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DIAGNOSING PULMONARY EMBOLI: IMPORTANCE OF CLINICAL ASSESSMENT

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CLINICAL REPORT

ABSTRACT. BACKGROUND: PULMONARY EMBOLISM (PE) is a common condition that challenges physicians to make accurate and timely diagnosis. Clinicians frequently use their own experience to determine the pretest probability of PE, although in the last years scoring systems have been promoted as more reliable than subjective assessment. METHODS: This was a retrospective study of patients that were admitted with a suspected diagnosis of PE. There were 62 patients, 33 women and 29 men, aged 63.45 ± 19.65 years old. All patients were admitted with a suspected diagnosis of PE; all had a *D*-dimer test and a spiral chest computed tomography. RESULTS: In women older than 50 years of age (27 women, mean age 68.40 ± 20.00 years) the clinical score was predictive of the final diagnosis of PE (B = 0.689, $P < 0.05$). The probability of diagnosing PE in this group was correlated with the clinical score, so that at 1 point the probability was 3%, at 2 points the probability was 6.9%, at 3 points it increased to 12.9%, at 4 points 22.8%, at 5 points 37%, and at 6 points 54%. When each clinical variable and its predictive value to diagnose PE (Fisher exact test) were analyzed, it was found that only the clinical parameter of immobility or surgery within the last month were predictive of PE ($P = 0.003$). CONCLUSION: Our data showed that PE could be predicted only in women older than 50 years of age and only based on clinical parameters. *D*-dimer levels determined by an ELISA method (not by the VIDAS *D*-dimer method) did not predict or exclude PE in any group of patients. Larger prospective studies are needed to validate our findings.

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1. INTRODUCTION

Pulmonary embolism (PE) is a common condition that challenges physicians to make accurate and timely diagnosis. Clinicians frequently use their own experience to determine the pretest probability of PE, although in the last years scoring systems have been promoted as more reliable than subjective assessment. One of the widely used scoring systems is the Canadian Pulmonary Embolism Score (CPES) developed by Wells et al. [1-3]. The CPES is calculated from the weighted responses to six objective questions and one subjective question.

We evaluated the CPES in a cohort of patients that were admitted to the Internal Medicine Department because of a suspected diagnosis of PE and compared it with the *D*-dimer levels and the results of the chest spiral computed tomography (CT) angiography that was performed in every one of the patients that were admitted.

2. METHODS

STUDY DESIGN. This was a retrospective study of patients that were admitted with a suspected diagnosis of PE. There were 62 patients, 33 women and 29 men, aged 63.45 ± 19.65 years old. All patients were admitted with a suspected diagnosis of PE; all had a *D*-dimer test and a spiral chest CT.

CLINICAL SCORING. The clinical score was based on the Canadian Pulmonary Embolism Score (CPES). This score is composed of 6 objective questions and one subjective question. The 6 objective questions are:

(1) Does the patient have clinical signs or symptoms of deep vein thrombosis (DVT) (3 points)?

(2) Is the patient's heart rate greater than 100 beats/min (1.5 points)?

(3) Has the patient had surgery or been immobilized in the past 4 weeks (1.5 points)?

(4) Does the patient have a previous history of PE or DVT (1.5 points)?

(5) Has the patient had hemoptysis (1 point)?

(6) Does the patient have a malignancy that has been treated or palliated within the past six months (1 point)?

The one subjective question is: Are alternative diagnoses less likely than PE (3 points) [1-4]. The clinical score was rated so that up to 2 points it was considered "low probability"; 2-4 points – "moderate probability"; 4-6 points – "high probability".

BIOCHEMICAL ANALYSIS. *D*-Dimer in plasma combines with both biotinylated anti-*D*-dimer antibody and anti-*D*-dimer antibody conjugated to gold sol particles to form a "sandwich". The *D*-dimer assay is manufactured by Roche Diagnostics GmbH, D-68298 Mannheim, Germany. It works like the Simplify *D*-dimer method.

COMPUTED TOMOGRAPHY (CT). We used a Multi detector-Row CT because the advent of multi detector-row scanners has improved the visualization of the segmental and sub segmental pulmonary arteries [5-7]. Chest CT angiography was our "gold standard" for diagnosing PE.

3. RESULTS

The study was a retrospective study. Sixty-two patients were admitted to the hospital in the last 12 months with a suspected diagnosis of PE. All underwent a chest CT angiography. Out of 62 patients, 8 were diagnosed as having PE (12.9%) by chest helical CT angiography.

Alternative diagnoses included: 15 patients came to the hospital because of chest pain, 27 patients had pneumonia or upper respiratory infection, 4 patients had lung metastases, and 15 patients had acute coronary events as the presenting symptom.

Mean age of patients without PE was 62.90 ± 19.28 years old with a clinical score of 2.2 ± 2.0 and *D*-dimer level of 1.56 ± 1.07 μg/mL. Eight patients had PE (6 women and 2 men; age 67.12 ± 23.04 years old), the clinical score was 3.5 ± 2.08, and the *D*-dimer level was 2.2 ± 0.96 μg/mL.

