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Full Length Article

# Reliability of diagnosing incidental pulmonary embolism in cancer patients



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#### ABSTRACT

*Background:* With the routine use of advanced multi-slice CT scanners, pulmonary embolism (PE) is increasingly detected as an incidental finding among cancer patients. Although this generally leads to therapeutic interventions, the accuracy of diagnosing PE on routinely performed contrast enhanced CT scans is unknown.

Methods: Consecutive cancer patients diagnosed with incidental PE were eligible for inclusion. Their CT images were reassessed in a blinded fashion by two thoracic radiologists. To ensure blindness, a total of 19 cancer staging CT images without PE were included. The inter-observer reliability for the presence of PE was calculated with use of Kappa statistics.

Results: A total of 62 incidental PE patients (mean age 64 years, 60% male) were included. All patients received anticoagulant treatment upon diagnosis. Level of agreement between the two expert readers was high: they disagreed on the presence of PE in only two patients (3.2%), resulting in a Kappa statistic of 0.93. After final consensus reading, it was concluded that the CT images of all 62 patients initially diagnosed with incidental PE were indeed positive for PE.

Conclusions: This study indicates that an incidental PE diagnosis is reliable and highly reproducible, despite the suboptimal reading conditions of a non-dedicated scan protocol.

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# 1. Introduction

As a consequence the increased use of more advanced CT imaging techniques, radiologists now increasingly report pulmonary embolism (PE) to be present on routinely performed contrast-enhanced CT examinations. This is in particular true for cancer patients, who display a high risk of developing venous thromboembolism (VTE), and frequently undergo CT scanning for reasons as tumor staging and treatment evaluation. Increased awareness among radiologists of incidental PE may also have contributed to the growing number of their reports. In recent literature, the reported prevalence of incidental PE diagnosed on routine cancer staging CT scans ranges from 1.9 to 4.4% [1,2].

By definition, these incidental findings are diagnosed on CT scans that are not primarily conducted to establish or rule out acute PE. The

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accuracy of diagnosing incidental PE on CT scans that were not performed according to a standardized CT pulmonary angiography (CTPA) imaging protocol is as yet unknown. Since a false positive diagnosis of PE, whether symptomatic or incidental, comes with the consequence of unnecessary exposure to anticoagulant therapy with its associated risk of bleeding complications, establishing this diagnostic accuracy is highly relevant. The present study therefore aimed to assess the reproducibility and inter-observer agreement of diagnosing incidental PE on cancer staging CT scans.

## 2. Methods

#### 2.1. Study Population

Consecutive adult patients with active malignant disease who were diagnosed with incidental PE between January 2003 and July 2012 in the Leiden University Medical Center were eligible for this study. The design and characteristics of this cohort study have, in part, been described previously [3]. Patients were identified using International Classification of Diseases (ICD) 9 codes for diagnosis of PE and a diagnosis of cancer. These included hospital discharge diagnoses as well as

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outpatient and emergency department encounters. Active malignancy was defined as cancer (either solid or hematologic) diagnosed within six months before the CT examination, recently recurrent or progressive cancer or any malignancy that deserved curative or palliative treatment within the previous six months. Incidental PE was defined as a diagnosis of PE detected on CT scans ordered for reasons other than the suspicion of acute PE (e.g. CT scans performed for cancer staging, treatment evaluation or cancer recurrence detection) [4]. This does not imply that all patients were asymptomatic from PE, however, any complaints did not result in a clinical suspicion of PE. The presence of (asymptomatic) DVT was not systematically investigated and no differentiation was made between possible in-situ thrombosis and true pulmonary emboli. Follow-up CT scans in order to assess pulmonary reperfusion were not performed. Institutional review board approval was waived for this observational and retrospective study.

# 2.2. Image Acquisition and Interpretation

Multi-detector CT scanners (4, 16-, 64-, and 320-slice CT scanners, Toshiba, Otawara, Japan) were used in all patients. Images were reconstructed with 1.0 mm slice thickness, if possible. For two patients, scanned with a 4-slice CT scanner, the slice thickness was 2 mm images and for one other patient only images with a slice thickness of 5 mm were available. The images were reassessed by two thoracic radiologists independently (LK and IH), who were blinded to the original CT report, location of the filling defect and clinical information of the patients. The radiologists were allowed to optimize reading by using post-processing tools such as stacking, adapting window-settings, and use of zoomfunction, as is used in clinical practice. PE was defined as the presence of at least one filling defect in the pulmonary artery tree. The reviewers' findings were reported on a pre-specified and standardized form, on which the following information was recorded: 1) the image quality of the CT examination regarding the level of confidence in PE diagnosis, i.e.: good confidence, uncertain, or not confident; and 2) contrast phase, i.e. late arterial (contrast delay approximately 30 sec.) or portal-venous (contrast delay approximately 70 sec.).

