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RESEARCH ARTICLE

The Accuracy of D-Dimer in Ruling Out Pulmonary Embolism in Low-Risk ED Patients: A Prospective Evaluation

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Abstract: ***Background:*** Pulmonary embolism (PE) is a severe disorder related to significant death and morbidity. Additionally, as it has nonspecific clinical manifestations and lacks a particular auxiliary examination, pulmonary embolism is related to elevated rates of missed diagnoses and misdiagnosis, which was a prevalent cause of medical disputes. Consequently, it is essential to attain a precise and early identification of pulmonary embolism. ***Aim:*** To assess the diagnostic accuracy of D-dimer in ruling out PE among emergency department (ED) cases, particularly those with low clinical probability. ***Patients and methods:*** This was prospective observational research conducted on 350 cases to evaluate the diagnostic accuracy of D-dimer testing in excluding PE among cases presenting to the emergency department with suspected acute pulmonary embolism, particularly focusing on those classified as low clinical probability. ***Results***: The mean age was 60.4 years; 57.4% were female. PE prevalence was 29.7% overall and 16.5% in the low-probability group (n=115). For all patients, D-dimer showed 100% sensitivity, 44.2% specificity, 46.6% PPV, and 100% NPV. In low-probability patients, sensitivity was 0%, specificity 42.7%, PPV 0%, and NPV 68.3%. **Conclusion:** D-dimer effectively rules out PE in the general ED population but has limited utility in low-risk patients, emphasizing the need for integrated clinical assessment.

Keywords: Pulmonary Embolism, D-Dimer, Wells Score.

INTRODUCTION

PE is a serious condition related to significant death and morbidity. Furthermore, as it lacks a specific auxiliary examination and has no specific clinical manifestations, pulmonary embolism is related to elevated rates of missed diagnoses & misdiagnosis, which was a prevalent source of medical disputes. Consequently, it is essential to obtain a precise and early identification of PE **(1)**.

PE is a severe condition characterized by a clot in a systemic blood vessel, typically a deep vein of the lower extremity, that migrates to the lung circulation, resulting in blockage and preventing distal blood flow **(2)**.

Risk factors for the progress of DVT or PE can be summarized by Virchow's triad: damage to the endothelial cells (catheterization, surgery, and trauma), hypercoagulability (obesity, malignancy, inflammatory conditions or severe infection, pharmacological agents, pregnancy, & hereditary coagulation disorders), and venous stasis (immobility). Cases with suspected acute pulmonary embolism typically exhibit dyspnea, low-grade fever, tachypnea, pleuritic chest pain, cough, tachycardia, and/or hemoptysis **(3).**

The application of clinical probability evaluation and D-dimer testing has demonstrated a reduction in the application of CT angiography in cases suspected of pulmonary embolism. Pulmonary embolism is excluded with a negative D-dimer test and a low or moderate clinical probability **(4)**.

D-dimer is a sensitive assay for pulmonary embolism, and a negative outcome may safely rule out pulmonary embolism in cases with low or intermediate clinical probability, thus obviating the requirement for imaging. D-dimer is a non-specific assay frequently yielding positive results even in the absence of pulmonary embolism. Traditionally, a reduced D-dimer threshold was utilized to classify data as positive or negative in order to enhance negative predictive value and sensitivity for thrombosis. Nevertheless, utilizing a reduced D-dimer threshold correlates with diminished specificity, hence constraining the clinical application of D-dimer testing, as limited cases will have a negative result even in the absence of pulmonary embolism **(5)**.

D-dimer levels rise approximately linearly with age, thereby diminishing the specificity of the unadjusted D-dimer test and limiting its efficacy in excluding pulmonary embolism in older cases. Many investigations have examined the efficacy and safety of age-adjusting the D-dimer cutoff levels utilized to safely exclude pulmonary embolism **(6)**.

The Geneva score and the Wells score the 1st version of the Geneva score incorporated non-clinical elements, demanding an X-ray of the chest and an arterial blood gas sample, hence constraining its widespread application among cases. A modified version comprising only clinical items has been developed and verified to address this constraint, designated as the 'Revised Geneva Score **(7)**.

