Thorax Online First, published on December 8, 2006 as 10.1136/thx.2006.062299

Prospective Evaluation of Unsuspected Pulmonary Embolism on Contrast Enhanced Multidetector CT (MDCT)

Dr Gillian Ritchie FRCR[*], Dr Simon McGurk[*] FRCR, Dr Catriona McCreath[*] FRCR, Catriona Graham[+] MSc, Dr John T Murchison[*] FRCR

[*]Department of Radiology
Royal Infirmary of Edinburgh
51 Little France Crescent
Old Dalkeith Rd
Edinburgh, UK
EH16 4SA

[+]Epidemiology and Statistics Core
Wellcome Trust Clinical Research Facility
The University of Edinburgh
Western General Hospital
Edinburgh, UK
EH4 2XU

Corresponding Author : Dr John T Murchison
Tel: 0131 242 3741
Fax: 0131 242 3742
E-mail: john.murchison@luht.scot.nhs.uk

Original Research

Keywords:
Pulmonary Embolism
Inpatients
Incidental Findings
Tomography, Spiral Computed

Word Count: 3261

Prospective Evaluation of Unsuspected Pulmonary Embolism (PE) on Contrast Enhanced Multidetector CT (MDCT)

Original Research

ABSTRACT

Aim

To quantify the incidence of unsuspected pulmonary emboli (PE) in an unselected in-patient population undergoing contrast enhanced multidetector CT (MDCT) thorax and to assess aetiological factors in their development.

Materials and Methods

All in-patients undergoing MDCT thorax over a ten month period were prospectively identified. Patients with previous or suspected current PE were excluded. CT scans were reviewed and the degree of contrast enhancement and presence of PE recorded. Where PE was found the level of most proximal thrombus was identified. Patient age, length of admission, slice scan thickness and clinical indication was noted.

Results

547 in-patients having undergone MDCT were identified. Following exclusions 487 remained.

5.7% (28/487) demonstrated PE. Unsuspected PE was more common with increasing age ($p<0.001$), identified in 9.2% (20/218) of all patients over 70 years and 16.7% (11/66) of over 80 year olds. 64.3% were at segmental or sub-segmental level. No other aetiological factor was identified which significantly increased the incidence of unsuspected PE

No significant difference was noted between 4- and 16-slice MDCT.

32.1% of incidental PE were not identified by the original reporting radiologists.

Conclusion

PE is an unsuspected finding on contrast enhanced MDCT thorax in 5.7% of all in-patients. This includes an incidence of 9.2% in patients > 70 years rising to 16.7% in over 80 years old. Most are peripheral and >30% are missed on initial review. PE should be routinely sought in all contrast enhanced MDCT of the chest irrespective of the indication for the CT scan.

INTRODUCTION

Pulmonary embolism (PE) is a common disease estimated to be a contributory factor in approximately 200,000 deaths per year in the United

States, occurring in 5-10% of hospital deaths.[1] PE is a difficult disease to positively diagnose clinically, presenting with varied and sometimes minimal symptoms that mimic a myriad of other pathologies. The actual annual incidence of PE is therefore difficult to determine but has been estimated at around 60-70 per 100,000 people.[2]

In the past PE was only ever firmly diagnosed after the diagnosis had been first considered by a clinician then proven by radiological study; either an isotope perfusion lung scan, a conventional pulmonary angiogram or in recent years a CT pulmonary angiogram (CTPA). With the advent of multidetector CT (MDCT), which allows assessment of the chest with thin section collimation using rapid acquisition, it is now possible to visualise the pulmonary arterial tree down to sub-segmental level on most contrast enhanced scans allowing unsuspected PE to be detected on routine MDCT of the chest.

METHODS

Patient Inclusion

Over a period of 10 months from 1st January 2004 to 13th October 2004, consecutive in-patients undergoing contrast enhanced MDCT chest for an indication other than suspected PE, were identified at a large teaching hospital. In-patients were selected for the patient study group as this was the population thought to be most at risk and in whom it was considered most likely that unsuspected PE might be detected. Patients were scanned either using either a 4 or 16 slice scanner (both Toshiba Aquilion series, Toshiba Medical Systems, Tokyo, Japan).

Patient details were recorded for the purpose of identification of the computer images and for accessing demographic information from the hospital database. From the request card, logbooks and hospital database, record was made of age, referring speciality, date of admission (to calculate length of hospital stay prior to scanning), scan slice thickness and brief clinical information or reason for referral. Recruited patients were hospital in-patients, from the wards, Admissions unit, Day Case Unit or Accident and Emergency (excluding trauma cases). Patients were excluded if they were suspected or known to have had a PE. CTPA studies were not included.

