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Wells Score to Predict Pulmonary Embolism in Patients with Coronavirus Disease 2019

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ABSTRACT

BACKGROUND: The association between coronavirus disease 2019 (COVID-19) and hypercoagulability has been extensively described, and pulmonary embolism is a recognized complication of COVID-19. Currently, the need for computed tomography pulmonary angiogram (CTPA) relies on the Wells score and serum D-dimer levels. However, because COVID-19 patients have a different thrombotic and inflammatory milieu, the usefulness of the Wells score deserves further exploration for this patient population. We aimed to explore the ability of the Wells score to predict pulmonary embolism in patients with COVID-19.

METHODS: In this retrospective study, patients found to have a CTPA and a COVID-19 diagnosis during the same admission were selected for analysis. Age and sex, CTPA results, and associated D-dimer levels were entered in a database. The Wells score sensitivity and specificity were calculated at different values, and the area under the curve of the receiver operating characteristic curve measured.

RESULTS: Of 459 patients with COVID-19, 64 had a CTPA and 12 (19%) had evidence of pulmonary embolism. Previous or current evidence of deep vein thrombosis, a Wells score above 4 points, and serum D-dimer levels 5 times above age-adjusted upper normal values were associated with pulmonary embolism. However, only 33% of patients with pulmonary embolism had a Wells score of 4 points or higher. The area under the curve of the receiver operating characteristic showed non-discriminating values (0.54)

CONCLUSIONS: Although a Wells score of 4 or more points predicted pulmonary embolism in our cohort, the outcome can be present even with lower scores.

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KEYWORDS: COVID-19; D-dimer; Pulmonary embolism; Wells score

INTRODUCTION

Coronavirus disease 2019 (COVID-19), first recognized in Wuhan, China, was declared a pandemic and has presented with heterogeneous signs and symptoms in more than 10 million people worldwide.[1] The association of COVID-19 with

hypercoagulability manifested as arterial and venous thrombosis has been extensively described. Deep vein thrombosis and pulmonary embolism (PE) are recognized complications of COVID-19; in fact, elevated D-dimer levels have been considered markers of increased mortality among these patients. Also, there is ongoing discussion regarding the benefit of treating these patients with anticoagulation, thrombolytics, or both.[2,3] The Wells score, a multi-point rule, has been used to predict PE in the general population since 1997.[4,5] Currently, the need for computed tomography pulmonary angiogram (CTPA) is determined by the Wells score and serum D-dimer levels.[5] However, because COVID-19 patients have a different thrombotic and inflammatory milieu, the usefulness of the

Wells score deserves further exploration for this patient population and is addressed in this article.

METHODS

This study was approved by The University of Texas at Houston institutional review board committee (HSC-MS-20-0542). Written informed consent for this study was waived. In this single-center retrospective study, the electronic records of patients aged over 17 years, confirmed to have COVID-19, and admitted between February 1 and July 15, 2020 to Lyndon B. Johnson Hospital in Houston, Texas, were reviewed. Patients found to have a CTPA and a COVID-19 diagnosis during the same admission were selected for analysis. Patient age and gender, CTPA results, and associated D-dimer levels were entered in a database. The Wells score was calculated for each of these patients. For patients aged over 50 years, age-adjusted D-dimer levels were used to define the expected normal value, in accordance with current guidelines.[5] For the patients with or without CTPA who died, we evaluated whether they had an autopsy and reported whether evidence for PE or infarction was noted (Figure).

Statistical Analysis

MedCalc version 12.3.0 (Mariakerke, Belgium) was used for the statistical analysis. Categorical variables were analyzed with the Fisher exact test, and discrete variables were analyzed with the Student t-test for unpaired samples. A 2-sided $P < .05$ was considered statistically significant. Sensitivity

> ### CLINICAL SIGNIFICANCE
> - Coronavirus Disease 2019 (COVID-19) is associated with hypercoagulability.
> - Currently, the need for Computed Tomography Pulmonary Angiogram (CTPA) relies on the Wells score together with serum D-dimer levels, but the value of this approach is unclear among patients with COVID-19.
> - In our cohort, a Wells score of four or more points predicted pulmonary embolism, though the outcome was frequently present with lower scores, behaving in a non-discriminative way.

and specificity of the Wells score were assessed for Wells score cutoffs of 1 to 6 and a receiver operating characteristic (ROC) curve was generated. The area under the curve (AUC) was calculated, and the location of shortest distance to 100% specificity and 100% sensitivity on the ROC curve was determined to delineate the optimal Wells cutoff score.

RESULTS

Between February 1 and June 30, 2020, 459 patients with COVID-19 were treated at Lyndon B Johnson Hospital. Of those, 64 (13%) had a CTPA performed during the emergency department or hospital visit.

