RETROSPECTIVE STUDY OF OPTIMISING THE USE OF COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAPHY (CTPA) FOR THE DIAGNOSIS OF PULMONARY EMBOLISM IN PLACES WITH LIMITED RESOURCES

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ABSTRACT

BACKGROUND

Aim of this study was to evaluate the use of computed tomography pulmonary angiography (CTPA) in the diagnostic evaluation of adult patients with a clinical suspicion of acute pulmonary embolism (PE) at our tertiary health centre and to determine whether pre-test probability assessment and D-dimer estimation lead to a more targeted approach to CTPA use in the local setting with limited resources.

MATERIALS AND METHODS

This was a two-year retrospective descriptive study of inpatients and outpatients referred to the pulmonology department for CTPA examination based on a clinical suspicion of acute pulmonary embolism (PE). Systematic sampling technique was employed in the selection of the patients who satisfied the inclusion criteria. The data was recorded in a Microsoft Excel spreadsheet. Statistical analyses were performed using SPSS Statistics 24.

RESULTS

Of the 220 patients sampled, 54 examinations (24.7%) returned a positive result for acute pulmonary embolism (PE), 101 examinations (45.7%) revealed no abnormal radiologic findings and 65 examinations (29.6%) revealed diagnoses other than PE. In the low probability category, 79.1% of the CTPA examinations were normal and revealed no PE and 20.9% of the examinations revealed pulmonary embolism. In the intermediate category, the majority of the cases (65 %) revealed evidence of PE and 35% were negative for PE. In the high probability category, all the patients (100%) had CTPA evidence of pulmonary embolism.

DISCUSSION

The use of CTPA, without having established the pre-test probability of the disease, will continue to result in overuse of the test and in an unjustified increase of costs and radiation load.

CONCLUSION

Pretest probability along with D-dimers test can be used in the triage of patients for performing computed tomography pulmonary angiography (CTPA) evaluation in limited resource setting.

KEYWORDS

Computed Tomography Pulmonary Angiography (CTPA), Pulmonary Embolism (PE), Wells Clinical Probability Score, D-Dimer Test.


BACKGROUND

Acute pulmonary embolism (PE) is a common and sometimes fatal disease. Clinical evaluation and diagnostic testing is necessary before starting anticoagulation, which is the mainstay of therapy for PE. The approach to the evaluation should be efficient because avoiding delays in initiating therapy reduces morbidity and mortality from PE.\textsuperscript{1,2}

Pulmonary embolism (PE) has a wide variety of presenting features, ranging from no symptoms to shock or sudden death.\textsuperscript{3-4} The most common presenting symptom is dyspnoea followed by pleuritic pain and cough. However, many patients including those with large PE have mild or nonspecific symptoms or are asymptomatic. Thus, it is critical that a high level of suspicion be maintained such that clinically relevant cases are not missed.

The most common symptoms in patients with PE were identified in the Prospective Investigation of Pulmonary Embolism Diagnosis II (PIOPED II) study.\textsuperscript{5} They include the following:

- Dyspnoea at rest or with exertion (73 percent).
- Pleuritic pain (44 percent).
- Cough (37 percent).
- Orthopnoea (28 percent).
- Calf or thigh pain and/or swelling (44 percent).
- Wheezing (21 percent).
- Haemoptysis (13 percent).
Common Presenting Signs on Examination Include,
- Tachypnoea (54 percent).
- Calf or thigh swelling, erythema, oedema, tenderness, palpable cords (47 percent).
- Tachycardia (24 percent).
- Rales (18 percent).
- Decreased breath sounds (17 percent).
- An accentuated pulmonic component of the second heart sound (15 percent).
- Jugular venous distension (14 percent).
- Fever, mimicking pneumonia (3 percent).

D-dimer
An elevated D-dimer alone is insufficient for the diagnosis of PE. In patients suspected of having PE, D-dimer levels are most useful when used in conjunction with clinical suspicion to facilitate clinical decision making for further testing. In general, for patients in whom PE is thought to be unlikely, a normal D-dimer (<500 ng/mL [fibrinogen equivalent units]) effectively excludes PE, and therefore, no further testing is required, including in patients who have had a prior PE, those with a delayed presentation, and women who are pregnant. In contrast, an elevated D-dimer (>500 ng/mL [fibrinogen equivalent units]) should raise the suspicion for PE and prompt further testing in patients who have a low clinical probability of PE.