Scan Parameters

Scan protocol varied depending on the indication for study. In most studies 100mls iodinated contrast was injected at between 3 and 4 mls per second

with the scan commencing at around 20 seconds post start of the contrast injection. Scan parameters are outlined in Table I.

Protocol	kV	Contrast and Concentration (mg/ml)	Contrast Volume (ml)	Table Feed (mm/rotation)	Pitch
Chest (16 slice)	120	Niopam 300	90	23	23
Aorta (16 slice)	120	Iomeron 400	100	23	23
Chest (4 slice)	120	Niopam 300	90	11	5.5
Aorta (4 slice)	120	Iomeron 400	100	11	5.5

Table I: Scan Parameters

Tube current (mA) is not given as this is controlled by in-built dose modulation software (Real EC, Toshiba Medical Systems, Tokyo, Japan).

Image Interpretation

All studies were initially reported as per routine practice in our institution. Subsequently, a single Consultant Thoracic Radiologist who was blinded to the initial report reviewed the studies. All images were assessed using a workstation allowing multi-planar reformatting. For each patient the degree of contrast enhancement and presence or absence of PE was noted. If the scan was positive the level of thrombus was recorded as central, lobar, segmental or sub-segmental. Contrast enhancement was classified as good (good enhancement of segmental and sub-segmental arteries), moderate (good enhancement of segmental but not of sub-segmental branches) or poor (inadequate enhancement of entire pulmonary arterial tree). Patients were excluded from the study at this stage if there was poor or absent contrast enhancement, if the lungs were only partially imaged or the images were not retrievable on the workstation (technical difficulties).

If scans were found to demonstrate pulmonary emboli which had not previously been reported, the appropriate clinical team were informed.

RESULTS

During the study period 547 consecutive in-patients undergoing MDCT thorax were identified from the scanner logbooks. 16 patients were excluded

due to absence of intravenous contrast, 25 due to incomplete lung imaging and 19 were excluded due to poor contrast enhancement.
Following exclusions a population of 487 study patients remained. These subjects were the in-patients with good or moderate contrast enhancement of the pulmonary arteries and no suspected or prior history of PE. Study group included 200 female (41%) and 287 male patients (59%). Median age 69 years (range 15-93 years).

28/487 scans demonstrated pulmonary emboli, an incidence of 5.7% in the total study population.

20/218 patients over 70 years old had unsuspected PE, an incidence of 9.2% in this cumulative grouping. This rises in the over 80 year age group to an incidence of 16.7% (11/66).

Median age of all patients with positive scan was 77 years, range 52-88 years. There was a statistically significant association between age group and the rate of unsuspected PE (χ^2=13.28, p=<0.001) with a significant difference in rate of PE with increasing age. The distribution of PE by age is recorded in table II although for the purposes of analysis the <50 and 50-59 age groups have been combined.

Age	Number	Number Positive	% Positive
<50 yrs	47	0	0
50-59	75	3	4
60-69	147	5	3.4
70-79	152	9	5.9
>80	66	11	16.7

Table II: Age Distribution of Studies

Of the positive scans, 27/28 (96.4%) showed good contrast enhancement, the one scan which showed only moderate enhancement had thrombus at a segmental level.

402/487 (82.5%) of the study patients were scanned on a 16-slice scanner, and images reconstructed at 1mm thickness, the incidence of PE among this subgroup was 24/402 (6.0%). 85/487 (17.5%) patients were scanned on a 4-slice scanner with slice reconstructions at either 2mm or 3mm. A total of

4/85 scans were positive for PE, an incidence of 4.7%. Of these, 3 were scanned with 3mm slice thickness. No statistically significant difference was noted between 4 and 16 slice scanners in their ability to identify unsuspected PE (p=0.80 using Fishers exact test). Distribution of proximal thrombus in the entire population is shown in Figure I. Image 1 is an example of sub-segmental thrombus in the right lower lobe, Image 2 demonstrates segmental level thrombus and Image 3 shows more proximal PE in the main pulmonary arteries bilaterally, all were unsuspected.

