DIAGNOSTIC ACCURACY OF D-DIMER FOR PULMONARY EMBOLISM: DETERMINATION OF AN OPTIMAL HIGH CUT-OFF VALUE

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Abstract: It might be difficult to diagnose acute pulmonary embolism (APE) in a timely manner since it is a potentially lethal illness. The preferred modality is now computed tomography pulmonary angiography (CTPA), which adds to the growing strain on CT scanners in emergency rooms.Objective: To evaluate the diagnostic role of D-dimer and determine an optimal cut-off value for predicting PE and retain a high sensitivity and negative predictive value (NPV) while lowering the need for CTPA.Methods: A retrospective analysis was conducted on 70 patients. Demographic data, D-dimer levels, and PE status were analyzed. ROC curve analysis was used to determine the optimal cut-off value, and sensitivity, specificity, PPV, and NPV were calculated. The results showed that the mean age was 57.8 ± 18.86 years, with 71.4% females. PE was present in 31.4% of patients. The optimal D-dimer cut-off value was 3500 ng/ml, yielding a sensitivity of 90.9%, specificity of 95.8%, PPV of 90.9%, and NPV of 95.8%. Higher D-dimer levels were associated with proximal PE. It is concluded that D-dimer demonstrated excellent diagnostic accuracy for PE. A higher cut-off value improved specificity while maintaining high sensitivity, supporting its clinical utility in both ruling in and ruling out PE.
Keywords: Computed tomography; pulmonary embolism; sensitivity

1. Introduction

Pulmonary embolism (PE) is a potentially fatal cardiovascular disorder caused by thrombotic emboli that clog pulmonary arteries, the majority of which originate from deep vein thrombosis. With a nonspecific clinical presentation ranging from severe dyspnea to sudden cardiac death, it is a major source of morbidity and mortality worldwide (Konstantinides et al., 2019; Stein et al., 2004). Early and precise identification is thus crucial to reducing negative outcomes; nevertheless, the diagnostic procedure remains difficult due to symptoms that overlap with other cardiopulmonary illnesses (Righini et al., 2008).

A frequently utilized biomarker in the diagnostic workup of suspected PE is D-dimer, a fibrin breakdown product produced during clot breakup. D-dimer testing is particularly helpful in ruling out PE in patients with a low to intermediate clinical likelihood because of its high sensitivity. In the past, a fixed cut-off value of 500 ng/mL was employed; however, this threshold has low specificity, especially in older patients and those with comorbid conditions like cancer, infection, or recent surgery, leading to a high rate of false-positive results and needless imaging studies (Schouten et al., 2013). Several approaches have been put forth in recent years to improve D-dimer testing's diagnostic efficacy. These include clinical probability-adapted thresholds and age-adjusted cut-off values used in the PEGeD and YEARS algorithms (Righini et al., 2014; van der Hulle et al., 2017; Kearon et al., 2019). By removing the necessity for computed

tomography pulmonary angiography (CTPA) and reducing patient exposure to radiation and contrast agents, these methods aim to maintain D-dimer's high sensitivity while boosting specificity. Despite these advances, there is ongoing discussion about the best D-dimer cut-off value for various patient demographics and therapeutic contexts. The purpose of this study is to examine and establish the best D-dimer threshold for detecting pulmonary embolism, with an emphasis on balancing diagnostic accuracy, safety, and clinical application.

2. Materials and Methods

The study was designed as a retrospective observational study, with the targeted respondents being adults (>18 years) presenting with clinical suspicion of PE at the emergency department. Computed Tomography Pulmonary Angiography (CTPA) was performed at the department of radiology at Almogrief Hospital in Ajdabia, Libya. The inclusion criteria focused on patients presenting with symptoms suggestive of PE (dyspnea, chest pain, hemoptysis, tachycardia), and the exclusion criteria included known anticoagulation therapy before presentation. The intended sample size was 50 participants. The procedures used included D-dimer testing, where for D-dimer positive or high clinical probability cases, CTPA was performed. Data analysis involved assessing sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of D-dimer. Additionally, ROC curve analysis was conducted for cutoff optimization.

3. Results analysis

Total of 70 patients were included in the final analysis. The mean age of the study population was 57.8 ± 18.86 years, with a median of 55 years (range: 24–99 years). Females constituted the majority of the sample (71.4%), while males accounted for 28.6%.

Table 1. Percentage of gender prediction, and Pulmonary Embolism confirmation

Variable	Category	Frequency (N)	Percentage (%)
Gender	Female	25	71.4%
	Male	10	28.6%
Presence of PE	No	24	68.6%
	Yes	11	31.4%

Pulmonary embolism (PE) was confirmed in 22 patients (31.4%), whereas 48 patients (68.6%) were PE-negative as shown in (Table 1). Receiver Operating Characteristic (ROC) curve analysis demonstrated excellent diagnostic accuracy of D-dimer in predicting pulmonary embolism (Table .2) The optimal cut-off value was identified at 3500 ng/ml, providing a sensitivity of 90.9% and a specificity of 95.8%.

Table 2. Diagnostic Performance of D-Dimer

Parameter	Value
Cut-off value	3500 ng/ml
Sensitivity	90.9%
Specificity	95.8%
PPV	90.9%
NPV	95.8%

The positive predictive value (PPV) was 90.9%, while the negative predictive value (NPV) was 95.8%, indicating strong reliability of the test in both ruling in and ruling out PE. Higher D-dimer levels were observed in patients with more proximally located pulmonary emboli, suggesting a positive association between clot burden and D-dimer concentration.

