Original Article

Values of the Wells and Revised Geneva Scores Combined with D-dimer in Diagnosing Elderly Pulmonary Embolism Patients

Dan-Jie Guo, Can Zhao, Ya-Dan Zou, Xu-Hang Huang, Jing-Min Hu, Lin Guo

Department of Cardiology, Peking University People's Hospital, Beijing 100044, China

Abstract

Background: Pulmonary embolism (PE) can be difficult to diagnose in elderly patients because of the coexistent diseases and the combination of drugs that they have taken. We aimed to compare the clinical diagnostic values of the Wells score, the revised Geneva score and each of them combined with D-dimer for suspected PE in elderly patients.

Methods: Three hundred and thirty-six patients who were admitted for suspected PE were enrolled retrospectively and divided into two groups based on age (≥65 or <65 years old). The Wells and revised Geneva scores were applied to evaluate the clinical probability of PE, and the positive predictive values of both scores were calculated using computed tomography pulmonary arteriography as a gold standard; overall accuracy was evaluated by the area under the curve (AUC) of receiver operator characteristic curve; the negative predictive values of D-dimer, the Wells score combined with D-dimer, and the revised Geneva score combined with D-dimer were calculated.

Results: Ninety-six cases (28.6%) were definitely diagnosed as PE among 336 cases, among them 56 cases (58.3%) were ≥65 years old. The positive predictive values of Wells and revised Geneva scores were 65.8% and 32.4%, respectively ($P < 0.05$) in the elderly patients; the AUC for the Wells score and the revised Geneva score in elderly was 0.682 (95% confidence interval [CI]: 0.612–0.746) and 0.655 (95% CI: 0.584–0.722), respectively ($P = 0.389$). The negative predictive values of D-dimer, the Wells score combined with D-dimer, and the revised Geneva score combined with D-dimer were 93.7%, 100%, and 100% in the elderly, respectively.

Conclusions: The diagnostic value of the Wells score was higher than the revised Geneva score for the elderly cases with suspected PE. The combination of either the Wells score or the revised Geneva score with a normal D-dimer concentration is a safe strategy to rule out PE.

Key words: D-dimer; Elderly; Pulmonary Embolism; Revised Geneva Score; Wells Score

INTRODUCTION

Pulmonary embolism (PE) is a common cardiopulmonary emergency, whose mortality is 30% if untreated,[1] but it would drop to 2–8% if treated appropriately.[2] The incidence of venous thromboembolism increases markedly with age,[3] and the mortality in elderly patients with PE is greater than in non-elderly patients.[4] The increasing prevalence of other cardiopulmonary diseases, such as chronic obstructive pulmonary disease or congestive heart failure, leads to rising rate of misdiagnosis and missed diagnosis of PE. Thus, it is necessary to explore suitable and noninvasive approaches for PE diagnosis in elderly patients.

Recently, several prediction rules make it possible to discriminate suspected PE patients in categories of clinical or pretest probability.[5-7] Two of the most extensively validated and widely used scores, the Wells and revised Geneva scores,[8,9] stratify patients into low, moderate, and high clinical probability groups. The two scores were validated and have become important strategies for accurate diagnosis, but there are few studies in elderly patients.[10] Therefore, this study aims to explore diagnostic values of the Wells and revised Geneva scores and their combination with D-dimer, for suspected PE in elderly patients.

METHODS

Patients

Three hundred and thirty-six consecutive patients with suspected PE due to chest pain, dyspnea, and hemoptysis who visited Peking University People's Hospital, between March 2006 and April 2011, were enrolled in this study. The elderly group was defined as ≥65 years of age.[3,10,11]

Assessment of clinical probability

For each suspected PE patient, the characteristics were recorded retrospectively, including gender, age, main

