Exclusion of acute pulmonary embolism: computed tomography pulmonary angiogram or D-dimer?

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ABSTRACT

Introduction: The aim of our study was to determine the accuracy of the D-dimer test in the exclusion of pulmonary embolism.

Methods: In 2006, 446 patients at our hospital underwent computed tomography pulmonary angiogram (CTPA) for the exclusion of pulmonary embolism. We selected patients with a clinical suspicion of pulmonary embolism, and who underwent both a CTPA examination and a D-dimer test performed within a period of five days. Pregnant women, patients with an allergy to intravenous contrast and those who were on anticoagulant therapy were excluded. Based on our criteria, 219 cases were selected. D-dimer test was performed using an immunoturbidimetric assay. A cut-off value of 500 ng/ml was selected as the upper limit to exclude thrombosis.

Results: There were 42 patients positive for pulmonary embolism on CTPA and all had elevated D-dimer values. There were 177 patients negative for pulmonary embolism on CTPA and 49 of them had normal D-dimer values. The sensitivity and specificity of the D-dimer test was 100.0 percent (95 percent confidence interval [CI] 91.6–100.0) and 27.7 percent (95 percent CI 21.2–34.9), respectively. The likelihood ratio for a positive test and negative test was 1.38 and 0, respectively.

Conclusion: The D-dimer test is suitable for screening patients with a clinical suspicion of pulmonary embolism. The indiscriminate use of CTPA results in unnecessary testing and elevates healthcare costs. Clinicians are urged to give due consideration to a D-dimer test result prior to requesting a CTPA examination.

Keywords: computed tomography pulmonary angiogram, D-dimer, pulmonary angiogram, pulmonary embolism

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INTRODUCTION

Acute pulmonary embolism is a common condition, especially in the hospitalised population. Delays in diagnosis and treatment often result in a high mortality rate.[1,2] Pulmonary angiography is regarded as the gold standard for the diagnosis of pulmonary embolism. Nevertheless, angiography is rarely performed because of its invasive nature, with significant morbidity and mortality.[3] Other more commonly used methods for the diagnosis of pulmonary embolism include the ventilation-perfusion scan, computed tomography pulmonary angiogram (CTPA) and serum D-dimer test. CTPA is now being increasingly utilised for the diagnosis of pulmonary embolism. Advances in technology from the previous single slice CT to the current ubiquitous 64-slice CT have enabled the radiologist to detect thrombus confidently up to the small sub-segmental branches of the pulmonary artery (Figs. 1–3). The accuracy of the CTPA has been well-established, as shown in the recent PIOPED II study that yielded positive predictive values of 97% for pulmonary embolism in a main or lobar artery.[4] This has led to the increasing use of CTPA. Clinicians have a low threshold in ordering CTPA as it is being perceived as a non-invasive examination, resulting in a low positive rate. In our institution, 446 examinations of CTPA were performed in the year 2006, with a positive rate of 20.4% (91 patients). This raises the concern of the over-usage of CTPA.

D-dimer is the terminal product of the fibrin degradation process. The presence of elevated D-dimer values is proof that a fibrin clot is present and the fibrinolytic system is active. An accurate D-dimer test could prevent the over-usage of CTPA, reduce radiation exposure and the potential complications related to intravenous contrast administration for patients who have an elevated D-dimer test value. The aim of our study was to determine the accuracy of the D-dimer test in the exclusion of pulmonary embolism.