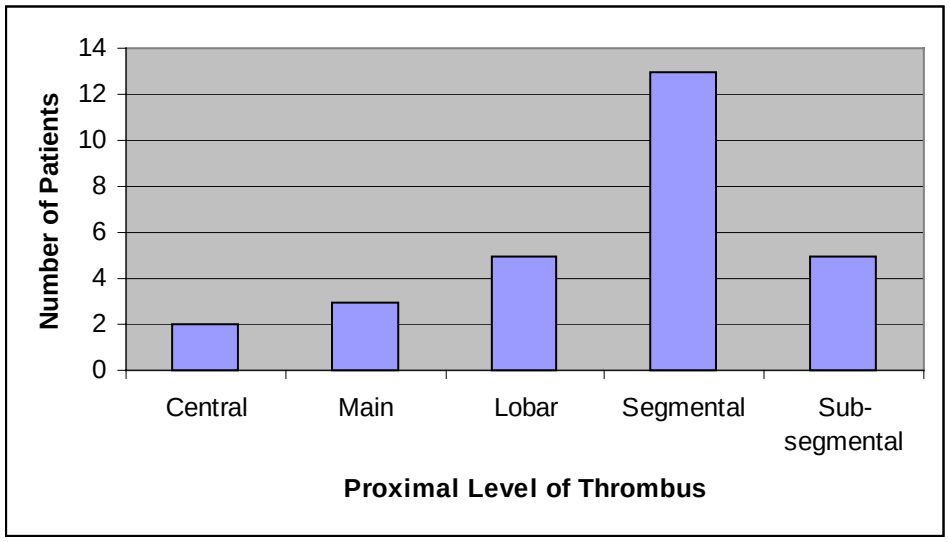

Figure I: Proximal Extent of Thrombus

19/28 (67.9%) of pulmonary emboli were positively identified on initial report. Of the 9 positive studies not identified at initial review, thrombus was segmental in 6 cases and sub-segmental in 3 cases. Distribution of involved lobes is summarised in figure II.

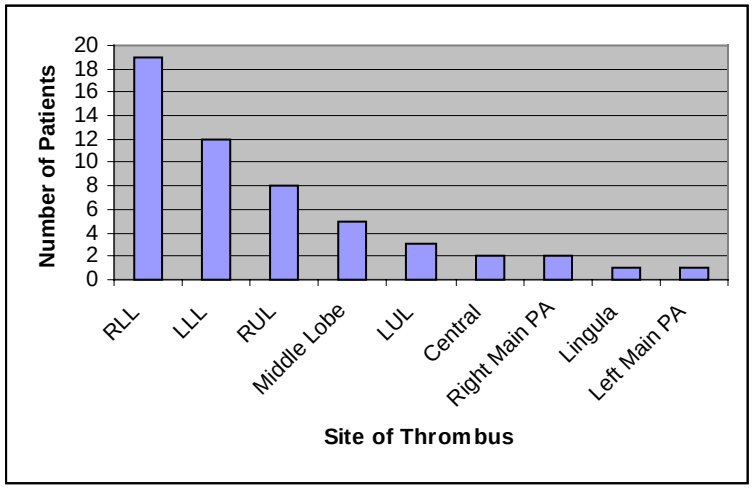

Figure II: Site of Thrombus

Referral speciality and clinical information given on the request card was used to determine any prior risk. The presumptive diagnosis of all patients at referral is illustrated in figure III. Most referrals, accounting for just over a third, were from the respiratory physicians (166/487), the general surgeons and general medical teams accounted for just over 10% of referrals each, with fewer referrals from GI medicine, the Transplant unit, geriatrics and ITU.

