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Wells score and prediction of pulmonary embolism in patients with coronavirus disease 2019 in Morocco

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Abstract

Aim: This study aimed to evaluate the performance of the WELLS score for the diagnosis of pulmonary embolism in patients with COVID-19 in Souss-Massa Regional Hospital Center. This article reviewed the diagnostic accuracy of the WELLS score associated with the dosage of D-dimer biomarkers.

Material and Methods: This retrospective observational descriptive and transversal study was conducted at Souss-Massa Regional Hospital Center, from March 15, 2021 to June 26, 2021.

Results: The study included 77 patients who underwent chest CT angiography due to oxygen desaturation associated with the values of the biological marker D - dimers. The most responsive antecedents were type II diabetes (41.00%), hypertension (17.9%), and heart disease (15.4%). The mean age of 47 patients with pulmonary embolism had an average age of 62.09 years (±13.31), including 40 men (85.1%) and 7 women (14.9%); 9 patients died, with no medical history available. Comorbidity factors presented in 80.85% (38/47 cases) of patients, the most frequent being type II diabetes 44.73% (17/38 cases), arterial hypertension 28.94% (11/38), heart disease 5.26% (2/38), chronic respiratory failure 2.63% (1/38), smoking history 10.52% (4/38), asthma patients were 5.26% (2/38), and tuberculosis patients were 2.63% (1 /38). Among these patients 38.29% died. The combination of the Wells score with the value of D-dimers can be useful to guide the appropriate care for his patients.

Discussion: The combination of the Wells score with the value of D-dimers can be useful to guide the appropriate care for his patients.

Keywords

WELLS Score, Pulmonary Embolism, Patients, COVID-19

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Introduction

Since the emergence of coronavirus disease-2019 (COVID-19) following infection with respiratory syndrome coronavirus 2 severe acute (SARS-CoV-2) [1], when the first cases of COVID-19 appeared, the clinical picture was constructed as a viral respiratory infection, the severity of which depended on the degree of parenchymal damage, damage thought to be responsible for the hypoxemia [2]. Then several reports described significant procoagulant events, including a life-threatening pulmonary embolism (PE), in these patients [3-7]. These thrombotic complications may be due to excessive inflammation, platelet activation, endotheliitis and stasis [8]. Studies reporting both arterial and venous thrombotic events in patients with COVID-19 have emerged in the literature, and emerging evidence suggests a high prevalence of pulmonary embolism cases in hospitalized patients with COVID-19 in care intensive [8, 9].

The detection of PE is established by a "diagnostic strategy", which has evolved over time, but computerized tomography (CT) angiography of the pulmonary arteries remains the gold standard for the detection of this disease thanks to its rapidity and the availability of highly sensitive scanning. To improve throughput and reduce the number of unnecessary CT scans, the routine use of PE prediction scores is recommended as a clinical decision aid [10]. Studies have demonstrated a reduction in imaging demands when pre-test use of clinical prediction rules is combined with rapid plasma D-dimer assays of cross-linked fibrin degradation products [11, 12]. This study aimed to evaluate the performance of the WELLS score for the diagnosis of pulmonary embolism in patients with COVID-19 in Souss-Massa Regional Hospital Center. as Also, the diagnostic accuracy of the WELLS score associated with the dosage of D-dimer biomarkers has been addressed in this article.

Material and Methods

This retrospective observational descriptive and transversal study was conducted at the Souss-Massa Regional Hospital Center (SMRHC), from March 15, 2021 until June 26, 2021, we selected consecutive hospitalized adult patients with confirmed SARS-coV2 infection and who underwent CT angiography due to suspicion of PE, and D-dimer biological examination. While the sample excluded from the study was any patient with an incomplete and unusable hospital file.

