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Clinical Consequences of an Indeterminate CT Pulmonary Angiogram in Cancer Patients

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Abstract

Our aim was to evaluate clinical management and outcomes in cancer patients who had an indeterminate Computed Tomographic Pulmonary Angiogram (CTPA) for the assessment of pulmonary embolus. We reviewed 1000 CTPA studies and identified 251 limited (indeterminate) CTPA. We examined follow-up imaging and reviewed clinical management decisions and any positive diagnosis of venous thromboembolic disease (VTE) within the subsequent 90 days.

60 patients (23.9%) had a follow-up imaging study within five days. 8 had a positive study for VTE disease within 5 days. 3 patients (1.2%) were placed on anticoagulation therapy based on the limited CT result.

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Introduction

Computed tomographic pulmonary angiography (CTPA) is widely used in the investigation of patients with suspected pulmonary embolus (PE) and has become the standard radiologic examination for the evaluation of patients with suspected PE in most institutions^{1–3}. The sensitivity of CTPA for PE has increased with the introduction of multidetector CT scanners and is now greater than 90%^{4,5}. In the multicenter PIOPED II study, 77% of the investigators recommended CT as the imaging modality of choice for suspected PE^{6,7}. Multidetector CT scanners can now demonstrate PE at the segmental and sub segmental pulmonary artery levels^{8,9}. Negative CTPA results are comparable to negative results on ventilation-perfusion (VQ) scans or conventional pulmonary angiography for the exclusion of PE^{4,5,10–19}. Unfortunately, similar to VQ scans, not all CTPA examinations will be conclusive in confirming or excluding a PE.

In the current literature, the percentage of limited or indeterminate CTPA ranges from 5.9 to 26%^{1,20–22}. Limitations may be due to respiratory motion artifact, streak artifact, extensive pulmonary parenchymal findings and poor opacification of the pulmonary arteries²³. The two major cause of an indeterminate result have been identified as motion artifact and poor opacification of the pulmonary arteries²¹. The clinical impact of a limited and therefore indeterminate CTPA can be potentially serious, as illustrated by similar data on clinical outcomes of an indeterminate VQ scan. VQ scans are indeterminate in up to 70% of cases²⁴ and follow up conventional angiograms have demonstrated PE in up to 33% of these cases^{25,26}.

Following a limited CTPA, the referring clinician is faced with a management dilemma. They can accept the report as a negative result and end their workup for PE, or choose to pursue the suspected diagnosis further, with repeat CTPA, Doppler ultrasound (US), or VQ scans. The implications for oncology patients are even more complicated, given their inherent increased risk of venous thromboembolic disease and frequently complicated surgical and medical issues. To date, no study has evaluated the clinical outcome of a limited CTPA in cancer patients.

Materials and Methods

Subjects

This retrospective study was approved by our institutional review board. The aim of this study was to evaluate the clinical outcome and management of oncology patients who had a limited CTPA and to assess whether the suspected PE diagnosis was further pursued with repeat CT imaging or alternative imaging modalities. As a secondary outcome, we evaluated for a positive diagnosis of venous thromboembolic disease within three months of the initial study.

CTPA reports at our institution are formally categorized into four separate groups, to standardise the terminology used to convey diagnostic certainty : (1) Positive for pulmonary embolism (2) Limited study showing no central pulmonary embolism; cannot evaluate for segmental or sub segmental emboli.(3) Equivocal for pulmonary embolism and (4) No

pulmonary embolism. CTPA are considered limited if, due to technical or other factors, evaluation for PE cannot be performed beyond the central pulmonary arteries (defined as main, right and left and lobar arteries), preventing diagnosis at the level of segmental and sub segmental branches. The designation of equivocal for PE at CTPA indicates that there is a possible small PE, but artifact cannot be excluded.

A PACS review in our tertiary cancer center identified 1000 consecutive CTPA performed between April 2010 and September 2010. Of these 1000 studies, a keyword search of all CT reports for limited PE yielded 251 patients who had a limited CT scan and were included in this study (mean age 58 years; 134 men, 117 women). No patient with a limited CTPA was excluded. The reason(s) for limitation was recorded and placed in one of six categories: respiratory motion, streak artifact from the superior vena cava, poor opacification in the pulmonary artery, extensive tumor or parenchymal disease, multiple reasons given or no reason given. For studies in which no reason was specifically given for the technical limitation, we reviewed the radiology report and recorded any new pleural or parenchymal disease mentioned elsewhere in the report; which may have been a cause for the study's limitation.

For all limited CTPA studies, the electronic medical records were reviewed for additional relevant imaging studies within the subsequent five days, including repeat CTPA, lower extremity Doppler venous US or V/Q scan. Use of anticoagulation and placement of an inferior vena cava filter were documented. The clinician's final impression of the study result (positive or negative) was documented, if recorded in the records. Age, sex and patient location at time of the initial study were recorded.

The electronic medical records and PACS were then reviewed for any repeat imaging studies within the 5–90 day period following the limited CTPA, to assess for a subsequent positive diagnosis of venous thromboembolic (VTE) disease. The number of positive studies was recorded for both the treated (anticoagulated) and untreated (not anticoagulated) groups.

