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ORIGINAL ARTICLE

Computed tomography for suspected pulmonary embolism results in a large number of non-significant incidental findings and follow-up investigations

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Abstract

Introduction Computed tomographic pulmonary angiograms (CTPAs) are often ordered to evaluate pulmonary embolism (PE) in the emergency department (ED). The increase use of CTPA has led to an increase in incidental findings, often of low clinical significance. Our objectives were to (1) assess the prevalence and clinical significance of incidental findings identified in patients evaluated with CTPAs for PE in the ED, (2) evaluate follow-up investigations for these incidental findings, and (3) assess the utility of routine chest X-rays done prior to CTPA.

Methods This is a historical cohort study of adult patients, presenting to two tertiary care EDs from January–December 2015, evaluated with CTPA for possible PE. Two reviewers' extracted data from electronic CT records in a standardized fashion with inter-rater reliability reported using the kappa statistic. We measured the prevalence of PE and stratified non-PE findings according to alternative diagnoses and incidental findings. Data were reported as mean and standard deviation (SD). Univariate analyses were performed with *t* test for continuous variables.

Results A total of 1708 studies were included (mean 62 years (SD 16.7), 56.9% female). PE was found in 233 (13.6%) patients. A total of 223 (13.1%) patients had an incidental finding, the majority of which included pulmonary nodules ($n = 83$, 37.2%) and adenopathy ($n = 26$, 11.6%). Of the incidental findings, 197 (88.3%) were non-significant and led to no definitive diagnosis of cancer. In patients who underwent both CTPA and chest X-ray, X-ray reports revealed the same diagnosis in 77% of PE-negative patients without missing a clinically significant incidental finding.

Conclusions Incidental findings are as common as a diagnosis of PE in patients undergoing CTPA. They are rarely clinically significant. Chest radiograph remains a reasonable initial investigation as it can aid in identifying alternative diagnoses especially in the setting of a low pre-test probability for PE.

Keywords Computed tomography · Incidental findings · Pulmonary embolism · Chest X-ray

Introduction

Pulmonary embolism (PE) is a clinically important diagnosis in the emergency department (ED) that is associated with significant morbidity and mortality. While several clinical decision rules have been derived to aid in the risk stratification of PE [1, 2], diagnostic evaluation is often required for patients with suspected PE.

Computed tomography pulmonary angiography (CTPA) has become the diagnostic imaging modality of choice in these patients. Given its widespread availability, high inter-observer agreement [3], speed, and accuracy, CTPAs are now preferred over other modalities such as the ventilation-perfusion (VQ) scan [4]. CTPA is frequently ordered even in patients with low clinical suspicion of PE owed in part to its ubiquity. This has also led to an increase in incidental findings; the prevalence and characterization of such findings have been reported in other literature, however their clinical significance has not been well described [5, 6]. Retrospective reports reveal

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that the prevalence of CT incidental findings in patients with suspected PE ranges from 15 to 30% [7–10]. These incidental findings often result in further investigations such as follow-up radiographic studies and other diagnostic interventions, exposing patients to unnecessary radiation and contrast [11–13]. Additionally, incidental findings such as pulmonary nodules can often be a source of great anxiety for patients as they lead to multiple follow-up investigations.

The primary aim of this study was to assess the prevalence and clinical significance of incidental findings on CTPA identified in patients with suspected PE. We also wished to evaluate follow-up CT studies for these incidental findings to determine those that led to a definitive diagnosis of cancer. In addition, routine chest X-rays are often ordered prior to CTPA to work up patients that may present with symptoms suggestive of an alternative diagnosis. Thus, our secondary aim of the study was to determine the diagnostic utility and performance of routine chest X-rays done prior to CTPA.

Methods

We included patients > 18 years of age undergoing CTPA to rule out the diagnosis of pulmonary embolism at two academic urban tertiary care EDs between January 01, 2015 and December 31, 2015. Our institutional electronic reports include an indication section that contains free text of important clinical information and indication for CT. Two reviewers (HB and OA) reviewed each indication section and 10% of these were reviewed by a third reviewer (RO) to ensure accurate data abstraction. Data was extracted as per guidelines put forward by Jansen et al. [14]. Data extracted were verified in multiple sources: emergency department record of treatment, consultant notes, and integrated progress notes. Two trained reviewers extracted data by standardized paper data forms. The data form was trialed on 20 patient records, refined and trialed on further 20 records. Training included 20 record data extractions by all three reviewers, data were compared and kappa calculated with clarification and oversight provided by the third reviewer (RO). In addition, 40% of total charts were reviewed by at least two reviewers and the Kappa statistic for inter-observer agreement was calculated.