The research aimed to evaluate the diagnostic precision of D-dimer in excluding PE among emergency

department cases, particularly those with low clinical probability.

MATERIAL AND METHODS

This was prospective observational research performed to assess the diagnostic accuracy of D-dimer testing in excluding pulmonary embolism among cases presenting to the emergency department with suspected acute PE, particularly focusing on those classified as low clinical probability. A total of 350 cases has been involved after meeting the inclusion criteria. Clinical probability was stratified using the Wells score, with low probability defined as a score of ≤1. This subgroup consisted of 115 patients.

Inclusion criteria: Age ≥ 18 years, presentation to the ED with symptoms indicative of PE (e.g., pleuritic chest pain, sudden dyspnea, tachypnea, hemoptysis, syncope, or signs of deep vein thrombosis), and assessed as **low clinical probability** for PE by Wells score (≤ 1 point).

Exclusion criteria: Cases have been excluded from the research if they have kidney insufficiency, hypersensitivity to IV contrast, pregnancy, or hemodynamic instability.

Methods

All patients have been subjected to the following:

Full medical history taking, stressing risk factors and symptoms indicative of pulmonary embolism; **physical examinations:** local and general chest examination for signs of pulmonary embolism and examination of the leg for signs of DVT; and **investigational studies: Routine laboratory investigations:** Complete blood count (CBC), kidney and liver functions, and arterial blood gases.

The Wells score has been determined for each case according to the following criteria: clinical symptoms and signs of DVT (3 points), pulmonary embolism as the most probable diagnosis (3 points), heart rate exceeding 100 bpm (1.5 points), surgery or immobilization within the preceding four weeks (1.5 points), history of DVT/PE (1.5 points), hemoptysis (1 point), & malignancy (1 point). Scores were classified as low (≤1), intermediate (2-6), or high (>6); however, no cases in this cohort exceeded a score of 5.

D-dimer Testing: Arterial blood has been utilized in conjunction with the Simplify D-dimer assay. Qualified respiratory therapists drew blood, often from the radial artery, collecting one milliliter in an arterial blood gas syringe comprising lithium-heparin. The D-dimer assay was subsequently conducted in the emergency department by the respiratory therapist utilizing a written protocol aligned with manufacturer recommendations.

CT pulmonary angiography: A standard CTPA protocol employs multidetector CT with an initial scout (topogram) from the lung apices to the diaphragm. Contrast is administered via a peripheral intravenous line, commonly 20–30 mL of iodinated contrast at 3–4 mL/s, followed by a saline flush. Scan timing is optimized using either bolus tracking (triggered at ~100 HU in the pulmonary artery) or a test bolus to determine peak enhancement. Acquisition uses thin slices (1–3 mm) during a single breath-hold, with low-kVp techniques (80–100 kVp) increasingly utilized to decrease radiation dose without compromising diagnostic image quality.

Ethical Consideration

The information obtained from participants is confidential. Prior to the participants' admission to the research, the study's aim, nature, and risk-benefit evaluation had been clarified to them. Informed consent has been obtained.

Statistical Analysis

Information has been analyzed applying the Statistical Package for the Social Sciences (SPSS) software application. Information has been presented as percentages and numbers for qualitative factors and as mean + SD for the quantitative information. The **significance level:** A P value under 0.05 denotes statistically significant outcomes.

RESULTS

Table (1): Demographic data in the examined group.

	All Patients N=350		***Low Probability N=115***	
	Mean	*±SD*	*Mean*	*±SD*
Age (years)	60.4	16.9	64.7	16.7
	N	*%*	*N*	*%*
Sex				
Female	201	57.4%	60	52.2%
Male	149	42.6%	55	47.8%
Medical history				
Chronic obstructive lung disease	59	16.9%	28	24.3%