Address for correspondence: Prof. Dan-Jie Guo,
Department of Cardiology, Peking University People's Hospital, Beijing
100044, China E-Mail: heartdanjie@medmail.com.cn

symptoms (dyspnea, chest pain, hemoptysis, syncope, unilateral lower limb pain), signs (heart rate, respiration rate, pain on lower limb deep vein at palpation and unilateral edema), and risk factors (previous deep vein thrombosis or PE, cancer, fracture within 4 weeks, immobilization or surgery within 4 weeks). The Wells and revised Geneva scores were applied to evaluate the probability of PE and the patients were classified into categories of clinical probability [Table 1]. The diagnosis of PE was ruled out if D-dimer test was normal in patients with Wells score ≤4 or revised Geneva score ≤3.[12]

Computed tomography pulmonary arteriography
Computed tomography pulmonary arteriography (CTPA) was used for PE diagnosis. Pulmonary artery signs of PE were central filling defects or eccentric partial filling defects surrounded by contrast medium, filling defects occupying the total vessel section and mural defects. CTPA was performed with a 64-row multidetector CT scanner (Lightspeed VCT, GE Healthcare). Scanning parameters were set as follows: Tube voltage of 120 kV and current of 300 mA, collimation of 0.6 mm, gantry rotation time of 0.4 s, and reconstruction increment of 1.25 mm. A mechanical injector was used for intravenous bolus injection of iopromide (Ultravist, 370 mg/ml; Bayer Schering Pharma, Germany) at a flow rate of 3.0–3.5 ml/s.

D-dimer test
D-dimer was measured by a high sensitive turbidimetric immunoassay (D-Dimer-0020008500, HemosIL™, Italy). The D-dimer kit consists of the latex reagent, reaction buffer, and D-dimer calibrator. The level of D-dimer is defined as normal if <500 ng/ml, abnormal if ≥500 ng/ml.

Statistical analysis
Chi-square test was used for comparison of categorical data, and Mann–Whitney U-test was used for comparison of continuous variables with a skewed distribution. The comprehensive degree of accuracy of both scores was compared using area under the curve (AUC) of receiver operating characteristic (ROC) curves. SPSS version 18.0 (SPSS Inc., Chicago, IL, USA) and MedCalc version 11.5.0.0 (MedCalc Software, Mariakerke, Belgium) were used for statistical analysis. Statistical significance was accepted at $P < 0.05$.

RESULTS
General characteristics
There were 196 elderly people (100 males and 96 females) with mean (standard deviation [SD]) age of 76.1 (6.2), and 140 nonelderly patients (81 males and 59 females) with mean (SD) age of 48.0 (11.4). By CTPA, PE was diagnosed in 96 (56 elderly patients, 40 nonelderly) of 336 patients, and the other 240 patients (49 respiratory failure, 48 chronic obstructive pulmonary disease, 39 pneumonia and bronchitis, 36 heart failure, 30 coronary atherosclerotic heart disease, 11 arrhythmia, 7 acute cerebral infarction, 20 unknown causes) were excluded PE. Table 2 shows the clinical characteristics of PE patients. For the symptoms, the incidence of dyspnea was significantly higher in elderly patients than in the nonelderly (75% vs. 48%, $P = 0.006$), while incidences of chest pain and hemoptysis were lower in elderly (chest pain: 16% vs. 38%, $P = 0.017$; hemoptysis: 2% vs. 18%, $P = 0.018$) patients. For signs, heart rate and respiration rate of elderly patients were higher than the non-elderly (heart rate: 95.0 ± 19.0 vs. 85.9 ± 13.7 beats/min, $P < 0.05$; respiration rate: 20.5 ± 3.7 vs. 18.9 ± 2.1 breaths/min, $P < 0.05$). And the arterial oxygen saturation was lower in elderly patients than the nonelderly ($92.7 \pm 6.2\%$ vs. $95.6 \pm 4.0\%$, $P < 0.05$).

