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Original Contributions

ASSESSING PRETEST CLINICAL RISK OF PULMONARY THROMBOEMBOLISM IN THE EMERGENCY DEPARTMENT: PROPOSAL OF A SIMPLE MODIFICATION TO THE WELLS' SCORE

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☐ **Abstract—Background: Clinical scores have been proposed to stratify the risk of pulmonary thromboembolism (PTE), although this approach suffers a low specificity and the unavoidable need for computed tomography pulmonary angiography (CTPA) scans. Objective: Our study aimed to investigate a simple modification to the already validated Wells' score to improve its diagnostic accuracy in the emergency department (ED). Methods: We retrospectively reviewed all CTPA scans performed in the ED setting to rule out PTE over a 1-year (2017) period. Clinical variables potentially associated with PTE were assessed to improve diagnostic accuracy of the Wells' score, thus introducing a modified Wells' score (mWells). Results: Four thousand four hundred thirteen CTPAs were identified, of which 504 were for suspected PTE. The prevalence of PTE was 23.9%. Among clinical data, only peripheral capillary oxygen saturation was consistently correlated with PTE at univariate (odds ratio 2.75 [95% confidence interval 1.61–4.73]) and multivariate (odds ratio 3.78 [95% confidence interval 2.13–6.72]) logistic regression analysis. The mWells' score had a higher area under the receiver operating characteristic curve compared with the original Wells' score: 0.71 (95% confidence interval 0.67–0.75) vs. 0.65 (95% confidence interval 0.61–0.69) ($p < .01$) and improved diagnostic accuracy. Conclusions: Current clinical stratification tools for PTE are characterized by low specificity, leading to an overuse of CTPA. mWells', rather than Wells', score showed a better predictive performance of PTE detection. Our results suggest that current diagnostic pathway for PTE may be improved by simple adjustments (i.e., mWells') of clinical prediction scores.**

☐ **Keywords—clinical prediction rules; emergency care; pulmonary embolism**

Reprints are not available from the authors.

INTRODUCTION

Pulmonary thromboembolism (PTE) is a complete or partial obstruction of ≥1 pulmonary arteries by blood clots originated from elsewhere in the body and moved to the pulmonary circulation through the bloodstream (1). PTE is the third more common cause of in-hospital cardiovascular death after myocardial infarction and stroke and represents one of the main causes of hospitalization in Europe (1). The overall annual incidence is estimated in 100–200 cases per 100,000 individuals (2). Signs and symptoms of PTE are poorly specific and include dyspnoea at rest (50%) or on exertion (27%), cough (22.9%), signs of deep vein thrombosis (DVT) (24%),

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chest pain (39%), and syncope (5%) (2). Each isolated sign/symptom evaluated either empirically or in combination using clinical scores do not show adequate diagnostic value in order to stratify the risk of having PTE in individual patients (3). Current guidelines recommend the use of validated clinical scores (e.g., Wells', PERC, or Geneva scores) and the D-dimer test to initially assess the risk of PTE and establish the need of further investigations. Despite the low specificity of such scores for PTE (10–65%), the association of a low or intermediate clinical probability with a normal D-dimer value confidently rules out PTE, reducing the need for additional testing (3). On the other hand, computed tomography pulmonary angiography (CTPA) is the gold standard imaging approach to safely rule out PTE when clinical pretest probability is intermediate or high. For this reason, its use quintuplicated between 2003 and 2007 despite an overall decrease of PTE prevalence, resulting in only 6.7–38.9% positive CTPA scans (4,5). The lower testing threshold may reduce the incidence of missed PTE but with adverse consequences, such as complications from intravenous contrast, radiation exposure, and an overall increased cost of care for the population at risk. Furthermore, as established by the American College of Chest Physicians consensus conference, this approach may lead to a high proportion of patients receiving inappropriate anticoagulant therapy while waiting for a diagnostic confirmation (1). Based on this background, the goal of our study was to assess the accuracy of the Wells' score in predicting the clinical risk of PTE in individuals with elevated pretest probabilities for PTE or low pretest probability with elevated D-dimer presenting to the emergency department (ED) of an Italian Third-Level University Hospital. Furthermore, we aimed at evaluating simple potential adjustments to the original model that might improve diagnostic accuracy in patients with suspected PTE by replacing the evaluation of the heart rate with the peripheral blood oxygen saturation because of its more substantial pathophysiological basis.

