In The Name of God
Thesis for specialty in radiology degree

Title:
The Association between Pulmonary CT Angiography Parameters with Clinical Outcome in Patients with Pulmonary Embolism

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Abstract

PURPOSE: To assess the association between pulmonary CT angiography (pCTA) with clinical outcome in patients with pulmonary embolism (PE).

METHODS: Prospective noncomparative analysis of pCTA studies of One hundred and forty-three patients with PE and documentation of pulmonary artery/aorta (PA/AO) ratio, right ventricular/left ventricular (RV/LV) ratio, superior vena cava (SVC) diameter, pulmonary obstruction index (POI), ventricular septal bowing (VSB), pulmonary infarction, need for ICU therapy, need for mechanical ventilation and mortality were recorded. Otherwise, Patients having CHF, chronic pulmonary thromboembolism, obstructive lung disease, severe interstitial lung disease, and vasculitis in addition to PE, as well as normal pCTA findings were excluded. Statistical significance of all tests was set at a $p$ level of less than 5%.

RESULTS: Mean duration of hospitalization was 9 ± 5 days. Fifty-five patients admitted to ICU; 34 received mechanical ventilation. Mean duration of ICU therapy was 3 ± 5 days and mortality rate was 10.5%. Significant positive associations of POI and pulmonary infarction with need for ICU therapy were shown ($P < 0.001$). RV/LV ratio, POI, and VSB significantly associated with mortality ($P < 0.001$).

CONCLUSIONS: The clinical course including need for ICU treatment and mechanical ventilation showed significant correlations with POI, VSB, and pulmonary infarction seen in CTA. Although, there were no statistically significant differences between pulmonary artery/aorta (PA/AO) ratio and superior vena cava (SVC) diameter with parameters of clinical course.
Keywords: Pulmonary CT Angiography parameters, pulmonary embolism, Clinical outcome
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Chapter 1: Introduction
1.1 INTRODUCTION:

Pulmonary CT angiography (pCTA) is gaining wider acceptance as a first-line and gold standard examination for detecting pulmonary embolism (PE) (1). Some studies have shown that pCTA is more cost-effective than conventional angiography in the work-up of patients suspected of having PE (2, 3). PE is a frequent missed clinical diagnosis that has absent or nonspecific associated radiographic findings (4). The mortality rate of PE decreased in proportion to last decades due to clinical suspicious and high accuracy of multi-detector CT (MDCT) angiography in detection of sub-segmental PE and advanced image processing techniques, such as multi planar reconstruction (MPR) or maximum intensity projection (MIP) reconstructed from isotropic volumetric data sets, that simplify demonstrating the sub-segmental PE (5, 6).

Prior studies demonstrated the importance of pCTA as a first-line imaging technique in patients suspected of having PE (7). Recently, many attempts have been made to classify patients according to their risk of death due to PE.

Previous large retrospective studies (8,9) and randomized trials on thrombolytics (10), have shown that clinical presentation are strong predictors of death due to PE.

However, efforts have been made to classify high risk patients based on imaging. Right-sided heart strain, demonstrated by echocardiography, have been shown to predict associated mortality in acute PE in several small prospective studies (11). Based on the results of echocardiography, several investigators have attempted to determine the prognosis of the results have been derived from CT.

They used different scoring system that can demonstrate relatively association between severity of PE and clinical outcome (7, 12).
The purpose of this study was to determine the pCTA images findings with need for ICU, need of mechanical ventilation, and mortality in affected patients. Besides, the method of our study was indirect effects of PE with measurement of SVC diameter, interventricular septum deviation, RV/LV, PA/AO, and POI.
1.2 Text & Literature Review

1.2.1 Acute Pulmonary Embolism

Imaging plays a crucial role in the diagnosis of pulmonary embolism (PE) and deep venous thrombosis (DVT), a spectrum of the same disease entity. PE is the third most common cause of cardiovascular death in the United States, following ischemic heart disease and stroke, with an annual incidence of 300,000 to 600,000 per year (13-14). Despite the high prevalence, PE is difficult to diagnose, with only 43 to 53 patients per 100,000 being accurately diagnosed, and up to 70% of clinically unsuspected PE diagnosed at autopsy (13, 15). In the past few decades, the incidence of PE has decreased by 45%, whereas that of DVT is unchanged (16-17). Death occurs in up to 90% of patients with unrecognized PE, whereas in treated patients PE accounts for less than 10% of deaths (18-19).

Rapid and timely diagnosis of this life-threatening disease is important to improve patient outcome as the signs and symptoms as well as ancillary tests are nonspecific. The recent rapid growth in CT technology over the past decade has seen the emergence of CT pulmonary angiography (pCTA) as the single first line test in the diagnosis of PE because of its high diagnostic accuracy and ability to provide alternate diagnosis for diseases of the lung parenchyma, pleura, pericardium, aorta, heart, thoracic lymph nodes, and mediastinum.

