Simplification of the Revised Geneva Score for Assessing Clinical Probability of Pulmonary Embolism

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Background: The revised Geneva score is a fully standardized clinical decision rule (CDR) in the diagnostic workup of patients with suspected pulmonary embolism (PE). The variables of the decision rule have different weights, which could lead to miscalculations in an acute setting. We have validated a simplified version of the revised Geneva score.

Methods: Data from 1049 patients from 2 large prospective diagnostic trials that included patients with suspected PE were used and combined to validate the simplified revised Geneva score. We constructed the simplified CDR by attributing 1 point to each item of the original CDR and compared the diagnostic accuracy of the 2 versions by a receiver operating characteristic curve analysis. We also assessed the clinical utility of the simplified CDR by evaluating the safety of ruling out PE on the basis of the combination of either a low-intermediate clinical probability (using a 3-level scheme) or a “PE unlikely” assessment (using a dichotomized rule) with a normal result on a highly sensitive D-dimer test.

Results: The complete study population had an overall prevalence of venous thromboembolism of 23%. The diagnostic accuracy between the 2 CDRs did not differ (area under the curve for the revised Geneva score was 0.75 [95% confidence interval, 0.71-0.78] vs 0.74 [0.70-0.77] for the simplified revised Geneva score). During 3 months of follow-up, no patient with a combination of either a low (0%; 95% confidence interval, 0.0%-1.7%) or intermediate (0%; 0.0%-2.8%) clinical probability, or a “PE unlikely” assessment (0%; 0.0%-1.2%) with the simplified score and a normal result of a D-dimer test was diagnosed as having venous thromboembolism.

Conclusion: This study suggests that simplification of the revised Geneva score does not lead to a decrease in diagnostic accuracy and clinical utility, which should be confirmed in a prospective study.

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A CLINICAL DECISION RULE (CDR) can be defined as an instrument containing variables obtained from history, physical examination, and simple diagnostic tests quantifying the likelihood of a diagnosis, prognosis, or likely response to treatment in an individual patient. Pulmonary embolism (PE) is clinically suspected in many patients who report respiratory or chest distress because of the nonspecific nature of the presenting signs and symptoms. Nevertheless, the prevalence of PE in this population is relatively low. Several CDRs have been developed to assist the clinician in diagnostic decision making. Correct implementation of CDRs in diagnostic strategies has been proven to decrease the need for expensive, time-consuming, and invasive diagnostic imaging procedures. Moreover, the venous thromboembolism failure rate is acceptably low in patients in whom PE is ruled out by various diagnostic criteria including a CDR and when anticoagulant treatment is withheld.

Although 2 CDRs for the pretest probability of PE have been extensively validated, ie, the Wells rule and the Geneva score, both have practical limitations. A fully standardized rule exclusively based on objective clinical items, the revised Geneva score, has been developed and validated recently. The revised Geneva score is independent of physicians’ implicit judgment, which makes this CDR objective and easily reproducible. The score consists of 8 different variables with different individual weights (Table 1), which might lead to miscalculations in acute patient care. Also, a more complicated score may be less likely to be used by clinicians or remembered correctly. Therefore, we evaluated whether a simplified version of the revised Geneva score in which each variable would be attributed 1 point (Table 1) would retain its diagnostic accuracy and clinical useful-
METHODS

PATIENTS

Data from 2 large prospective diagnostic trials that included patients with suspected PE were used and combined for the validation of the simplified revised Geneva score.3,4

In the first trial (study A), consecutive patients with suspected PE admitted to the emergency department of 3 teaching hospitals (Geneva University Hospital, Geneva, Switzerland; Angers University Hospital, Angers, France; and Hôpital Européen Georges-Pompidou, Paris, France) between August 1, 2002, and November 30, 2003, were eligible for inclusion. The Geneva score was assessed in all patients before diagnostic testing.7 In patients with either a low or intermediate probability, plasma D-dimer levels (VIDAS D-Dimer Exclusion Test; bioMerieux, Marcy l’Etoile, France) were measured. Pulmonary embolism was ruled out in patients with a level below the cutoff value of 500 ng/mL (to convert to nanomoles per liter, multiply by 5.476 × 10−3). Patients with a D-dimer level greater than 500 ng/mL as well as patients with high clinical probability underwent proximal venous-compression ultrasonography of the lower limbs and multidetector-row computed tomography (CT). Patients with CT findings indicating PE or patients with respiratory distress in combination with ultrasonography (CT). Patients with CT findings indicating PE or patients with respiratory distress in combination with ultrasonography (CT). Patients with CT findings indicating PE or patients with respiratory distress in combination with ultrasonography (CT).