METHODS

We retrospectively reviewed all CT scans performed at our institution from January to December 2017 to identify all the CTPAs requested from the ED to exclude or confirm a suspected diagnosis of PTE. After the identification of CTPAs, we extracted clinical data from our institutional electronic database including demographics, presenting and accompanying symptoms, medical history, and vital signs (systolic and diastolic blood pressure, heart rate, and peripheral blood oxygen saturation [SpO_2]) according to the items of Wells' score (6). Investigated patients were admitted to the ED at our institution, a large tertiary University Hospital assisting >350,000 inhabitants living in the district. All CTPAs were performed following an institutional standardized protocol. Scans were acquired in inspiratory apnea in caudocranial direction using a 64-slice multidetector scanner (General Electric). As contrast agent, 60 mL of iomeprol 350 mg/ml (Bracco Diagnostics, Milan, Italy) were used, at an optimal flow of 4 mL/s. Three visualization windows were used, 1 dedicated to TPE, 1 for pulmonary parenchyma, and 1 for mediastinum. All data were extracted simultaneously by 2 investigators blinded to the final diagnosis. Disagreements between the 2 investigators were managed by reviewing the case with the support of a third reviewer. No cases were excluded from our analysis. According to Wells' score, a predefined score is assigned (if present) to each of 8 clinical criteria reported in Table 1 (6). Notably, information about the item 2 could not be directly obtained from clinical records because of the subjective nature of this item. Many authors have identified this item as the main source of interobserver variability of the Wells' score (7). The Wells' score predictivity against CTPA-detected PTE was tested using logistic regression analysis and the evaluation of the area under the receiver operating characteristic (AUROC) curve. We built univariate and multivariate logistic regression models including the selected clinical variables of the Wells' score. Subsequently, we modified the original Wells' score by replacing the variable "heart rate >100 beats/min" with the variable "SpO_2 <90%" while maintaining the same scoring system. The AUROC of the modified Wells' score (mWells) was compared with the original one using the method proposed by DeLong et al. Descriptive data were reported as mean ± standard deviation (SD) and median (25th–75th percentiles) for continuous variables and as number (percentage) for categorical variables. Comparisons between groups were performed using the Student *t* test, and $\div^2$ as appropriate. All analyses were performed using SPSS software (version 22; IBM

Table 1. Clinical Criteria Evaluated in This Study

Item No.	Signs	Points
1	Clinical signs and symptoms of DVT	3
2	PTE is the first diagnosis or equally likely	3
3	Heart rate >100 beats/min	1.5
4	Immobilization for ≥3 days or surgery in the previous 4 weeks	1.5
5	Previous, objectively diagnosed PTE or DVT	1.5
6	Hemoptysis	1.5
7	Malignancy with treatment within 6 months or palliative care	1
8	SpO_2 <90%	1.5

DVT = deep venous thrombosis; PTE = pulmonary thromboembolism; SpO_2 = peripheral blood oxygen saturation.
Items 1 to 7 according to Wells' score (6).