Diabetes mellitus	59	16.9%	27	23.5%
Coronary artery disease	38	10.9%	21	18.3%
Malignancy	107	30.6%	13	11.3%
Cerebrovascular event	7	2%	5	4.3%
Hypertension	148	42.3%	62	53.9%
Congestive heart failure	46	13.1%	26	22.6%
Thromboembolic disease	50	14.3%	5	4.3%
Autoimmune disease	23	6.6%	5	4.3%
Pregnancy	5	1.4%	2	1.7%

Table 1 shows that the mean age of all cases was 60.4 years, compared to 64.7 years in the low probability group. Among all patients, 57.4% were women and 42.6% were men, while in the low probability group, 52.2% were women and 47.8% were men. The prevalence of comorbidities in all patients versus the low probability group was chronic obstructive lung disease: 16.9% vs. 24.3%; diabetes mellitus: 16.9% vs. 23.5%; coronary artery disease: 10.9% vs. 18.3%; malignancy: 30.6% vs. 11.3%; cerebrovascular event: 2.0% vs. 4.3%; hypertension: 42.3% vs. 53.9%; congestive heart failure: 13.1% vs. 22.6%; thromboembolic disease: 14.3% vs. 4.3%; autoimmune disease: 6.6% vs. 4.3%; and pregnancy: 1.4% vs. 1.7%.

Table (2): Clinical findings in the studied group.

	All Patients N=350		***Low Probability N=115***	
	N	*%*	*N*	*%*
Clinical findings				
Chest pain	139	39.7%	43	37.4%
Dyspnea	313	89.4%	98	85.2%
Syncope	13	3.7%	5	4.3%
Hemoptysis	26	7.4%	2	1.7%
Signs of deep vein thrombosis	41	11.7%	3	2.6%

Table 2 shows that among all patients, the most common clinical finding was dyspnea, reported in 89.4%, compared to 85.2% in the low probability group. Chest pain was present in 39.7% of all patients and 37.4% of those with low probability. Syncope occurred in 3.7% of all patients versus 4.3% in the low probability group. Hemoptysis was observed in 7.4% of all patients but only 1.7% in the low-probability group. Signs of deep vein thrombosis were noted in 11.7% of the overall group, compared to 2.6% in the low probability group.

Table (3): Wells scale in the studied group.

	All Patients N=350		***Low Probability N=115***	
	N	*%*	*N*	*%*
Wells scale				
0	26	7.4 %	26	22.6%
1	89	25.4%	89	77.4%
2	131	37.4%	-	
3	86	24.6%	-	
4	16	4.6%	-	
5	2	0.6%	-	

Table 3 shows that based on the Wells scale, among all patients, the most frequent scores were 2 points (37.4%), followed by 1 point (25.4%), 3 points (24.6%), and 0 points (7.4%). Scores of 4 and 5 were less common, reported in 4.6% and 0.6% of patients, respectively. In the low probability group, 77.4% of patients had a score of 1, while 22.6% had a score of 0; no patients in this group had scores of 2 or higher

Table (4): Outcome in the studied group.

	All Patients N=350		***Low Probability N=115***	
	N	*%*	*N*	*%*
Outcome				
Pulmonary embolism	104	29.7%	19	16.5%
Death	18	5.1%	2	1.7%

Table 4 shows that among all patients, pulmonary embolism was confirmed in 29.7%, compared to 16.5% in the low probability group. The overall mortality rate was 5.1%, while it was lower in the low-probability group at 1.7%.

Table 5: Performance of D-dimer Test for Diagnosing Pulmonary Embolism in All Patients.

D-dimer	*Pulmonary Embolism for all patients*		*Total*
	Positive	*Negative*	
Positive	104	219	223
Negative	0	27	27
Total	104	246	
Sensitivity	100%		
Specificity	44.2%		
PPV	46.6%		
NPV	100%		

Table 5 illustrates the specificity and sensitivity of the D-dimer test for detecting PE. The sensitivity is 100%, indicating that the test identified all true positive cases. However, the specificity is relatively low at 44.2%, meaning there are many false positive results. The positive predictive value (PPV) is 46.6%, and the negative predictive value (NPV) is 100%, confirming that a negative D-dimer test efficiently excludes pulmonary embolism.

Table 6: Performance of D-dimer Test for Diagnosing PE for Low Probability Population.