METHODS

A retrospective review of the radiology information system of our hospital, a tertiary referral centre with 1,200 beds, was performed for the year 2006. Reports of CTPA were reviewed. This was correlated with the D-dimer tests. The

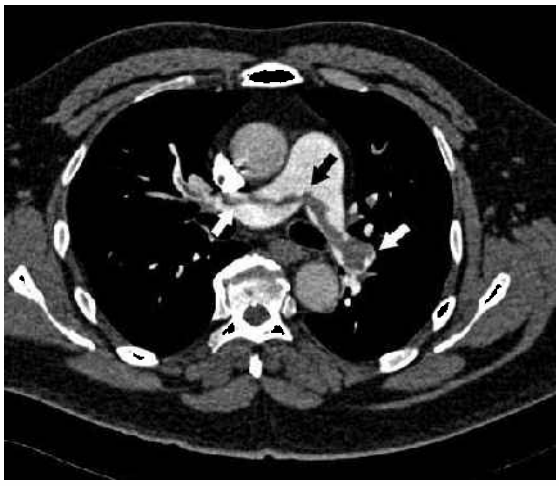

Fig. 1 Axial CT image shows a saddle embolus involving both main pulmonary arteries (arrows).

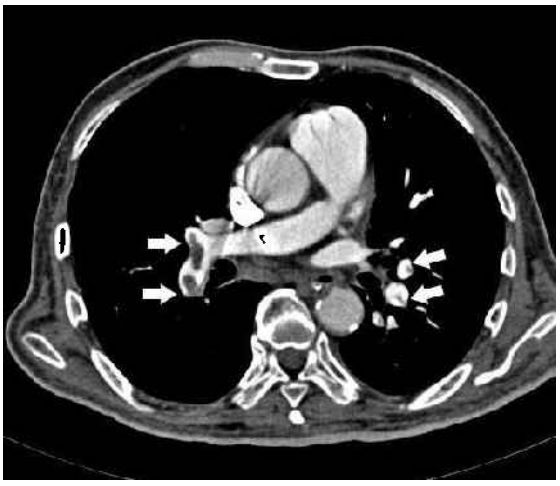

Fig. 2 Axial CT image shows emboli at the right middle and bilateral lower lobar pulmonary arteries (arrows).

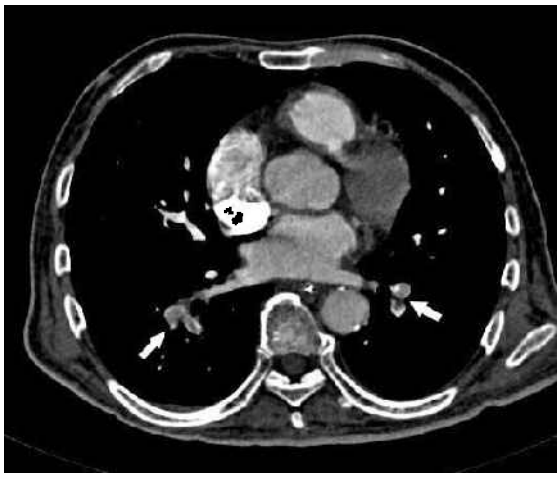

Fig. 3 Axial CT image shows emboli in both the lower lobar segmental pulmonary arteries (arrows).

entry criteria of our study were: patients who presented with a clinical suspicion of pulmonary embolism and underwent both CTPA and serum D-dimer test within a period of five days. Exclusion criteria were: pregnant women, patients with an allergy to intravenous contrast agent, and those on anticoagulant therapy.

All CTPA examinations were performed with multi-detector scanners using a standard protocol. The CT machines were either Somaton Sensation 16 or Somaton Sensation 64 (Siemens, Erlangen, Germany). Intravenous iodinated contrast agent (Omnipaque 350) was delivered at a rate of 3 ml/sec via mechanical injectors, either Stellant (Medrad, PA, USA) or Dual Shot (Nemoto, Japan). A total of 90 ml of contrast was administered. The bolus tracking method was employed, with a triggering point of 100 HU at the pulmonary trunk to ensure optimal opacification of the pulmonary arteries. The data obtained was reconstructed at 1-mm slice thickness with a 0.8-mm slice increment and reviewed at Centricity picture archival and communication systems (PACS) workstations (GE Healthcare, Waukesha, WI, USA).