CT Angiography Technique

All CTPA studies were performed with either a 16-MDCT scanner (Lightspeed 16, GE Healthcare) or a 64-MDCT scanner (Lightspeed VCT 64 or CT750HD, GE Healthcare). Images were acquired in a caudal to cranial direction from 2 cm below the domes of the diaphragm to the aortic arch, in a single breath-hold in the supine position. Using an 18-gauge peripheral venous line, an intravenous injection of 40 ml of saline, then 80 ml Omnipaque 350 followed by another 40 ml of saline was administered at a rate of 4cc/sec using Smartprep for bolus timing. These parameters were unchanged during the study period.

Images were reviewed on a picture archiving and communication system monitor (PACS), (Centricity, GE Healthcare). All inpatient, urgent care center and intensive care unit (ICU) studies were double read by a radiology resident or fellow and an attending radiologist. All outpatient studies were single read by an attending radiologist.

Statistical Analysis

Continuous variables were described using the median and range while categorical variables were summarized by frequency and percent. Statistical comparisons were made using Fisher's exact test. Significance was defined as $p < 0.05$. All analyses were conducted using SAS v.9.2 software (SAS Institute, Cary, NC, USA).

Results

Of the initial 1000 consecutive CTPA studies, 107 (10.7%) studies were interpreted as positive for PE and 600 (60.0%) were negative for PE. 251 (25.1%) were reported as limited for central PE - cannot evaluate for segmental or sub segmental emboli and 42 studies (4.2%) were interpreted as equivocal for PE (Figure 1).

Most patients were either inpatients or referred from the urgent care center (Table 1). No reason was given for the study limitation in 184 studies (73.3%). The most commonly mentioned limitation was respiratory motion, in 23 cases (9.2%). Other causes for study limitation are listed in Table 2. Of the 184 studies where no specific reason was documented for the study limitation, our review found that 74 of 184 (40.2%) had new parenchymal or pleural findings documented elsewhere in the report.

In total, 60 of 251 patients (23.9%) with limited CTPA had further imaging to investigate for VTE disease within a five day period. 191 patients (76.1%) had no repeat imaging within the first 5 days. Of the 60 re-imaged patients, 16 had documented notes indicating that the clinician considered the CTPA negative, but these 16 patients then had repeat or additional imaging to assess for VTE within five days. Of the 60 re-imaged patients, 54 patients (90.0%) had a lower extremity US, 5 (8.3%) had a VQ scan and 1 patient (1.7%) had a repeat CTPA. No patient had digital subtraction pulmonary angiography. 8 of the 60 re-imaged patients (13.3%) had a positive study-all lower extremity DVT.

Overall, most (207 of 251, 82.5%) of the limited CTPA studies were treated as a negative study by the clinician, with either documentation to that effect in the medical notes or, where no opinion was recorded, subsequent clinical decisions to support this opinion (i.e. no therapeutic intervention or no re-imaging within 5 days) (Table 3). No significant association was found between a positive follow up imaging study and the clinician's final impression of the limited CTPA (US $p = 0.200$ and V/Q $p = 1.00$).

17 of 251 patients (6.8%) were already on therapeutic doses of anticoagulation therapy prior to the limited CTPA. Only 3 (1.2%) patients were started on anticoagulation therapy based on the limited CTPA result alone. Of these, one patient had an incidental catheter-related superior vena cava thrombosis detected on the limited CTPA, and was anticoagulated for this reason. One patient was started on anticoagulation after the limited CTPA, but subsequently had a positive lower extremity Doppler ultrasound for DVT ten days later. The third patient was anticoagulated because of the limited CTPA result alone, without any positive study for VTE disease and was continued on treatment for 9 months. In total, 20 patients (8.0%) were already on or commenced anticoagulation therapy over the course of

this study (the treated group). 231 (92.0%) patients were never anticoagulated (the untreated group).

One patient's anticoagulation therapy was stopped within the 5 day period after the limited CTPA. The treatment had been commenced a week prior to the CT study, because of a positive ultrasound for lower extremity DVT. Due to pre-existing relative contraindications to anticoagulation treatment, the decision was made to place an IVC filter several days after the limited CTPA, and the anticoagulation was thus stopped.

We reviewed PACS for any additional relevant imaging studies within the 5–90 day period following the initial CT. Within this time frame, 92 of the 251 patients (36.7%) had additional imaging studies to assess for new or recurrent venous thromboembolic disease (Table 4). 1 of 20 patients (5.0%) in the treated group and 12 of 231 (5.2%) patients in the non-treated group had a positive study ($p=1.00$; Table 5).

8 patients (3.2%) died within 5 days of the limited CTPA. 81 patients (32.3%) in total had died by the end of the three month period. 155 patients (61.8%) in total had no additional imaging studies to investigate for VTE disease either within the acute 5-day period or within 5–90 days following the limited CTPA.