Clinical Probability Testing
Hospital identification numbers of the sampled cases were used to review the patient records which were searched for clinical parameters used to retrospectively work out Wells? pre-test probabilities. Of the pre-test clinical probability scores available, the Wells test was chosen for its simplicity and the fact that its parameters were easy to obtain.

Diagnostic accuracy was greatest when CTPA was combined with prior clinical probability, as determined by the Wells criteria:
- Wells criteria and modified Wells criteria: clinical assessment for pulmonary embolism.

<table>
<thead>
<tr>
<th>Clinical symptoms of DVT (leg swelling, pain with palpation)</th>
<th>3.0</th>
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<tbody>
<tr>
<td>Other diagnosis less likely than pulmonary embolism</td>
<td>3.0</td>
</tr>
<tr>
<td>Heart rate &gt;100</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilisation (≥23 days) or surgery in the previous four weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Previous DVT/PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>1.0</td>
</tr>
<tr>
<td>Malignancy</td>
<td>1.0</td>
</tr>
<tr>
<td>Probability Score</td>
<td></td>
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<tr>
<th>Traditional clinical probability assessment (Wells criteria)</th>
</tr>
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<tbody>
<tr>
<td>High</td>
</tr>
<tr>
<td>Moderate</td>
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<tr>
<td>Low</td>
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<tr>
<th>Simplified clinical probability assessment (Modified Wells criteria)</th>
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<tr>
<td>PE likely</td>
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<tr>
<td>PE unlikely</td>
</tr>
</tbody>
</table>

Patients with a low pre-test probability (Wells score <2) and a normal or low-probability V/Q scan had a less than 4 percent chance of having a PE.

Patients with a high clinical probability (Wells score >6) and a high-probability scan had a 96 percent chance of having a PE.

Patients with all other combinations were considered indeterminate and had probability of PE that ranged from 6 to 88 percent.

Demographic profiles, including patients age and gender, were recorded. The charts were searched for records of symptoms and signs to suggest deep vein thrombosis (DVT) at or around the day of examination. Symptoms looked for include:
- Upper or lower limb pain
- Swelling
- Discolouration of skin along with other
- Respiratory symptoms.

Signs included upper or lower limb tenderness, positive Homans’ sign, prominent superficial veins and discolouration of the skin. Patients were then grouped into those with clinically suspected or confirmed deep vein thrombosis (DVT), those with no evidence of deep vein thrombosis (DVT) and a third category of unknown for the cases with insufficient data in relation to deep vein thrombosis (DVT).

Heart-rate recordings on the day of the CTPA examination were reviewed and patients were grouped into those with heart-rates of 100 per minute or more and those with heart-rates less than 100 per minute. Patients with heart-rates of at least 100 per minute were given 1.5 points. Chart reviews also included recorded evidence of immobilisation such as travel history, surgery in the preceding four weeks. Patients with a history of immobilisation were allocated 1.5 points.

History of previous venous thromboembolic disease including DVT and PE were allocated 1.5 points. Recorded histories of haemoptysis were searched for and patients with a history of haemoptysis were allocated 1.0 point. Reviews further included history to suggest the presence of a recent malignancy or patients on palliative therapy. Patients with a positive history of malignancy were allocated 1.0 point. Points were tallied and patients who had scores more than > 4 were allocated the high clinical probability and scores ≤4.0 were allocated low clinical probability.

Findings in relation to PE were reported as either PE present or not and whether acute or chronic. Acute PE was defined as a partial or complete filling defect of the pulmonary arterial system.

Chronic PE was defined as the presence of direct pulmonary artery signs (complete or partial filling defect, the presence of an eccentric or calcified thrombus), signs related to pulmonary hypertension and/or signs of systemic collateral supply.

CTPA results were reviewed and patients were grouped into confirmed PE, no abnormal findings or normal study and alternate diagnosis.