To ensure control and blindness of the expert readers, a number of 19 cancer staging CT examinations without reported PE were included, originating from the same inclusion period as the CT scans with incidental PE, with a similar distribution of late arterial and portal-venous contrast phase.

# 2.3. Statistical Analysis

The proportion of cases, with its corresponding 95% confidence interval (CI), in whom the expert readers' interpretations were concordant was calculated. The kappa-coefficient was calculated to assess the rate of agreement upon PE diagnosis in the total sample of CT scans. SPSS version 20 (SPSS Inc, Chicago, IL), was used for all analysis.

### 3. Results

A total of 65 consecutive patients diagnosed with incidental PE were identified during the study period. We were unable to retrieve the original CT images in three patients, and those were excluded from the present analyses. Mean age of the remaining 62 patients was 64 years, and 60% of the patients were male (Table 1). The most prevalent malignancies were lung cancer (18%) and colorectal cancer (11%). The main indications for the CT examinations were primary diagnosis (24%), staging (27%), or treatment evaluation (32%) of the malignant disease. In 20 patients (32%) expert reading identified central PE, in 41 patients (66%) segmental PE and in 1 patient (1.6%) subsegmental PE.

All patients were treated with anticoagulant agents following the diagnosis of incidental PE. In three patients (4.8%), a CTPA was conducted following the identification of PE on the staging CT, which confirmed the presence of PE in all three cases (Fig. 1). The expert radiologists only

Table 1
Patient characteristics.

Age in years (mean $\pm$ SD)	64 ± 15
Male sex (n, %)	37 (59.7)
BMI (mean $\pm$ SD)	$25.5 \pm 3.9$
Inpatient (n, %)	21 (33.9)
Recent immobilization (n,%)	26 (41.9)
Recent surgery (n,%)	9 (14.5)
Previous VTE (n, %)	3 (4.8)
Primary tumor site (n, %)	
Lung	11 (17.7)
Breast	6 (9.7)
Colorectal	7 (11.3)
Other GI	12 (19.4)
Gynecological	6 (9.7)
Other solid	13 (21.0)
Hematologic	7 (11.3)
Thrombus localization (n, %)	
Central	20 (32)
Segmental	41 (66)
Subsegmental	1 (1.6)

**Note:** BMI, body mass index; VTE, venousthromboembolism; GI, gastro-intestinal

evaluated the initial CT scans on which PE was found, and were unaware of these CTPAs.

The contrast phase was late arterial in 14 patients and portal-venous in 48 patients. In 13 patients (21%), incidental PE was diagnosed on an abdominal CT without a complete chest CT examination. In 60 of the 62 patients diagnosed with incidental PE, the expert readers agreed on the presence of PE. In two patients (3.2%), either one of the observers refuted the presence of PE whereas the other observer confirmed the presence of PE. Of these 2 patients, 1 patient was diagnosed with incidental PE with the most proximal PE in the central pulmonary artery on a 64-slice CT-scanner with contrast in the portal-venous phase. The second patient was diagnosed with incidental PE with the most proximal PE in a subsegmental pulmonary artery on a 16-slice CT-scanner with contrast in the portal-venous phase. Thus, the proportion of agreement on the presence of PE between the initial report and expert reading was 96.7% (60/62; 95% CI: 88.8-99.6%). Regarding the level of confidence of diagnosis, one reader classified 61 of the incidental PE diagnoses as good confidence for PE and one as non-confident, whereas the other reader classified 60 as good confident, one as non-confident, and one as uncertain/non-confident. After consensus reading, it was concluded that PE was present in all 62 patients. Both readers did not identify PE in any of the 19 control scans. In the total sample of 81 patients with and without PE, Kappa analysis revealed a Kappa statistic of 0.93 (p < 0.001) for the dichotomous categories 'PE present' versus 'PE absent' after first reading by the expert readers.

### 4. Discussion

The results of this study indicate that diagnosing incidental PE on CT scans that were conducted for other reasons than a clinical suspicion of PE, is reliable with excellent inter-observer agreement. None of the incidental PE diagnoses were found false positive according to the final consensus evaluation of two experts.

Our observed Kappa level compares well to the level of interobserver agreement found for diagnosing PE with the use of dedicated CTPA, which has repeatedly been reported to be good [5–7]. Of note, CTPA is currently widely considered the imaging test of choice for the diagnosis of acute PE [8].

The importance of accurately diagnosing PE, including incidental episodes, lies in the therapeutic consequences that come with this diagnosis. The current consensus is that cancer patients with established VTE should continue anticoagulation as long as the cancer is active [9]. For incidental PE, a similar therapeutic approach as towards symptomatic

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