Wells score

The original Wells score, published in 2000, includes clinical parameters: history of PE or deep vein thrombosis (DVT), heart rate greater than 100/min, recent surgery or immobilization, clinical signs of DVT, hemoptysis and presence of cancer. It also includes a criterion titled "an alternative diagnosis is less likely than PE" [13]. For this last criterion, the formulation of which is not very intuitive, the reasoning can be carried out as follows: if it is estimated that PE is the most probable diagnosis, three points are added to the score. If, however, an alternative diagnosis is deemed as likely or more likely than PE, no points are added to the total score. Although this score item is predictive of the presence of PE [14].

Data collection

Data collection is based on a survey form consisting of 3 parts: sociodemographic and biological, the Wells score and the results of the chest CT angiography. The survey sheet form was completed after reviewing all hospital records of the COVID-19 patient and it was completed by ourselves.

Statistical analysis of the data was performed using SPSS (statistical package for social science) version 13 statistical software. Quantitative variables were expressed as mean ± the standard deviation, and the qualitative variables were presented as tables, numbers and frequencies. The sensitivity and specificity of the D-dimer biomarkers were assessed by a receiver operating characteristic (ROC) curve.

The area under the curve (AUC) and 95% confidence intervals (CI) were calculated to assess the strength of any association. This study complied with ethical and regulatory considerations of the institutional agreement of the Souss-Massa Regional Hospital Center (SMRHC) for the realization of this research. We also wanted to respect the anonymity and the confidentiality through the codification of the identification data, and not to have conflicts of related interests.

Results

During the study period, 85 of the patients were referred to the COVID-19 services and underwent a chest CT angiography at the level of the medical radiology service, of which 8 patients were excluded due to the predefined exclusion criteria, the demographic and clinical characteristics of people with and without PE are shown in Table 1.

The 77 patients included underwent chest CT angiography due to oxygen desaturation associated with the values of the biological marker D - dimers, 47/77 (61.00%) were positive for pulmonary embolism and 30/77 (39.00%) were negative (Figure 1).

The incidence of patients hospitalized in the medical department was 49.4%, while 50.6% in the intensive care resuscitation unit COVID-19, of which 32 (82.1%) were males and 7 (17.9%) were females.

The most responsive antecedents were type II diabetes (41.00%), hypertension (17.9%), and heart disease (15.4%). The mean age of 47 patients with pulmonary embolism was 62.09 years (±13.31), including 40 men (85.1%) and 7 women (14.9%); 9 patients died with no medical history available. Comorbidity factors in patients are represented by 80.85% (38/47 cases), the most frequent being type II diabetes 44.73% (17/38 cases), arterial hypertension 28.94% (11/38), heart disease 5.26% (2/38), chronic respiratory failure 2.63% (1/38), smoking history 10.52% (4/38), asthma patients accounted for 5.26% (2/38), and tuberculosis patients accounted for 2.63% (1 /38). Among these patients, 38.29% died.

Wells Score

The numbers and proportions with a low Wells score < 2 were 47/77 (41%), intermediate 2-6 were 28/77 (36.4%), with a high > 6 were 2/77 (2.6%). The most frequently present Wells score items were immobilization ≥ 3 days or recent surgery (n = 53), heart rate > 100/min (n = 25) and "less likely alternative diagnosis" (n = 11).

Only one patient had a history of deep vein thrombosis or pulmonary embolism, DVT symptoms were confirmed in (n=6) patients. The frequency of all Wells score components is shown in Tables 1 and 2.