Table 2. General Characteristics of the Study Cohort

	Patients with PTE (n = 120)	Patients without PTE (n = 384)	*p* Value
Age, years ± SD	77 ± 12	75 ± 14	.49
Female sex, n (%)	65 (54)	202 (52)	.78
Presentation, n (%)			
Chest pain	12 (10)	58 (15.1)	.76
Dyspnea	46 (39.2)	97 (25.1)	.007
Syncope	8 (6.7)	60 (15.7)	.014
Other	52 (43.3)	151 (39.4)	.46
Dysrhythmia	1 (0.8)	11 (2.9)	.31
sBP, mm Hg ± SD	135 ± 25	134 ± 27	.50
dBP, mm Hg ± SD	77 ± 14	77 ± 14	.81
HR, beats/min ± SD	89 ± 18	88 ± 22	.27
SpO_2, % ± SD	93 ± 5	95 ± 4	<.001
Wells' score ± SD	4.75 ± 1.71	3.98 ± 1.16	<.001
mWells' score ± SD	6.25 ± 1.71	5.48 ± 1.16	<.001

dBP = diastolic blood pressure; HR = heart rate; PTE = pulmonary thromboembolism; sBP = systolic blood pressure; SD = standard deviation; SpO_2 = peripheral blood oxygen saturation.

Corp., Armonk, NY). This study was conducted in accordance with the Helsinki Declaration. As no individual patient identification was involved and all assays/tests were part of clinical routine practice, a simplified review board approval by the local ethics committee was deemed unnecessary.

RESULTS

We retrieved a total of 4413 computed tomography scans performed during the predefined period; of these, 504 were CTPAs (corresponding to 504 individual patients) performed to rule out or confirm a suspected diagnosis of PTE in the ED setting, and these were included in the present study. The general characteristics of the study cohort have been summarized in Table 2. A diagnosis of PTE was confirmed in 120 patients (23.9%). No significant differences were observed between patients with PTE and those in which PTE was excluded except for a significantly lower SpO_2 and a higher total Wells' score. In univariate logistic regression analysis, SpO_2 significantly predicted a confirmed diagnosis of PTE (OR 2.75 [95% confidence interval 1.61–4.73]; $p < .01$) (Table 3). Amongst Wells' score items (no cases of "hemoptysis" were reported in our population), only items 1 and 5 significantly predicted a confirmed PTE at univariate and multivariate logistic regression analyses (Table 3). ROC curves were built to valuate the diagnostic accuracy of both Wells' and mWells' scores (Figure 1). The AUROC of mWells' was significantly higher than that of the original Wells' score (0.71 vs. 0.65; $p < .01$). Table 4 shows the sensitivity, specificity, positive

Table 3. Univariate and Multivariate Logistic Regression Analysis

	Univariate		Multivariate Model 1		Multivariate Model 2	
	OR (95% CI)	*p* Value	OR (95% CI)	*p* Value	OR (95% CI)	*p* Value
Age	1.01 (0.99–1.03)	.12				
Male sex	0.94 (0.63–1.42)	.78				
sBP <90 mm Hg	0.95 (0.26–3.52)	.94				
SpO_2 <90%	2.75 (1.61–4.73)	<.001			3.78 (2.13–6.72)	<.001
Item no.						
1	5.88 (3.39–10.19)	<.001	5.54 (3.15–9.74)	.001	6.44 (3.60–11.48)	<.001
3	1.14 (0.7–1.84)	.6	1.25 (0.75–2.09)	.4		
4	1.36 (0.67–2.75)	.4	1.49 (0.7–3.15)	.3	1.47 (0.68–3.17)	.32
5	3.3 (1.72–5.69)	<.001	2.76 (1.43–5.35)	<.001	3.08 (1.59–6.01)	<.001
6	NE	NE	NE	NE	NE	NE
7	0.78 (0.43–1.41)	.41	0.69 (0.36–1.30)	.25	0.71 (0.38–1.35)	.3

NE = not evaluable (lack of cases); sBP = systolic blood pressure; SD = standard deviation; SpO_2 = peripheral blood oxygen saturation. Model 1 includes Wells' score. Model 2 includes the modifide Wells' score.
Item 1, clinical signs and symptoms of DVT. Item 3, heart rate >100 beats/min. Item 4, immobilization ≥3 days OR surgery in the previous 4 weeks. Item 5, previous objectively diagnosed PE or DVT. Item 6, hemoptysis. Item 7, malignancy on treatment ≤6 months or palliative care.

