Received:
18 October 2017

Revised:
11 April 2018

Accepted:
18 April 2018

<https://doi.org/10.1259/bjr.20170806>

Cite this article as:

Myat Moe MM, Redla S. Incidental pulmonary embolism in oncology patients with current macroscopic malignancy: incidence in different tumour type and impact of delayed treatment on survival outcome. *Br J Radiol* 2018; **91**: 20170806.

SHORT COMMUNICATION

Incidental pulmonary embolism in oncology patients with current macroscopic malignancy: incidence in different tumour type and impact of delayed treatment on survival outcome

¹MAUNG MAUNG MYAT MOE, FRCP, MD, MSc and ²SRIDHAR REDLA, FRCR

¹Department of Oncology, North Middlesex University Hospital, London, UK

²Department of Radiology, Princess Alexandra Hospital, Harlow, UK

Address correspondence to: Dr Maung Maung Myat Moe
E-mail: maungmoe@hotmail.com

Objectives: To evaluate the incidence and outcome of incidental pulmonary embolism (iPE) in patients with current macroscopic malignancy and delayed anticoagulation due to late reporting of CT scan.

Methods: Reports of CT thorax with i.v. contrast done on oncology patients between 1 January 2015 and 31 December 2015 in two district general hospitals in UK were reviewed. Electronic patient records of iPE patients were reviewed for demographic and treatment information.

Results: 26 iPEs were reported in 1,604 scans (731 patients), incidence 1.6%; female = 15; median age = 66 (range 32–90); main artery = 10; lobar artery = 8; segmental = 7; subsegmental = 1; median time (range) from scan to reporting = 1 day (0–60); scan to anticoagulation = 5 days (0–61) (three had no treatment); scan to death = 7 months (1–22+) with nine still alive and two lost

to follow up. All had metastatic disease. There was no sudden death. None of the patients whose anticoagulation started more than 5 days after the iPE CT scan died within 3 months. iPE was absent in all repeat staging CT scans (done average 3.4 months after the anticoagulation) in 16 patients, without any anticoagulation in one patient with segmental iPE.

Conclusion: Incidence of iPE in patients with current macroscopic malignancy is low—1.6%—mostly seen in lung, breast and colorectal cancer probably due to frequency of imaging. A few days' delay in anticoagulation does not appear to have an impact on the risk of sudden cardiac death.

Advances in knowledge: This study tells us that iPE is infrequent, that it can be treated appropriately with anticoagulation, but this does not necessarily need to begin on the same day of diagnosis.

INTRODUCTION

Cancer patients have increased risk of venous thromboembolism compared to general population—up to 50-fold in pancreatic cancer.¹ Pulmonary embolism causes symptoms such as chest pain, haemoptysis, dyspnoea and death especially if left untreated. Cancer patients had 94% probability of death from Venous Thromboembolism within 6 months compared to 29% in patients without cancer.² National Institute for Health and Care Excellence of UK recommended initiation of anticoagulation therapy in patients suspected of having pulmonary embolism if the diagnostic investigation was not going to occur within 4 hours.³

Incidental pulmonary embolism (iPE) is defined as “pulmonary embolism (PE) detected on CT thorax (with i.v. contrast) other than CT pulmonary angiogram (CTPA)” which is

the gold standard investigation for PE.⁴ No data is available with regard to iPE on how commonly, or how quickly it could progress into symptomatic, straight to fatal PE, or resolve spontaneously without any anticoagulation therapy. It is not practical or ethical to find answers to these questions by withholding the treatment in patients with confirmed iPE. Clinicians in UK, as well as world-wide, treat iPE in the same way as symptomatic PE diagnosed on CTPA.^{5,6} Due to the shortage of radiologists in UK, many radiology departments are facing the problem of significant delay in reporting non-urgent (outpatient), routine staging CT scans. As a result, iPE found on these scans are left untreated for some time after the scan. This gives us an opportunity to find out the effect of delayed treatment on iPEs.

The aim of this study is to evaluate the incidence and outcome of iPE in oncology patients with current

macroscopic malignancy taking into account the delay in initiating anticoagulation therapy because of late reporting.