Aim of Study
To evaluate the use of computed tomography pulmonary angiography (CTPA) in the diagnostic evaluation of adult patients with a clinical suspicion of acute PE at our tertiary health centre and to determine whether pre-test probability...
assessment and D-dimer estimation lead to a more targeted approach to CTPA use in the local setting with limited resources.

Objectives
To determine the diagnostic yield of computed tomography pulmonary angiography (CTPA) in the local setting.
To compare the pre-test probability scores to the outcomes of the computed tomography pulmonary angiography (CTPA) examinations.
To compare both pre-test probability along with D-dimer test to the outcomes of the CTPA.

MATERIALS AND METHODS
Study Area
The study was conducted at a tertiary health centre in Guntur, Andhra Pradesh, India.

Study Design
Retrospective descriptive study of patients.

Study Population
Patients referred to the pulmonology department for CTPA examination based on a clinical suspicion of acute pulmonary embolism (PE). The study population included both inpatients and outpatients attending the hospital.

Statistical Design
Retrospective two-year study and systematic sampling technique was employed in the selection of the patients who satisfied the inclusion criteria. The data was recorded in a Microsoft Excel spread sheet. Statistical analyses were performed using SPSS Statistics 24.

Inclusion Criteria
Adult patients (>14 years) referred for CTPA examination on the basis of a clinical suspicion of PE, for the first time, in the period 01/04/2014 to 01/04/2016 at a tertiary health centre.

Exclusion Criteria
1. Younger patients (< 14 years)
2. Technically non-diagnostic or
3. Inadequate studies
4. Follow-up CTPAs performed on the same patients
5. CTPAs performed for indications other than PE.

Ethical and Medico-Legal Aspects
The study was a retrospective descriptive study of the patients that were subjected to CTPA on the basis of a clinical suspicion of PE. The study only commenced after full ethical approval was granted. It was reviewed and approved by the Medical Research and Ethics Committee (MREC) of the NTR University and Institutional approval.

A total of 220 patients were selected from the study population using a systematic sampling technique following a random start. D-dimer results were reviewed and patients were categorised as positive, negative and unknown. The data was recorded in a Microsoft Excel spread sheet. Statistical analyses were performed using SPSS Statistics 24.

RESULTS
A total of 412 computed tomography pulmonary angiography (CTPA) examinations were performed in the period 01/03/2014 to 01/03/2016.

A total of 220 patients met the inclusion criteria.

D-dimer results were reviewed and patients were categorised as positive, negative and unknown. The data was recorded in a Microsoft Excel spread sheet. Statistical analyses were performed using SPSS Statistics version 24.

The patients sampled had a mean age of 41.30 with a standard deviation of 18.73.

Of the sampled patients, 65.9% were female and males accounted for 34.1% (Fig 1).

Of the 220 patients sampled, 54 examinations (24.7%) returned a positive result for acute pulmonary embolism (PE), 101 examinations (45.7%) revealed no abnormal radiologic findings and 65 examinations (29.6%) revealed diagnoses other than PE (Fig 2).

Wells clinical probability scores were worked out and assigned. One hundred thirty patients (59.2%) were in the low probability category, 69 patients (31.3 %) were in the...
intermediate probability category and twenty patients (9.5%) were in the high probability category (Fig:3).

**Figure 3. Wells Clinical Probability Score**

In the low probability category, 79.1% of the computed tomography pulmonary angiography (CTPA) examinations were normal and revealed no pulmonary embolism (PE) and 20.9% of the examinations revealed pulmonary embolism (Fig 4). In the intermediate category, the majority of the cases (65%) revealed evidence of PE and 35% were negative for PE. In the high probability category, all the patients (100%) had CTPA evidence of pulmonary embolism (Fig 4).

**Figure 4. Correlating Wells Probability with CTPA**

**D-Dimer**

Of the sampled patients, 78.2% had D-dimer estimation performed and D-dimer test results were unknown or not done in 21.8%. Of the patients that had D-dimer tests performed, 55% were positive and 45% returned were negative (Table 1).

Seventy-five percent (75%) of the patients with negative D-dimers had normal CTPA studies and PE was confirmed in 22%. Of the patients with positive D-dimer test results, 45.1% were normal with PE being confirmed in 44.6% (Table 1).

