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ORIGINAL ARTICLE

Diagnostic accuracy of D-dimer assay in detection of Pulmonary Embolism in patients presenting in emergency department

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ABSTRACT

Background: Pulmonary embolism is the lethal condition that is associated with higher rate of mortality in cardia patients. The diagnosis of the acute pulmonary embolism is frequently observed in patients presenting in emergency department or during hospitalization. Level of D-dimer may be assessed by blood test to help the physicians to diagnose the thrombosis. Literature showed variable evidence regarding predictive accuracy of D-dimer for detection of pulmonary embolism. So to get local data, we conducted this study.
Aim: To determine the diagnostic accuracy of D-dimer assay for detection of pulmonary embolism in patients of acute myocardial infarction presenting in emergency department taking CTPA as gold standard
Methods: Cross - sectional study conducted in Cardiology Department , Punjab Institute of Cardiology, Lahore for a period of six months from 1-9-2018 to 1-3-2019. One hundred patients, fulfilled the selection criteria were enrolled from emergency. Then blood sample was taken for evaluation of D-dimer level. Reports were checked and D-dimer level was noted. Pulmonary embolism was labeled as positive on D-dimer, if D-dimer level ≥500 and was labeled as negative if D-dimer level <500. Then all patients underwent CTPA. Pulmonary embolism labeled as positive if there was mass filling defects detected as dark spot on angiogram. All the data was collected by using the proforma. Data analysis as done in SPSS v. 21.
Results: The mean age of patients was 54.03±10.26years. There were 40 (40) males and 60 (60%) females. The mean BMI of patients was 27.57±4.35kg/m^2. There were 46 (46%) patients with diabetes mellitus while 61 (61%) patients had hypertension. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 82.6%, 72.2%, 71.7%, 83.0% and 77.0%, respectively taking CTPA as gold standard.
Conclusion: Thus the D-dimer is accurate enough that it can help to predict pulmonary embolism and can help to prevent at least negative cases to undergo CTPA.
Keywords: Acute myocardial infarction, pulmonary embolism, D-dimer, computed tomography pulmonary angiography

INTRODUCTION

Pulmonary embolism is a dangerous disease that has a high death rate.[1] Its diagnosis remains difficult, and the use of medical instruments has risen sharply.[2] In myocardial infarction patients who presented in the emergency room, pulmonary embolism was confirmed to occur 42.1 percent of the time.[3] When patients come to the emergency room or are admitted to the hospital, the clinical condition of acute pulmonary embolism is often considered. Since signs are non-specific and anticoagulant therapy has serious effects, objective examinations to confirm or deny the diagnosis have become standard of care[4].

Men have a mortality risk associated with AMI that is about three times that of women. It is more common in black patients than in white patients, with the difference disappearing by the age of 75. Coronary mortality is lower in the Hispanic population than it is in the black and white populations[5]. Pulmonary embolism is a potentially fatal disease that affects many people. The majority of patients who die from a pulmonary embolism die within the first few hours of the occurrence. Despite advances in diagnostic technology, pulmonary embolism detection delays are normal and a serious problem[6] .

Large pulmonary embolism is second only to sudden heart arrest as a cause of sudden death. The patient and clinician are at risk of losing the diagnosis due to the uncertainty of appearance. The difficulty is that the "classic" diagnosis of pleuritic chest pain, shortness of breath, and hypoxia is uncommon. Patients who died suddenly of pulmonary embolism have been complaining of nagging symptoms for weeks before dying, according to studies. In the weeks leading up to their deaths, 40% of these patients have seen a doctor[7].

The number of pulmonary embolism tests increased by a factor of six between 1997 and 2000, owing primarily to the widespread use of computed tomographic pulmonary angiography (CTPA), though the incidence of pulmonary embolism in the emergency room declined during the same time, with some reports from North America reporting as low as 5%.[8] D-dimer is a fibrin degradation element, and is a small protein fragment found in the blood after fibrinolysis breaks down a blood clot. It gets its name from the fact that it's made up of two D fragments of the fibrin protein linked together by a cross-link. A blood examination can be used to assess D-dimer concentration in order to detect thrombosis[9].

Rationale of this study is to determine the diagnostic accuracy of D-dimer assay for detection of pulmonary embolism in patients presenting in emergency department. Literature showed variable evidence regarding diagnostic accuracy of D-dimer for detection of pulmonary embolism. Moreover, no local data available in this regard. So, in routine patients would undergo CTPA instead of screening with D-dimer on initial stages or in emergency and the specificity of D-Dimer is found to be low which create a dispute whether to ignore negative cases on D-dimer or must undergo CTPA. So to get local data, we want to conduct this study whether the D-dimer, we want to conduct this study. So that pulmonary embolism can be detected and diagnosed on basis of D-dimer and burden of cardiologists can be reduce by reducing unnecessary CTPA.

