

Are all pulmonary embolism clinical decision rules equal?

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Clinical question

Are four common clinical decision rules, in combination with normal D-dimer results, comparable in their ability to clinically exclude the diagnosis of pulmonary embolism?

Article chosen

Douma RA, Mos ICM, Erkens PMG, et al. Performance of 4 clinical decision rules in the diagnostic management of acute pulmonary embolism: a prospective cohort study. *Ann Intern Med* 2011;154:709-18.

Objective

To directly compare the performance of four different clinical decision rules, the Wells rule, revised Geneva score, simplified Wells rule, and simplified revised Geneva score, in combination with D-dimer results, to exclude pulmonary embolism.

there had been no previous direct comparison of all four rules in one study.

POPULATION STUDIED

This study enrolled inpatients and outpatients from seven hospitals (academic and nonacademic) in the Netherlands suspected clinically of suffering an acute first-time PE. A PE was suspected when sudden-onset dyspnea, deterioration of existing dyspnea, or sudden-onset pleuritic chest pain was present. Patients were excluded for the following reasons: age under 18 years, life expectancy < 3 months, treated with low-molecular-weight or unfractionated heparin > 24 hours before assessment, treated with vitamin K antagonists, previously diagnosed with PE, had a contraindication to computed tomography (CT), pregnancy, or unable to return for follow-up.

Keywords: clinical decision rule, D-dimer, pulmonary embolism, revised Geneva score, simplified revised Geneva score, simplified Wells rule, Wells rule

BACKGROUND

Two clinical decision rules (CDRs) for pulmonary embolism (PE) are the most widely used in daily practice, the Wells rule (WR) and the revised Geneva score (RGS).^{1,2} Although both CDRs rely on clinical indicators to calculate a patient's probability for PE, the latter uses only objective criteria, whereas the former also uses clinician judgment. Simplified versions of these CDRs have emerged: the simplified Wells criteria (SWR) and the simplified revised Geneva score (SRGS).^{3,4} Paired head-to-head comparisons have been published.⁵⁻⁷ Prior to the Douma and colleagues study,

STUDY DESIGN

This was a prospective cohort study in which all patients underwent clinical probability assessment and high-sensitivity quantitative D-dimer testing (the exact D-dimer assay differed among study sites) between July 2008 and November 2009. An enrolment of at least 753 patients was necessary based on a 20% prevalence of PE and a power of 90%. PE was deemed "unlikely" if the WR was ≤ 4 points, the SWR was ≤ 2, the RGS was ≤ 5, and the SRGS was ≤ 2. Physicians entered clinical data relevant to the CDRs via a computerized program, which instructed the physician on the next step based on CDR and D-dimer results: PE was

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considered “clinically excluded” when all four CDRs were deemed PE unlikely and the D-dimer was negative; CT was required to exclude PE if at least one of the CDR results was positive or if the D-dimer was positive.

Patients in whom PE was excluded were followed up in 3 months by telephone. Patients were instructed to return to hospital if symptoms of venous thromboembolism (VTE) occurred.

OUTCOMES MEASURED

The primary outcomes were as follows: 1) the ability of each CDR to correctly categorize patients as PE likely or unlikely; 2) the proportion of patients in whom PE was excluded on the basis of an unlikely CDR and a normal D-dimer; 3) the incidence of VTE following the clinical exclusion of PE; 4) the sensitivity, specificity, and receiver operating characteristics of each CDR.

RESULTS

Of the 1,023 patients with suspected PE, 807 participants (644 outpatients and 163 inpatients) were entered in the study.

PE was deemed unlikely using all four CDRs in 434 patients. Of that group, 169 patients had a normal D-dimer, thereby ruling out PE. Two-hundred sixty-five patients had elevated D-dimers despite all four CDRs rating them as being unlikely to have a PE, 243 patients had discordant CDR results, and 130 patients were CDR likely across all CDRs. These 629 patients underwent CT; PE was diagnosed in 184. Several protocol violations occurred, including seven patients undergoing CT despite not being indicated, detecting one PE.

Of those with a normal CT scan, one patient developed PE, six developed deep vein thrombosis and one patient was lost to follow-up.

Discordance between the scores occurred in 29% of patients, occurring most frequently between the WR and the RGS and least frequently between the original CDRs and their simplified versions.

Sensitivity of CDRs alone for PE was 52% (95% CI 45–59), 65% (95% CI 58–72), 53% (95% CI 46–60), and 49% (95% CI 42–56) for the WR, SWR, RGS, and SRGS, respectively. When combined with a normal D-dimer, sensitivity was 99.5% (95% CI 97–100) for all four CDRs.