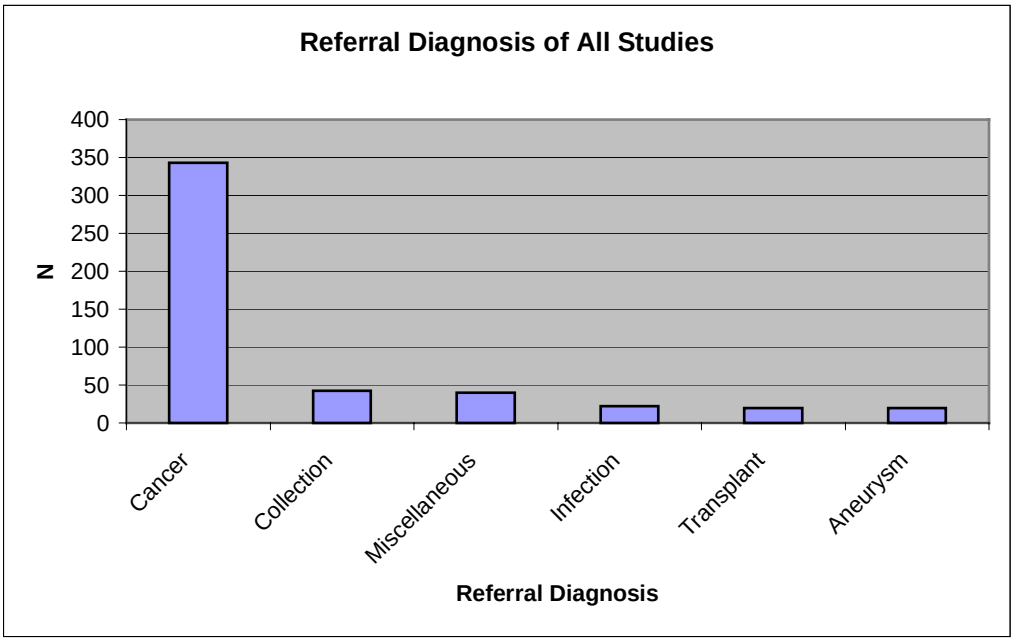

Figure III: Presumptive Diagnosis at Referral

Cancer refers to any patient with known or suspected cancer, mediastinal or pulmonary mass. Collection covers patients being imaged to evaluate pleural or pericardial collections. Infection includes patients with slow to resolve pneumonia or sepsis. Transplant identifies a group of patients being assessed for hepatic and renal transplantation. Aneurysm covers patients with thoracic aneurysm as well as patients suspected of having acute aortic syndrome. Miscellaneous describes a heterogeneous group with diverse presumptive diagnoses including pulmonary fibrosis, emphysema, collapse, hoarseness and dysphagia.

Studies were performed as determined by clinical urgency, based largely on information provided on patient request card. At our institution the vast majority of in-patient CT scans are performed within 3 days of request.

Of the positive studies 18/28 (64.3%) were carried out for confirmed or presumed malignancy. Of the total study population, 343 studies (70.4%) were carried out for confirmed or presumed malignancy. There was no evidence of a statistically significant difference in the proportion of PE cases in those with suspected malignancy (18/343, 5.2%) compared to the proportion of PE in non-malignancy (10/144, 6.9%). Difference in

proportions is -1.7% with a 95% CI for difference (-6.47%, 3.08%), p=0.486 (binomial test for proportions).

Median duration of in-patient admission prior to scan was 3 days, (range 0-255 days). Distribution of hospital stay for positive scans is recorded in Figure IV.

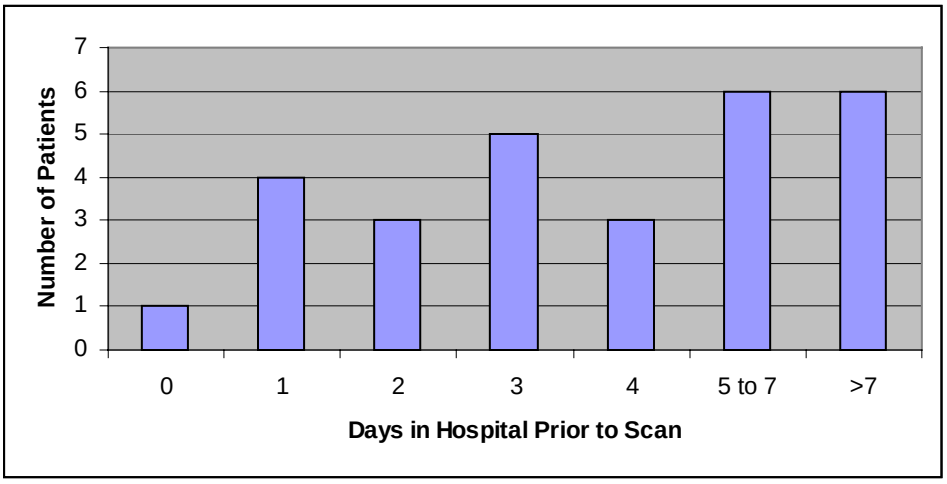

Figure IV: Days in Hospital prior to Diagnosis of PE

Looking at grouped hospital stays (0-1, 2-3, 4-6 and 7+ days) there was no statistically significant relationship between length of hospital stay and likelihood of finding unsuspected PE (χ^2=2.169, p=0.538).

