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## New Technologies, Diagnostic Tools and Drugs

# Validity and clinical utility of the simplified Wells rule for assessing clinical probability for the exclusion of pulmonary embolism

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### Summary

The recently introduced simplified Wells rule for the exclusion of pulmonary embolism (PE) assigns only one point to the seven variables of the original Wells rule. This study was performed to independently validate the simplified Wells rule for the exclusion of PE. We retrospectively calculated the prevalence of PE in the "unlikely" probability categories of the original Wells (cut-off  $\leq 4$ ) and the simplified Wells rule (cut-off  $\leq 1$ ) in 922 consecutive patients with clinically suspected PE from a multicenter cohort study. We compared the three-month incidence of venous thromboembolism (VTE) in patients with an unlikely probability and a normal D-dimer test using both scores, and the proportion of patients with this combination (clinical utility). The proportion of patients categorized as PE "unlikely" was similar using

the original (78%) and the simplified (70%) Wells rule. The prevalence of PE was 13% (95% confidence interval [CI], 11–16%) and 12% (95%CI, 9.7–15%) for the original Wells and simplified Wells "unlikely" categories, respectively. None of the patients with PE "unlikely" and a normal D-dimer test experienced VTE during three-month follow-up. The proportions of patients in whom further tests could safely be withheld based on PE "unlikely" and a normal D-dimer test was 28% (95%CI, 25–31%) using the original and 26% (95%CI, 24–29%) using the simplified Wells rule. In this external retrospective validation study, the simplified Wells rule appeared to be safe and clinically useful, although prospective validation remains necessary. Simplification of the Wells rule may enhance the applicability.

### Keywords

Pulmonary embolism, diagnosis, clinical decision rule, Wells rule, D-dimer

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### Introduction

Many diagnostic algorithms for patients with clinically suspected pulmonary embolism (PE) have been investigated for their safety and utility. Due to the low prevalence of PE, confirming the diagnosis in the minority of patients who have the disease, while safely excluding it in the majority of patients that are suspected of, but do not have the disease, is challenging. In recent years, much attention has been given to the role of clinical decision rules to objectively assess clinical probability, and several rules have been designed and validated (1–5). The usefulness of clinical assessment in combination with a D-dimer test, has been shown in several management studies. In the 20–40%

of patients with a low clinical probability score in combination with a normal D-dimer result the diagnosis can be safely ruled out and no further diagnostic work-up for PE is necessary (6–10). The Wells PE rule, introduced in 2000, is composed of seven variables obtained from medical history and physical examination (Table 1) (4). It has gained popularity in Europe and North America and has been implemented in several guidelines for the diagnostic work-up of patients with suspected pulmonary embolism (11, 12). The Wells rule assigns different points to the variables, which renders the calculation of a patient's individual score somewhat cumbersome. Recently a simpler version of the Wells rule was proposed, by assigning the same weight (one point) to each of the seven variables in the Wells rule (Table 1)

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**Table 1: Wells score – original and simplified.**

Condition	Points 'original' Wells	Points 'simple' Wells
Clinical signs of DVT	3	1
Heart rate > 100/min	1.5	1
Recent surgery or immobilization	1.5	1
Previous PE or DVT	1.5	1
Haemoptysis	1	1
Cancer	1	1
Alternative diagnosis less likely than PE	3	1
Cut-off for PE unlikely	≤4	≤1

PE = pulmonary embolism; DVT = deep venous thrombosis. Adapted from: Wells et al.<sup>4</sup> and Gibson et al.<sup>13</sup>

(13). In this derivation set, the 'simplified' Wells PE rule showed a similar diagnostic accuracy and clinical utility compared to the 'original' Wells rule (13). The goal of the present study is to validate this simplified Wells rule for the exclusion of PE in another cohort of patients (14).

## Methods

For the present analysis data from a prospective management study were used (14). This study validated a diagnostic strategy for suspected PE, based on clinical probability, D-Dimer test, compression ultrasonography and helical computed tomography (CT). The study was performed in three teaching hospitals in Geneva and Lausanne, Switzerland and Angers, France. It was approved by the Ethics Committee of the Department of Medicine, Geneva University Hospital; the Ethics Committee of the Lausanne Medical School; and the Comité consultative de Protection des Personnes dans la Recherche Biomédicale des Pays de la Loire in Angers. All patients gave written informed consent for their participation in the study.