Discussion

Venous thromboembolic disease is commonly encountered in oncology patients. However, in 82.5% of the cases in our study, the clinicians considered the limited CTPA a negative study, and often did not proceed with further diagnostic or therapeutic measures. Only 1.2% of the patients in this study were given anticoagulation following a limited CTPA. This contrasts with a previous paper by Jones and Wittram²¹, who found that only 22% of their indeterminate CTPA studies were clinically interpreted as negative. Just 23.9% of our patients were further investigated with repeat imaging within 5 days, with either lower extremity US, repeat CT or V/Q scan. This percentage was again lower than in the Jones et al paper, in which 33% of patients with indeterminate CTPA underwent follow-up imaging²¹.

The percentage of CTPAs considered limited in our study was high, at 25.1%, but was similar to that in a study published by Abujudeh et al. in 2009²⁰. They reviewed 2151 CTPA reports and found that 21% of their cases were only considered negative for PE as far as the central pulmonary arteries and 5% were completely non-diagnostic. They classified a further 8% of their exams as suboptimal but diagnostic. Abujudeh et al concluded that more experienced radiologists (> 10 years experience), subspecialty thoracic imagers and radiologists reporting independently as a single reader were more likely to report technical limitations in studies. Our study did not assess the experience of the reporting radiologists. It may also be that the standard PE reporting lexicon used at our institution, which is incorporated into a report template, encourages people to report any technical limitations in a study, ensuring that clinicians are not falsely assured of a negative result in a suboptimal scan.

Our population group was composed entirely of oncology patients, which is a very select population and the significance of a limited CTPA has not been previously studied in this group. 38 patients (15.1%) had a diagnosis of primary lung cancer, with associated parenchymal abnormalities, which may have attenuated or obscured the pulmonary arterial tree. 10 (4.0%) of the patients were inpatients in the ICU. Studies have shown that CTPA in an ICU patient group may be more likely to be technically limited, because of the severity of the underlying conditions that lead to the ICU admission ²⁷.

Clinical decision making was not uniform across our studied population, with no algorithm available to guide clinical decision making on which patient to treat in these situations. The number of patients who died within the three month period was high, at 32.2%; however, these were all oncology patients, many with advanced metastatic disease. Reassuringly, our three month event rate for VTE after the acute period was similar in both the treated and untreated patients. This leads us to believe that the rate of missed PE in the untreated patients following the indeterminate CTPA was not high and that clinicians at our institution are using clinical criteria appropriately to treat those patients whom they are most concerned about.

Our study had several limitations. It was a retrospective study, which made it difficult to collect complete data for certain variables, particularly the clinician's impression of the study result. The 5 day acute period was arbitrarily selected, however this was based on our clinical opinion that a thromboembolic event occurring within that time period was likely to be related to the same event that prompted the CTPA study, rather than a new, separate event.

Despite the reassuring finding of similar three-month rates of VTE within the treated and untreated groups, it is still a potential medico-legal concern that most clinicians considered a limited CTPA to be a negative study and did not investigate further. While we did not find evidence that this adversely affected our patient group, the potential for serious, adverse outcomes at an individual level should not be ignored. We feel that further education of clinicians is still prudent; to ensure that the true limitations of a "limited"CT PA are fully understood.

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Figure 1.
Results of 1000 consecutive CTPA

Table 1

Patient characteristics

Median age at CT, years (range)	58.0 (18.0–92.0)
Sex	N (%)
Men	134 (53.4)
Women	117 (46.6)
Cancer type	N (%)
Breast	34 (13.5)
Lower Gastrointestinal	16 (6.4)
Upper Gastrointestinal	14 (5.6)
Genitourinary	22 (8.8)
Gynecological	18 (7.2)
Head & Neck	17 (6.8)
Hepatobiliary	11 (4.4)
Leukemia & Lymphoma	22 (8.8)
Lung	38 (15.1)
Prostate	14 (5.6)
Other	45 (17.9)
Patient location,	N (%)
Inpatient, including Intensive Care Unit	148 (60.0)
Urgent Care Center	76 (30.3)
Outpatient	27 (10.8)

Table 2

Reasons documented for limited study

Reason	No. of studies (%)
No reason given	184 (73.3)
Respiratory motion artifact	23 (9.2)
Extensive tumor/parenchymal disease	14 (5.6)
Poor opacification of pulmonary arteries	9 (3.6)
Streak artifact from SVC	5 (2.0)
More than one reason given	16 (6.4)

Table 3

Clinician impression of the limited CTPA

Clinician impression	No of studies (%)
Negative	207 (82.5)
Positive	8 (3.2)
No impression available	36 (14.3)

Table 4

Type of imaging done within 5–90 days

Study type	N (%)
CTPA	6 (6.5)
Lower extremity Doppler ultrasound	71 (77.2)
V/Q scan	1 (1.1)
CT + Ultrasound	10 (10.9)
V/Q scan + Ultrasound	4 (4.3)

Table 5

Incidence of VTE in treated vs untreated patients within 5–90 days

Group	No. of positive studies (%)
Treated patients (n = 20)	1 (5.0)
Untreated patients (n = 231)	12 (5.2)

Group	Study result, No. (%)		p-value
	Positive	Negative	
Treated patients (n = 20)	1 (5.0%)	19 (95%)	1.00
Untreated patients (n = 231)	12 (5.2%)	219 (94.8%)	