > 50 years, (11) hypoxemia, and (12) estrogen. The 13 implicit factors studied were (1) female gender, (2) pregnancy or postpartum state, (3) thrombophilic condition (noncancer related, eg, factor V Leiden mutation, antiphospholipid antibody syndrome, sickle cell disease), (4) smoking, (5) sudden onset of symptoms, (6) substernal chest pain, (7) pleuritic chest pain, (8) dyspnea, (9) inactive malignancy, (10) obesity, (11) fever, (12) tachypnea, and (13) family history of VTE.

Main outcome measures. The primary outcome was PE or DVT during the index ED visit or during the subsequent 45 days.

Results. A total of 7940 ED patients who underwent formal testing for PE were ordered by 477 unique clinicians. After 45-day follow-up, 7.2% ($n = 568$) of these patients met the criterion standard definition of having PE or DVT. Of the 25 predictor variables studied, 9 of the 12 explicit and 8 of the 13 factors were associated with VTE. The strongest associations were those validated based on pre-existing prediction model factors: patient history of VTE (odds ratio [OR] = 2.90), unilateral leg swelling (OR = 2.60), surgery within 4 weeks (OR = 2.27), estrogen use (OR = 2.31), pulse oximetry saturation < 95% (OR = 2.10), active cancer (OR = 1.92), and immobilization exclusive of travel (OR = 1.72). Of the implicit factors newly studied, positive associations were found with thrombophilic condition (noncancer related) (OR = 1.99), pleuritic chest pain (OR = 1.53), and family history of VTE (OR = 1.51). Three implicit factors with negative associations included female gender (OR = 0.60), currently smoking (OR = 0.60), and substernal chest pain (OR = 0.60).

Conclusion. The presence of noncancer-related thrombophilia, pleuritic chest pain, and family history of VTE increases the risk of having a PE or DVT. These, in addition to already published criteria for PE prediction rules, may be used to guide clinicians in the need for additional diagnostic testing.

Commentary

Failure to diagnose PE is associated with high morbidity and mortality. For this reason, clinicians have increasingly relied on diagnostic testing (whether in the form of D-dimer testing, V/Q scans, and now CT angiography) for ambulatory patients who present with symptoms suspicious for PE. Over the last decade, at least 9 multiple clinical prediction rules have been proposed to assist the evaluation of patients suspected of having a PE and or VTE [1]. The primary objective of these proposed models is to determine the pretest probability of having a PE and determine in which patients PE can be safely ruled out. Ideally, this would assist the clinician in differentiating which patients are lower risk versus higher risk of having a VTE. Lower risk patients that are identified should not require additional testing. Despite the plethora of prediction rules available to clinicians, diagnostic approaches to evaluating for the presence of PE remains heterogeneous, unstructured, and with no widespread use of clinical prediction rules [1,2]. Additionally, only a minority of the prediction factors are commonly shared by many of the proposed prediction rules.

Courtney et al [3–6] attempt to validate 12 factors used in 4 published prediction rules while studying 13 additional factors that “were absent from prior models but (are) commonly used in routine care as an indication to test for PE” with a prospective, multicenter observational cohort. As expected, results of their study indicate the majority of factors used in previous prediction rules were significantly associated with risk of PE or VTE within 45 days of ED evaluation. The strongest associations were found with patient history of VTE, unilateral leg swelling, recent surgery, estrogen use, oxygen saturation < 95%, active cancer, and immobilization. Other non-prediction rule factors (implicit factors) significantly associated with increased risk of VTE were patient history of thrombophilia, pleuritic chest pain, and family history of VTE. These findings further distinguish the most important variables that may assist clinicians in increasing or decreasing their suspicion of PE. Simplifying the many prediction rules into a set of factors most greatly associated with risk of VTE may clarify a clinician’s diagnostic approach to evaluating patients suspected of having a PE. As suggested by study investigators, clinicians may

opt to document the presence or absence of these significant predictors during the decision-making process on whether or not to further test for pulmonary embolism.

Limitations of this study include the inability of investigators to evaluate long-term causal associations between predictor variables and the studied outcomes of PE and DVT. While follow-up of subjects was extended over a short period to 45 days, the study findings were not longitudinal and thus not reliable for causal associations and the development of VTE over time.

Applications for Clinical Practice

Documenting the presence (or absence) of patient history of VTE, unilateral leg swelling, recent surgery, estrogen use, oxygen saturation < 95%, active cancer, immobilization, patient history of thrombophilia, pleuritic chest pain, and family history of VTE may assist clinicians in heightening (or reducing) the need for further diagnostic evaluation of pulmonary embolism.

—Review by Ula Hwang, MD, MPH

References

1. Ceriani E, Combescure C, Le Gal G, et al. Clinical prediction rules for pulmonary embolism: a systematic review and meta-analysis. *J Thromb Haemost* 2010 Feb 9.
2. Squizzato A, Miceli E, Galli M, et al. Diagnosis and management of venous thromboembolism: results of a survey on current clinical practice. *Thromb Res* 2010;125:134–6.
3. Wells PS, Anderson DR, Rodger M, et al. Derivation of a simple clinical model to categorized patients’ probability of pulmonary embolism: increasing the models utility with SimpliRED D-dimer. *Thromb Haemost* 2000;83:416–20.
4. Kline JA, Nelson RD, Jackson RE, et al. Criteria for the safe use of D-dimer testing in emergency department patients with suspected pulmonary embolism: a multicenter U.S. study. *Ann Emerg Med* 2002;39:144–52.
5. Kline JA, Mitchell AM, Kabrhel C, et al. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. *J Thromb Haemost* 2004;2:1247–55.
6. Le Gal G, Righini M, Roy PM, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. *Ann Emerg Med* 2006;144:165–71.