The predictive values of the Wells score and the revised Geneva score in the elderly group
Proportion of patients ultimately diagnosed with PE for

Table 1: The Wells and the revised Geneva score

Wells score		Revised Geneva score	
Variable	**Points**	**Variable**	**Points**
Previous DVT or PE	1.5	Age >65 years	1
Recent surgery or immobilization	1.5	Previous DVT or PE	3
Cancer	1	Surgery or fracture within 1-month	2
Hemoptysis	1	Active malignancy	2
Heart rate >100 beats/min	1.5	Unilateral lower limb pain	3
Clinical signs of DVT	3	Hemoptysis	2
Alternative diagnosis less likely than PE	3	Heart rate 75–94 beats/min	3
		Heart rate ≥95 beats/min	5
		Pain on lower limb deep vein at palpation and unilateral edema	4
Clinical probability (3 levels)	Total	Clinical probability (3 levels)	Total
Low	0–1	Low	0–3
Intermediate	2–6	Intermediate	4–10
High	≥7	High	≥11
Clinical probability (2 levels)		Clinical probability (2 levels)	
PE unlikely	0–4	PE unlikely	0–3
PE likely	>4	PE likely	>3

DVT: Deep vein thrombosis; PE: Pulmonary embolism.

Table 2: Clinical presentation in elderly and nonelderly patients with PE

Clinical presentation	≥65 years n = 56	<65 years n = 40	χ^2/u	P
Cancer, n (%)	8 (14)	9 (23)	1.08	0.299
Previous DVT/PE, n (%)	4 (7)	4 (10)	0.02	0.901
Recent surgery or immobilization, n (%)	17 (30)	7 (18)	2.06	0.151
Dyspnea, n (%)	42 (75)	19 (48)	7.62	0.006*
Chest pain, n (%)	9 (16)	15 (38)	5.71	0.017
Hemoptysis, n (%)	1 (2)	7 (18)	5.63	0.018
Syncope, n (%)	4 (7)	5 (13)	0.28	0.594
Unilateral lower limb pain, n (%)	6 (11)	10 (25)	3.43	0.064
Temperature (°C)	36.7 ± 0.7	36.9 ± 0.4	776.00	0.041
Heart rate (beats/min)	95.0 ± 19.0	85.9 ± 13.7	780.50	0.012
Respiration rate (breaths/min)	20.5 ± 3.7	18.9 ± 2.1	833.50	0.028
Blood pressure (mmHg)				
Systolic pressure	128.5 ± 17.5	126.0 ± 18.6	991.00	0.335
Diastolic pressure	73.1 ± 9.9	77.3 ± 12.0	927.50	0.144
Arterial oxygen saturation (%)	92.7 ± 6.2	95.6 ± 4.0	622.50	0.011

DVT: Deep vein thrombosis; PE: Pulmonary embolism. *P < 0.05.

the Wells and revised Geneva group in the elderly, and non-elderly patients are presented in Figure 1a and b.

For the elderly people, the positive predictive value of the Wells score was significantly higher than that of the revised Geneva score (65.8% vs. 32.4%, P < 0.01). It was also similar for non-elderly patients: 65.6% and 32.4% (Mantel–Haezel test: P < 0.01) respectively [Figure 1c, d]. For the elderly people, there was no significant difference between the overall accuracies of the Wells (0.682, 95% confidence interval [CI]: 0.612–0.746) and revised Geneva scores (0.655, 95% CI: 0.584–0.772) as determined by the area under ROC curves (P = 0.389) [Figure 2]. The AUC for the Wells score and the revised Geneva score in nonelderly patients was 0.732 (95% CI: 0.650–0.803) and 0.633 (95% CI: 0.548–0.713) respectively, with statistically significant difference (P = 0.010) [Figure 3].

Negative predictive values for D-dimer only or combined with either the Wells score or the revised Geneva score
D-dimer

There were 63 cases with D-dimer <500 ng/ml in the elderly patients, 59 cases of whom were ruled out PE by CTPA, thus the negative predictive value was 93.7%; while there were 45 cases of D-dimer <500 ng/ml in the nonelderly patients, 42 cases of whom were finally ruled out by CTPA, with the negative predictive value of 93.3% [Table 3]. The negative values were similar, with no statistically significant difference (P = 1.000).