Coagulation measurements

A total of 71 patients had positive D-dimer results and 6 had negative. D-dimer values were significantly higher in people

Table 1. Clinical and demographic characteristics of the study population

		Patients With PE	Patients without PE	Total
Age		62.4 (±13.31)	65.67 (±13.31)	63.48 (±13.33)
Gender	Female	7 (14.9%)	9 (30%)	16 (20.8%)
	Male	40 (85.1%)	21 (70%)	61 (79.2%)
Medical history	Diabetes	17	10	27
	high blood pressure	11	5	16
	Chronic respiratory failure	1	5	6
	asthma	2	0	2
	Tuberculosis	1	1	2
	heart disease	2	7	9
	smoking	4	1	5
	tumor pathology	0	1	1
	no medical history	9	5	14
Department	Medical department	22	16	38
	Reanimation	25	14	39
Death	Yes	19	14	33
	No	28	16	44
Score wells	Low	29	18	47
	Intermediate	17	11	28
	High	1	1	2

*Sex ratio of patients with pulmonary embolism 5.71
*Sex ratio of patients without PE: 2.33
*The mortality rate in patients hospitalized in intensive care with PE: 46 %
PE: pulmonary embolism, *: The standard deviation

Table 2. Criteria for prediction tests (Wells score)

		n (%)
Features	Symptoms of Lower Limb Deep Vein Thrombosis	6 (7.8%)
	Alternative diagnosis less likely than PE	11 (14.3%)
	Heart rate > 100 beats /min	25 (32.5%)
	Recent surgery or immobilization>3 days	53 (68.8%)
	Previous DVT or PE	1 (1.3%)
	Hemoptysis	2 (2.6%)
	Cancer	2 (2.6%)

Table 3. Thoracic involvement data of patients with COVID-19 and patients with CT angiographic evidence of pulmonary embolism

		Frequency
Pulmonary embolism	Yes	47 (61%)
	No	30 (39%)
Type of pulmonary embolism	Bilateral distal	28 (59.6%)
	Unilateral distal	16 (34.3%)
	Bilateral proximal	2 (4.3%)
	Unilateral proximal	1 (2.1%)
Extent of COVID-19	Mild (<25%)	5 (6.5%)
	Moderate (25%-50%)	11 (14.3%)
	Severe (50%-75%)	22 (32.5%)

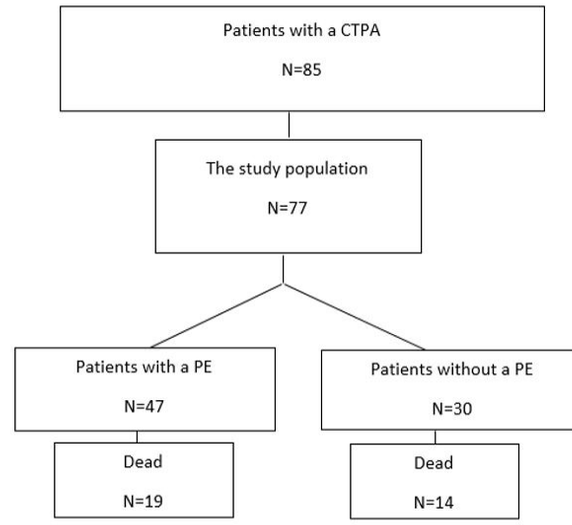

Figure 1. Study Flowchart

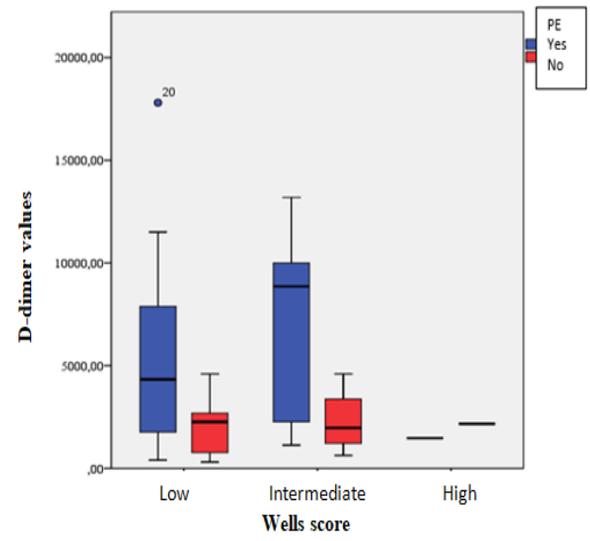

Figure 2. Distribution of D-dimer values in patients with low, intermediate and high probability of pulmonary embolism