## Patients and management

Consecutive outpatients presenting to the emergency department with a clinical suspicion of acute PE were included between October 2000 and June 2002. Predefined exclusion criteria were: ongoing anticoagulant treatment for reasons other than venous thromboembolism; contraindication to CT scan (known allergy to iodine contrast agents or at risk of allergic reaction); creatinine clearance below 30 ml/minute (min) as calculated by the Cockcroft formula; informed consent impossible due to cognitive impairment; patient refusal; suspected massive pulmonary embolism with shock; pregnancy; estimated survival less than three months; and follow-up not possible. The results of this diagnostic workup have been published previously (14). Briefly, the study design was as follows: clinical probability was assessed in all patients using the Geneva score (3), with an option to override by implicit assessment in case of a physician's disagreement with the score. The seven items required to compute

the Wells PE rule were also collected, allowing retrospective calculation of this score. After assessing the clinical probability, a D-Dimer test was performed (enzyme-linked immunosorbent assay (ELISA), Vidas D-dimer; Biomérieux, Marcy l'Etoile, France). PE was considered ruled out if the D-dimer level was below 500 µg/l. These patients were not treated with anticoagulants and were followed up. Those with an abnormal D-Dimer level underwent proximal lower-limb venous compression ultrasonography (CUS), and were treated with anticoagulants if CUS disclosed a proximal deep venous thrombosis (DVT). All patients with a normal CUS proceeded to helical CT. Patients with an inconclusive CT or those with a normal CT but a high clinical probability underwent further testing (pulmonary angiography or ventilation-perfusion lung scan). Patients were followed by their family physicians and received a telephone-interview by one of the study coordinators at the end of the three-month follow-up period.

## Validation of original and simplified Wells scores

In this analysis, we calculated the proportion of patients attributed to two probability categories; "PE unlikely" and "PE likely", and the prevalence of PE per category, using both the original and the simplified Wells PE rule. The cut-offs for the "PE unlikely" category were a score of four points or less for the original Wells rule (4), and a score of one point or less using the simplified Wells rule (13). To gain further insight into the distribution of patients categorized by the simplified Wells rule, we elected to calculate the prevalence of PE in two subcategories within the likely probability category, resulting in a trichotomous decision rule (results available in the Appendix online at [www.thrombosis-online.com](http://www.thrombosis-online.com)).

To compare the different scores for safety and utility, we assessed the prevalence of PE in the unlikely probability groups (low prevalence endorsing safety) during three months of follow-up and the size of these unlikely probability groups (large groups endorsing clinical utility). Because clinical decision rules are most often used together with the result of a D-dimer test, the proportion of patients with an unlikely clinical probability together with a normal D-dimer test result were determined to calculate the proportion of patients in whom PE could be excluded and further tests could be safely withheld.

## Statistical analysis

For each score, 1) the proportion of patients classified in each clinical probability group, 2) the prevalence of PE in each group, and 3) the three-month thromboembolic risk in patients left untreated on the basis of the combination of clinical probability assessment and results of the D-dimer test, were estimated with their 95% confidence intervals (CI). Clinical characteristics of study patients with or without all required data to compute the Wells rule were compared using a chi<sup>2</sup>-test for qualitative variables, and a Student t-test for continuous variables.

## Results

### Patient characteristics

A total of 965 consecutive outpatients with clinical suspicion of PE were included in the study. In this cohort, the overall preva-

**Table 2: Distribution of patients in the unlikely and likely clinical probability category of the two decision rules and corresponding prevalence of PE.**

Decision rule	Proportion of patients in total % (95% CI) [N]		Prevalence of PE % (95% CI) [N]	
	Unlikely	Likely	Unlikely	Likely
Original Wells rule	78% (76–81%) [722/922]	22 % (19–25%) [200/922]	13% (11–16%) [95/722]	56% (49–63%) [112/200]
Simplified Wells rule	70% (67–73%) [644/922]	30% (27–33%) [278/922]	12% (9.7–15%) [77/644]	47% (41–53%) [130/278]

PE = pulmonary embolism.

lence of PE at the time of initial presentation was 23% (n = 222). In 43 of the 965 patients data on the variables of the Wells PE rule were missing (the most frequently missing variable was ‘alternative diagnosis less likely’), leaving 922 (96%) analyzable patients for the present analysis. The patients in whom the Wells rule could not be calculated had a slightly higher rate of confirmed PE [35% (15/43) vs. 23% (207/922) p = 0.06], less patients complained of chest pain [54% (23/43) vs. 71% (658/922) p = 0.01], and there were more symptoms of DVT (33% (14/43) vs. 20% (183/922) p = 0.04). The groups were otherwise comparable. In the original cohort, patients with a normal D-dimer test (n=268) did not receive further investigations and none of them experienced VTE during the three months follow-up (0.0%, 95% CI 0.0–1.4%).