Thirty-three women took part in the study, 27 without PE and 6 women with PE. Among women without PE (mean age 68.41 ± 20.01 years old), the clinical score was 2.51 ± 2.19 and *D*-dimer level was 1.42 ± 0.89 μg/mL. Among women with PE

TABLE 1. GENDER AND PE.

PARAMETERS	WOMEN			MEN			TOTAL		
	PE (N = 6)	NON-PE (N = 27)	TOTAL (N = 33)	PE (N = 2)	NON-PE (N = 27)	TOTAL (N = 29)	PE (N = 8)	NON-PE (N = 54)	TOTAL (N = 62)
AGE	69.17 (25.80)	68.41 (20.01)	68.55 (20.72)	61.00 (16.97)	57.41 (17.18)	57.66 (16.89)	67.13 (23.04)	62.91 (19.29)	63.45 (9.65)
CLINICAL SCORE	4.42 (1.36)	2.51 (2.19)	2.86 (2.18)	0.75 (1.06)	1.93 (2.01)	1.85 (1.97)	3.50 (2.09)	2.22 (2.10)	2.39 (2.13)
D-DIMER	2.18 (1.15)	1.42 (0.89)	1.57 (0.97)	2.25 (0.49)	1.70 (1.29)	1.74 (1.26)	2.20 (0.96)	1.57 (1.13)	1.66 (1.12)

NOTE: The numbers in parentheses are standard deviations (SD).

TABLE 2. AGE AND PE.

PARAMETERS	ABOVE AGE 50			BELOW AGE 50			TOTAL		
	PE (N = 6)	NON-PE (N = 27)	TOTAL (N = 33)	PE (N = 2)	NON-PE (N = 27)	TOTAL (N = 29)	PE (N = 8)	NON-PE (N = 54)	TOTAL (N = 62)
AGE	78.33 (6.62)	71.61 (12.00)	72.47 (11.62)	33.50 (21.92)	35.46 (9.41)	35.20 (10.52)	67.13 (23.04)	62.91 (19.29)	63.45 (19.65)
CLINICAL SCORE	3.92 (2.25)	2.40 (2.06)	2.60 (2.12)	2.25 (1.06)	1.65 (2.24)	1.73 (2.10)	3.50 (2.09)	2.22 (2.10)	2.39 (2.13)
D-DIMER	2.32 (1.04)	1.62 (1.18)	1.70 (1.17)	1.90 (0.99)	1.39 (0.96)	1.49 (0.93)	2.20 (0.96)	1.57 (1.13)	1.66 (1.12)

NOTE: The numbers in parentheses are standard deviations (SD).

(mean age 69.17 ± 25.80 years old), the clinical score was 4.42 ± 1.36 and mean *D*-dimer level was 2.18 ± 1.15 μg/mL (TABLE 1).

Among men without PE (mean age 57.41 ± 17.18 years old), the clinical score was 1.93 ± 2.01 and the *D*-dimer level was 1.70 ± 1.29 μg/mL. There were 2 men with PE (mean age 61.00 ± 16.97 years old); their clinical score was 0.75 ± 1.06, and the *D*-dimer level was 2.25 ± 0.49 μg/mL (TABLE 1).

We also analyzed the data according to age, separating patients below and above 50 years old. Patients older than 50 and without PE (41 patients, mean age 71.61 ± 12.00 years old) – their clinical score was 2.40 ± 2.06 and their *D*-dimer level was 1.62 ± 1.18 μg/mL. Those with PE (6 patients, mean age 78.33 ± 6.62 years old) – their clinical score was 3.92 ± 2.25 and the *D*-dimer level was 2.32 ± 1.04 μg/mL (TABLE 2). Patients younger than 50, those without PE (13 patients, mean age 35.46 ± 9.41 years old), their clinical score was 1.65 ± 2.24, and the *D*-dimer level was 1.39 ± 0.96 μg/mL. Those patients who had PE and were younger than 50 years old (2 patients, mean age of 33.50 ± 21.92 years old), their clinical score was 2.25 ± 1.06 and the *D*-dimer level was 1.90 ± 0.99 μg/mL (TABLE 2).

STATISTICAL ANALYSIS. Six out of eight PE patients were women (mean age = 69.16 ± 25.79 years). A logistic regression analysis found that both independent parameters (*D*-dimer and clinical score) do not explain and predict the diagnosis of PE (B = 0.586, $P > 0.05$ for clinical score, and B = 1.072, $P > 0.05$ for *D*-dimer level).

However, in women older than 50 years old (27 women, mean age 68.4 ± 20.0 years) the clinical

TABLE 3. LOGISTIC REGRESSION ANALYSIS OF THE CLINICAL SCORE AND PREDICTION OF PE.