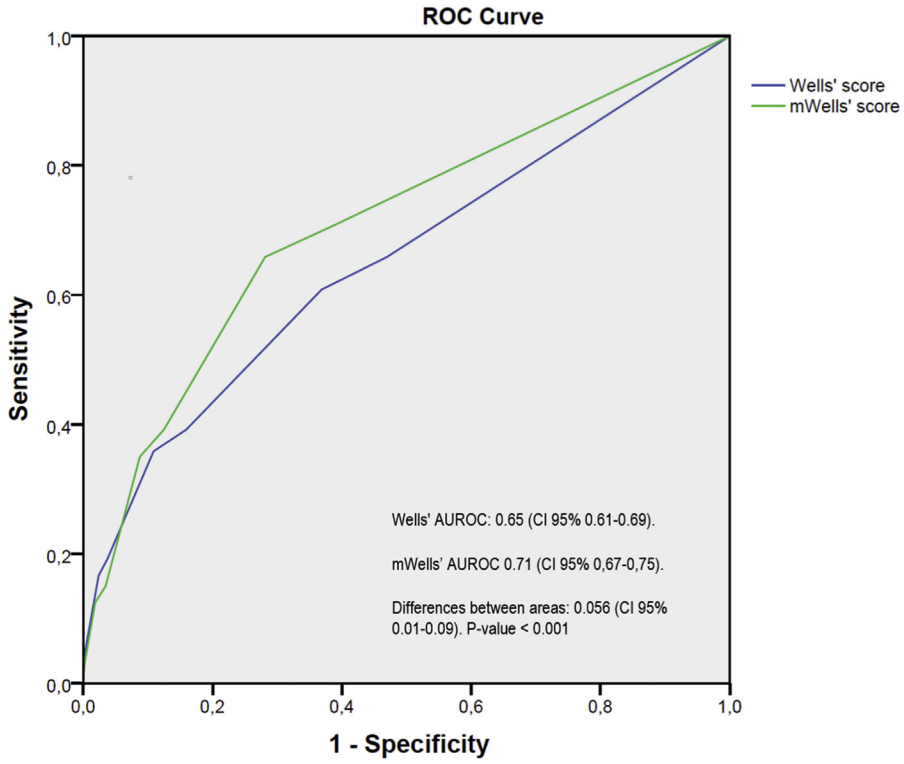

Figure 1. Receiver operating characteristic (ROC) curve of the Wells' and modified Wells' (mWells') scores. Note that the mWells' score has a higher area under the ROC (AUROC) curve indicating a better diagnostic accuracy compared with Wells' score AUROC data. CI = confidence interval.

predictive value, negative predictive value, and accuracy of the Wells' score and the mWell's score using the well-established cutoff for the total score of 4 points.

DISCUSSION

The main aim of our study was to evaluate the performance of the Wells' score in stratifying the risk of PTE in the ED setting. The prevalence of PTE in our retrospective cohort of patients undergoing CTPA was 23.9%, comparable to that observed in previously published studies; the most common presentation symptom was dyspnea (27.6%), followed by chest pain (13.5%), syncope (13.3%), and dysrhythmia (2.8%) (5,8). In 40% of cases a prevailing symptom was not identifiable, thus we used the class "other" to collate a wide range of nonspecific symptoms barely identifiable at admission. Similar data were reported in the literature, except for dyspnea, whose prevalence is generally estimated to be >50% of cases (9). This difference may be attributed to the retrospective identification of the main symptom at admission in place of a structured symptom interview. However, our results underline the wide heterogeneity of PTE clinical presentation and the lack of clinical "red flags" for establishing a correct diagnosis using simple stratification tools. In our cohort, the sensitivity and specificity of the Wells' score were relatively low (both ~61%), confirming that despite multiple attempts to build clinical diagnostic pathways to select patients with high PTE probability, there is still a lack of adequate specificity for stratifying those worthy of CTPA (3). Furthermore, in our cohort, only items 1 and 5 of the original score were significantly associated with the odds of having PTE, further corroborating the clinical

