Original article

Comparison of non-invasive diagnostic tests to multi-detector CT pulmonary angiography for the diagnosis of pulmonary embolism

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ABSTRACT

Context: Acute pulmonary embolism (PE) remains a diagnostic and therapeutic challenge to physicians. There are various non-invasive diagnostic modalities been suggested to diagnose pulmonary embolism.
Aim: We tried to find the performance of various non-invasive investigations in comparison to multi-detector Computerized Tomography (MDCT pulmonary angiography for the diagnosis of PE).
Settings and design: A prospective cohort study was conducted in 80 hospitalized medical patients.
Materials and methods: There were 80 patients with Wells score > 2 who were included. The de-mographic data, non-invasive investigations, and MDCT pulmonary angiography were conducted in these patients. The sensitivity (SEN), specificity (SPE), positive predictive value (PPV), and negative predictive value (NPV) were calculated for each test.
Results: Out of 80 patients, 77.5% patients were with Wells score 3–6 and 22.5% patients were with Wells score more than 6. The test with highest sensitivity was D-dimer (SEN − 90%, $P = 0.091$) followed by PAH on TTE (SEN − 83%, PPV − 86%, $P = 0.006$). The most specific test was ECG showing S1Q3T3 (SPE − 100%, $P = 0.421$), followed by Wells score > 6 (SPE − 91%, $P = 0.211$). There was no test with sensitivity and specificity more than 90%
Conclusion: In all patients with intermediate to high-risk probability MDCT pulmonary angiography is the most accurate test to diagnose PE and should be performed at the earliest. The combination of 2-dimensional ECHO and D-dimer can be used in patients with a high clinical suspicion of PE on pre-test probability where MDCT pulmonary angiography is not possible.

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1. Introduction

Pulmonary embolism (PE) is a potentially life-threatening con-dition that can cause significant morbidity and mortality.[1] Pulmo-nary embolism (PE) and deep vein thrombosis (DVT) represents the spectrum of same disease, and clinically most important PE origi-nates from proximal DVT of the leg veins.[1,2] Data from a post-mortem study conducted in a tertiary care hospital in India, showed an overall incidence of PE to be 15.9% in 1000 autopsies of adult medical patients.[3] Moreover, PE was a terminal event in almost 80% of these patients.

The timely diagnosis of PE still remains a challenge for the physicians. Various clinical criteria and diagnostic modalities have been put forth from time to time for early and accurate diagnosis of PE. Though, pulmonary arteriography has conventionally been the gold standard for the diagnosis of PE however during the last two decades, computed tomography pulmonary arteriography (CTPA) has revolutionized the imaging of PE in adults.[4,5] The CTPA has sensitivity and specificity of more than 90% when compared to conventional pulmonary arteriography.[4–6] However, with modern multi-detector Computerized Tomography (MDCT) pulmonary angiography the sensitivity has increased further to more than 95%.[7] This means in a single negative study with MDCT pulmonary angiography, one can safely exclude highly sensitive for PE.[7,8]

However, in the patients where CTPA could not be done either due to critical condition (shock or hypotension) of the patient or history of contrast hypersensitivity, other investigations like D-dimer lower limb venous Doppler and trans-thoracic echocardi-ography (TTE) can be used to diagnose PE.[7,9–11] The sensitivity and specificity of each of these diagnostic modalities as compared to

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MDCT pulmonary angiography is not properly validated. We did this study aiming to find the test performance of pre-test probability using Wells score, non-invasive investigations with MDCT pulmonary angiography in the diagnosis of PE.

2. Materials and methods

This prospective cohort study was conducted in a tertiary care hospital in New Delhi. The study was approved from the Ethics Committee of the hospital. The Wells score (low < 2; intermediate 2–6; high > 6 or more) was used for pre-test clinical probability in all the patients.[12] Patient's with a clinical suspicion of PE and a Wells score of greater than two were taken into study from September 2008 to August 2010.

The exclusion criteria were patient's with a known contraindication to MDCT (known allergy to contrast agents), Wells prediction score of less than two and pregnant patients.

One hundred and sixty two patients were screened on the basis of history, physical examination and Wells score and 80 hospitalized patients based on clinical presentation and Wells scoring system more than two were evaluated. All these patients were subjected to electrocardiogram (ECG), arterial blood gas (ABG), D-dimer testing, chest X-ray, bilateral lower limb venous Doppler, TTE and 64 slice MDCT pulmonary angiography.

All the MDCT pulmonary angiography examinations were performed with 64 slice scanner MDCT (Toshiba Aquilion, Japan) using 50–70 ml of 350 mg nonionic iso-osmolar contrast (fonexal, omnipaque). A hypodense intraluminal filling defect causing partial or total obliteration of vascular lumen in segmental and subsegmental arteries with or without corresponding increase in the diameter of the affected vessel was taken as positive result for PE on MDCT. For D-dimer levels, Nycocard D-dimer, quantitative test based upon immunometric flow principle was used. The values less than 0.3 mg/L were considered normal.