We pre-defined study variables and created a data abstraction template in Microsoft Excel along with a coding manual to streamline the data collection process. Patient demographic data, their Canadian Triage and Acuity Scale (CTAS) score, and disposition location were all recorded. Radiology reports were documented in terms of PE and non-PE findings (alternative diagnoses), along with any incidental findings identified. We also reviewed chest radiographs that were performed prior to undergoing CTPA. For incidental findings, we also reviewed any follow-up CT investigations for up to 2 years and recorded any finding that led to a biopsied diagnosis of cancer.

CTPA parameters and reporting

CTPA for diagnosing or excluding PE was performed using a 64-slice MDCT scanner (Siemens Sensation 64, Forchheim, Germany). Scan parameters were collimation 64* 0.6 mm with 100 kV and 200 mAs, rotation time 0.5, with pitch of 1.4 and a 4D automatic tube current modulation (CARE dose 4D Automatic Exposure Control, Erlangen, Germany). Intravenous contrast medium (Ultravist 300, Bayer Pharma AG, Berlin, Germany; 100 ml at 4 ml/s) was administered via an 18G peripheral cannula, followed by a saline chase of 40 ml at 4 ml/s. Images were reconstructed at 1-mm axial, sagittal, and coronal slices in soft kernel. Image data sets were transmitted to an archiving and communication system called PACS (Impax 4.5, AGFA Gevaert, Mortsel, Belgium) for diagnostic interpretation using standard window settings with possibility to change such settings without restrictions. CTPA was considered to be of non-diagnostic quality to detect PE if there was insufficient opacification (subjective interpretation of available contrast in the pulmonary arteries, Hounsfield units < 200) of the vessels or in case of major artifacts. For CTPA evaluation, a structured reporting format was used by the radiologists.

Outcomes

Our primary outcome was the prevalence of incidental findings. An incidental finding was defined by any previously unknown finding that was identified in the radiologist's final report. Findings that required either clinical or radiological follow-up, as determined by the radiologist, were also recorded. "Immediate" follow-up was defined as follow-up within 0 to 3 months; "non-immediate" was defined as follow-up within 3 to 6 months; "less urgent" was defined as follow-up > 6 months or no follow-up. We evaluated follow-up CTs that were done over a 2-year period to determine which of the incidental findings led to a significant diagnosis. Accordingly, we defined an incidental finding to be significant if it led to a cancer diagnosis or a diagnosis requiring treatment.

Our secondary outcome was a positive chest X-ray for a clinically significant diagnosis that could explain patient's presenting complaint.

Statistics

Descriptive statistics were performed for all variables. Continuous variables were expressed as mean (standard deviation) and categorical variables were expressed as numbers (percentages). Patient demographics were compared between

CT groups. Univariate analyses were performed with Student *t* test for continuous variables and Cochran-Mantel-Haenszel test for categorical variables. The level of statistical significance was set at 0.05. A sample size of 770 was calculated based on an expected difference in prevalence between significant and non-significant incidental findings of 80% ($\alpha = 5\%$, Power = 90%).

Results

A total of 1708 patients (62 years (SD 16.7), 56.9% female) undergoing CTPA to rule out PE in 1 year were included (Fig. 1; Table 1**)**. Two hundred thirty-three cases of PE were detected, 173 CTPA reports yielded an alternative explanation for the patient's presentation, and 223 reports identified an incidental finding. Most patients presented with a CTAS triage score of 2 or 3. Those who were PE positive were found more likely to be admitted (128/233, 55%), whereas individuals with PE negative studies were more likely to be discharged home (766/1079, 71%). Clinical or radiological follow-up was recommended in 152 (72%) studies that identified an incidental finding, of which 26 yielded significant findings that led to newly identified and/or biopsied cancer diagnoses.

Prevalence of PE and non-PE findings

Our overall diagnostic yield for PE was 13.6% with the majority being lobar and segmental PEs. One hundred seventy-three patients (10.1%) had findings that supported alternative diagnoses. These included pneumonia that were further characterized as lobar, multi-lobar, or interstitial; mass effect that included any process having a mass effect on the mediastinum, lungs, or pleural space; pericardial effusion; pneumomediastinum that included mediastinal emphysema or pneumatosis; and pneumothorax. The most common pathologic finding included pneumonia, noted in 130 patients (7.6%), followed by pulmonary masses found in 22 patients (1.3%). We then looked at chest radiographs that were taken concurrently in the ED. Of the 173 patients that had an alternative diagnosis made on CTPA, 77% had the same non-PE diagnosis on chest radiograph reports (Table 2).