Table .3 Correlation between PE Location and D-Dimer

Location of PE	Mean D-Dimer Level (ng/ml)
Right main pulmonary	6840.0
Left 2nd & 3rd order	6300.0
2nd & 2rd order	6234.0
Bilateral 1st & 2nd order (Saddle)	6123.5
Bilateral 2nd & 3rd order	5678.0
2nd & 3rd order	4637.0
3rd order	4200.0
1st, 2nd & 3rd order (Saddle)	3500>0

Diagnostic Performance of D-DimerA Receiver Operating Characteristic (ROC) analysis was performed to determine the effectiveness of D-Dimer levels in predicting the presence of PE. Area under the Curve (AUC): 0.9792 An AUC close to 1.0 indicates excellent diagnostic accuracy. Optimal Cut-off Value: 3500 ng/ml Based on Youden's Index (maximizing Sensitivity + Specificity). Sensitivity: 90.91%, Specificity: 95.83%> Furthermore, correlation between PE Location and D-Dimer. Table (3) shows the mean D-Dimer levels categorized by the specific site/location of the pulmonary embolism. Generally, more central or extensive involvements (e.g., main pulmonary or saddle) tend to be associated with higher D-Dimer levels.

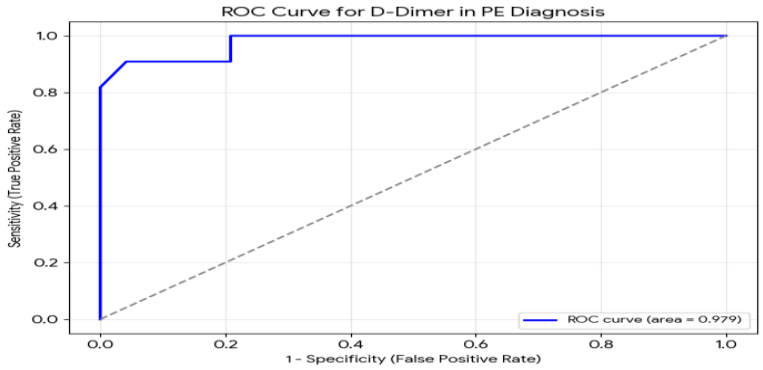

Figure 1. Receiver operating characteristic curve for PE diagnosis by D-dimer level (ng/mL)

4. Discussion

Based on the statistical analysis of the 70 cases in the dataset, the following academic discussion explores the diagnostic utility of D-Dimer, the impact of demographic variables, and the clinical implications of the findings.

4.1. Diagnostic Efficacy of D-Dimer

The ROC analysis yielded an area under the Curve (AUC) of 0.979, which is categorized as "excellent" diagnostic accuracy. This aligns with global literature where D-Dimer is recognized as a highly sensitive biomarker for excluding Pulmonary Embolism (PE).

Optimal Cut-off: The calculated cut-off in this study was 3500 ng /ml, resulting in a sensitivity of 90.91% and specificity of 95.83%. Comparison with Standard Thresholds: Most clinical guidelines utilize a standard cut-off of 500 ng/ml. The significantly higher threshold found in this study (3500 ng/ml) suggests that the positive cases in this specific sample presented with high clot burdens or advanced symptoms, whereas the "No PE" group maintained relatively lower levels despite age-related increases.

4.2. The Influence of Age on D-Dimer Performance

Age-D-Dimer Correlation: The analysis showed a weak positive correlation (r = 0.2618$). While not statistically significant in this small sample ($p > 0.05$), the trend supports the biological reality that D-Dimer levels naturally rise with age due to subclinical fibrin deposition and decreased renal clearance. When comparing age groups, the AUC remained high, but the "No PE" baseline was higher in the >60 age group (1317.9 ng/ml) than in the < 60 group (1109.7 ng/ml). This reinforces the academic consensus for using age-adjusted cut-offs (Age × 10) to avoid over-diagnosis and unnecessary imaging in older patients.

4.3. Anatomical Correlation (Location of PE)

A critical finding in the data is the relationship between the anatomical location of the thrombus and the D-Dimer concentration. Proximal vs. Distal: Higher mean D-Dimer levels were observed in (Main Pulmonary) (6840 ng/ml) and (Saddle) (6123.5 ng /ml) emboli. This is consistent with the physiological understanding that a larger thrombus surface area provides more substrate for fibrinolysis, leading to higher levels of circulating D-Dimer.

4.4. Gender and Demographic Distribution

The sample was predominantly female (71.4%). While gender is not typically considered a primary risk factor for PE compared to clinical conditions (like surgery, immobility, or malignancy), academic studies often monitor gender distribution to ensure there is no diagnostic bias. In this dataset, the high AUC suggests that D-Dimer remained a robust predictor regardless of gender distribution.

5. Conclusion

The data confirms that D-Dimer is a powerful screening tool for PE. However, the high optimal cut-off found here (3500 ng/ml) suggests a population with high-acuity presentations. In a broader clinical setting, adhering to a lower, age-adjusted threshold is necessary to ensure that smaller but clinically significant emboli are not missed. The correlation between clot location and D-Dimer levels further suggests that D-Dimer magnitude may serve as a proxy for the severity of the pulmonary obstruction.

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