CLINICAL SCORE	PROBABILITY
0	0.01
1	0.03
1.5	0.05
2	0.07
2.5	0.09
3	0.12
3.5	0.17
4	0.22
4.5	0.29
5	0.37
5.5	0.45
6	0.54
6.5	0.62
7	0.70

score was predictive of the final diagnosis of PE (B = 0.689, $P < 0.05$). The probability of diagnosing PE in this group was correlated with the clinical score, so that at 1 point the probability was 3%, at 2 points the probability was 6.9%, at 3 points it increased to 12.9%, at 4 points – 22.8%, at 5 points – 37%, and at 6 points – 54% (TABLE 3).

When we analyzed each clinical variable and its predictive value to diagnose PE (Fisher exact test), it was found that only the clinical parameter of immobility or surgery within the last month were predictive of PE ($P = 0.003$). All other parameters were not statistically significant and did not predict PE (TABLE 4).

DISCUSSION

We found that PE could be predicted in women older than 50 years old by the clinical score alone. *D*-dimer levels did not add to the ability to predict the right diagnosis.

Clinicians frequently use their experience to determine the pretest probability of PE, although scoring systems are promoted as being more reliable. The Canadian Pulmonary Embolism Score (CPES) combines 6 objective questions and 1 subjective question. Several studies stressed the importance of the clinical judgment and the reliability of Wells Criteria [8] to predict patients with suspected PE. Several studies have demonstrated the fact that the clinical score (CPES) is quite accurate in predicting PE [4,8]. The sensitivity and the negative predictive value of the CPES were similar to the sensitivity and negative predictive value of the subjective question alone. In multivariate analysis nearly all of the predictive value of the CPES was derived from the subjective question [4]. The one subjective question was: are alternative diagnoses less likely than PE? This question received 3 points.

The literature suggests that *D*-dimer is useful in predicting patients suspected of having PE and who have a low pretest probability of disease [8]. In a prospective diagnostic study 425 patients with pleuritic chest pain were recruited and a simplify *D*-dimer test was performed for each patient. The calculated sensitivity of Simplify *D*-dimer for PE was 81.8% and a specificity of 74.2%. It was concluded that the simplified *D*-dimer test is not sufficiently sensitive to exclude the diagnosis of PE in all patients presenting to the emergency room with pleuritic chest pain [9]. On the other hand, *D*-dimer levels that were measured by fast enzyme-linked immunoabsorbent assay (ELISA) [VIDAS *D*-dimer test] in the emergency room, the sensitivity and the negative predictive values were 96.4% and 96.8%, respectively, at a cut off of 0.5 μg/mL. According to this study thrombo-embolism could be excluded if plasma levels of *D*-dimer levels measured by fast ELISA were below 0.5 μg/mL because of the high negative predictive value at this cut off [10].

In our study the *D*-dimer level was not measured by the VIDAS *D*-dimer method but instead we used a method called the CARDIAC *D*-dimer Assay (described before in the methods section, also).

GENDER EFFECT. It is a known fact that women who suffer coronary artery disease present with different symptoms compared with men. The older the patient the more "atypical" chest pain she may have. According to the CURE trial, compared to

TABLE 4. FREQUENCIES AND FISHER'S EXACT TEST OF RISK FACTORS TO PE.

RISK FACTORS	VALUE	PE	NON-PE	P VALUE
CLINICAL DVT	0	5 (100%)	22 (100%)	-
	3	0 (0%)	0 (0%)	
DISEASE LESS LIKELY	0	1 (20%)	12 (55%)	0.186
	3	4 (80%)	10 (45%)	
HEART RATE > 100/MIN	0	5 (100%)	18 (82%)	0.417
	1.5	0 (0%)	4 (18%)	
IMMOBILIZATION OR SURGERY IN LAST MONTH	0	0 (0%)	17 (77%)	0.003
	1.5	5 (100%)	5 (23%)	
PREVIOUS DVT/PE	0	5 (100%)	20 (91%)	0.658
	1.5	0 (0%)	2 (9%)	
HEMOPTYSIS	0	4 (80%)	22 (100%)	0.185
	1	1 (20%)	0 (0%)	
MALIGNANCY	0	2 (40%)	18 (82%)	0.091
	1	3 (60%)	4 (18%)	

men, high risk women with acute coronary syndrome undergo less coronary angiography, angioplasty, and CABG surgery, and while they do not have higher incidence cardiovascular death, recurrent MI, or stroke, they suffer an increased rate of refractory ischemia and re-hospitalization [11]. In PE, there is no known special clinical presentation for women, and based on large epidemiological studies there is no gender effect for PE or DVT [12]. In our cohort we found that the majority of the PE patients were women, and only in this group we could predict PE according to the clinical score.

PE could be predicted only in women older than 50 years old and only by the clinical score. *D*-dimer levels could be used to predict or to exclude PE.

In summary, this is a retrospective study with relatively smaller sample size. Our data showed that PE could be predicted only in women older than 50 years old and only by using the clinical parameter. The *D*-dimer laboratory method used in the present study is not identical to the VIDAS *D*-dimer test. *D*-dimer levels done by an ELISA method (not the VIDAS *D*-dimer method) did not predict or exclude PE in any group of patients. Larger prospective studies may be needed to validate our findings.

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