D-dimer	*Pulmonary Embolism for Low Probability Population*		*Total*
	Positive	*Negative*	
Positive	0	55	55
Negative	19	41	60
Total	19	96	115
Sensitivity	0%		
Specificity	42.7%		
PPV	0%		
NPV	68.3%		

Table 6 illustrates the diagnostic accuracy of the D-dimer test among cases with reduced clinical probability of pulmonary embolism. The sensitivity is 0%, indicating the test failed to identify any true positive cases in this group. Specificity is 42.7%, reflecting a moderate rate of correctly identifying those without the condition. The positive predictive value (PPV) is 0%, showing no true positives among positive test outcomes, while the NPV is 68.3%.

DISCUSSION

Our research stated that the mean age of all cases was 60.4 years, compared to 64.7 years in the low probability group. Among all patients, 57.4% were women and 42.6% were men, while in the low probability group, 52.2% were women and 47.8% were men. The prevalence of comorbidities in all patients versus the low probability group was chronic obstructive lung disease: 16.9% vs. 24.3%; diabetes mellitus: 16.9% vs. 23.5%; coronary artery disease: 10.9% vs. 18.3%; malignancy: 30.6% vs. 11.3%; cerebrovascular event: 2.0% vs. 4.3%; hypertension: 42.3% vs. 53.9%; congestive heart failure: 13.1% vs. 22.6%; thromboembolic disease: 14.3% vs. 4.3%; autoimmune disease: 6.6% vs. 4.3%; and pregnancy: 1.4% vs. 1.7%.

Kearon et al. (8) aimed to evaluate whether a variable D-dimer threshold, determined by clinical probability, may safely exclude an identification of pulmonary embolism without additional imaging in a cohort of 3,133 cases exhibiting signs or symptoms of PE, of which 2,017 were involved in the research. The mean age was fifty-two, with two-thirds being female. During clinical evaluation, eighty-seven percent of cases exhibited a low probability.

Kline et al. (9) aimed to determine whether a D-dimer assay can efficiently exclude PE via yielding a posttest probability of pulmonary embolism under one percent in low-risk, symptomatic ED cases. Their research encompassed 2,302 cases (mean age, 45 ± 16 years; thirty-one percent men), of whom 108 were diagnosed with PE.

Our study found that among all patients, the most common clinical finding was dyspnea, reported in 89.4%, compared to 85.2% in the low probability group. Chest pain was present in 39.7% of all patients and 37.4% of those with low probability. Syncope occurred in 3.7% of all patients versus 4.3% in the low probability group. Hemoptysis was observed in 7.4% of all patients but only 1.7% in the low-probability group. Signs of deep vein thrombosis were noted in 11.7% of

the overall group and 2.6% in the low probability group.

In the research conducted by Van der Hulle et al (10)., the objective was to assess a new and simplified diagnostic strategy for suspected acute pulmonary embolism. Throughout the three-month monitoring, eighteen cases were identified with symptomatic venous thromboembolism (0.61%, ninety-five percent CI 0.36–0.96).

Our study found that, based on the Wells scale, among all patients, the most frequent scores were 2 points (37.4%), followed by 1 point (25.4%), 3 points (24.6%), and 0 points (7.4%). Scores of 4 and 5 were less common, reported in 4.6% and 0.6% of patients, respectively. In the low probability group, 77.4% of patients had a score of 1, while 22.6% had a score of 0; no patients in this group had scores of 2 or higher.

Consistent with our research, Harringa et al. (11) aimed to evaluate the efficacy of D-dimer testing in eliminating the requirement for cross-sectional imaging in cases categorized as "non-high risk" for pulmonary embolism. They stated a significantly greater occurrence of PE in the high-risk group in comparison with the "non-high-risk" group when stratified via the Wells' Score (p-value equal to 0.03).

Furthermore, (12) aimed to evaluate the clinical diagnostic efficacy of the revised Geneva score, the Wells score, & each of them combined with D-dimer for suspected pulmonary embolism in aged cases. The Wells score exhibited a PPV of 65.8%.