METHODS AND MATERIALS

CT scans performed on oncology patients between 1 January 2015 and 31 December 2015 were identified from the database in radiology departments in two district general hospitals in a cancer network in England. CT scans were performed using Phillips Ingenuity 128 channel (slices) scanner with a slice thickness of 3 mm at 1.5 mm increments. Omnipaque-300 (Iohexol) was used as i.v. contrast (60–70 ml bolus per patient). Pulmonary embolism was detected as filling defects in pulmonary arteries (main pulmonary, lobar, segmental, subsegmental). CTPAs and CTs with no i.v. contrast were excluded. Initially CT reports were reviewed. CT scans with no macroscopic malignant disease, either primary or metastases, were excluded. Information on age, sex, primary diagnosis, most proximal location of iPE (pulmonary main artery or lobar or segmental or subsegmental artery) were collected from the CT scan reports. Electronic hospital records of patients with iPE were reviewed for start dates of anticoagulation therapy and drugs prescribed. Dispense of anticoagulation drug was confirmed with the pharmacy as all the treatments were initiated in the hospital. Survival status was checked against the hospital electronic record and most recent encounter with hospital services such as blood tests and outpatient clinics.

FINDINGS

2147 CT scans with i.v. contrast were identified. 543 scans were excluded due to the absence of macroscopic disease (no iPE was reported in any of these CT scans) leaving 1604 scans belonging to 731 patients eligible for this study. Breakdown of scans for different tumour type is shown in [Table 1](#).

A total of 26 patients with iPE were identified. All patients had metastatic disease. All were re-staging CT scans to assess the disease progression status, arranged as outpatient except one which was done on an inpatient admitted for pain and general deterioration, and was found to have a fungating breast cancer on examination. Subsequent staging CT scan found bone mets and iPE. None of the patients—including one inpatient—had signs and symptoms indicative of PE that warrant CTPA. 58% of patients were female. Median age was 66 (range 32–90). Locations of iPE (most proximal artery) are 10 in main pulmonary artery, 8 in lobar, 7 in segmental and 1 in subsegmental artery. The time from CT scan to reporting ranges from 0 to 60 days with the median of 1 day. (0 day means the same day as the scan.)

23 patients had anticoagulation with low molecular weight heparin: 22 = enoxaparin; 1 = dalteparin. Median time from iPE CT scan to anticoagulation is 5 days (range 0–61 days), more than 23 days in five patients. Treatment was usually initiated straight away after the report but in six patients it took 3, 5, 9, 9, 13 and 18 days respectively. This is because of difficulty in getting contact with patients, and unawareness of the CT report by the clinical team. Nobody required inpatient treatment for iPE.

Disappearance of iPE was documented in subsequent staging CT scan reports in 16 patients who had scans repeated at a later date.

Table 1. Incidence of iPE in different tumour types

	Patients	Scans	Scans with iPE (% of total scans)
Lung	235	587	9 (1.5%)
Breast	148	267	5 (1.9%)
Colorectal	142	310	5 (1.6%)
Oeso/gastric	72	163	2 (1.2%)
Mesothelioma	8	19	1 (5.3%)
CUP	15	30	1 (3.3%)
Bladder	15	31	1 (3.2%)
NET	1	1	1 (100%)
Prostate	41	87	1 (1.2%)
Anal	1	2	0
Brain	1	1	0
H & N	8	18	0
Heptaobiliary	10	20	0
Melanoma	3	4	0
Ovary	3	4	0
Pancreas	26	58	0
Skin	2	0	0
Total	731	1604	26 (1.6%)

iPE, incidental pulmonary embolism.

The interval between the anticoagulation and the CT with no PE ranged from 1.1 to 4.9 months with one patient at 8.1 months (Mean = 3.5 months; Median = 3.4 months). Spontaneous resolution of a segmental iPE was discovered in a 77-year-old patient with small cell lung cancer on chemotherapy when his staging CT scan was reported on the same day as CTPA done 3 weeks later for dyspnoea. CTPA was negative for PE. The patient was subsequently anticoagulated.

