Diagnostic accuracy of d-dimer test in diagnosing pulmonary embolism in emergency department

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Abstract

Objective: To determine the diagnostic accuracy of D-dimer assay in diagnosing pulmonary embolism taking findings of CTPA as the gold standard.**Study design:** Retrospective Cross-sectional study **Place and Duration** This study was conducted in Ziauddin University Hospital Karachi from March 2022 to March 2023 **Methodology:** Both male and female patients aged 18 years or above presenting with chest pain and dyspnea for a duration of one hour or more were included. Blood sampling was done and the sample was drawn from the easily accessible superficial vein. CTPA was performed on a 16-slice CT scanner. Patients were positioned supine and with arms raised above the head and a scan was commenced from lung bases to apices in a single breath hold. Scans were reported on the workstation.**Results:** This study had 187 patients in total. The patients were 55.09 ± 12.98 years old on average. There were 132 patients (70.6%) who were over 45 years old and 55 (29.4%) who were under 45 years old. There were 92 women and 95 men in total, or 50.8% and 49.2%, respectively. There were 84 (44.9%) obese patients and 103 (55.1%) non-obese patients. The mean level of D-dimer was 2.17 ± 1.41 microgram/ml**Conclusion:** It can be concluded that D-dimer level measurement is a safe and sensitive method for identifying pulmonary embolism. This could result in the avoidance of unnecessary exposure to ionizing radiation in the form of CTPA and may help to initiate PE treatment promptly.

Keywords: D-dimer, pulmonary embolism, CTPA,

Introduction

Pulmonary embolism (PE) occurs as a result of occlusion of pulmonary arteries or its branches from dislodgement of thrombus elsewhere in the body. PE is commonly originated as dislodgement of deep /venous thrombosis (DVT) in lower limbs. Various genetic and acquired risk factors play an important role in its development.[1] Common risk factors include immobilization for prolonged periods, presence of any venous catheter, recent orthopedic surgery, pregnancy, cancer, use of oral contraceptive pills (OCPs) or smoking.[2] PE may be hemodynamically stable or unstable requiring inotropic support or vasopressors. PE is thought to be the third most common cardiovascular disease following coronary artery disease and stroke.[3]

A prompt diagnosis of PE is quite essential because of its association with increased mortality and morbidity. Approximately 30% of patients with untreated PE usually die as compared to 8% of the patients with treated PE.[4, 5] Patients with PE may present with pleuritic chest pain, shortness of breath and cough with or without hemoptysis. Central PE may cause severe dyspnea. Patients are usually tachycardic and tachypneic on examination. Patients

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may also undergo sudden onset cardiac arrest. Chest radiographs and computed tomography pulmonary angiograms (CTPA) are frequently ordered in the evaluation of such patients. Chest X-ray may be normal or may reveal Hampton hump or pulmonary vessel cutoff.[6] CTPA is highly diagnostic for PE. This is due to the fact that visualization of pulmonary vasculature is usually up to the subsegmental level with CTPA.[7] However, there are certain conditions when CTPA becomes contraindicated, such as in patients with an allergy to contrast material or renal insufficiency.

D-dimer is a commonly performed test for the evaluation of acute thrombotic conditions of the body. D-dimer is made from blood clot degradation in the body as a result of fibrinolysis.[8] Its levels can aid in thrombosis diagnosis. According to a previous study, the use of D-dimer assay has a sensitivity of 96.2% and a specificity of 50.0% in diagnosing PE.[9] Controversies still exist regarding the use of D-dimer in cases of PE. PE has a prevalence of approximately 19%.[10] The aim of this study is to determine the diagnostic accuracy of D-dimer assay in diagnosing PE taking findings of CTPA as the gold standard.

Methodology

Operational definitions

Pulmonary embolism on d-dimer

Pulmonary embolism was labelled as positive on D-dimer if its value exceeds or exceeds 1.3 microgram/ml.

Pulmonary embolism on ctpa

On CTPA, pulmonary embolism was defined as the presence of a filling defect in the main or segmental pulmonary arteries.