### Group size and prevalence of PE

The original Wells rule identified a slightly larger proportion of patients as ‘unlikely’ compared to the simplified Wells rule: 722 (78%, 95% CI 76–81%) and 644 (70%, 95% CI 67–73%) respectively (Table 2).

The prevalence of PE per clinical probability category is detailed in Table 2. The prevalence of PE in the unlikely categories (Table 2) is comparable for the two rules (13% and 12%, respectively).

### Safety and clinical utility of the clinical decision rules combined with D-dimer testing

Because none of the patients with a normal D-dimer result suffered from VTE during follow-up in the original cohort, the incidence of VTE in patients with an unlikely probability for PE in combination with a normal D-dimer was 0%, similar for both scores (Table 3). The clinical utility of the scores, expressed as the proportion of patients in whom further tests could be safely withheld using the clinical decision rule and D-dimer test is comparable for both scores (Table 3).

## Discussion

In this analysis, the original Wells PE rule and the simplified Wells PE rule display similar diagnostic accuracy and clinical utility for the exclusion of PE. Compared to the results obtained in the derivation study of the simplified rule, the incidence of VTE in patients categorized as “PE unlikely” and a normal D-dimer result is similar (0.5% in the derivation study [13] vs. 0.0% in this analysis), while the proportion of patients with such a combination was slightly lower (26% compared to 30% in the derivation study [13]). Both figures are comparable to the results

obtained when using the original Wells rule. In the present study, the prevalence of PE in the unlikely clinical probability category was similar using the simplified Wells rule compared with the original Wells rule. Also, the clinical utility of the simplified rule, reflected by the proportion of patients not requiring further testing based on clinical assessment and D-dimer result, was roughly similar to that of the original and more complicated Wells rule.

As this analysis was performed in a multicenter cohort completely distinct from that which served to derive the simplified one-point Wells rule, we believe that our results provide additional validity to this rule, which could be easier to compute by busy clinicians. Indeed, it appears that assigning the same weight to each variable did not reduce predictive accuracy. Also, simplifying the dichotomized Wells rule did not reduce its clinical utility, as the proportion of patients in whom further testing could be avoided using D-dimer testing and the simplified rule is not significantly lower than that obtained by the original classification (Table 3).

There are several aspects of this study that require comment. First, various steps can be identified in the development of a clinical decision rule, from the derivation to the justified widespread implementation in daily practice (15). Although validated in a cohort of patients independent of the derivation set, the retrospective character of this exploratory study will not necessarily guarantee the same results in a prospective validation study – which is necessary before use in clinical practice.

The Wells PE rule (both original and simplified) was computed retrospectively in this patient cohort, in which another rule, the Geneva score, was used to guide patient management. Although all the information necessary to compute the Wells

**Table 3: Safety and clinical utility of the different scoring options of the clinical decision rules combined with D-dimer testing.**

Strategy	Incidence of VTE during three months follow-up		Proportion of patients in whom further tests could be withheld
	n	%, 95 CI %	%, 95 CI %
Original Wells ≤4 and normal D-dimer	0/246	0.0, 0.0–1.5	28, 25–31
Simplified ≤1 and normal D-dimer	0/234	0.0, 0.0–1.6	26, 24–29

VTE = venous thromboembolism.

**What is known about this topic?**

- Clinical decision rules are a safe and useful tool in the diagnostic management of pulmonary embolism (PE).
- The calculation of a patient's individual score can be cumbersome, because different points are assigned to the variables. This does not enhance applicability.
- Recently, the simplified Wells rule, which assigns only one point for each variable, was introduced and showed similar diagnostic accuracy and clinical utility compared to the 'original' Wells rule in the derivation study.

**What does this paper add?**

- In this study, the simplified Wells rule was independently validated in a large multicenter cohort of patients with clinically suspected PE, and it appeared safe and clinically useful.
- The straightforwardness of this simplified one-point Wells rule may enhance clinical applicability and could be a good alternative to the more complicated rules.

rule was acquired prospectively before any test was performed, there were 43 patients in whom the Wells rule could not be calculated. These patients had a slightly higher rate of PE and associated DVT, and "alternative diagnosis less likely" was the most frequently missing variable. It is conceivable that the suspicion of PE was higher in these 43 patients. Because it is only a limited proportion of the entire cohort and these patients were left out of

the analysis for both rules, the interference in the comparison among the rules is only limited.