At the time of this study nine patients were still alive and two lost to follow up due to migration abroad. The time from CT scan to death ranges from 1 month to over 22 months, with the median of 7 months. Only three patients died within 2 months—at 31, 42 and 59 days, respectively—and they had anticoagulation within 0, 1 and 3 days, respectively, of iPE CT scan. Review of clinical notes confirmed that there was no sudden death. All deaths were expected and attributable to the malignant disease.

DISCUSSION

Incidence of iPE in oncology patients with current macroscopic disease is low—1.6%—in our retrospective study that represented our daily practice. This is slightly higher than the rate of 1.5% reported by Hulle et al in their big cohort of 13,590 unselected outpatient oncology patients.⁷ The majority of our patients are lung, breast and colorectal cancer patients. This is probably because of these cancers being common tumour types and the frequency of scanning during their relatively long course of metastatic disease and multiple lines of

treatment. We cannot identify any specific tumour type for highest incidence of iPE due to the small number of cases. Our study confirmed that iPE can occur in any part of the pulmonary arteries including main arteries, staying silent for at least a certain period in oncology patients with current macroscopic malignant disease. Spontaneous resolution of one segmental artery iPE was noted in one patient on 10 weeks interval CT scan. Similar spontaneous resolution had also been reported in the literature for subsegmental iPEs.⁸ Although it is fair to say that iPE may not be fatal for at least a few days without any anticoagulation therapy, more research is needed to select patients whose iPE would resolve without any intervention or progress to symptomatic or even fatal PE to prevent side effects from unnecessary anticoagulation therapy in patients already affected by the burden of malignant disease. Hulle et al reported weighted-pooled 6-month risk of 12% for progression of untreated iPE to symptomatic PE in cancer patients.⁷ However, the difference in 6-month mortality between treated and untreated iPE did not seem to be statistically significant—37% (95%confidence interval 29–44) vs 47% (95%confidence interval 28–66).⁷ Sun et al reported a much worse survival for no treatment compared to anticoagulation therapy for iPE (6.1 vs 30.9 months) in lung cancer patients but did not report if the disease status played a major role in not giving anticoagulation therapy or was the main cause of death.⁹ Abdel-Razeq et al reported sudden death within 1 month of iPE in up to 26.5% (nine patients including two untreated iPE patients.).¹⁰ However a study from a large tertiary cancer centre reported 30 days mortality among 135 iPEs who had treatment in outpatient setting as 1% but did not report how many of these were iPE related.¹¹

A limitation of our study is that only scan reports were reviewed rather than CT images to exclude any iPE that might have been missed at the time of reporting. Multirow detector CT images

with 1.25 mm thickness are essential for not missing iPE.¹² Previous studies revealed that 30–66% of iPE were not reported in routine practice.^{12,13} Up to 27% of iPE can be confined to subsegmental arteries¹⁴ and there could be a significant number of scans with subsegmental iPE not being reported. However our study actually represents the real world experience. We managed to evaluate the incidence of iPE specifically in patients who have macroscopic malignancy, either primary or metastases, at the time of the scan while most of the published studies reported incidence on unselected oncology patients with or without macroscopic cancer at the time of scanning.

Hypoxaemia and central location (main and lobar artery) of iPE have been reported to be significant determining factors for death.¹¹ Our study showed that it could take a few days to get anticoagulation therapy started in an outpatient setting due to communication issues. The current standard of care for PE, either incidental or symptomatic, is to give anticoagulation. Therefore it may be advisable to have CT images examined for at least main pulmonary and lobar artery iPE in patients with concurrent macroscopic malignancy, either primary or metastases before patients leave the radiology department.

CONCLUSION

Incidence of iPE in patients with current macroscopic malignancy is small—only 1.6% in our study—and mostly seen in lung, breast and colorectal cancer, likely to be due to the frequency of imaging in these tumour patients. There is often a delay in reporting non-urgent CT scans, and subsequently late commencement of anticoagulation for iPE. However this delay in treatment doesn't seem to cause sudden cardiac death, suggesting some iPE may not need treatment like symptomatic PE. This warrants more research to identify certain kind of iPEs that could be safely left untreated for better quality of life in advanced cancer patients.

