** AFP Journal Club

The Story Behind the Study

Pulmonary Embolism Rule-Out Criteria: A Clinical Decision Rule That Works

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Purpose

In AFP Journal Club, three presenters review an interesting journal article in a conversational manner. These articles involve "hot topics" that affect family physicians or "bust" commonly held medical myths. The presenters give their opinions about the clinical value of the individual study discussed. The opinions reflect the views of the presenters, not those of AFP or the AAFP.

Article

Kline JA, Courtney DM, Kabrhel C, et al. Prospective multicenter evaluation of the pulmonary embolism rule-out criteria. *J Thromb Haemost*. 2008;6(5):772-780.

For more information on evidence-based medicine (EBM) terms, see the EBM Toolkit at http://www.aafp.org/afp/ebmtoolkit.

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Is there a clinical prediction rule that can reliably exclude the presence of a pulmonary embolism (PE), and thus avoid the use of computed tomography (CT) in patients believed to be at very low risk?

Bob: Let's start with a case. A 42-year-old woman presents to your clinic saying that she awoke that morning with pleuritic right infrascapular pain. It is not associated with cough, hemoptysis, fever, or chills. She has no anterior chest pain, leg pain or swelling, or shortness of breath at rest. She has not traveled recently. She takes no medications, and doesn't use birth control pills. Her medical history is unremarkable, and she has no personal or family history of venous thromboembolism. Physical examination reveals normal vital signs, and she has good breath sounds bilaterally.

A couple of causes for this patient's discomfort quickly come to mind. Then you get this nagging thought: Could this be a PE? Although it's very unlikely, you think: Should I just order the chest CT and stop worrying?

This month's article demonstrates the validity of the Pulmonary Embolism Rule-Out Criteria (PERC; *Table 1*¹) and should reassure your decision to forgo CT in patients at very low risk of PE.

What does this article say?

Bob: In the past few years, a number of clinical decision rules have been produced that purportedly help family physicians make clinical decisions. Before a clinical decision rule can be implemented in clinical practice, it must be:

- Rigorously derived from a large group of patients
- Tested on a new population of patients (internal validation)
- Tested in a wide variety of clinical settings outside of the original study site (external validation); I like to refer to this as the "road test."

The eight-factor PERC rule was developed in 2004, and a small internal validation study was then completed.² This month's article is the large external validation series. It included 8,138 prospectively enrolled patients from 13 emergency departments (12 in the United States, one in New Zealand) who had suspected PE. The emergency department physicians documented the presence or absence of each PERC factor, with their degree of suspicion about the presence of a PE prior to any testing. Workups were then performed, and outcomes were followed over the next 45 days.

The PERC rule had high sensitivity for ruling out PE. Of the 1,666 patients who answered "no" to all eight questions, only 15 (1%) had a PE (95% confidence interval, 0.6% to 1.6%), with one death. Applying

Table 1. Pulmonary Embolism Rule-Out Criteria

Is the patient > 49 years?

Is the pulse rate > 99 beats per minute?

Is pulse oximetry < 95% on room air?

Does the patient have current hemoptysis?

Is the patient taking exogenous estrogen?

Does the patient have a history of venous thromboembolism?

Has the patient had surgery or trauma requiring hospitalization in the past four weeks?

Does the patient have unilateral leg swelling?

NOTE: If the patient is considered to be at very low risk of pulmonary embolism (< 15% risk) based on the physician's pretest suspicion, and answers "no" to all eight questions, the criteria results are considered negative.

Adapted with permission from Kline JA, Courtney DM, Kabrhel C, et al. Prospective multicenter evaluation of the pulmonary embolism rule-out criteria. J Thromb Haemost. 2008;6(5):773.

this to the patient presented earlier, PE could reasonably be excluded, avoiding CT.

Should we believe this study?

Mark: Yes—the authors correctly performed all of the steps to create a valid clinical decision rule. This study, the external validation study, is the step most investigators don't successfully pull off. We previously covered the San Francisco Syncope Rule,³ which appeared promising until it was tested outside of San Francisco ("road test"), where it was found to be unreliable.