In this cohort, none of the patients with a normal D-dimer test result suffered from VTE during follow-up. As a result this assay had a negative predictive value of 100% for excluding clinically significant PE. This might seem optimistic considering the fact that there are several studies that indicated that it was not safe to manage patients on the D-dimer test result alone; in patients in whom PE is likely further diagnostic testing is usually advocated (16–19). However, the observed negative predictive value of 100% has no impact on our analysis, since this uncertainty is reflected by the 95% CI of the three-month thromboembolic risk (i.e. PE could be missed in 1.6% of the patients with an unlikely simplified Wells score and a normal D-dimer). This confidence interval is narrow, and a lower negative predictive value using another or the same D-dimer assay would have the same influence whether using the original or the simplified one-point Wells rule. Finally, it is currently advised that exclusion of PE in patients is based on the outcome of a clinical decision rule in combination with a D-dimer test result.

In conclusion, in this retrospective external validation, the simplified Wells rule appears to have the same predictive accuracy as the original rule and a similar clinical utility for the exclusion of PE. Also, it appears safe to rule out PE in combination with D-dimer measurement. The straightforwardness of the rule may enhance applicability, as it appears that in daily clinical practice even a relatively simple summing equation can lead to mistakes. With a more straightforward and simple rule, already with two positively scored items the physician knows that further (imaging) testing is necessary. The simplified one-point Wells rule may be a good alternative to more complicated rules, albeit that prospective validation remains necessary.

**References**

1. 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 US study. *Ann Emerg Med* 2002; 39: 144–152.
2. Miniati M, Prediletto R, Formichi B, et al. Accuracy of clinical assessment in the diagnosis of pulmonary embolism. *Am J Respir Crit Care Med* 1999; 159: 864–871.
3. Wicki J, Perneger TV, Junod AF, et al. Assessing clinical probability of pulmonary embolism in the emergency ward: a simple score. *Arch Intern Med* 2001; 161: 92–97.
4. Wells PS, Anderson DR, Rodger M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost* 2000; 83: 416–420.
5. 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: 165–171.
6. Wells PS, Anderson DR, Rodger M, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and d-dimer. *Ann Intern Med* 2001; 135: 98–107.
7. van Belle A, Buller HR, Huisman MV, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. *J Am Med Assoc* 2006; 295: 172–179.
8. Ten Cate-Hoek AJ, Prins MH. Management studies using a combination of D-dimer test result and clinical probability to rule out venous thromboembolism: a systematic review. *J Thromb Haemost* 2005; 3: 2465–2470.
9. Perrier A, Roy PM, Sanchez O, et al. Multidetector-row computed tomography in suspected pulmonary embolism. *N Engl J Med* 2005; 352: 1760–1768.
10. Goekoop RJ, Steeghs N, Niessen RW, et al. Simple and safe exclusion of pulmonary embolism in outpatients using quantitative D-dimer and Wells' simplified decision rule. *Thromb Haemost* 2007; 97: 146–150.
11. Qaseem A, Snow V, Barry P, et al. Current diagnosis of venous thromboembolism in primary care: a clinical practice guideline from the American Academy of Family Physicians and the American College of Physicians. *Ann Fam Med* 2007; 5: 57–62.
12. British Thoracic Society guidelines for the management of suspected acute pulmonary embolism. *Thorax* 2003; 58: 470–483.
13. Gibson NS, Sohne M, Kruij MJ, et al. Further validation and simplification of the Wells clinical decision rule in pulmonary embolism. *Thromb Haemost* 2008; 99: 229–234.
14. Perrier A, Roy PM, Aujesky D, et al. Diagnosing pulmonary embolism in outpatients with clinical assessment, D-dimer measurement, venous ultrasound, and helical computed tomography: a multicenter management study. *Am J Med* 2004; 116: 291–299.
15. McGinn TG, Guyatt GH, Wyer PC, et al. Users' guides to the medical literature: XXII: how to use articles about clinical decision rules. Evidence-Based Medicine Working Group. *J Am Med Assoc* 2000; 284: 79–84.
16. Kelly J, Hunt BJ. A clinical probability assessment and D-dimer measurement should be the initial step in the investigation of suspected venous thromboembolism. *Chest* 2003; 124: 1116–1119.
17. Ginsberg JS, Wells PS, Kearon C, et al. Sensitivity and specificity of a rapid whole-blood assay for D-dimer in the diagnosis of pulmonary embolism. *Ann Intern Med* 1998; 129: 1006–1011.
18. Di Nisio M, Squizzato A, Rutjes AW, et al. Diagnostic accuracy of D-dimer test for exclusion of venous thromboembolism: a systematic review. *J Thromb Haemost* 2007; 5: 296–304.
19. Gibson NS, Sohne M, Gerdes VE, et al. The importance of clinical probability assessment in interpreting a normal D-dimer in patients with suspected pulmonary embolism. *Chest* 2008; in press.