In the second study (study B), the clinical effectiveness of a simplified algorithm using the dichotomized Wells rule was evaluated.4 Only patients from the Leiden Medical University Hospital who participated in that study were included in the present analysis. Pulmonary embolism was considered to be excluded if the diagnosis of PE was unlikely (Wells score ≤4) in combination with a normal quantitative D-dimer test result. When the Wells score was 4 or less in combination with an increased D-dimer value (>500 ng/mL) or when the diagnosis of PE was likely (Wells score >4), the diagnosis of PE was established by CT. Patients in both studies were followed up for 3 months. Patients with confirmed venous thromboembolism were brought back for reexamination. All other patients were instructed to report any new signs of venous thromboembolism to their general practitioner or to the emergency department of the participating hospitals. At the end of the 3-month follow-up period, all patients were interviewed by telephone and were asked to disclose all health-related events since their hospital discharge. The family physician was contacted whenever a possible event was disclosed by the interim history, and charts were reviewed if a patient was readmitted to the hospital for any cause or died during the follow-up period. Recurrent venous thromboembolism was diagnosed according to standard criteria. Both studies were approved by the ethics committees of all participating hospitals, and all patients provided written informed consent before they were enrolled.

In study A, D-dimer testing was part of the diagnostic workup of all patients with either a low or intermediate probability according to the Geneva score.7 In study B, D-dimer tests were performed only in patients with a Wells score of 4 or less. This resulted in missing D-dimer data for 69 patients in the low- and intermediate-probability group and for 29 patients in the unlikely clinical probability group as assessed by the simplified revised Geneva score.

ASSESSMENT OF THE REVISED GENEVA SCORE

In study A,3 the data collection form was identical to that used in the derivation study of the revised Geneva score, allowing retrospective calculation of the simplified revised Geneva score for each patient. In study B,4 the Wells rule was used for assessing clinical probability. The revised Geneva score comprises 4 variables not included in the Wells rule: age, unilateral lower-limb pain, heart rate, and signs of deep venous thrombosis (pain on lower-limb deep venous palpation and unilateral edema). The 4 variables absent from the original database were extracted from the medical charts in a prespecified standard way by 2 independent observers after blinded of the diagnosis (PE or no PE) by a third person not involved in the data extraction. Lower-limb pain and signs of deep venous thrombosis were routinely recorded in patient charts in the setting of a clinically suspected PE. Therefore, there were no missing data.

In the simplified revised Geneva score, all variables were given 1 point if present (Table 1). Because of the weight of heart rate in the original score, we attributed 1 point to a heart rate between 75 and 94 beats/min and an additional point for a heart rate of 95 beats/min or more.

DATA ANALYSIS

Patient characteristics and outcomes of both studies were combined in a single database. Optimal cutoff points for the simplified Geneva score were determined by a receiver operating curve analysis.
characteristic (ROC) analysis. To account for the existence of both 3-level (low, intermediate, or high clinical probability) and 2-level (PE unlikely or likely) schemes in clinical practice, we set cutoff points for both schemes. Accuracy of the simplified revised Geneva score and the revised Geneva score was compared by means of the area under the curve (AUC) in ROC analyses of the continuous score and of the 3-level classification scheme. Comparing the AUC for the continuous scores was designed to compare the original and simplified rule more precisely, using all possible point scores. However, the continuous score is not meant for clinical use. We studied the clinical course of patients with a normal D-dimer result in different clinical probability categories using the simplified revised Geneva score. Statistical analysis was performed by using SPSS software (SPSS for Windows 14.0.2; SPSS Inc, Chicago, Illinois). 