By taking the sensitivity of PE as 96.2%[9], specificity as 50.0%[9], the prevalence of PE as 19%[10], and margin of error as 8%, the calculated sample size came out to be 187.Non-probability consecutive sampling technique was used. Both male and female patients aged 18 years or above presenting with chest pain and dyspnea for a duration of one hour or more were included

Patients with already diagnosed PE and presenting for follow-up after treatment or with a history of treated PE or currently on anti-coagulation treatment for any hematological condition or with already known contrast allergy and already diagnosed with hepatic or renal impairment were excluded from the study

After discussing the advantages and disadvantages of the study with the patients, informed consent was obtained. Blood sampling was done and the sample was drawn from the easily accessible superficial vein. CTPA was performed on a 16-slice CT scanner. Patients were positioned supine and with arms raised above the head and a scan was commenced from lung bases to apices in a single breath hold. Scans were reported on the work station.

In order to analyse the data, SPSS version 22.0 was used. The formula for quantitative variables was mean +/- standard deviation. They described qualitative characteristics as frequency +/- percentage. A 2x2 table was used to calculate the D-dimer's sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy, using the CTPA results as the gold standard.

Stratification was used to control the effect modifiers. After stratification, the following metrics were calculated: sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy.

Results

A total of187 patients were included in this study. The mean age of the patients was 55.09 ± 12.98 years. There were 55 (29.4%) patients with ≤45 years of age and 132 (70.6%) with >45 years of age. A total of95 (50.8%) were males and 92 (49.2%) were females. There were 84 (44.9%) obese patients and 103 (55.1%) non-obese patients. The mean level of D-dimer was 2.17 ± 1.41 microgram/ml.

Table 1 provides a summary of the patients' initial characteristics

Table 1:Baseline characteristics of the patients (n=187)

	n	%
Age, years	55.09 ± 12.98‡	
≤45 years	82	40.6
>45 years	120	59.4
Gender		
Males	95	50.8
Females	92	49.2
Obesity		
No	103	55.1
Yes	84	44.9
Diabetes		
No	161	86.1
Yes	26	13.9
Hypertension		
No	168	89.8
Yes	19	10.2

‡mean±SD, n: number

Pulmonary embolism on D-dimer was found in 129 (69.0%) of the patients while on CTPA, pulmonary

embolism was found in 143 (76.5%) of the patients (As shown inTable 2).

Table 2:D-dimer and CTPA findings (n=187)

D-dimer findings	CTPA findings		Total
	Positive	Negative	
Positive	118	11	129
Negative	25	33	58
Total	143	44	187

Using histopathological findings as the gold standard, it was discovered that the D-dimer's sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were 82.52%, 75.00%, 91.47%, 56.90%, and 80.75%, respectively, in the diagnosis of pulmonary embolism.

Table 3 displays the post-stratification sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy for baseline parameters including age and gender.

Table 3:Stratification according to baseline characteristics (n=187)

	Age		Gender	
	≤45 years	>45 years	Male	Female
Sensitivity	83.33%	82.18%	83.56%	81.43%
Specificity	61.54%	80.65%	77.27%	72.73%
PPV	87.50%	93.26%	92.42%	90.48%
NPV	53.33%	58.14%	58.62%	55.17%
Diagnostic Accuracy	78.18%	81.82%	82.11%	79.35%

Stratification was also done with respect to co-morbid such as obesity, diabetes and hypertension, results are shown in Table 4.

Table 4:Stratification according to obesity, diabetes and hypertension (n=187)

	Obesity		Diabetes		Hypertension	
	Absent	Present	Absent	Present	Absent	Present
Sensitivity	80.77%	84.62%	81.10%	93.75%	81.25%	93.33%
Specificity	84.00%	63.16%	73.53%	80.00%	77.50%	50.00%
PPV	94.03%	88.71%	91.96%	88.24%	92.04%	87.50%
NPV	58.33%	54.55%	51.02%	88.89%	53.36%	66.67%
Diagnostic Accuracy	81.55%	79.76%	79.50%	88.46%	80.36%	84.21%

Discussion

In emergency departments, PE is a frequently encountered condition. Thromboembolism of the veins is a predisposing condition of PE. This may be attributed to the triad of Virchow, which refers to increased coagulability, venous stasis and injury to endothelium. Certain hereditary and acquired risk factors predispose to venous thromboembolism. Protein C and S deficiency, factor V Leiden mutation and prothrombin gene mutation are included among genetic/hereditary risk factors, whereas immobilization of longer periods, malignancy, obesity, pregnancy, or any recent surgery.[1] Clinical assessment is important to evaluate the probability of PE.