The Wells score combined with D-dimer

There were 58 elderly patients whose Wells scores ≤4 and D-dimer <500 ng/ml, and all of them were excluded PE by CTPA; while 42 cases were all excluded PE by CTPA in the non-elderly. The negative predictive values of the Wells score ≤4 combined with normal D-dimer were 100% in both groups [Table 3].

Table 3: PPV and NPV for the patients (%)

Items	≥65 years		<65 years	
	PPV	NPV	PPV	NPV
Wells score	65.8	80.4	65.6	82.4
Revised Geneva score	32.4	81.5	32.4	75.4
D-dimer	39.0	93.7	41.2	93.3
Wells score with D-dimer	40.6	100	43.2	100
Revised Geneva score with D-dimer	32.3	100	38.8	100

PPV: Positive predictive value; NPV: Negative predictive value.

The revised Geneva score combined with D-dimer

There were 25 elderly patients whose Geneva scores ≤3 and D-dimer <500 ng/ml, and all of them were ruled out PE by CTPA; while 32 cases were also fully ruled out PE by CTPA in the other group. The negative predictive values of the revised Geneva score ≤3 combined with normal D-dimer were 100% in both groups [Table 3].

Comparison of negative predictive values for D-dimer only or combined with either the Wells score or the revised Geneva score

There was no significant difference for negative predictive value between normal D-dimer and the Wells score ≤4 combined with normal D-dimer (93.7% vs. 100%, P = 0.149) in elderly patients. The negative values of normal D-dimer and revised Geneva score ≤3 combined with normal D-dimer were also similar (93.7% vs. 100%, P = 0.470) in elderly patients.