DISCUSSION

Terminology and Significance of Unsuspected PE

Previous studies[3,4] have described the finding of pulmonary embolism, in situations where this is not suspected, as *incidental* PE. In this study we have chosen to use the term *unsuspected* PE, previously also used by Gosselin *et al.*[5] The term incidental to some suggests clinical insignificance. We feel there is little evidence to support the implication that these emboli are nessessarily of less clinical significance just because they are identified as an incidental finding.

Recent meta-analysis of necropsy studies has demonstrated that pulmonary embolism remains a common condition where there is discrepancy between clinically suspected and necropsy proven cause of death.[6] The significance of small pulmonary emboli has been called in to question. While discussion as to the importance of small emboli is beyond the scope of this article, a comprehensive summary of the evidence regarding small pulmonary emboli is contained in a recent editorial by Goodman.[7] It is of note that of the

emboli identified in this study, 18/28 were at segmental or sub-segmental level and might be classified as small.

Identification and Estimates of Prevalence of PE

Contrast enhanced CT, specifically CTPA, has become the first line investigation in many centres in the diagnosis of pulmonary embolism due to a high inter-observer agreement,[8] identification of unsuspected pathologies[9] and because it is a cost effective method of imaging PE.[10]

Unsuspected PE has previously been demonstrated in patients undergoing contrast enhanced CT of the chest for reasons other than suspected PE. Using older technologies in a study of 1879 patients undergoing contrast enhanced helical CT thorax, Winston *et al*[4] identified 18 patients with unsuspected PE, estimating the prevalence at 1%. A similar study by Gosselin *et al*[5] demonstrated an overall rate of 1.5%, with up to 5% of in-patients demonstrating PE. More recently, with a 4 slice MDCT, Storto *et al*[3] found incidental PE in 4% of 474 in-patients. No previous studies have reported rates of unsuspected PE using 16-slice MDCT.

Our study has shown an overall rate of unsuspected PE of 5.7%. We identified only those in-patients in whom PE was an unexpected finding. Due to the exclusion of CTPA examinations and patients with a known PE, this figure must be an underestimation of the actual prevalence of PE in the hospital population. The fact that we are now identifying these unsuspected PE on a regular basis implies that PE is much more common than previously appreciated. Many of the unsuspected PE, were in the smaller segmental and sub-segmental arteries. Whilst large central PE may seem more likely to be clinically apparent, peripheral emboli are also important because of the tendency to cause pulmonary infarction, pleuritic chest symptoms and as a possible prelude to larger potentially life threatening emboli. Until the natural history of these smaller PE is better understood it remains the responsibility of the radiologist to report them and of the clinician to define the therapy. We cannot conclude from this study whether or not patients with unsuspected PE should be anticoagulated or not. We would expect that the larger emboli at least require treatment. Evidence is uncertain as to optimal management so far as the smaller asymptomatic emboli are concerned. In our institution clinicians certainly still consider all detected PE as significant and treat as such. The question which our study does raise is whether PE, and in particular small PE, are more common than previously recognised. If this is the case then these small PE may be of lesser clinical

significance than larger clinically evident PE and may merit a different management strategy. A possible strategy, which would need to be fully evaluated, would be to do leg U/S in patients with unsuspected or asymptomatic emboli, to look for possible DVT and avoid anticoagulation if negative.

Spatial Resolution and Identification of PE

The higher incidence of PE demonstrated in our study compared to previous studies may be due to improved spatial resolution. Previous work has indicated that MDCT increases conspicuity of small, peripheral arteries.[11,12] Several studies have also demonstrated increased sensitivity for detection of pulmonary embolism in sub-segmental vessels using MDCT.[13-15] Patel *et al*[16] have previously demonstrated that MDCT scanning demonstrates more PE and in smaller vessels than single slice scanning. In addition, the same study demonstrated that using MDCT decreasing slice thickness from 2.5mm to 1.25 mm improved visualisation of segmental and sub-segmental vessels and PE.

If spatial resolution is the principal determining factor in identification of peripheral emboli, it is perhaps not surprising that our data demonstrates more incidental PE in patients scanned using a 16 slice scanner with 1mm slice thickness than in a 4 slice scanner with a 2 or 3mm slice thickness. The difference in this study between 4 and 16-slice scanning was not statistically significant. This likely reflects the small number of positive studies identified.

In this study, only 67.9% of the positive scans were initially reported as showing PE. In all 9 cases (32.1%) where PE was not identified, thrombus was at segmental level or more distally. This data suggests that smaller clots are more easily overlooked and highlights the need to include a thorough assessment of pulmonary arteries in all contrast enhanced thoracic CT scans.