The D-dimer test was performed using immuno-turbidimetric assay Liatest D-DI (Diagnostica Stago, Paris, France). A cut-off value of 500 ng/ml was selected as the upper limit to exclude thrombosis.[5,6] The median time of D-dimer testing is one day with an interquartile range (IQR) of 0–2 days. There were 446 patients who underwent CTPA for the exclusion of pulmonary embolism in 2006. Based on our criteria, a total of 219 cases were eligible, while 227 cases were excluded mainly because no D-dimer test was performed within the time period specified.

Data analysis was performed with Stata version 9.2 (College Station, TX, USA). The proportion of positive pulmonary embolism in the eligible cases was 19.2% and in the excluded cases, 21.6%. The median age for the eligible cases was 68 years (IQR 53–79), while that for the excluded cases was 70 years (IQR 56–80). The gender distribution in the eligible and excluded groups was 94:125 and 105:122 (male:female), respectively. There was no statistically significant difference in terms of the proportion of positive pulmonary embolism (chi-square test, $p = 0.528$), median age (Wilcoxon rank-sum test, $p = 0.201$), and male to female distribution (chi-square test, $p = 0.479$) between the group of patients with and without the D-dimer test. The level of significance was set at 5%. The profile of the cases based on the available biodata is summarised in Fig. 4.

RESULTS

Based on our sample size of 219 patients, 42 patients were positive for pulmonary embolism on CTPA. All the patients had an elevated serum D-dimer test value. There were 177 patients negative for pulmonary embolism on CTPA, of which 49 had a normal D-dimer test. In

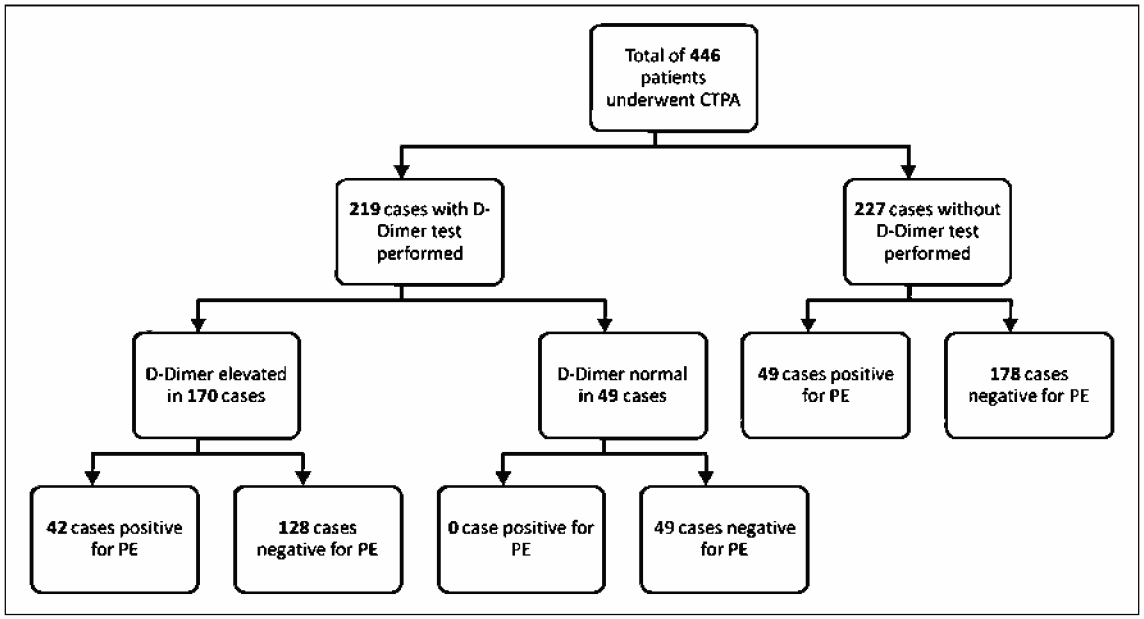

Fig.4 Algorithm shows the profile of the 446 cases which underwent CTPA.
CTPA: computed tomography pulmonary angiogram; PE: pulmonary embolism.