REFERENCES

- Epstein AS, O'Reilly EM, O'Reilly E. Exocrine pancreas cancer and thromboembolic events: a systematic literature review. *J Natl Compr Canc Netw* 2012; **10**:7: 835–46. doi: <https://doi.org/10.6004/jnccn.2012.0087>
- Levitan N, Dowlati A, Remick SC, Tahsildar HI, Sivinski LD, Beyth R, et al. Rates of initial and recurrent thromboembolic disease among patients with malignancy versus those without malignancy. Risk analysis using Medicare claim data. *Medicine* 1999; **78**:5: 285–. doi: <https://doi.org/10.1097/00005792-199909000-00001>
- NICE. Venous thromboembolism in adults: diagnosis and management Quality standard [QS29]. Update in June, 2015. Website accessed on 18.10.17. Available from: <https://www.nice.org.uk/guidance/qs29>.
- Khorana AA, O'Connell C, Agnelli G, Liebman HA, Lee AY, Agnes L. Incidental venous thromboembolism in oncology patients. *J Thromb Haemost* 2012; **10**:12: 2602–4. doi: <https://doi.org/10.1111/jth.12023>
- Franklin JM, Rahman N, Gleeson FV, Fergus G. The clinician's response to a report of an incidental pulmonary embolism detected on multidetector CT. *Postgrad Med J* 2011; **87**: 746–9. doi: <https://doi.org/10.1136/pgmj.2011.118497>
- den Exter PL, van Roosmalen MJ, van den Hoven P, Klok FA, Monreal M, Jiménez D, et al. Physicians' management approach to an incidental pulmonary embolism: an international survey. *J Thromb Haemost* 2013; **11**: 208–13. doi: <https://doi.org/10.1111/jth.12040>
- van der Hulle T, den Exter PL, Planquette B, Meyer G, Soler S, Monreal M, et al. Risk of recurrent venous thromboembolism and major hemorrhage in cancer-associated incidental pulmonary embolism among treated and untreated patients: a pooled analysis of 926 patients. *J Thromb Haemost* 2016; **14**: 1: 105–13. doi: <https://doi.org/10.1111/jth.13172>
- Chiu V, O'Connell C. Management of the incidental embolism. *AJR Am J Roentgenol* 2017; **208**: 485–8. doi: <https://doi.org/10.2214/AJR.16.17201>
- Sun JM, Kim TS, Lee J, Park YH, Ahn JS, Kim H, et al. Unsuspected pulmonary emboli in lung cancer patients: the impact on survival and the significance of

- anticoagulation therapy. *Lung Cancer* 2010; **69**:3: 330–6. doi: <https://doi.org/10.1016/j.lungcan.2009.11.015>
10. Abdel-Razeq HN, Mansour AH, Ismael YM. Incidental pulmonary embolism in cancer patients: clinical characteristics and outcome--a comprehensive cancer center experience. *Vasc Health Risk Manag* 2011; **7**: 153–8. doi: <https://doi.org/10.2147/VHRM.S17947>
11. Banala SR, Yeung SJ, Rice TW, Reyes-Gibby CC, Wu CC, Todd KH, et al. Discharge or admit? Emergency department management of incidental pulmonary embolism in patients with cancer: a retrospective study. *Int J Emerg Med* 2017; **10**: 19. doi: <https://doi.org/10.1186/s12245-017-0144-9>
12. Tresoldi S, Flor N, Luciani A, Lombardi MA, Colombo B, Cornalba G. Contrast enhanced chest-MDCT in oncologic patients. Prospective evaluation of the prevalence of incidental pulmonary embolism and added value of thin reconstructions. *Eur Radiol* 2015; **25**:11: 3200–6. doi: <https://doi.org/10.1007/s00330-015-3739-7>
13. Bach AG, Meyer HJ, Taute BM, Surov A. The frequency of incidental pulmonary embolism in different CT examinations. *Br J Radiol* 2016; **89**: 1058. doi: <https://doi.org/10.1259/bjr.20150737>
14. O'Connell C, Razavi P, Ghalichi M, Boyle S, Vasan S, Mark L, et al. Unsuspected pulmonary emboli adversely impact survival in patients with cancer undergoing routine staging multi-row detector computed tomography scanning. *J Thromb Haemost* 2011; **9**: 305–11. doi: <https://doi.org/10.1111/j.1538-7836.2010.04114.x>