DISCUSSION

In this study, the positive predictive value of the Wells score was higher than that of the revised Geneva score among the elderly group. The negative predictive values
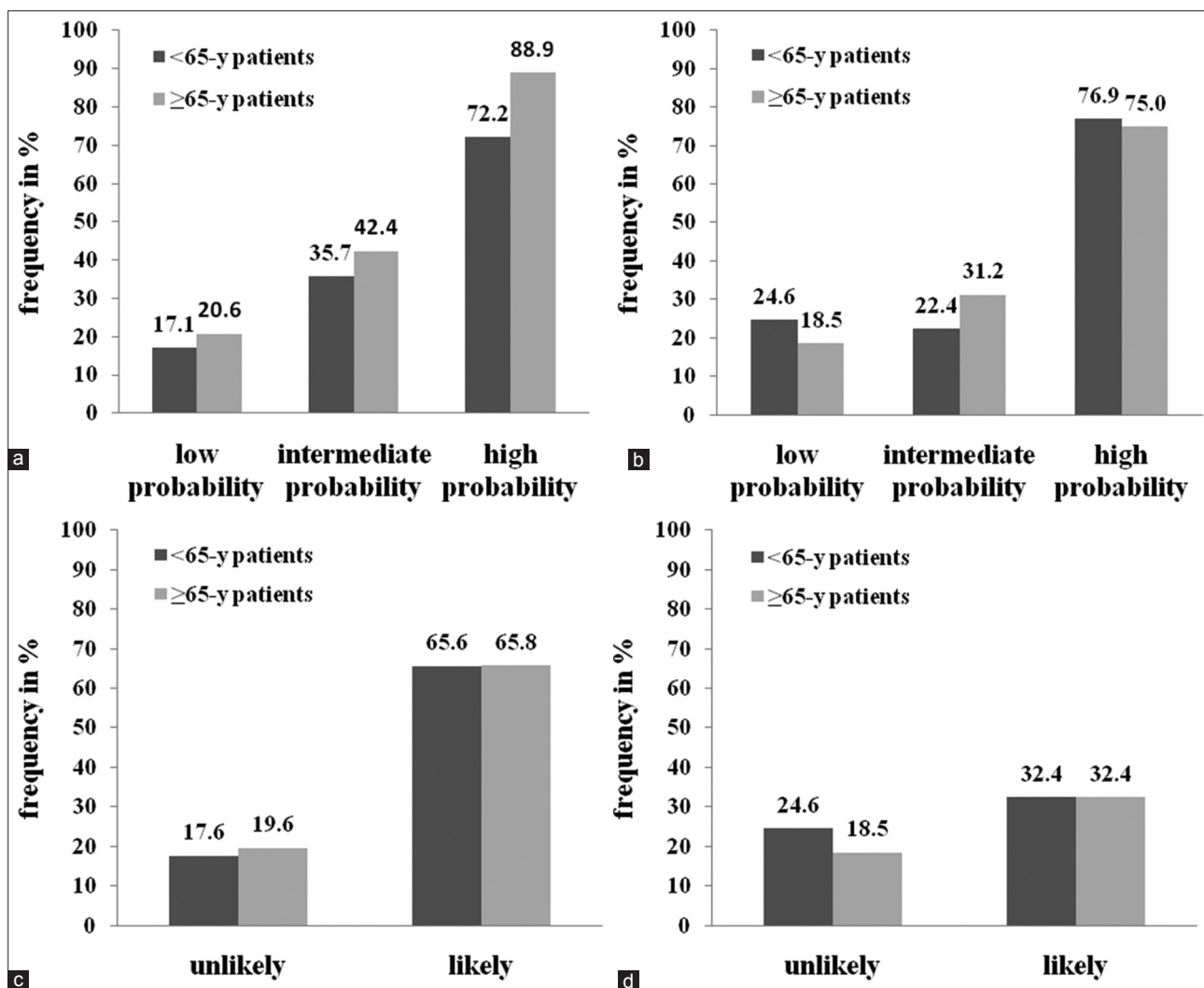
Figure 1: Frequency of pulmonary embolism in patients with different clinical probability according to age. (a) Frequency of pulmonary embolism (PE) in 3-level clinical probability categories of Wells score; (b) Frequency of PE in 3-le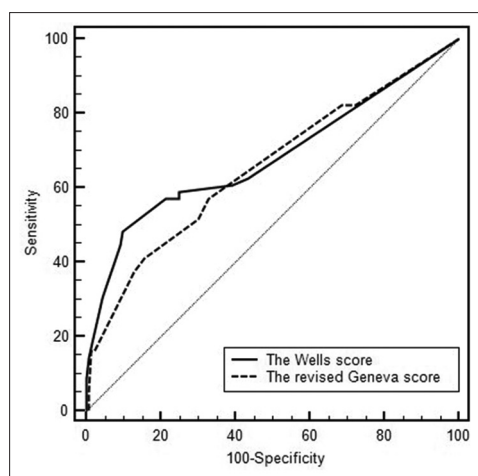vel clinical probability categories of revised Geneva score; (c) Frequency of PE in 2-level clinical probability categories of Wells score; (d) Frequency of PE in 2-level clinical probability categories of revised Geneva score.

Figure 2: Receiver operating characteristic curves of Wells score and revised Geneva score for the elderly patients.
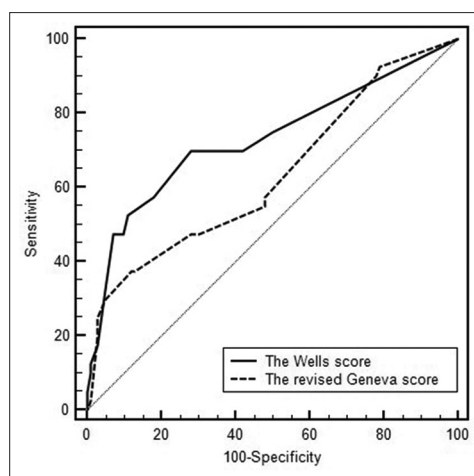

Figure 3: Receiver operating characteristic curves of Wells score and revised Geneva score for the nonelderly patients.

of D-dimer combined with either the Wells score or revised Geneva score were both 100% in the elderly patients,

which is more specific of negative prediction for PE than D-dimer only.