Bilateral lower limb venous Doppler was performed by blinded (not aware of MDCT results) senior radiologist and positive diagnosis of DVT was based on failure to compress the vascular lumen and absence of normal phasic Doppler signals arising from changes to venous flow. TTE was performed by blinded senior cardiologist who was not aware of other results and MDCT findings. On TTE, pulmonary artery systolic pressure (PASP) > 25 mm of Hg in absence of previous history of pulmonary artery hypertension (PAH) and new right ventricle dysfunction (RVD) where taken as positive findings suggestive of PE. Chest X-ray findings like presence parenchymal opacity, oligemia, raised hemi-diaphragm, atelectasis and pleural effusion were considered findings suggestive of PE. The sensitivity (SEN), specificity (SPE), positive predictive value (PPV), and negative predictive value (NPV) were calculated for each test in comparison to MDCT pulmonary angiography. The test performance in term of accuracy was taken with sensitivity and specificity more than 90%. Primary objective of the study was to establish sensitivity, specificity, and test performance of clinical prediction score (Wells score) and non-invasive investigations as compared to MDCT pulmonary angiography in the diagnosis of PE.

3. Results

A total of 80 consecutive medical hospitalized with clinical suspicion of PE and Wells score of more than two patients were included in the study. Out of these, 52 (65%) were males and 28 (35%) were females (Table 1).

The most common presenting complaint among the study group was shortness of breath (97.5%), followed by chest pain (85%) and cough (72.5%) (Table 2). The patients were subjected to clinical pre-test probability for PE using Wells score. Only the patients with

Table 1
Demographic characteristics of the patients.

Demographic characteristic Age group	No. of male patients	No. of female patients	Total
<25	8 (10%)	0 (0%)	8 (10%)
26–50	16 (20%)	8 (10%)	24 (30%)
51–75	24 (30%)	18 (22.50%)	42 (52.50%)
>75	4 (5%)	2 (2.50%)	6 (7.50%)
Total	52 (65%)	28 (35%)	80

Wells scoring more than 2 were included in the study. There were 62 (77.5%) patients with Wells score 3–6 (intermediate risk of PE) and 18 (22.5%) patients with Wells score more than 6 (high-risk for PE). The test with highest sensitivity was D-dimer (SEN – 90%, $P = 0.091$) followed by PAH on TTE (SEN – 83%, PPV – 86%, $P = 0.006$). The most specific test was ECG showing S1Q3T3 (SPE – 100%, $P = 0.421$), followed by Wells score > 6 (SPE – 91%, $P = 0.211$) (Table 3). There was no test with sensitivity and specificity more than 90%.

The combination of positive 2-dimensional ECHO and D-dimer in patients with Wells score > 6 had specificity of 100% and sensitivity of 34.45%.

4. Discussion

Acute PE remains a life-threatening disorder that continues to challenge diagnostically and therapeutically contemporary physicians. In classic historical studies, PE has been shown to be fatal in up to 5–30% of patients if left untreated.[13,14] On an average 22% of patients die with PE even before a diagnosis is made.[15] However, timely anticoagulation therapy can reduce the risk of fatal PE to less than 2%.[16,17] Hence, expedient diagnosis is crucial for prompt initiation of therapy and can improve outcomes of these patients.[17]

The signs and symptoms of PE are non-specific and may be absent in 50–60% of the patients.[18] In our study too, shortness of breath was the most common symptom but was again non-specific.[16,19] Therefore, various investigations and algorithms have been suggested for the diagnosis of PE. The accuracy of a particular diagnostic test involves a trade-off between sensitivity and specificity. A test that is highly sensitive can reduce morbidity and mortality associated with PE by allowing prompt treatment. On the other hand, a highly specific test can reduce morbidity, mortality, and management costs not only by avoiding incorrect treatment but also by avoiding risky confirmatory tests, as well. The modern MDCT pulmonary angiography is highly sensitive and specific for the diagnosis of PE and a single negative study can safely exclude PE.[8]

However, the MDCT pulmonary angiography requires transfer of the patient to CT scan suite and administration of contrast, which may not always be feasible and safe, especially if the patient is critically ill with multi-organ dysfunction. This has led to the development of various clinical prediction algorithms and non-

Table 2
Presenting complaints.

Presenting complaint	Number	%
Shortness of breath	78	97.5
Chest pain	68	85
Hemoptysis	6	7.5
Cough	58	72.5
Fever	50	62.5
Altered sensorium	22	27.5
Death	2	2.5

Table 3
Calibration of various tests with MDCT pulmonary angiography.