The widespread availability and use of pCTA has made the diagnosis of PE easier in most cases, but has raised the need for optimal use of this technique in the
appropriate patient population, in order to minimize unnecessary medical radiation exposure.

Pretest risk stratification using Wells criteria, clinical probability scores, assessing premorbid conditions, past history, and a thorough clinical examination should precede an appropriate, timely, and accurate diagnostic test (20-21). In some common scenarios like pregnancy and in critically ill patients, the diagnosis of PE still remains challenging.

1.2.2 Ventilation-Perfusion Scintigraphy

Combined ventilation and perfusion (V/Q) scintigraphy had been the imaging technique of choice for decades. A V/Q scan with normal findings essentially excludes pulmonary embolism with an NPV (Negative Predictive Value) close to 100%, thereby precluding the use of anticoagulation, whereas a high-probability scan is highly specific for the diagnosis of PE, allowing definitive treatment. In the original PIOPED (Prospective Investigation of Pulmonary Embolism Diagnosis) study only 14% of patients had a normal V/Q scan and 13% a high probability V/Q scan, rendering a definitive diagnosis in only a small group of patients; most (73%) had an indeterminate (non-diagnostic) or low-probability test result (22). This high degree of uncertainty makes initiation of definitive anticoagulant therapy difficult because of risk of bleeding and necessitates additional tests to diagnose or exclude pulmonary embolism. The criteria for reporting V/Q scans have improved significantly (23). Recent use of V/Q scanning with SPECT allows 3-dimensional visualization of segments previously not identified on planar imaging, such as the medial basal segment of the right lower lobe. The lung segments are more clearly defined and can be viewed in any orthogonal
plane, resulting in better detection and characterization of defects (24). SPECT also improves image contrast, thus decreasing the rate of intermediate scan reports. Large-scale trials are needed to fully assess this modality and compare its performance with pCTA. Currently the definitive primary role of V/Q scanning is in patients where pCTA is contraindicated as in severe renal impairment or history of iodine or contrast allergy.

1.2.3 Catheter Pulmonary Angiography

Catheter pulmonary angiography has been considered as the reference test for the diagnosis of PE since the late 1960s. However, the invasive nature and expense of the study along with a small but definite risk in morbidity has contributed to its underutilization. Two studies, done 12 years apart in 1240 patients, showed that following an inconclusive V/Q scan result, catheter pulmonary angiography was performed in less than 15% of patients (25-26). Many patients were treated with anticoagulants without a definitive result. Accurate diagnosis is important, as anticoagulants themselves account for significant morbidity (up to 6.5%), that increases with age and with comorbid conditions (27-28).

With the newer generation of MDCT (multidetector CT) scanners, the role of catheter pulmonary angiography as the gold standard test has been questioned and is considered to be flawed, particularly at the subsegmental level (29-30). The interobserver agreement at the subsegmental level on the original PIOPED study was reported to be only 66% (22). In PIOPED II, in the 20 discordant cases, PE was missed at the lobar, segmental, and subsegmental levels in 13 patients; 8 of 13 were at the
subsegmental level (31). The current role of catheter pulmonary angiography is when pCTA is inconclusive, or when the clinical findings are discordant with pCTA results.

1.2.4 CT Pulmonary Angiography

Incidental detection of PE was first documented by Sinner in 1978 (32). The advent of single-detector helical CT in the early 1990s, made it possible to obtain volumetric datasets with good contrast in a single breath-hold, allowing diagnosis predominantly of central and segmental PE. With rapid evolvement of CT technology, the CT diagnosis of PE has been a subject of much research in the past couple of decades, and has resulted in pCTA becoming a first-line imaging test at many centers (33). pCTA is a relatively safe, accurate, readily available and cost-effective noninvasive test that not only diagnoses PE, but also provides diagnosis of alternative pathologies in the thorax accounting for patient symptoms, particularly in the inpatient and emergency department settings. Faster multidetector scanners have set the way for a potential new gold standard test. With newer 128 and higher slice scanners, the sensitivity and specificity is likely to increase albeit at a cost of increased radiation.

1.2.5 Advances in MDCT

MDCT has several advantages over SDCT (single detector CT) in the diagnosis of PE, which include improved z-axis resolution, shorter scan times, reduction in volume of contrast, and the ability to do a combined pCTA/CT venography (CTV) exam at the same setting with a single bolus of contrast.

Advances in MDCT technology with improved gantry rotation speeds and increased detector width allow rapid acquisition of large volumetric datasets over a
greater craniocaudal distance than with SDCT. While reduction in slice collimation with SDCT results in a longer breath hold and a likelihood of increased respiratory motion artifact, with MDCT reduction in slice thickness leads to better visualization of subsegmental pulmonary arteries, with 94% of fifth order and 74% of sixth order pulmonary arteries being visualized (34-36).