We found that heart rate and respiration rate in elderly PE patients were higher than those of the nonelderly, which was similar to the previous report.[13] The reason might be as followings: Most elderly patients with PE also had cardiopulmonary comorbidities such as chronic obstructive pulmonary disease or congestive heart failure, which impairs cardiopulmonary function, so that they have poor hypoxic tolerance. The manifestations of patients with hypoxia would be dyspnea or tachycardia. So if there are unknown causes of the signs above, clinicians should have a high index of suspicion of PE.

Some researchers applied the Wells score[8] and the revised Geneva score[9] for diagnosis of patients with suspected PE. Although it has been proved that the Wells score is used more generally and has a higher predictive value,[14] one item of the score "alternative diagnosis less likely than PE" is highly subjective and influenced by other factors in the rule,[15] which reduces its diagnostic value and reproducibility.[16] While the revised Geneva score consists entirely of objective clinical items, which would be less influenced by the clinical experience. However, Penaloza *et al.*[17] reported that compared with the revised Geneva score, the Wells score appeared to be more convenient and accurate. The same conclusion was obtained by Calisir *et al.*[18] But there were few studies focused on the elderly PE patients. It was shown in this study that the positive predictive value of the Wells score was higher than that of the revised Geneva score among the elderly group. The possible reason of the result may be as follows: In 2-level scoring systems, 4 points was the cut-off value in Wells score to categorized patients as "PE unlikely" or "PE likely," while 3 points was used in revised Geneva score. This may lead more cases categorized as "likely PE" evaluated by revised Geneva score, and thus decrease the positive predictive value of it. It is necessary to find an appropriate cut-off value in 2-level scoring system of revised Geneva score. The AUCs were similar in both rules for the elderly patients while the AUC of the Wells score was larger than revised Geneva score for the nonelderly group. This is likely due to a variety of other diseases, which the elderly patients were often concomitant with. The individual symptoms were complicated or atypical, so it was difficult for the subjective item in the Wells score to assess the elderly patients. Unlike nonelderly, the clinical diagnostic value of the Wells score was not superior to the revised Geneva score in elderly patients.

There was a high percentage (71.4%) of suspected patients who were finally excluded from PE diagnosis by CTPA, similar to the previous report.[19] Consequently, it is necessary to find a method with high negative predictive value so that unnecessary diagnostic tests could be avoided. Plasma D-dimer is a degradation product of cross-linked fibrin, levels of which are elevated in plasma in the presence of an acute clot because of simultaneous activation of coagulation and fibrinolysis. It is available for excluding PE.[20,21] However, the negative predictive value of D-dimer is about 94% in all subjects.[22] In the elderly group of this study, the negative predictive value of D-dimer was 93.7%. When a normal D-dimer combined with the Wells score ≤4, it reached to 100%, which is similar as a meta-analysis result.[23] Similarly, when a normal D-dimer combined with the Geneva score ≤3, the negative predictive value reached to 100%. The combination of using either Wells or revised Geneva score with a normal D-dimer was a safe strategy to rule out PE for elderly cases. Through chi-square tests, negative predictive values for D-dimer only or combined with either the Wells score or the revised Geneva score were similar. This may be due to the small number of patients in this study. Further studies with more cases are needed.

Admittedly, this study also has some limitations: Limited samples and follow-up. In addition, the cardiac troponin T, NT-proBNP or echocardiography of the patients which were required for risk stratification were not analyzed. However, with high diagnostic value, either the Wells score or the revised Geneva score was a simple and applicable method for risk stratification without using the items mentioned above.

In conclusion, for elderly cases, the Wells score appeared to be a more accurate rule, with which could reduce the rate of misdiagnosis and avoid unnecessary tests; D-dimer is of greater value in excluding PE when combined with Wells score or revised Geneva score.

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