The median age of the 64 patients was 55 ± 16 years. Thirty-five (55%) were male. Twelve of these patients (19%) had radiologic evidence of PE (10 segmental and 7 subsegmental, with some overlapped). The median Wells score for the cohort was 2 ± 2 (range 0-10.5). The characteristics of patients with and without PE on CTPA were compared (Table). The AUC of the ROC for an optimal value of Wells score between 1 and 2 was 0.54, suggesting nearly no discrimination.
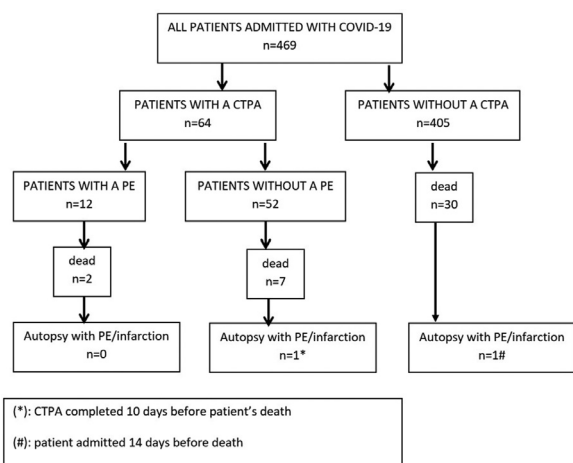
One patient without a CTPA died 14 days after admission and had evidence of subsegmental PE in the autopsy. One patient had autopsy evidence of subsegmental microinfarctions despite a negative CTPA 10 days earlier.

DISCUSSION

In our cohort, the radiologic incidence of PE was 19%. Current and prior evidence of deep vein thrombosis and serum D-dimer levels 5 times or more above the age-adjusted expected normal value predicted PE. The Wells score was significantly higher in the group with PE; however, 4 of the 12 patients with PE had a score of 0 points. The score value commonly recommended to evaluate for PE (>4) was more common among our patients with PE than those without.

The subjective component of the Wells score "Is PE the most likely diagnosis?" was not a good predictor in our series. As a rule of thumb, clinicians will answer "Yes" to this question when the chest x-ray is normal and the patient has other elements suggestive of PE, such as tachycardia and hypoxemia. Most patients admitted with COVID-19 have striking radiological abnormalities assumed to be the cause of such presentations. Moreover, this question, when positive, adds 3 points to the final score and has been criticized as being subjective and dependent on the accrual of points from other categories.[6] Finally, the Wells score altogether has been questioned regarding its ability to accurately predict PE in critically ill patients; consistent with this notion, in our cohort, the AUC of the ROC showed non-discriminatory values.[7]


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          ALL PATIENTS ADMITTED WITH COVID-19
                      n=469
                        |
          ┌─────────────┴─────────────┐
  PATIENTS WITH A CTPA         PATIENTS WITHOUT A CTPA
        n=64                          n=405
          |                             |
  ┌───────┴───────┐                     |
PATIENTS WITH A PE  PATIENTS WITHOUT A PE    dead
     n=12               n=52               n=30
       |                  |                  |
     dead               dead                 |
     n=2                 n=7                  |
       |                  |                  |
 Autopsy with PE/   Autopsy with PE/    Autopsy with PE/
 infarction         infarction         infarction
    n=0                n=1*               n=1#
```

(*): CTPA completed 10 days before patient's death

(#): patient admitted 14 days before death

Figure   Distribution of patients with coronavirus disease 2019 at Lyndon B. Johnson Hospital.

Table   Comparison of Patients With and Without Radiologic Evidence of Pulmonary Embolism (N = 64)

	Patients with PE (n = 12)	Patients without PE (n = 52)	P Value
Male sex, no., (%)	7 (58)	28 (52)	1.00
Age, mean (SD)	59 (12)	54 (17)	.27
Clinical current DVT, n, (%)	2 (17)	0 (0)	**.03**
Previous DVT, no., (%)	3 (25)	2 (4)	**.04**
Is PE the most likely diagnosis? no., (%)	4 (33)	5 (9)	0.06
Wells score >4 no., (%)	3 (25)	2 (4)	**.04**
Wells score, mean (SD), (range), μg/mL	3.13 (3.8) (0-10.5)	1.57 (1.3) (0-6)	**.02**
Serum D-dimer level, mean (SD), μg/ml	6.8 (4)	2.7 (4)	**.005**
D-dimer > age-adjusted normal value	n=10	n=46	
2 times, no., (%)	9 (90)	28 (61)	.14
5 times, no., (%)	8 (80)	13 (28)	**.004**
10 times, no., (%)	6 (60)	6 (13)	**.004**

DVT = deep vein thrombosis; PE = pulmonary embolism; SD = standard deviation.

Not surprisingly, the higher the serum D-dimer level, the more likely PE was observed. However, this may represent selection bias, because although not always documented in the records, elevated serum D-dimer may have been the reason to order the CTPA. Serum D-dimer elevation has been previously documented as a marker of severity, even predicting mortality in patients with COVID-19.[8,9]

Only the patients deemed by doctors as needing a CTPA (13% of those with COVID-19) were entered in the analysis. Although this fact limits our knowledge of how the Wells score would have performed in the remaining 87%, the AUC of the ROC supports our overall findings.

In conclusion, in our cohort, a Wells score above 4 was significantly associated with PE, but the sensitivity and specificity of the score were unreliable. Serum D-dimer elevation also predicted PE, but in the setting of COVID-19 this feature may represent the severity of disease, regardless of the existence of demonstrable thrombosis.

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