Jill: There are a couple of other appealing features of the PERC rule. It is fairly simple. Clinical decision rules that require too many steps are not useful during a patient encounter. For example, the Boston Syncope Criteria has 25 criteria⁴; this is too many for a physician to remember or use. The eight questions in the PERC rule are easily accessible, requiring no intricate lab or radiology studies. Therefore, the rule can be used in both the emergency department and office settings.

Mark: And look at that nice, tight 95% confidence interval. Patients who are deemed very low risk and who answer "no"

to all eight questions no doubt have a negligible risk of PE.

Jill: A clinical decision rule that gives a 99% clinical probability of no PE, allowing the physician to avoid workup (e.g., D-dimer test, CT), is impressive. In comparison, 14 validation studies of the Wells Criteria revealed that 1.3% to 27.9% of patients deemed to be low risk had a PE.⁵ It appears that the PERC rule is far more sensitive.

Bob: There is no perfect clinical decision rule because they can't account for every potential clinical variable. For example, suppose the patient in our case scenario carries the gene for factor V deficiency, her mother died of a PE at 35 years of age, and the patient just flew back from China. None of these variables can be accounted for in the clinical decision rule. That is why the physician's "gestalt" (pretest probability) must be considered. In the case of the PERC rule, if the physician suspects that the chance of PE is greater than 15%, the clinical decision rule should not be applied, and diagnostic testing should be performed.

What should the family physician do?

Bob: The PERC rule has been validated in 12 additional studies performed in six different countries, and it continues to demonstrate consistently high sensitivity.⁶ In fact, at my community hospital, we found that if we had applied the PERC rule in every patient who received chest CT to rule out PE, we would have decreased CT use by 22% and not missed any PEs.⁷

Mark: We previously discussed the carcinogenic properties associated with CT.⁸ A validated clinical decision rule that gives physicians the confidence to avoid chest CT in low-risk patients is a real step forward.

Jill: We must also remember that CT in low-risk patients does not always give us the correct answer. The PIOPED II (Prospective Investigation of Pulmonary Embolism Diagnosis II) study revealed that when CT is performed in low-risk patients, the result is a false positive 42% of the time.⁹

If you conduct a journal club and want to know the next article that will be discussed, or if you would like to suggest an article for discussion, e-mail afpjournal@aafp.org with "AFP Journal Club" in the subject line.

Journal Club

Main Points

- The PERC rule is a validated clinical decision rule that assists decision making when patients are deemed to be at very low risk of PE.
- The PERC rule has better sensitivity than the Wells Criteria for ruling out PE.
- CT in patients deemed to be at low risk of PE has a high false-positive rate.

EBM Points

 Clinical decision rules need to go through a rigorous process of derivation, internal validation, and external validation before widespread adoption.

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REFERENCES

- Kline JA, Courtney DM, Kabrhel C, et al. Prospective multicenter evaluation of the pulmonary embolism ruleout criteria. J Thromb Haemost. 2008;6(5):772-780.
- Kline JA, Mitchell AM, Kabrhel C, Richman PB, Courtney DM. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. *J Thromb Haemost*. 2004;2(8):1247-1255.
- 3. Dachs RJ, Graber MA, Darby-Stewart A. Is the San Francisco Syncope Rule reliable? *Am Fam Physician*. 2009;80(6):558-559.
- 4. Grossman SA, Fischer C, Lipsitz LA, et al. Predicting adverse outcomes in syncope. *J Emerg Med.* 2007;33(3):233-239.
- 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;8(5):957-970.
- Singh B, Parsaik AK, Agarwal D, Surana A, Mascarenhas SS, Chandra S. Diagnostic accuracy of pulmonary embolism rule-out criteria: a systematic review and meta-analysis. Annals Emerg Med. 2012;59(6):517-520.
- 7. Dachs RJ, Kulkarni D, Higgins GL 3rd. The Pulmonary Embolism Rule-Out Criteria rule in a community hospital ED: a retrospective study of its potential utility. *Am J Emerg Med*. 2011;29(9):1023-1027.
- 8. Dachs RJ, Graber MA, Darby-Stewart A. Cancer risks associated with CT scanning. *Am Fam Physician*. 2010;81(2):111-114.
- 9. Stein PD, Fowler SE, Goodman LR, et al.; PIOPED II Investigators. Multidetector computed tomography for acute pulmonary embolism. *N Engl J Med*. 2006;354(22):2317-2327. ■