The objective of the study was to determine the diagnostic accuracy of D-dimer assay for detection of pulmonary embolism in patients of acute myocardial infarction presenting in emergency department taking CTPA as gold standard

MATERIAL AND METHODS

This cross sectional study was conducted in Cardiology Department, Punjab Institute of Cardiology, Lahore for a period of six months from 1-9-2018 to 1-3-2019 after permission from IRB. Sample size of 100 patients is calculated with 95% confidence level, and taking expected percentage of pulmonary embolism i.e. 42.1% with sensitivity of D-dimer i.e. 90% with 9% margin of error and specificity of D-dimer i.e. 37.5% with 11% margin of error.

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Sampling technique used was non-probability, consécutive sampling.

Inclusion criteria: Patients of age 40-75 years of either gender presenting with AMI (ST elevations >0.5mm on ECG with continuous chest pain, troponin T >100mIU) presenting within 12 hours of symptoms were included.

Exclusion criteria: Patients who had previous valvular or rheumatic heart disease, underwent coronary artery bypass grafting or PCI or previous AMI, diastolic dysfunction before AMI or already with pulmonary embolism or DVT and taking treatment were not included in the research

Data Collection Procedure: 100 patients, fulfilled the selection criteria were enrolled from emergency. Consent was taken before enrolment. Their demographics were also taken. Then blood sample was taken in a 3cc disposable syringe. All the obtained samples were sent to the pathology laboratory for evaluation of D-dimer level. Reports were checked and D-dimer level was noted. Patients were labelled as positive or negative. Pulmonary embolism was labeled as positive on D-dimer, if D-dimer level ≥500 and was labeled as negative if D-dimer level <500. Then all patients underwent CTPA for confirmation of pulmonary embolism. On CTPA, it was labeled as positive if there was mass filling defects detected as dark spot on angiogram and was labeled as negative if pulmonary vessels are filled with contrast, and appear white. All the data was collected by using the proforma.

Analysis Plan: The data was analysed in SPSS v. 21. 2 x 2 contingency table was generated to calculate the sensitivity, specificity, PPV, NPV & overall accuracy of D-dimer keeping CTPA as gold standard.

RESULTS

The mean age of patients was 54.03±10.26years. There were 40 (40) males and 60 (60%) females. The mean BMI of patients was 27.57±4.35kg/m^2. There were 46 (46%) patients with diabetes mellitus, and 61 (61%) had hypertension. The mean D-dimer level of patients was 541.34±264.90 (Table 1).

The sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 82.6%, 72.2%, 71.7%, 83.0% and 77.0%, respectively taking CTPA as gold standard (Table 2).

Data was stratified for age of patients. In patients aged 40-60years, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 82.9%, 75.7%, 76.3%, 82.4% and 79.2%, respectively taking CTPA as gold standard. In patients aged 61-75 years, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 81.8%, 64.7%, 60.0%, 84.6% and 71.4%, respectively taking CTPA as gold standard. Data was stratified for gender of patients. In male patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 86.4%, 77.8%, 82.6%, 82.4% and 82.5%, respectively taking CTPA as gold standard. In female patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 79.2%, 69.4%, 63.3%, 83.3% and 73.3%, respectively taking CTPA as gold standard. Data was stratified for BMI of patients. In normal BMI patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 88.2%, 75%, 79%, 85.7% and 82.8%, respectively taking CTPA as gold standard. In overweight patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 73.3%, 66.7%, 64.7%, 75% and 69.7%, respectively taking CTPA as gold standard. In obese patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 85.7%, 75%, 70.6%, 88.2% and 79.4%, respectively taking CTPA as gold standard. Data was stratified for diabetes. In diabetic patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 80%, 66.7%, 94.1%, 33.3% and 78.3%, respectively taking CTPA as gold standard. In non-diabetic patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 100%, 72.9%, 31.6%, 100% and 75.9%, respectively taking CTPA as gold standard. Data was stratified for hypertension. In hypertensive patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 82.6%, 73.3%, 90.5%, 57.9% and 80.3%, respectively taking CTPA as gold standard. In non-hypertensive patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 0%, 71.8%, 0%, 100% and 71.8%, respectively taking CTPA as gold standard. Table 3

Table 1: Demographics of patients

	Mean ± SD, F (%)
n	100
Age (years)	54.03 ± 10.26
Gender	
Male	40 (40%)
Female	60 (60%)
BMI (kg/m^2)	27.57 ± 4.35
Diabetes	
Yes	46 (46%)
No	54 (54%)
Hypertension	
Yes	61 (61%)
No	39 (39%)
D-dimer level	541.34 ± 264.90

Table 2: Accuracy of D-dimer for prediction of pulmonary embolism taking CTPA as gold standard