<table>
<thead>
<tr>
<th>D-Dimer Result</th>
<th>CTPA Result</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Confirmed PE</td>
</tr>
<tr>
<td>Negative</td>
<td>58</td>
<td>17</td>
</tr>
<tr>
<td>Positive</td>
<td>43</td>
<td>42</td>
</tr>
<tr>
<td>Total</td>
<td>101</td>
<td>59</td>
</tr>
</tbody>
</table>

Table 1. D-Dimer Test Result VS. CTPA Result

Patients in the low probability group, with negative D-dimer estimation, all returned negative computed tomography pulmonary angiography (CTPA) results. Nineteen percent (19%) of intermediate probability category cases with negative D-dimers returned positive CTPA results.

**Chest Radiography**

A total of 45.2% of the sampled patients had abnormal chest x-rays, 15.2% had normal chest x-rays and chest x-ray results were unknown in 39.6% of the cases (Fig 5).

**Common Findings Include:**

Atelectasis or pulmonary parenchymal abnormalities (46%), pleural effusion (47 percent).

Usually Hampton’s hump and Westermark’s sign are rare, but should raise the suspicion for PE. Hampton’s hump is a shallow, wedge-shaped opacity in the periphery of the lung, with its base against the pleural surface. Westermark’s sign is the demonstration of a sharp cut-off of pulmonary vessels with distal hypoperfusion in a segmental distribution within the lung. These signs were positive only in 8% of the cases in our study.

**Figure 5. PIE Chart showing Chest Radiography Results**

Of the patients with normal CXRs, 74.4% had no abnormal findings at CTPA and 15.3% had confirmed PE, 10.3% patients had alternate diagnosis. Of the patients with abnormal CXRs, 43.7% were negative (Fig 6) for PE and PE was confirmed in 33.1%, remaining 23.2% had alternate diagnosis (Fig 6). Patients with unknown CXRs, 51.3% had confirmed PE and 23.3% had no abnormalities at CTPA, remaining 25.4% had alternate diagnosis.

**Figure 6. Chest Radiography vs. CTPA Results**

**Lower Limb Ultrasound**

Colour Venous Doppler results were negative in 16.3% of the patients, 15.2% were positive and results were unknown in 68.5% of the cases. Of the patients with no current DVT, 82.7%
returned normal CTPA. 17.3% of these cases (fig 7) returning a positive PE result.

In total, 81.4% of the patients with current DVT returned positive CTPA results in relation to PE and 18.6% were (fig 7) normal CTPA results.

Figure 7. Lower limb DVT ultrasound vs. CTPA

Alternate Diagnosis

DISCUSSION

CTPA (computed tomography pulmonary angiography) is the investigation of choice in patients with a high clinical suspicion of pulmonary embolism (PE) and in those with pre-existing pulmonary disease. Clinical evaluation and diagnostic testing is necessary before starting anticoagulation, which is the mainstay of therapy for PE. The approach to the evaluation should be efficient because avoiding delays in initiating therapy reduces morbidity and mortality from pulmonary embolism (PE).

Results from the current study showed that 59.2% of the CTPA examinations performed at our hospital were in the low probability pre-test category. These results suggest overuse of the CTPA technique and possibly poor choice in the selection of patients undergoing the CTPA without checking Wells pre-test probability of the sampled cases, 31.3% were in intermediate probability and 9.5% were in the high probability category (fig 3).

In the low probability category, 79.1% of the CTPA examinations were normal and revealed no PE and 20.9% of the examinations revealed pulmonary embolism. In the intermediate category, the majority of the cases (65%), revealed evidence of PE and 35% were negative for PE. In the high probability category, all the patients (100%) had CTPA evidence of pulmonary embolism.

In total, 24.7% of the examinations performed were positive for PE (Figure 2). A total of 45.7% of the studies revealed no radiologic abnormality and a further 29.6% of the examinations revealed alternate diagnoses. The high percentage of alternate diagnoses underlines the fact that a more targeted approach is necessary in the evaluation of these patients and that possible pickup of an alternate diagnosis cannot justify CTPA use in low probability cases. The examinations that revealed alternate diagnoses showed cardiac disease in 37% of the cases. Congestive cardiac failure was the most common cardiac condition followed by right-sided heart failure. Pulmonary parenchymal disease was present in 33% of the examinations that revealed alternate diagnoses. Consolidation, pulmonary tuberculosis and interstitial lung disease were the most common lung parenchyma diseases. Pleural disease accounted for 20% of the alternate diagnoses and pleural effusion was the most common finding in these cases. Mediastinal disease accounted for 8% and airways disease for 2% of the alternate diagnoses in our study (Figure 8).