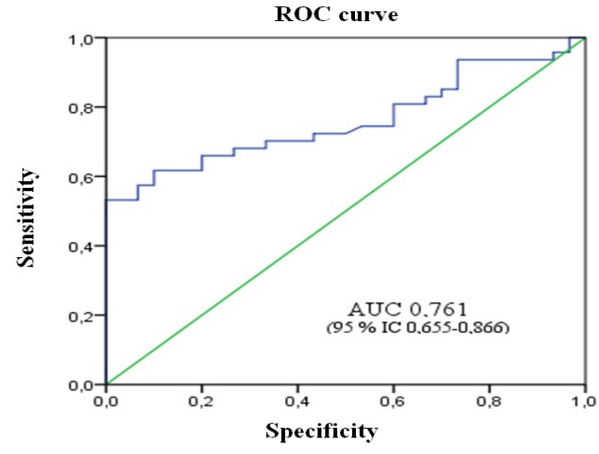

Figure 3. Receiver operating characteristic (ROC) curve for D-dimer for the diagnosis of pulmonary embolism

with confirmed PE. The prevalence of PE increased with higher D-dimer levels. Figure 2 shows the performance of different combinations of D-dimer values and Wells score in predicting pulmonary embolism at hospitalization, with higher values seen in people with PE in the probability groups weak and intermediate pre-test.

The performance of the D-dimer assay to determine EP is represented by a receiver operating characteristic (ROC) curve (Figure 3). The area under the curve (AUC) was 0.761 (95% confidence interval (CI) 0.655-0.866). Above 4849 ng/ml, D-dimer has a positive predictive value for PE; this threshold had a sensitivity of 0.532 and a specificity of 1.

The D-dimer values are homogeneous in patients who do not present with PE and have a low or intermediate probability, while they are heterogeneous in those who present with PE and have a low or intermediate probability, therefore do not share the same D-dimers because the values are more scattered.

CT angiography result

In the 77 patients, the overall involvement of the lung parenchyma was less than 25% in 5 patients (6.5%), between 25% and 50% in 11 (14.3%) patients, between 50 and 75% in 22 (32.5%) patients and more than 75% in 30 (39%) patients. Among patients with confirmed PE, the majority presented with distal PE 93.62% (n=43), of which 28/44 were bilateral, and 16/44 were unilateral. Whereas only 6.4% (n= 3) presented with a proximal PE (Table 3).

Discussion

Our study provides information on the cumulative incidence of pulmonary embolism in patients hospitalized for COVID-19 pneumonia in the COVID-19 departments of the Souss-Massa Regional Hospital Center. We found 47 patients with proven PE and COVID-19 pneumonia out of 77 chest CT angiograms performed. These data support the hypothesis that COVID-19 patients have an increased thromboembolic risk that tends to manifest as pulmonary arterial thrombosis [12, 15]. Hospitalization in intensive care and especially mechanical ventilation were associated with the occurrence of PE. The high rate in intensive care (53.2%; 25 patients out of 77) is consistent with the current bibliography, but seems higher than most studies, especially compared to a recent meta-analysis showing an overall rate of 30.4% of patients in intensive care [16, 17]. Helms et al reported a higher rate (67.3%) in patients with acute respiratory distress syndrome (ARDS) related to COVID-19 compared to patients with ARDS due to other causes [18]. The importance of these clinical incidence rates is further underlined by a recent series of 12 consecutive autopsy reports showing the presence of PE in 58% of cases, which were not recognized until death [19].

It should be noted that a large proportion of patients hospitalized in intensive care has a mortality rate of 46%, this can be explained by the high comorbidity rate in these patients, mainly diabetes 80%, hypertension 60%, and heart disease with 50% [20, 21].

