Diagnostic Yield of D-dimer In Pulmonary Embolism

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ABSTRACT

Objective — *To determine the diagnostic yield of D-dimer in combination with multi-detector computed tomography (MDCT) in patients with clinical symptoms and signs of acute pulmonary embolism.*

Study design — *Cross sectional observational study.*

Place & Duration of study — *This study was carried out in Radiology Department Rashid Hospital Dubai UAE, from October 2011 to September 2012.*

Methodology — *In patients with clinical symptoms and signs of acute pulmonary embolism, D-dimer and MDCT were performed. Pulmonary angiography was performed to compare the results. For descriptive purpose the patients were divided into four groups. The sensitivity, specificity, false positive rate, false negative rate, positive predictive value and negative predictive value were calculated.*

Results — *There were total of 151 patients of whom 97 (64.2%) were males and 54 (35.8%) females. The mean age of the patients was 47.26 + 16.16 year. Shortness of breath was noted in 104 (68.9%, p = 0.000), chest pain in 88 (58.3%, p = 0.042) and cyanosis in 57 (37.7%, p= 0.061) patients. The D-dimer test was positive in 80 (53.0%) patients while CT angiogram in 56 (37.1%) patients. In 52 patients both D-dimer and MDCT angiogram were positive, while 65 patients had normal D-dimer and CT angiogram. The sensitivity of D-dimer in combination with CT angiogram was 92.85%, specificity 68.42%, false positive rate 31.57%, false negative rate 7.14%, positive predictive value 63.41%, negative predictive value 94.20% and accuracy 77.48%.*

Conclusion — *D-dimer is an easy, non-invasive, safe, efficient and cost effective method of diagnosis in clinically suspected cases of pulmonary embolism.*

Key words — *Pulmonary embolism, D-dimer, MDCT pulmonary angiogram*.

INTRODUCTION:

Pulmonary embolism (PE) is an obstruction of the major artery of the lung or one of its branches, by an embolus travelled from elsewhere in the body through the blood stream. PE is most frequently caused by an embolus dislodged from the deep veins of the legs or pelvis, but occasionally by embolization of air, fat, amniotic fluid and talc in drugs of intravenous drug abuser. The risk of PE increased in bed ridden, polytrauma and carcinoma patients and those with hematological abnormalities.[1] In USA it occurs in 0.6 million people resulting in 50,000 to 200,000 deaths per year.[2] The clinical presentation is usually due to right heart failure. The usual presentation is difficulty in breathing, chest pain on inspiration, cyanosis, tachycardia, collapse or even death.[1] The mortality of PE in undiagnosed or untreated patient varies from 26- 30%.[3]

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The clinical diagnosis of PE is based on different criterias like Wells score and Geneva rule. The score of >6.0 has high probability, while score of <2.0 has low probability on Wells score.[4] The typical findings on electrocardiography are long S wave in lead I,

long Q wave in lead III and inverted T wave (S1Q3T3) which occurs only in 12-50% of the people with diagnosis, but also occur in 12% without diagnosis.[5] The echocardiography shows right ventricular dysfunction with typical appearance of Mc Connell's sign (akinesia of mid-free wall but normal motion of the apex). The echocardiography has 77% sensitivity and 94% specificity.[6]

The X-ray chest shows pulmonary congestion of the effected lung and sometimes typical signs like Westermark sign and Hampton hump are seen.[7] Ventilation/perfusion scan (V/Q scan) shows decrease perfusion of the effected artery, while ventilation is normal. This method is obsolete because of the more widespread availability of CT technology.[8] D- dimer is widely used nowadays as its sensitivity ranges from 91 to 97% in various studies and the specificity varies between 40 to 70%.[9] CT pulmonary angiography is a pulmonary angiogram without cardiac catheterization. Single slice spiral CT has sensitivity of 69% and specificity of 84%.[10] Multi-detector computerized tomography pulmonary angiogram has the sensitivity of diagnosing PE of more than 95%.[11] This means that in a single negative study of MDCT pulmonary angiogram, one can safely exclude PE.

This study was performed to find out the diagnostic accuracy of the D-dimer test as compared to MDCT angiogram in order to diagnose the PE and making a decision to start the treatment without any delay.

METHODOLOGY:

This study was conducted on patients with clinical diagnosis of pulmonary embolism in Radiology Department, Rashid Hospital Dubai UAE, from October 2011 to September 2012. Patients with signs and symptoms of PE were included. Those who had previous episode of PE and known cases of pulmonary disease, were excluded. Detailed history and physical examination were performed. The clinical probability rules like 'Simplified Wells rule' and 'Simplified revised Geneva score' were considered in establishing the diagnosis. Initially electrocardiography and chest radiography were performed to augment the clinical diagnosis.

Patients were divided into four groups. Group I included those patients in whom clinical diagnosis of PE was made and was confirmed by both D-dimer and MDCT Pulmonary angiogram.

Group II included those patients in whom clinical diagnosis of PE was made and D-dimer test was negative. In these patients positive MDCT pulmonary angiogram confirmed the diagnosis.

Group III included patients in whom clinical diagnosis of PE was made and D-dimer test were negative. In these patient negative MDCT pulmonary angiogram excluded the diagnosis.

Group IV included those patients in whom clinical diagnosis of PE was made and D-dimer test was positive. In these patients negative MDCT pulmonary angiogram excluded the diagnosis.