particular, no patient with a normal D-dimer test was positive for pulmonary embolism on CTPA in our study. The sensitivity and specificity of the D-dimer test was 100.0% (95% confidence interval [CI] 91.6–100.0) and 27.7% (95% CI 21.2–34.9), respectively. The likelihood ratio for positive and negative tests were 1.38 and 0, respectively. The clinical records of the patients were reviewed at three months follow-up to look for a diagnosis of thromboembolism. No false positive or negative case was detected. Due to the retrospective nature of the study, the assessment was mainly clinical, as the patients did not have repeat CTPA or D-dimer tests.

DISCUSSION

Pulmonary embolism is a fairly common disease in the hospital setting and can be life-threatening. However, the signs and symptoms are often very non-specific, with vague presentations of shortness of breath and chest pain. There are established criteria, such as the Wells' criteria,[7] to assess the clinical likelihood of pulmonary embolism. However, they can be subjective and certainly not all physicians adhere to them. In daily practice, pre-test probability is usually not assessed with scoring systems or D-dimer tests before a CTPA is ordered. We believe this is because the CTPA is regarded as a quick and relatively non-invasive means for excluding pulmonary embolism. However, CTPA is not without its drawbacks. Although radiation exposure for CTPA is lower compared to the catheter pulmonary angiogram, it is still significant with a mean dosage of 4.2 (range 2.2–6.0) mSv.[8] Intravenous contrast administration also has known side effects of contrast-related allergic reaction and contrast-induced nephropathy.

The D-dimer test is available around the clock in our institution and the final result can be obtained within one hour. The high sensitivity of 100% (95% CI 91.6–100) at the threshold value of 500 ng/ml ensures that pulmonary embolism will not be missed. In addition, the likelihood ratio for a negative test of 0 implies that there is a conclusive change from pre-test to post-test probability for the exclusion of pulmonary embolism. The high sensitivity and likelihood ratio for a negative test of D-dimer have also been established in various other studies.[9-12]

In our study sample, 49 patients with a normal D-dimer test had a negative CTPA. This group of patients could have avoided unnecessary CTPA testing if the D-dimer value had been taken into consideration before ordering the CTPA. These 49 patients, representing 22.4% of our study sample, could have avoided unnecessary radiation and potential complications related to contrast administration. Although we selected 49% of all CTPA done in 2006, the positive rate in both groups with and without contemporaneous D-dimer tests was similar. The profile based on the available biodata is also similar. We believe that the results can be extrapolated to the group who did not have D-dimer tests.

Based on the results we obtained, the D-dimer test is a useful tool for screening patients with a clinical suspicion of pulmonary embolism, prior to subjecting them to CTPA. This has economic implications. In our institution, a D-dimer test costs $35, while CTPA costs $425. Significant

healthcare cost savings can be achieved in our study sample if patients with normal D-dimer did not have a CTPA [($425–$35) × 49 = $19,110]. Individual calculations are required for other institutions and circumstances, but we expect similar results to be seen. The positive predictive value of the D-dimer test remains limited as a result of increased sensitivity. Excluding overriding clinical factors, such as a high risk based on clinical scoring systems, we do not recommend CTPA for further testing if the D-dimer test is within the normal range. Various other studies have also recommended no further testing required for the exclusion of pulmonary embolism in the low and intermediate risk groups, if a D-dimer test is normal.[13,14] The D-dimer test is a quick, easily available and non-invasive test. It is an excellent test for the exclusion of pulmonary embolism, especially in the low and intermediate risk groups of patients. The indiscriminate use of CTPA will result in unnecessary testing and elevate healthcare costs. Hence, we urge clinicians to give due consideration to the D-dimer test result prior to subjecting their patients to CTPA for the exclusion of pulmonary embolism.

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