According to our data, PE was more likely in case of Wells score <6 points and D-dimer value ≥4849 ng/ml. These results are similar to the study by Kampouri et al, which was conducted at the University Hospital of Lausanne, Switzerland, on a sample of 443 patients who concluded that the combination of the Wells score with the value of D-dimers at the Admission can be a useful tool to guide empiric anticoagulant therapy when diagnostic imaging is not possible or available [22]. Moreover, our data suggest that D-dimer has a positive predictive value for thrombotic events of approximately 90% when values >4849 ng/ml.

In our case series of patients with a low to moderate pre-test probability of pulmonary thromboembolism, 61.7% and 60%, respectively showed signs of PE on chest CT angiography, with 7 out of 10 patients with EP having a score of 0 points. Additionally, considering the true prevalence of pulmonary embolism in our small cohort of COVID-19 patients, we found an increase greater than the prevalence reported by the original study by Wells et al [23].

However, in the retrospective cohort study by Monfardini et al, they described an increased risk of PE in patients with a moderate to high pre-test probability [16]; this observation could be explained by the subjective component of the Wells score "Is PE the most probable diagnosis?" was not a good predictor in our series. Three points are added to the final score based on the presence of the differential diagnosis of PE; this question, when positive, has been criticized as subjective and dependent on the accumulation of points from other categories. Knowledge of the risk factors for PE in COVID-19 patients is crucial to establish the indication for pulmonary CT angiography because of the logistical difficulty involved in the practice of this technique: mobilization of patients, acute respiratory failure, iatrogenic contrast, risk of transmission of the virus and optimization of resources, in a situation of saturation of care [24]. There is some debate as to whether the PE observed in COVID-19 represents a true "thrombosis embolization" or whether it may be localized "immunothrombosis"; in our series, PE was mostly (59.6%) distal bilateral, so PE probably did not have an impact on prognosis.

Several limitations of our work are worth mentioning. First, this is a single-center retrospective study; thus, the results may not be generalized safely due to our small sample size, as well as to fully exclude a selection bias related to the possibility that some patients meeting our inclusion criteria are not referred for chest CT angiography because they had contraindications to the administration of iodinated contrast agents or because CT examinations were temporarily unavailable due to the number of patients requiring chest CT without injection for triage purposes.

Conclusion

The present research showed that pulmonary embolism appears to be a common complication of SARS-CoV-2 infection, especially in intensive care. The combination of the Wells score with the value of D-dimers can be useful to guide the appropriate care for his patients. Our data discourage the use of a stepwise increase in D-dimer threshold alone.