Our research found that among all patients, pulmonary embolism was confirmed in 29.7%, compared to 16.5% in the low probability group. The overall mortality rate was 5.1%, while it was lower in the low-probability group at 1.7%.

Consistent with our research, Chaari et al. (13) aimed to evaluate the efficacy of the Wells score, revised Geneva score, and age-adjusted D-dimer in identifying pulmonary embolism in critically diseased cases. Sixty-seven cases have been involved. Pulmonary embolism has been confirmed in twenty-seven cases, constituting 40.3% of the total.

Gupta et al. (14) aimed to evaluate the effectiveness of clinical risk algorithms and a quantitative immunoturbidimetric d-dimer assay in cases of pulmonary computed tomography angiography for suspected acute pulmonary embolism. The study excluded 118 cases due to the absence of a D-dimer assay, while 281 cases have been categorized as having a low clinical probability of pulmonary embolism.
Our study reported on the specificity and sensitivity of the D-dimer test for detecting PE. The sensitivity is 100%, indicating that the test identified all true positive cases. However, the specificity is relatively low at 44.2%, meaning there are many false positive results. The PPV is 46.6%, and the NPV is 100%, confirming that a negative D-dimer test effectively rules out PE.
In agreement with our study, Harringa et al., (11) stated that D-dimer testing had one hundred percent sensitivity and NPV.

With regard to Kline et al. (9), the D-dimer test exhibited an overall sensitivity of 80.6% (ninety-five percent CI, 71.8 to 87.5%) and a specificity of 72.5% (ninety-five percent CI, 70.6 to 74.4%).

Patel et al. (15) conducted a systematic assessment of the D-dimer assay's performance, revealing pooled estimations of sensitivity at 0.97 (ninety-five percent confidence interval [CI], 0.96-0.98) and specificity at 0.41 (ninety-five percent CI, 0.36-0.46).

Our study reported illustrated the diagnostic accuracy of the D-dimer test among cases with low clinical probability of PE. The sensitivity is 0%, indicating the test failed to identify any true positive cases in this group. Specificity is 42.7%, reflecting a moderate rate of correctly identifying those without the condition. The PPV is 0%, showing no true positives among positive test results, while the NPV is 68.3%.

In contrast with our study, Adrita (16) aimed to evaluate the diagnostic accuracy of D-dimer testing in ruling out pulmonary embolism among low-risk emergency department cases. The pooled sensitivity & specificity of D-dimer testing (500 nanogram per milligram threshold) in low-risk patients were 97.8% (95% CI: 95.9-98.9%) and 54.7% (ninety-five percent CI: 51.2-58.1%), respectively. The NPV was 99.7% (ninety-five percent CI: 99.4-99.9%).

Also, Gupta et al., (14) in the low clinical probability group, the D-dimer assay demonstrated a sensitivity of 100% and an NPV of one hundred percent, indicating that all true cases of pulmonary embolism were detected and that a negative result effectively ruled out the condition. However, the specificity was only 25%, reflecting a high rate of false positives.

Additionally, Kline et al., (17) aimed to avoid unnecessary diagnostic testing in ED cases with suspected PE by safely recognizing cases that have a reduced probability of PE, applyingthe rule in the low-risk sensitivities of 96% and 100%, respectively.

CONCLSION

The study showed that the D-dimer test demonstrated excellent performance in ruling out pulmonary embolism among the overall patient population, with a sensitivity and NPV of 100%, ensuring that no cases were missed when the test result was negative. However, its specificity was relatively low (44.2%), leading to a high rate of false positives and limiting its

utility as a confirmatory tool. In contrast, among cases with low clinical probability of pulmonary embolism, the test's diagnostic value was markedly reduced, with a sensitivity of 0% and NPV of only 68.3%, indicating poor ability to detect true positive cases in this subgroup. These results suggest that while D-dimer testing is greatly beneficial for excluding pulmonary embolism in the general emergency department setting, it has limited diagnostic benefit in low-risk patients, highlighting the requirement for careful integration with clinical assessment tools like the Wells score to guide decision-making.

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