Pulmonary embolism on		**CTPA**		**Total**
		Positive	**Negative**	
D-Dimer	Positive	38	15	53
	Negative	8	39	47
Total		46	54	100

Sensitivity = 82.6%, Specificity = 72.2%, PPV = 71.7%, NPV = 83.0% and Diagnostic accuracy = 77.0%

Table 3: Accuracy of D-dimer for prediction of pulmonary embolism taking CTPA as gold standard stratified for effect modifiers

	Age (years)		**Gender**		**BMI**			**Diabetes**		**Hypertension**	
	<60	**>60**	**Male**	**Female**	**Normal**	**Overweight**	**Obese**	**Yes**	**No**	**Yes**	**No**
Sensitivity	82.9	81.8	86.4	79.2	88.2	73.3	85.7	80.0	100	82.6	0
Specificity	75.7	64.7	77.8	69.4	75.0	66.7	75.0	66.7	72.9	73.3	71.8
PPV	76.3	60.0	82.6	63.3	79.0	64.7	70.6	94.1	31.6	90.5	0
NPV	82.4	84.6	82.4	83.3	85.7	75.0	88.2	33.3	100	57.9	100
Diagnostic accuracy	79.2	71.4	82.5	73.3	82.8	69.7	79.4	78.3	75.9	80.3	71.8

DISCUSSION

Two principles guide the diagnosis process of acute lung embolism. Firstly, precise and fast diagnosis of the patients with lung embolism is essential since pulmonary embolism may be lethal and because of the possibility of severe bleeding.[10] This leads to the needless possibility of lung embolism or bleeding and can often be fatal if a wrong diagnosis is made. Second, the use of individual diagnostic trials in isolation can cause potential pulmonary embolism to be mismanaged. Therefore, integrated testing procedures are favoured, including a mixture of several diagnostic measures[11,12].

The rate of pulmonary embolism will vary significantly from race to race; with variations found probably attributed not to real incidence but to differences in diagnostic precision. In infants, the average prevalence is much lower than in adults[13].

A longitudinal cohort research by female nurses showed that idiopathic embolism is associated with hours sitting every week. Women who reported that they had been sat for more than 40 hours a week were more than twice as risky as women who

reported that they were sat for fewer than ten hours a week in both 1988 and 1990[14]. D-dimer (or D-dimer) is a fibrous degradation agent that is degraded by fibrinolysis after a small protein fragment in the blood has been degraded. This is because it comprises two D-fibrin protein fragments that are linked together[15].

Radio-exposure, a number of complications arising from contrast dye administration and over diagnosis, is synonymous with CTPA, which replaces pulmonary angiography as the first-line scan test. In a first or recurring episode of clinically suspected pulmonary embolism, CTPA can be largely prevented for 20 to 30% of patients using structured algorithm. This should consistently include a clinical decision rule, in addition to the D-dimer blood test and/or CTPA, to determine how likely it is to present pulmonary embolism.[16] The mean D-dimer amount was 541.34±264.90 in our sample. In 53(53%) patients, D-dimer was positive. In 46 (46%) patients, CTPA was positive. The sensitivity, precision, PPV, NPV and diagnostic accuracy of the diagnostics of D-dimer is 82.6%, 72.2%, 83% and 77%, respectively. There was a sensitivity of 88% to 96% and the specificity ranged from 48% to 53%[17]. Yousaf et al., found that sensitivity of D-dimer was 90% while specificity was 37.5%, for diagnosis of pulmonary embolism[18].

The highest sensitivity (79–100%) of enzyme-connected immunosorbent tests is for detection of D-dimers; their specificity (25%–100%) is usually too limited to be used as a diagnostic tool. Furthermore, they take time, and are too costly to conduct in healthcare conditions with the most immediate need. Assays on latex agglutination avoid such issues, but sacrificial sensitivity (22-88%) is used during the method. The recent use of the SimpliRED D-dimer test has increased, since it usually approaches 95% of the NPV, but these results have been obtained from patients with limited pre-test clinical probabilities for deep venous thrombosis pulmonary embolism[19].

This is in line with the findings of Patrick et al., who claimed that the D-dimer assay was not appropriate for the sole purpose of excluding or confirming venous tribulation. They observed the sensitivity, specificity, NPV and PPV of D-dimer were 78%, 41%, 84%, and 34% respectively for detection of pulmonary embolism[20].

CONCLUSION

Thus the D-dimer is accurate enough that it can help to predict pulmonary embolism and can help to prevent at least negative cases to undergo CTPA. Now we have got the local evidence and can implement D-dimer in routine instead of going for CTPA directly on initial stages or in emergency. So that pulmonary embolism can be detected and diagnosed on basis of D-dimer and burden of cardiologists can be reduce by reducing unnecessary CTPA.

Conflict of interest: Nil

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