These data reinforce the need to combine it with PE risk stratification scores, in particular the WELLS score. Therefore, the use of chest CT angiography should be encouraged in patients who present with a low and intermediate WELLS score associated with a threshold D-dimer value >4849 ng/ml, this feature may represent the severity of the disease.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References
1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020; 382(8):727-33
2. Bertoletti L. COVID-19: pulmonary embolism or pulmonary endothelitis? Journal of Vascular Medicine. 2021; 46(5): 28.
3. Sakr Y, Giovini M, Leone M, Pizzilli G, Kortgen A, Bauer M, et al. Pulmonary embolism in patients with coronavirus disease-2019 (COVID-19) pneumonia: a narrative review. Ann Intensive Care. 2020; 10: 124.
4. Casey K, Iteen A, Nicolini R, Auten J. COVID-19 pneumonia with hemoptysis: acute segmental pulmonary emboli associated with novel coronavirus infection. Am J Emerg Med. 2020. 38(7): 1544. e1-1544. e3.
5. Foch E, Allou N, Vitry T, Masse L, Allyn J, Andre M, et al. Pulmonary embolism in a returning traveller with COVID-19 pneumonia. J Travel Med. 2020; 27(5):taaa063. DOI: 10.1093/jtm/taaa063.
6. Rotzinger D.C, Beigelman-Aubry C, Von Garnier C, Qanadli S.D. Pulmonary embolism in patients with COVID-19: time to change the paradigm of computed tomography. Thromb Res. 2020; 190: 58-9.
7. Lushina N, Kuo J.S, Shaikh HA. Pulmonary, cerebral, and renal thromboembolic disease in a patient with COVID-19. Radiology. 2020; 296(3): E181-3.
8. Bikdeli B, Madhavan M V, Jimenez D, Chuich T, Dreyfus I, Driggin E, et al. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up: JACC state-of-the-art review. J Am Coll Cardiol. 2020; 75(23): 2950-73.
9. Poissy J, Goutay J, Caplan M, Parmentier E, Duburcq T, Lassalle F, et al. Pulmonary embolism in patients with COVID-19: awareness of an increased prevalence. Circulation. 2020; 142(2): 184-6.
10. Venkatesh A.K, Kline JA, Courtney D.M, Camargo C. A, Plewa M.C, Nordenholz KE, et al. Evaluation of pulmonary embolism in the emergency department and consistency with a national quality measure: quantifying the opportunity for improvement. Arch Intern Med. 2012; 172(13): 1028-32.
11. Goekoop RJ, Steeghs N, Niessen RW, Jonkers GJ, Dik H, Castel A, et al. Simple and safe exclusion of pulmonary embolism in outpatients using quantitative D-dimer and Wells' simplified decision rule. Thromb Haemost. 2007; 97(1): 146-50.
12. Righini M, Van Es J, Den Exter PL, Roy PM, Verschuren F, Ghuysen A, et al. Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. JAMA. 2014; 311(11): 1117-24.
13. Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent 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(03): 416-20.
14. Klok F, Karami Djurabi R, Nijkeuter M, Huisman MV. Alternative diagnosis other than pulmonary embolism as a subjective variable in the Wells clinical decision rule: not so bad after all. J Thromb Haemost. 2007; 5(5): 1079-80.
15. Schmidt P, Vasquez J, Gagliano B, Moore A. J, Robert C. S. Ascending aortic thrombus with multiple emboli associated with COVID-19. In: Baylor University Medical Center Proceedings. London: Taylor & Francis; 2021.p.178-179.
16. Monfardini L, Morassi M, Botti P, Stellini R, Bettari L, Pezzotti S, et al. Pulmonary thromboembolism in hospitalised COVID-19 patients at moderate to high risk by Wells score: a report from Lombardy, Italy. Br J Radiol. 2020; 93(1113): 20200407.
17. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. J Thromb Haemost. 2020; 18(6): 1421-4.
18. Klok FA, Kruip MJHA, Van der Meer NJM, Arbous MS, Gommers D A MPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020; 191: 145-7.
19. Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med. 2020; 46(6): 1089-98.
20. Wichmann D, Sperhake JP, Lütgehetmann M, Steurer S, Edler C, Heinemann A, et al. Autopsy findings and venous thromboembolism in patients with COVID-19: a prospective cohort study. Ann Intern Med. 2020. 173(4): 268-77.
21. Touahri R, Kaouan H, Messoudi M, Katem A, Ketfi A. Acute pulmonary embolism in patients with COVID-19, a retrospective study. Journal of Respiratory Diseases News.2022; 14(1): 248.
22. Bompard F, Monnier H, Saab I, Tordjman M, Abdoul H, Fournier L, et al , Pulmonary embolism in patients with COVID-19 pneumonia. Eur Respir J. 2020; 56(1). DOI: 10.1183/13993003.01365-2020
23. Kampouri E, Filippidis P, Viala B, Méan M, Pantet O, Desgranges F, et al. Predicting venous thromboembolic events in patients with coronavirus disease 2019 requiring hospitalization: an observational retrospective study by the COVIDIC Initiative in a Swiss University Hospital. BioMed research international. 2020;34.
24. Wells PS, Anderson D R, Rodger M, Stiell I, Dreyer J F, Barnes D, 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(2): 98-107.

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