**RESULTS**

Study A included 756 outpatients. They had a mean (SD) age of 60 (19) years, and 454 were female (60.1%). The overall prevalence of PE in this cohort was 25.6% (194 patients). However, owing to missing values mainly for heart rate, the revised Geneva score could not be computed in 7 patients, leaving 749 for the present analysis, including 192 patients with PE (25.6%). Three hundred and 681 patients (64.9%) were designated unlikely to have PE and proportions of the population in the 3-level and 2-level clinical probability categories.

In selecting the optimal cutoffs for the 3-level scheme, a low clinical probability was defined as a score of 0 or 1 point, an intermediate probability as 2 to 4 points, and a high probability as 5 points or more (Figure 1 and Figure 2). With the use of these cutoff points, 378 patients (36.0%) were assigned to the low clinical probability category (prevalence of PE, 7.7% [95% confidence interval [CI], 5.2%-10.8%]), 629 patients (60.0%) to the intermediate clinical probability category (prevalence of PE, 29.4% [26.5%-33.1%]), and 42 patients (4.0%) to the high clinical probability category (prevalence of PE, 64.3% [48.0%-78.5%]). The optimal cutoff for the 2-level scheme was 3 points, patients with a score of 0 to 2 being categorized as unlikely to have PE and those with a score of 3 or more as likely to have PE (Figure 1); 681 patients (64.9%) were designated unlikely to have PE (prevalence of PE, 12.9% [10.5%-15.7%]) and 368 patients (35.1%) were designated likely to have PE (prevalence of PE, 41.6% [36.5%-46.8%]). Flowcharts for both dichotomized and trichotomized rules are shown in Figure 3 and Figure 4.

We compared the AUC for the revised Geneva score and simplified revised Geneva score (Figure 2). The AUC of the continuous score was 0.75 (95% CI, 0.71-0.78) for the revised Geneva rule and 0.74 (0.70-0.77) for the simplified revised Geneva rule. The AUC of the 3-level classification scheme was 0.70 (0.66-0.74) for the revised Geneva score and 0.68 (0.64-0.72) for the simplified revised Geneva score.

Finally, we studied the clinical utility of the simplified revised Geneva score. Of all patients in the combined patient population with a normal result of the D-dimer test, in whom PE was excluded (n=361), 2 patients were lost during follow-up and an additional 10 received anticoagulant therapy for reasons other than PE. These patients were excluded from the analysis. During 3 months of follow-up, no patient with a low (0 of 219 [0%; 95% CI, 0.0%-1.7%]) or intermediate (0 of 130 [0%; 0.0%-2.8%]) clinical probability score by the simplified revised Geneva score and a normal D-dimer result at inclusion was subsequently diagnosed as having venous thromboembolism (Figure 3). When the 2-level rule was used, no patient with an unlikely clinical probability (0 of 318 [0%; 0.0%-1.2%]) was subsequently diagnosed as having venous thromboembolism after the 3-month follow-up period (Figure 4).

This study shows that it is possible to simplify the revised Geneva score without decreasing the diagnostic accuracy of the rule. The distribution of the patient proportions by the simplified revised Geneva score in both trichotomized and dichotomized categories and the prevalence of PE in these categories were comparable to those of the original revised Geneva score as well as to 3 other validated CDRs: the Wells rule, the Geneva score, and the rule by Kline et al. The simplified revised Geneva score is clinically useful and might safely rule out PE when combined with a normal D-dimer result using a highly sensitive assay. Indeed, in this cohort, the venous thromboembolism failure rates were extremely low in patients with normal D-dimer results and a low-intermediate clinical probability (3-level scheme) or a “PE unlikely” as-
essment (2-level score). The simplified score would likely be easier to compute and may reduce computational errors in clinical practice in busy environments with a heavy workload.