Characterization of incidental findings

A total of 223 incidental findings were identified by the CT studies (Table 3). These included pulmonary nodules (any nodule measuring < 3 cm located in the lung parenchyma); pulmonary mass (any lesion measuring > 3 cm located in the lung parenchyma); mediastinal mass (any mass identified within the mediastinum); adenopathy (any new lymph node > 1 cm, further characterized based on origin, including mediastinal, hilar, paratracheal, axillary, and abdominal); and non-pulmonary mass (any mass identified in the liver, spleen, pancreas, adrenal, gallbladder, or bone). Other incidental findings included thyroid nodules (any nodules identified in the thyroid gland), breast nodules (any nodules identified in the breast tissue), cardiomegaly (newly identified enlargement of

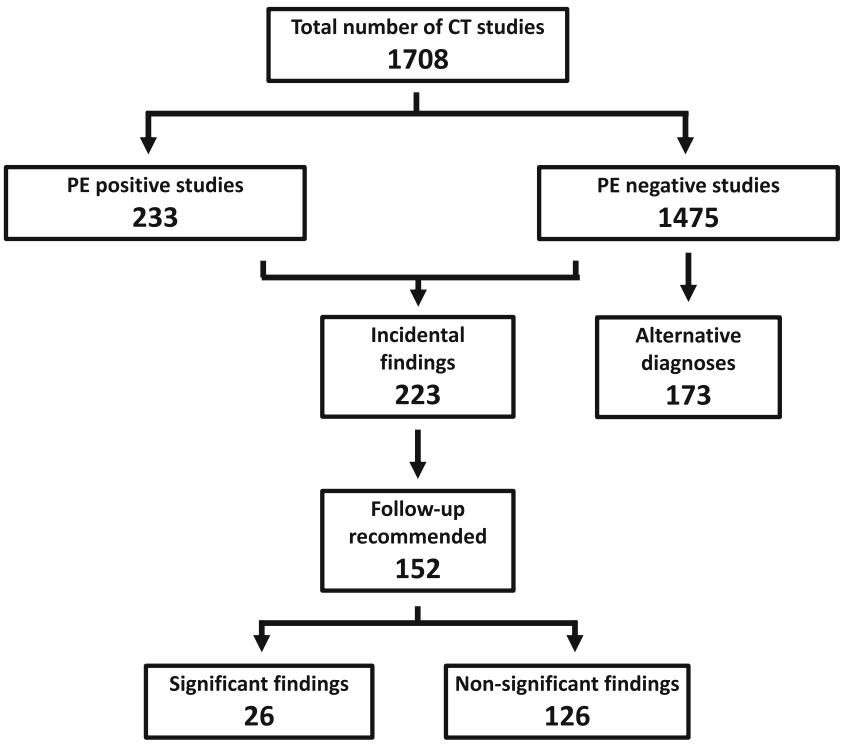

Fig. 1 Summary of results

Table 1 Summary characteristics of patient population ($N = 1708$)

Computed tomography pulmonary angiography group	Age (± SD)	Sample size, *n* (%)	Canadian Triage and Acuity Scale Score (%)				Disposition (%)		
			1	2	3	4	Home	Admitted	Transferred
PE studies	62.2 (± 16.7)	233 (13.6)	2.6	56.7	39.1	1.3	41.7	55.2	3.1
Alternative diagnosis studies	65 (± 15.3)	173 (10.1)	1.1	55.9	41.4	1.6	51.9	41.7	6.4
Incidental findings	66 (± 15.5)	223 (13.1)	0	52.3	45.7	2.0	59.8	34.1	6.1
Negative studies	61 (± 17.2)	1079 (63.2)	0.9	50.2	46.1	2.8	70.5	26.3	3.2

the heart as determined by the radiologist), and degenerative bone findings (any process identifying degenerative bone disease). Pulmonary findings were common: 83 reports found pulmonary nodules (37.2%) and 22 reports identified pulmonary masses (9.9%). Other common incidental findings were mediastinal adenopathy (5.8%), mediastinal masses (4.9%), and cardiomegaly (7.6%).

We stratified incidental findings according to the follow-up recommendations provided by the radiologist. Overall, there were a total of 152 incidental findings for which further imaging was recommended (Table 4). These included both immediate (0–3 months) and non-immediate (3–6 months) follow-up. After evaluating follow-up CTs, we identified a total of 26 significant incidental findings that led to a definitive diagnosis of cancer, confirmed by pathology. There were a total of 253 follow-up CTs done over a 2-year period for the non-significant findings, and 48 follow-up CTs for significant findings. Nine percent of total follow-up CTs yielded significant results of cancer diagnosis. There was no statistical significance ($p = 0.27$) while comparing the number of CTs ordered between significant and non-significant incidental findings. From our database of 1708 CT studies, our prevalence for significant and non-significant findings was 1.5 and 7.4%, respectively. This approximates to 17 CT scans required to identify one significant incidental finding.