In this study the cut off value of D-dimer for positive cases was considered to be equal or more than 0.5mg/dl. CT angiogram was performed by the 64-slices MDCT scanner to acquire the images of thorax in caudo-cranial direction. The venous access was taken in all cases by ante-cubital vein and contrast was given. Images were taken with standard algorithm and viewed with IMPAX software. The saddle embolus at the bifurcation of the pulmonary artery or thrombus burden in the lobar branches of both main pulmonary arteries were considered to be the positive CT angiogram for PE. The CT angiogram in this study was considered to be the gold standard.

All the data was recorded on data sheet. The results were analyzed by using the SPSS version 20.0. The mean age with standard deviation and gender ratio were calculated. The frequency distribution of clinical features, D-dimer and CT angiogram were calculated. The Chi square value, confidence interval and p value were also calculated. The p value < 0.05 was considered to be significant. The D-dimer test sensitivity, specificity, false positive rate, false negative rate, positive predictive value, negative predictive values and accuracy were also determined.

RESULTS:

This study was conducted on 151 patients who presented with clinical diagnosis of pulmonary embolism. The age of the patients ranged from 21-88 year, with mean age of 47.26 +16.16 year. Majority of the patients (n=93, 61.1%) were below the age of 50 year (table I). There were 54 (35.8%) females and 97 (64.2%) males with female to male ratio of 1:1.8. Majority of the patients (n=92, 60.9%) were indoor patients of different specialties, while 59 (39.1%) were outdoor patients.

The prominent symptoms and signs included shortness of breath in 104 (68.9%) patients and pain in the chest in 88 (58.3%) patients . Clinical presentations like pain in the chest, shortness of breath and cyanosis were found to be significant (table II). The D-dimer test was found positive in 80 (53.0%) patients. The CT angiogram was positive

Table I: Age of Patient Presented With Acute Pulmonary Embolism

Age groups (Year)	Frequency (n)	Percentage (%)
21-30	24	15.9
31-40	33	21.9
41-50	36	23.8
51-60	25	16.6
> 60	33	21.9
Total	151	100%

Table II: Patients Characteristics at the Time of Presentation

Groups of Patients	Pain in Chest Chi Square 4.13 df 1 95% CI:0.017-0.089 P 0.042	Shortness of Breath Chi Square 21.51 df 1 95% CI:0.00- 0.02 P 0.000	Cyanosis Chi Square 9.06 df 1 95% CI:0.00-0.02 P 0.003	Tachycardia Chi Square 3.50 df 1 95% CI:0.02-0.097 P 0.061
Group I	47 (53.8%)	49 (47.11%)	34 (58.64%)	45 (70.31%)
Group II	4 (4.5%)	3 (2.88%)	2 (3.50%)	2 (3.12%)
Group III	23 (26.13)	38 (36.53%)	13 (22.80%)	7 (10.93%)
Group IV	14 (15.90)	14 (13.46%)	8 (14.03%)	10 (15.62%)

in 56 (37.1%) patients. There were 52 patients in whom both D-dimer and CT angiogram were positive, while 65 patients had normal D-dimer and CT angiogram.

When the diagnostic capability of D-dimer was compared with CT angiogram as a gold standard in the clinically suspected cases of PE, its sensitivity was 92.85%, specificity 68.42%, false positive rate 31.57%, false negative rate 7.14%, positive predictive value 63.41%, negative predictive value 94.20% and accuracy 77.48%.

DISCUSSION:

D-dimer formed by the degradation of cross-linked fibrin is the best currently available laboratory marker of coagulation activation.[12] It is clinically used when there is suspicion of deep venous thrombosis (DVT), PE and disseminated intravenous coagulation (DIC). D-dimer test can avoid a significant proportion of imaging tests and is less invasive as revealed in present study.[13]

The prevalence of DVT and PE is 20% or less among clinically suspected individuals.[14]Diagnosing PE requires both clinical assessment and objective testing because the clinical features are non- specific and investigation can be either false positive or negative. The initial step in the diagnostic process is to stratify patients into high, moderate and low risk categories. This was not done in present study. In a study conducted in a tertiary care hospital on 80 patients revealed that 42 patients (52.50%) were between the age of 51-75 year with male preponderance (n=52, 65%).[15] Our results were not mirror image of that study as 36 patients (23.8%) were in 5th decade of life and 64.2% were males. In the same study the most common presenting complaint was shortness of breath in (97.5%) while in current study shortness of breath occurred in 68.9% patients.

Various studies have demonstrated that the D-dimer sensitivity is between 93-95% and specificity 50% in the diagnosis of thrombotic disease.[16] In a meta-analysis the pooled sensitivity of the ELISA assays for diagnosing pulmonary embolism was 95% and the specificity 45%.[17] In our study the D-dimer test was found to be positive in 80 (53.0%) patients with sensitivity of 92.85% and specificity 68.42%.

There were few limitations of our study. This study did not address the false positive and false negative results. The false positive results may be due to laboratory technical error of improper dilution, presence of liver disease etc. The false negative results may be due to early or delayed collection of sample for testing. The timing of clinical presentation

and sample collection were also not the part of our study.

CONCLUSIONS:

D-dimer a non-invasive test with a good diagnostic yield but technical laboratory errors and associated diseases can make it less accurate. The clinical diagnosis along with D-dimer is a recommended tool for diagnosing PE.

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