Several studies have shown D-dimer assays to have a high negative predictive value and to be a sensitive but nonspecific marker of PE. However, different sensitivity for several D-dimer assays has been described in the literature. Less sensitive tests yield a lower negative predictive value for the same pretest probability of PE. As a consequence, the proportion of patients with suspected PE in whom D-dimer testing can safely be used to exclude PE depends on both the prevalence of the disease and the sensitivity of the D-dimer assay. This is why we adopted 2 different schemes. Table 3 shows the post-test probability of PE for various combinations of clinical probability categories and D-dimer assays. The upper limit of the 95% CI of the 3-month thromboembolic rate after negative pulmonary angiography is 2.7%. Using this 3% as the upper posttest probability limit above which it is no longer safe to rule out PE by the combination of clinical probability and a negative D-dimer result, Table 3 shows that, with a 3-level score, a less sensitive D-dimer assay would exclude PE safely only in low-probability patients, whereas the same assay would still be safe in the patients in whom PE was unlikely by using the 2-level score. For this reason, a less sensitive assay would rule out PE in more patients and therefore be more useful in combination with the dichotomized rule because there are more patients categorized as PE unlikely than in the low clinical probability category. Conversely, the 3-level score would be more useful when a highly sensitive assay is used because it would safely rule out PE in both the low and intermediate probability groups, which would regroup a higher number of patients than the PE unlikely category. In the present study, a highly sensitive quantitative D-dimer assay with a reported sensitivity of 95% to 98% was used, and the out-

Figure 2. Receiver operating characteristic curves. A, Continuous revised Geneva score (RGS) and simplified RGS. B, Three-level categorized RGS and simplified RGS.

Figure 3. Flowchart of patients showing outcomes by 3-level simplified revised Geneva score. *One patient was lost to follow-up and 3 patients were treated with anticoagulant therapy for reasons other than pulmonary embolism (PE). †One patient was lost to follow-up and 7 patients were treated with anticoagulant therapy for reasons other than PE. CI indicates confidence interval.
come of 3-month follow-up was good in either low-
intermediate probability or PE unlikely categories. However, a physician using the simplified revised Geneva score in combination with a D-dimer assay with a lower sensitivity should probably restrict its use to the low clinical probability category of the 3-level score to exclude PE.

The AUC of the ROC curve of the simplified score was not lower than that of the original score. Given that the original score assigned very different weights to the individual variables, at least some loss of predictive accuracy would have been expected, and this might therefore seem surprising. Because this is also true for the ROC curve using all the score values and not only 2 cutoff values, this observation is not due to cutoff selection in this particular population.

This study has limitations. We performed a retrospective analysis, which can be subject to various biases. We acknowledge that prospectively studying the clinical utility and outcomes in a new sample would be the best way of testing our hypothesis. Nevertheless, the revised Geneva score could be calculated in more than 99% of patients. Also, the original cohorts prospectively included consecutive patients with minimal loss to follow-up (0.5% in study A and 0.1% in study B). There were some differences in general characteristics between the 2 study populations, ie, mean age and prevalence of PE. However, the prevalence of PE according to the number of points in the simplified revised Geneva score was similar in the 2 groups (data not shown), which actually adds validity to the simplified score. Finally, by study design, D-dimer results were not available for all patients. Data were missing in 9 patients (2.4%) with low clinical probability, in 60 patients (9.5%) with intermediate clinical probability, and in 29 patients (4.3%) designated as PE unlikely.

In summary, our data indicate that simplification of the revised Geneva score does not decrease the score’s diagnostic accuracy and clinical utility. Prospective outcome studies are needed, however, to confirm our findings.

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Table 3. Posttest Probability of PE According to Sensitivity of DD and Clinical Probability Category as Assigned by Simplified Revised Geneva Score

<table>
<thead>
<tr>
<th>Clinical Probability, %</th>
<th>3-Level Scheme</th>
<th>2-Level Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of PE</td>
<td>Low Intermediate High</td>
<td>PE Unlikely PE Likely</td>
</tr>
<tr>
<td>Posttest PE</td>
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<td></td>
</tr>
<tr>
<td>Highly sensitive DDb</td>
<td>8 29 64</td>
<td>13 42</td>
</tr>
<tr>
<td>Less sensitive DDb</td>
<td>1 3 12</td>
<td>1 5</td>
</tr>
<tr>
<td>Low-sensitivity DDb</td>
<td>1 6 23</td>
<td>2 11</td>
</tr>
<tr>
<td></td>
<td>2 9 29</td>
<td>3 14</td>
</tr>
</tbody>
</table>

Abbreviations: DD, D-dimer test; PE, pulmonary embolism.

b Figures for sensitivity and specificity are extracted from Di Nisio et al.16

c Sensitivity, 97%; specificity, 40%.

d Sensitivity, 90%; specificity, 60%.

e Sensitivity, 85%; specificity, 65%.

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REFERENCES