Table 2 Computed tomographic findings of PE and alternative diagnoses ($N = 406$)

Finding	Number of studies, *n* (%)	Percentage of chest radiographs in ED with same finding (%)
Pulmonary embolism	233 (14)	0
Main pulmonary artery	91 (5)	–
Lobar and segmental	124 (8)	–
Sub-segmental	18 (1)	–
Computed tomographic finding supporting alternative diagnoses	173 (10)	76.8
Infiltrate	130 (8)	
Lobar	59 (4)	95.6
Multi-lobar	28 (2)	88.5
Diffuse/interstitial	43 (3)	57.9
Mass effect		
Pulmonary	22 (1)	100
Pleural	1 (< 1)	100
Mediastinal	5 (< 1)	100
Pericardial effusion	11 (1)	11.1
Pneumomediastinum	3 (< 1)	33.3
Pneumothorax	1 (< 1)	0

Discussion

Our study demonstrated that incidental findings, such as a pulmonary nodule or adenopathy, are as common as a diagnosis of PE in patients undergoing CTPA. Many of these incidental findings were non-significant as revealed by follow-up CT imaging. We also observed a large number of negative CT studies, indicating a rise in the non-selective use of CTPA and a subsequent increase in the prevalence of incidental findings. Since it is now a common practice to employ a low-dose CTPA protocol, as in our centers, an increase use of CTPA in patients with suspected PE is commonly seen [15, 16]. Hall et al. have reported a high prevalence of incidental findings compared to PE in a similar population to ours (24% incidental findings vs. 9% PE) [7]. Nonetheless, our prevalence of PE (13.6%) is similar to rates observed in literature, ranging from 9 to 18% [7, 8, 17, 18]. However, the high prevalence and non-significance of the incidental findings observed are largely attributed to the rising incidence of CTPA use in current practice. Our study thus highlights the implications of CTPA overuse and the growing opportunity for standardization of the test for patients with suspected PE.

In our study, we observed a large number of incidental findings that required diagnostic follow-up within a year as per radiologist recommendations. Follow-up CT studies revealed that the majority of incidental findings were non-significant. This may be due to the fact that many low-risk pulmonary nodules were followed up, suggesting the need for better adherence to guidelines such as those provided by the Fleischner Society [19]. There were six significant findings

Table 3 New incidental findings from CT reports being evaluated for PE ($N = 223$)

Incidental findings	Number of studies		
	Immediate follow-up recommended[a]	Non-immediate follow-up recommended[b]	Less urgent or no follow-up
Pulmonary			
Nodule	36	34	13
Mass	14	8	0
Emphysema	0	0	4
Other pathology	0	2	12
Pleural			
Mass	2	1	0
Sub-pleural nodule	1	0	1
Other pathology	0	1	2
Mediastinal mass	8	2	1
Pneumoperitoneum	2	0	0
Adenopathy			
Mediastinal	6	6	1
Hilar	0	4	4
Paratracheal	0	1	0
Axillary	2	0	1
Abdominal	0	1	0
Non-pulmonary mass			
Liver	3	3	0
Spleen	1	0	0
Pancreas	3	0	1
Adrenal	1	3	0
Gallbladder	2	0	0
Bone	1	0	0
Abdominal process	2	1	2
Thyroid nodule	2	2	0
Breast nodule	1	4	1
Thrombosis	1	0	0
Cardiomegaly	0	0	17
Coronary artery calcification	0	0	1
Degenerative bone finding	0	0	1

[a] Immediate follow-up is defined as diagnostic follow-up between 0–3 month as recommended by the radiologist

[b] Non-Immediate follow-up is defined as diagnostic follow-up between 3 month–1 year as recommended by the radiologist

(8.6% of total incidental findings) that led to a definitive diagnosis of lung cancer. Based on low-dose CT screening for lung cancer in high-risk patients in the USA, malignant findings ranged between 1 to 10% [20] results that are similar to our study. We also reported that approximately 17 CT scans had to be performed to identify one significant incidental finding. While the prevalence of significant incidental findings is low, our study demonstrates the utility of CTPA in identifying a clinically reasonable number of conditions warranting treatment. However, follow-up for incidental findings may need to be re-evaluated, either by extending the time interval between repeating a CT for low-risk incidental findings or risk stratifying patients so that their follow-up is appropriately managed [19]. Of the CTPA reports that identified pulmonary nodules ($N = 83$), we identified 65 reports (78.3%) that adhered to the Fleischner guidelines. This would subsequently lead to a 19% decrease in follow-up CTs. While this may not represent a significant reduction, it highlights an opportunity to re-evaluate follow-up for low-risk pulmonary nodules.