COMMENTARY

With the emergence of multiple CDRs to stratify patients as PE “likely” or “unlikely,” the Prometheus Study Group’s comparison of the four most commonly used CDRs is appropriate and timely. The authors present a well-designed prospective study enrolling consecutive patients. They presented their results using a flow chart to track patients through their study and present comprehensive data in the body and appendix of the article.

However, this study uniquely excluded patients with a previous diagnosis of PE. As this criterion is in all four CDRs, this raises questions of an overrepresentation of low-risk patients in the study population and would seem to limit the applicability of the study’s results to all ED patients.

The gold standard for PE was CT angiography. In patients in whom PE had been clinically excluded, the gold standard for PE was the absence of VTE over the a follow-up of 3 months. Although the latter rule-out criterion has seen widespread use, the specificity and sensitivity of CT angiography would suggest that, as the sole criterion, it may not be an ideal gold standard.

The results of this study showed sensitivity of the CDRs alone ranging from 49 to 65%. When the additional criterion of a positive D-dimer test was added, sensitivities became similar, suggesting that D-dimer results played a considerable role.

Compared to the original studies, this study had a slightly higher prevalence of PE in CDR-unlikely patients using the WR and the SRGS and a comparable prevalence with the SWR.^{1,2,4}

Of the patients in whom PE was excluded after the initial CT scan, seven developed a VTE. Whether the original CT scan of these patients missed the seminal clot (poor sensitivity) or the VTE developed later in a higher-risk patient cannot be determined. Not all seven patients had a D-dimer and should not have had one based on clinical risk stratification, so no comment can be made on the role (or lack thereof) of D-dimer in these patients.

Discordance among the four CDRs was high (29%). Despite this, only one PE was detected in the low-clinical likelihood group (also having a positive D-dimer). It would seem intuitive that the incidence of PE increases as the number of positive CDR criteria increases, but this was not found to be true in this study. Whereas the CDR-unlikely group had a PE prevalence of 12%, the CDR discordant group—where some CDRs indicated a risk and other CDRs did not—had only one patient with a PE.

This would suggest that, rather than risk stratification, a binomial yes/no approach might be more appropriate.

CONCLUSION

This observational study affirmed the ability of CDRs to identify low-risk patients, especially when combined with a normal D-dimer. In that low-risk cohort, the miss rate was 0.5% (95% CI 0–3), similar to the miss rate reported in the literature for each CDR.^{2,8} Exclusion of patients with a history of PE has no bearing on the low-risk categorization in this study as these patients would all be considered “at risk” when presenting with the clinical symptoms associated with VTE.

Competing interests: None declared.

REFERENCES

1. Wells PS, Anderson DR, Rodger M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the model's utility with the SimpliRED D-dimer. *Thromb Haemost* 2000;83:416-20.
2. Le Gal G, Righini M, Roy PM, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. *Ann Intern Med* 2006;144:165-71.
3. Klok FA, Mos IC, Nijkeuter M, et al. Simplification of the revised Geneva score for assessing clinical probability of pulmonary embolism. *Arch Intern Med* 2008;168:2131-6, doi:10.1001/archinte.168.19.2131.
4. Douma RA, Gibson NS, Gerdes VE, et al. Validity and clinical utility of the simplified Wells rule for assessing clinical probability for the exclusion of pulmonary embolism. *Thromb Haemost* 2009;101:197-200.
5. Klok FA, Kruisman E, Spaan J, et al. Comparison of the revised Geneva score with the Wells rule for assessing clinical probability of pulmonary embolism. *J Thromb Haemost* 2008;6:40-4, doi:10.1111/j.1538-7836.2007.02820.x.
6. Calisir C, Yavas US, Ozkan IR, et al. Performance of the Wells and revised Geneva scores for predicting pulmonary embolism. *Eur J Emerg Med* 2009;16:49-52, doi:10.1097/MEJ.0b013e328304ae6d.
7. Wong DD, Ramaseshan G, Mendelson RM. Comparison of the Wells and revised Geneva scores for the diagnosis of pulmonary embolism: an Australian experience. *Intern Med J* 2011;41:258-63, doi:10.1111/j.1445-5994.2010.02204.x.
8. Pasha SM, Klok FA, Snoep JD, et al. Safety of excluding acute pulmonary embolism based on an unlikely clinical probability by the Wells rule and normal D-dimer concentration: a meta-analysis. *Thromb Res* 2010;125:e123-7, doi:10.1016/j.thromres.2009.11.009.