Table 4. Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, and Accuracy of Wells' Score and Modified Wells' Score Using the Well-Established Cutoff for the Total Score of 4 Points

Score	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Accuracy, % (95% CI)
Wells' score	61.54 (55.49–70.91)	61.56 (55.99–66.92)	34.22 (29.75–38.99)	83.12 (79.12–86.44)	61.56 (56.74–66.21)
mWells' score	64.17 (54.9–72.91)	71.23 (66.92–76.19)	41.62 (36.66–46.75)	86.44 (83.26–89.09)	69.92 (65.7–73.9)

CI = confidence interval.

heterogeneity of this disease, risk factors, and management policies. For this reason, we modified the original score by substituting item 3, the least performing item, with a simple clinical measure (SpO_2 <90%). From a pathophysiological standpoint, it is well known that PTE affects the ventilation/perfusion ratio, promoting a functional right-to-left shunt, thereby decreasing blood oxygenation (10). In our population, SpO_2 was consistently associated with PTE, justifying its use in our model. The new mWells' score showed higher sensitivity and specificity and better overall accuracy compared with the original Wells' score, providing the basis for a more accurate selection of patients needing further investigation in the ED setting.

Limitations

Despite providing additional information on a clinical topic of major interest, our study has several limitations that should be acknowledged. The retrospective nature of our data hampered the access to the full set of patients' information, including variables that may potentially affect the probability of having PTE. In addition, our case-finding process started from a review of all subjects undergoing CTPA, thus excluding those patients with suspected PTE who underwent other diagnostic pathways (e.g., ventilation perfusion scintigraphy) because of contraindications to CTPA. A major limitation of our study was the retrospective design. As a result, we could not assign a score to item 2 of the Wells' criteria. Based on our routine clinical practice and the 2016 European Society of Cardiology guidelines on pulmonary embolism, we assumed that a CTPA was performed in patients with a high pretest risk of PTE or in patients with low pretest risk but with high D-dimer plasma levels. Therefore, we decided to systematically assign +3 points on item 2 to all patients (see Table 1).

CONCLUSION

In conclusion, available clinical risk stratification tools suffer insufficient specificity to clearly identify patients who should benefit from a CTPA, avoidable in a subset of cases. Overuse of CT scans not only increases the risk of undesired effects related to the procedure itself (e.g., ionizing radiation and contrast media reactions). The refinement of simple clinical decision rules may improve diagnostic accuracy in the ED setting and can contribute to health care system sustainability. In our cohort of patients at high risk of having PTE, a minor modification (substituting tachycardia with oxygen desaturation) in the original Wells' score led to a significant improvement in the ability of this tool to discriminate patients requiring additional testing. Our study suggests that clinical decision making may be further improved with a minor modification of Wells' score. However, further studies are needed to confirm the accuracy of our model in nonselected patients with suspected PTE.

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ARTICLE SUMMARY

1. Why is this topic important?

Many efforts have been made to improve the diagnosis of patients with suspected pulmonary thromboembolism (PTE). Clinical scores can be used to stratify the risk of PTE, although this approach suffers from low specificity and the unavoidable need of computed tomography pulmonary angiography (CTPA) scans.

2. What does this study attempt to show?

In this study we investigated a simple modification to the already validated Wells' score to improve its diagnostic accuracy in the emergency department. We demonstrate that improving our capability in identifying patients worthy of additional testing is still possible.

3. What are the key findings?

In the 504 patients (of 4413 CTPAs) with suspected PTE, the prevalence of PTE was 23.9%. Only peripheral blood oxygen saturation consistently correlated to PTE at univariate and multivariate logistic regression analysis. The modified Wells' score had a higher AUROC compared with the original Wells' score and improved the diagnostic accuracy.

4. How is patient care impacted?

Our study can provide support to further advancement in detecting patients with PTE. If confirmed by further research, the modified Wells' score could select better patients who are worthy of instrumental investigations, avoiding unnecessary CTPA scans or perfusion lung scintigraphy and the related potential adverse effects and costs.