In the present study, we evaluated the use of D-dimer in diagnosing PE taking findings of CTPA as the gold standard. The present study was conducted on a larger sample size and incorporated variables such as diabetes, hypertension and obesity to see their effect on the accuracy of the D-dimer assay.

Our study results have shown a high sensitivity of D-dimer assay in diagnosing pulmonary embolism. Another previous study has reported a higher sensitivity of D-dimer as compared to our study.[11] This could be attributed to the large sample size of that study. Another previous study has shown a higher sensitivity of D-dimer as compared to our study.[9] Another larger sample size study demonstrated a higher sensitivity of D-dimer as compared to our study.[12] Another study showed a lower sensitivity as compared to our study.[13]

Our study results have demonstrated a high specificity of D-dimer assay in diagnosing PE. A previous study has shown a lower specificity of D-dimer for PE.[9] This difference could be due to the small sample size of that study. A very low specificity of D-dimer was also reported by another study,[11] and this contrasts with the finding reported in our study. Another study reported almost comparable, but slightly lower specificity of D-dimer assay as compared to our study.[14] That study utilized a point-of-care D-dimer assay for evaluation and this could have resulted in lower specificity. Another difference in specificity could be due to differences in population genetics.

The results of our study have shown that sensitivity was higher in younger patients as compared to older patients. A similar result has been shown by another study, but in that study, the threshold for higher sensitivity was age <50 years, whereas, in our study, the age threshold was age <45 years.[15]

Our study results have demonstrated the high sensitivity and accuracy of D-dimer in diagnosing PE in obese patients. Obesity is a known risk factor for PE and the risk is increased more in patients who are morbidly obese.[16] An increasing sensitivity and diagnostic accuracy could be due to an increased incidence of thromboembolism in obese patients. The risk is greater in young obese patients.[17]

Our study results have demonstrated an increased diagnostic accuracy and sensitivity of the D-dimer assay in diagnosing PE in diabetic patients. Diabetic patients may have an unstable atherosclerotic disease with apropensity to develop embolism. Moreover, D-dimer levels in diabetic patients with atherosclerosis are increased[18] and this might be a possible reason for increased sensitivity and diagnostic accuracy.

According to the results of our study, the sensitivity and diagnostic accuracy of the D-dimer assay were high in females. However, another previous study has shown a lower sensitivity of D-dimer in females for

diagnosing PE.[19] Another previous study has shown that D-dimer positivity among males was higher as compared to females.[20]

Our research has some drawbacks. First of all, this was a retrospective study done at just one institute. Our failure to assess the diagnostic accuracy pertinent to the diagnosis was another weakness of our study. Thirdly, because complete data were not available retrospectively, we were unable to stratify the findings according to low, intermediate, or high probability.

Another limitation of our study was that we did not stratify the results on the basis of presenting complaints of the patients. The fifth limitation of our study was that on CTPA, the location and type of embolism were not stratified. According to a study, mean D-dimer levels were higher with embolism in main pulmonary arteries as compared to segmental arteries.[21] Considering this association, it can be postulated that there might also be a difference in accuracy.

Despite these limitations, we believe to the best of our knowledge that this study determines the diagnostic accuracy of D-dimer on a larger sample size and incorporates co-morbid conditions such as obesity, diabetes and hypertension. It is recommended that further studies should be carried out regarding age-specific D-dimer assay and also incorporating variables of location of embolism, to get further insight into the related clinical problem.

Conclusion

It can be concluded that D-dimer level measurement is a safe and sensitive method for identifying pulmonary embolism. This could result in the avoidance of unnecessary exposure to ionizing radiation in the form of CTPA and may help to initiate PE treatment promptly.

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