D-dimer levels are elevated in plasma in the presence of an acute clot because of simultaneous activation of coagulation and fibrinolysis. A normal D-dimer level renders acute pulmonary embolism (PE) or deep venous thrombosis (DVT) unlikely. Although D-dimer is very specific for fibrin, the specificity of fibrin for VTE is poor because fibrin is produced in a wide variety of conditions, such as cancer, infection, inflammation, dissection of the aorta, and therefore D-dimer is not useful for confirming pulmonary embolism (PE). Data from a study conducted by van E N and colleagues,9 CTPA can be withheld if Wells score is in low probability and a negative D-dimer result (efficiency) was estimated using fixed (≤500 µg/L and age-adjusted (age × 10 µg/L >50 years) D-dimer thresholds.

The results of the most commonly adopted strategy to evaluate patients who are clinically suspected of having PE which show that the combination of the absence of definite risk factors and negative D-dimer test results could be used to substantially decrease the number of CTPA examinations performed in an emergency department.

Of the patients that had D-dimer tests performed, 75% were positive and 25% returned negative (Table 1).

Patients in the low probability group with negative D-dimer estimation all returned negative CTPA results. Eighteen percent of intermediate probability category cases with negative D-dimers returned positive CTPA results. The use of alternate interpretation of the Wells criteria, where scores of 4 or less are considered PE unlikely, and more than 4 PE likely, suggests that CTPAs can be safely withheld in the PE unlikely cases. The patients sampled had a mean age of 41.3 with a standard deviation of 18.73 and ranged from 14 to 72. Of the sampled patients, 65.9% were female and males accounted for 34.1% (Figure 1). Of the female patients, 50.9% were in the reproductive age group. As a result of the increased clinical use of CTPA, and its well-documented high radiation exposure, serious concerns have been raised about the possibility of increased incidence of cancers in the future. That is why it is important to select patients for CTPA correctly.

Many studies provide evidence that suggests that a substantial number of CTPAs could be avoided simply by adhering to the information derived from clinical history and D-dimer test determination. In the current study, only 78.2% of the sampled patients had D-dimer estimation performed. The combination of negative D-dimers and a low probability
category returned no PE positive CT examinations. This highlights the value of D-dimer estimation in the workup of these patients and the fact that more than 20% of the sampled cases did not have D-dimers performed clearly suggests that clinicians should be encouraged to use this D-dimer test in the triage of patients for performing computed tomography pulmonary angiography (CTPA) evaluation.

The current study was a retrospective review of pre-test probability scores, which were worked out based on chart entries. The study population was heterogeneous, as it included in and outpatients, and chart entries prior to CTPA were of varying quality between these groups. The CT scans were reported by different observers of varying experience and this also served as a limiting factor for this study.

CONCLUSIONS

Pulmonary embolism (PE) remains a very challenging disease to diagnose. The myriad of alternate diagnoses clearly highlights the magnitude of the challenge clinicians are faced with in the clinical evaluation of the patients suspected of having PE. The results of the current study demonstrate that the majority of CTPA examinations performed at our institute had Wells low probability scores. These results suggest overuse of the CTPA technique and possibly poor choice in the selection of patients undergoing the examination. The results raise serious concerns about the radiation dose delivered to patients, which could have been avoided and further highlight the importance of correct patient selection prior to CTPA examination. The results further support the use of pre-test probability assessment in combination with D-dimer estimation prior to computed tomography pulmonary angiography (CTPA) evaluation in the local setting. CTPA is an accurate and readily available diagnostic test for the diagnosis or exclusion of pulmonary embolism (PE). However, use of CTPA, without having established the pre-test probability of the disease, will continue to result in overuse of the test and in an unjustified increase of costs and radiation load to the patients.

REFERENCES