We identified an alternative diagnosis in 11.7% of CTs that were negative for PE. Similar rates were observed by Chandra and colleagues and van Strijen and colleagues [21, 22]. The most common alternative diagnosis that explained patient symptoms was pneumonia. Of the patients that showed infiltrates on CT imaging, a large proportion had findings consistent with pneumonia on chest radiographs that were taken concurrently in the ED. The high proportion of positive chest radiographs with similar CT diagnosis may indicate the need for chest radiographs to be ordered routinely prior to further investigation for PE. As such, if one has a low pre-test probability for PE, chest X-ray remains a reasonable initial investigation. Because our inclusion population included patients who underwent CTPA for suspected PE, we were only able to identify those who had concurrent chest radiographs performed in the ED. Thus, we could not determine how many significant incidental findings, if any, would be missed if clinicians acted on chest radiographs alone. Retrospectively, looking at patients who had CTPA-diagnosed significant incidental findings (i.e., those that led to a definitive diagnosis of cancer); there were no patients whose radiographs identified those incidental findings. So, while chest radiographs can be used as a reasonable initial exam, the decision to perform CTPA is not unreasonable as it may identify clinically significant incidental findings. However, attention can be given to X-ray results that demonstrate a clear alternative diagnosis before deciding on further imaging. Further prospective research is required to identify any negative outcomes associated with acting on chest radiograph results alone in the low-risk PE patient population.

Limitations

We reviewed the radiology indication report and not patient charts. Therefore, we were unable to assess the entire clinical criteria a physician was using to order the CTPA, or why a physician would order a CTPA when a chest X-ray has an obvious consolidation. Our CT studies were read by different radiologists of varied opinions and this may be missing or overcalling incidental findings. Some used Fleischner guidelines and provided documentation of their use and some

Table 4 Incidental findings requiring diagnostic follow-up ($N = 152$)

Incidental findings	Findings for which further imaging was recommended	Non-significant findings*	Follow-up CTs	Significant findings**	Follow-up CTs
Pulmonary					
Nodule	70	64	116	6	14
Mass	22	15	36	7	11
Pleural					
Sub-pleural nodules	1	1	2	0	–
Mass	3	2	4	1	2
Mediastinal mass	10	6	18	4	7
Pneumoperitoneum	2	2	2	0	–
Adenopathy					
Mediastinal	12	9	21	3	7
Axillary	2	2	5	0	–
Mass					
Liver	6	4	9	2	4
Spleen	1	1	2	0	–
Bone	1	1	3	0	–
Pancreas	3	3	7	0	–
Adrenal	4	4	5	0	–
Gallbladder	2	1	2	1	1
Abdominal process	3	2	3	1	1
Thyroid nodule	4	4	6	0	–
Breast nodules	5	4	10	1	1
Thrombosis	1	1	2	0	–
Total, *n* (%)	152	126 (82.9)	253	26 (17.1)	48
Mean number of follow-up CT scans (± SD)			2.08 (0.52)		1.67 (0.55)
p value***				0.27	

*Findings that did not lead to a definitive diagnosis (i.e., benign pulmonary nodule)

**Findings that lead to a definitive diagnosis (i.e., newly identified and biopsied lung cancer)

***Univariate analysis (*t* test) comparing number of CT ordered between significant findings and non-significant findings

provided their expert recommendation for follow-up, so there was some inconsistency in the CT reports. While it would be challenging to objectively assess the variability of these CT reports, our main purpose of the study was to determine the prevalence and clinical implications of incidental findings by identifying their follow-up investigations. Our study was at two academic emergency departments and thus may not be generalizable; however, we found a similar rate of PE diagnosis as seen in the literature in our cohort. Although all CTPAs were assessed according to a pre-specified protocol, it cannot be ruled out that some of our patients were misclassified as having PE, an alternative finding, or an incidental finding. However, this obviously reflects routine clinical practice of the diagnostic process of suspected PE. We did not use specific criteria for incidental findings; rather, we used the radiologist recommendation. This reflects current practice whereby physicians order further imaging based on radiology recommendation rather than a personal interpretation of the primary images or report.

Conclusion

Incidental findings are as common as a diagnosis of PE in patients undergoing CTPA. They are rarely clinically significant. Chest radiograph remains a reasonable initial investigation as it can aid in identifying alternative diagnoses especially in the setting of a low pre-test probability for PE.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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