Abnormal test	MDCT positive for PE 58 (n)	MDCT negative for PE 22 (n)	Total 80 (n)	SEN	SPE	PPV	NPV
Well's score > 6	16	2	18 (22.50%)	28%	91%	89%	32%
Abnormal	36	10	46 (57.5%)	69%	55%	78%	35%
S1Q3T3 on ECG	8	0	8 (10.00%)	14%	100%	100%	32%
Hypoxemia (PaO$_2$ < 60 mmHg)	12	4	16 (20%)	21%	82%	75%	28%
Level > 0.3 mg/l	52	16	68 (85.0%)	90%	27%	77%	50%
Doppler − suggestive of DVT	38	4	42 (52.5%)	66%	82%	91%	47%
2D-ECHO positive for PAH	48	8	56 (70.00%)	83%	64%	86%	58%
2D-ECHO positive for RVD	36	4	40 (50.00%)	62%	82%	90%	45%

invasive diagnostic techniques for early and accurate diagnosis of PE. However, the majority of studies that have evaluated diagnostic algorithms for PE have been performed in the emergency department setting.[7,8]

In our study of hospitalized patients with Wells score greater than 2, PE was detected in 58 patients (73%) using MDCT pulmonary angiography. Wells score is important in initial risk stratification of patients with PE, with wells score of more than 6 having a specificity of 91%, but is not accurate enough in isolation to predict PE. In our study, the prevalence of PE in high-risk group was around 89% which is higher as compared to that reported in PIOPED study.[20] This may be due to use of more sensitive MDCT pulmonary angiography as compared to the ventilation perfusion scan or may be due to the inter-observer variability of one subjective item in the score (alternative diagnosis less likely than PE).[21,22] No single non-invasive investigation when used in isolation could predict PE with sufficient accuracy as compared to MDCT pulmonary angiography (i.e., sensitivity and specificity more than 90%) (Table 3). Among the various non-invasive tests studied, D-dimer had the highest sensitivity but poor specificity (SNS − 90% SPE − 27%; P = 0.091). The ECG showing S1Q3T3 had highest specificity but again was poorly sensitive (SNS 14%, SPE 100%; P = 0.421).

We also compared the performance of the combination of tests like 2D ECHO and D-dimer in patients with intermediate to high probability of PE (Wells score ≥ 3, Wells score > 6) (Table 4). The combination of positive 2-dimensional ECHO and D-dimer in patients with Wells score > 6 had specificity of 100%, and hence, can be used in place of MDCT pulmonary angiography when it cannot be performed. However, if patients are negative on 2-dimensional ECHO and D-dimer, the patients still should be taken for MDCT pulmonary angiography in high clinical probability of PE as the combination has poor sensitivity. Similar findings with combination of these tests have been reported by other studies.[23,24]

There are few limitations of our study, firstly our study included patients who were hospitalized for medical reasons, and therefore, the results cannot be generalized to other patients. However, the incidence and outcome of PE is different in surgical patients and ICU patients, and may be biased by other confounding factors. Secondly, we did not perform pulmonary arteriography in patients who did not have evidence of pulmonary embolism on MDCT pulmonary angiography. Recent studies have observed risk of subsequent symptomatic PE in those patients in whom pulmonary embolism was excluded by CT was comparable to the risk reported after a normal pulmonary angiogram.[7,25] Also, MDCT pulmonary angiography has been recommended as a first line test by most of the international guidelines,[26,27] hence, we tried to compare non-invasive diagnostic tests with MDCT pulmonary angiography. Finally, we did not look into impact of positive CT pulmonary angiography on the outcome of the patients as this was a test performance study for evaluation of non-invasive diagnostic tests to MDCT pulmonary angiography.

5. Conclusion

We recommend that a clinical pre-test probability using Wells score may be done in all patients with patients with clinically suspected pulmonary embolism. In all patients with intermediate to high risk probability, MDCT pulmonary angiography is the most accurate test to diagnose PE and should be performed at the earliest. The combination of 2-dimensional ECHO and D-dimer can be used in patients with a high clinical suspicion of PE on pre-test probability where MDCT pulmonary angiography is not possible.

Conflicts of interest

All authors have none to declare.

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Table 4
Performance of combination of tests.

Tests	SEN	SPE	PPV	NPV
Wells score ≥ 3 + D-dimer > 0.3 + any of positive echo findings	62.07%	54.55%	78.26%	35.29%
Wells score > 6 + D-dimer > 0.3 + any of positive echo findings	34.45%	100%	100%	36.67%

Sensitivity (SEN), specificity (SPE), positive predictive value (PPV), negative predictive value (NPV).

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