Reducing the reconstruction thickness decreases partial volume averaging and also results in better visualization of the obliquely oriented middle lobe and lingual arteries, in which an estimated 20% of emboli occur (29). Reducing the slice thickness also improves the interobserver agreement for diagnosis of PE (37).

1.2.6 CT Pulmonary Angiography Technique

With rapidly advancing MDCT technology, the techniques and protocols are continually evolving. Precise techniques vary between the different generation of scanners and between vendors. The imaging acquisition on the current generation of scanners includes the entire lungs with resolution of 1.25 mm or less. The aim is to perform the study at thinnest slice collimation with a single short breath hold in full suspended respiration. With the 64-slice and higher generation scanners, it is possible to obtain the entire study with a breath hold of less than 5 seconds. In intubated patients, because of the short acquisition time, respiration can be suspended for the duration of the study. With such short breath holds, it does not matter whether the scan is acquired in a caudocranial or craniocaudal direction.

Power injectors are required for rapid contrast delivery to obtain adequate enhancement of the pulmonary arteries. An 18- to 20-gauge intravenous cannula is
placed in the antecubital vein. The degree and quality of pulmonary arterial enhancement depends on the amount and concentration of contrast, injection rate, and the scan delay. On the 64-slice scanner we use 70 mL of contrast (Isovue 370, Bracco Diagnostics, New Jersey) for pCTA imaging of the chest alone, and for a combined CTPA/CTV study we use 120 mL of contrast (Isovue 370 Bracco Diagnostics) at 4 mL/s. A greater degree of arterial enhancement can be achieved by increasing the rate of contrast, independent of the concentration of iodine contrast medium.

1.2.7 Timing Bolus/Bolus Tracking

The timing of contrast bolus administration is critical to obtain optimal opacification of the pulmonary arteries. Incorrect timing is a common cause of suboptimal studies. A fixed scan delay of 20 to 25 seconds was used especially for SDCT and early generation of MDCT scanners, which leads to adequate opacification of the pulmonary arteries in at least 85% of patients with normal cardiac function. However, with the current generation of scanners, a timing bolus or bolus tracking method is more commonly used to optimize opacification of pulmonary arteries.

A timing bolus is usually performed by injecting 15 to 20 mL of intravenous contrast material and placing a region of interest in the pulmonary trunk to obtain a time-density curve from which the scan delay can be calculated. When comparing empirical delay with test bolus, Hartmann and colleagues reported that despite objective improvement in pulmonary artery enhancement, there was no significant difference in image quality (38). Additionally, 16% of the studies had to be excluded because of uninterpretable time density curves.
Alternatively, bolus tracking method can be used with a cursor in the main pulmonary artery that triggers scanning at a preset threshold. For the 16-slice scanner, the scan is triggered when a threshold of 120 HU is reached and for the 64-slice scanner, at the first sight of contrast in the pulmonary artery. A timing or bolus tracking method should be used in patients with suspected or known cardiac dysfunction because the optimal scan delay time can be 40 seconds or more.

In larger patients, a larger volume of high-density contrast should be injected at a higher flow rate to improve the signal to noise, a higher kVP should be used, and images should be acquired at thicker collimation of 2.0 to 2.5 mm to decrease quantum mottle.

**1.2.8 Image Interpretation**

Given the large volume datasets and the increased number of images generated for these studies, pCTA is now routinely read off a dedicated work station or PACS system and not on hard copy images. The window level and width are adjusted on the fly while scrolling to optimally visualize the opacified pulmonary arterial lumen. At some institutions, coronal and sagittal reformats are routinely generated to aid fast review of the pulmonary arterial tree. In an interobserver study evaluating the utility of multiplanar reconstructions in pCTA, the authors report that generated sagittal and coronal reformats do not increase diagnostic accuracy, but do increase reader agreement and reader confidence, and may decrease interpretation time (Espinosa et al, presented at Society of Thoracic Radiology Annual Meeting, 2008).
The paddle wheel technique helps delineate the vessel and its branches in continuity as the artery radiates from the hilum, allowing visualization of the extent of thrombus burden on a single image. There is no significant difference between the paddle wheel technique and axial images for detecting central PE (39-40). However, for the diagnosis of peripheral pulmonary emboli, there is significantly lower sensitivity and specificity for the paddle wheel method alone without the concurrent use of axial images (39).

### 1.2.9 CT Findings of Pulmonary Embolism

**Direct Findings**

The diagnosis of PE is made on CT by direct visualization of a low attenuation filling defect that partially (Fig. 1.1) or completely occludes a contrast filled artery.

![Figure 1.1. Low attenuation filling defect](image)