Aetiological Factors in Unsuspected PE

Age:

Older patients are significantly more likely to develop symptomatic thrombo-embolic disease.[2,17,18] This study demonstrates that older people are also more likely to develop unsuspected PE. Most dramatically

illustrated, in the over 80 age group who were found to have PE in 16.7% of cases (Table II). We recognise that age may be a surrogate for other risk factors known to be associated with an increased risk of PE such as malignancy, immobility or heart failure.

Malignancy:
The suggestion that rates of incidental PE are higher in patients with confirmed or presumed malignancy is not new. In a sub-group assessment following the PIOPED study, 14 of 20 patients proven to have unsuspected pulmonary embolism as the principal cause of death at autopsy had advanced associated diseases, with malignancy in 4 patients.[19] The link between thrombo-embolic disease and malignancy is further suggested by the finding of an increased risk of the diagnosis of malignancy in the 2 years following diagnosis of venous thrombo-embolism in a large retrospective study.[20] In a recent paper regarding incidental PE, Storto *et al* have noted that 70% of patients with incidental PE had malignancy.[3]

No statistically significant correlation between malignancy and incidence of PE was noted in this study. The reasons for this are uncertain but may reflect in part the small number of positive cases and the fact that the great majority of patients having a contrast enhanced CT of thorax fell into this category and that many of the scans were for presumed, rather than confirmed malignancy.

Hospital Admission:
No significant association is seen in this study between length of hospital admission and presence of PE. Hospital in-patient stays are now relatively short. The average stay for all patients scanned in this study was only three days and 17 of the 28 positive cases were identified within five day of admission. We would suggest that at least some of these emboli had been present prior to admission. We would also suggest that for patients with longer admissions, the use of low molecular weight heparin (LMWH) as prophylaxis might have a protective effect, this information however was not easily available during this study.

The rate of unsuspected in-patient PE will not reflect the general out-patient incidence. This population theoretically should have fewer risk factors for PE and therefore presumably a lower incidence.[3]
A small number of outpatient scans were inadvertently assessed before exclusion from our study. Of 43 such studies, 4 patients (9.3%) showed

incidental PE. This is at odds with the suggestion that prolonged hospital admission increases the rate of PE, but is felt likely to be spuriously high due to small patient numbers involved and a larger study is needed in this out-patient group.

CONCLUSIONS

Unsuspected PE is present in 5.7% of in-patients having contrast enhanced MDCT thorax. The detection of these thrombi suggests that the actual prevalence of PE in the hospital population is greater than previously appreciated. The incidence increases significantly with age with 9.2% of the over 70 year old, and 16.7% of the over 80 year old population affected. We showed no statistical correlation with the length of admission or associated malignancy.
In this study >30% of emboli are missed on initial review, all of these were found in segmental or subsegmental vessels, but the clinical significance of these smaller thrombi remains uncertain. Routine assessment of the pulmonary arteries should be considered standard practice when reporting any contrast enhanced MDCT thorax.

ETHICS APPROVAL

Institutional approval was obtained for the study.

COMPETING INTERESTS

None.

LICENCE FOR PUBLICATION STATEMENT

REFERENCES

1. Pineo GF. New developments in the prevention and treatment of venous thromboembolism. *Pharmacotherapy*. 2001;**21**:51S-55S.

2. Silverstein MD, Heit JA, Mohr DN, *et al*. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. *Arch Intern Med* 1998;**158**:585-593.

3. Storto ML, Di CA, Guido F, *et al*. Incidental Detection of Pulmonary Emboli on Routine MDCT of the Chest. *AJR Am J Roentgenol* 2005;**184**:264-267.

4. Winston CB, Wechsler RJ, Salazar AM, *et al*. Incidental pulmonary emboli detected at helical CT: effect on patient care. *Radiology* 1996;**201**:23-27.

5. Gosselin MV, Rubin GD, Leung AN, *et al*. Unsuspected pulmonary embolism: prospective detection on routine helical CT scans. *Radiology* 1998;**208**:209-215.

6. Roulson J, Benbow EW, Hasleton PS. Discrepancies between clinical and autopsy diagnosis and the value of post mortem histology; a meta-analysis and review. *Histopathology* 2005;**47**:551–559.

7. Goodman LR. Small Pulmonary Emboli: What Do We Know? *Radiology* 2005;**234**:654-658.

8. Blachere H, Latrabe V, Montaudon M, *et al*. Pulmonary embolism revealed on helical CT angiography: comparison with ventilation-perfusion radionuclide lung scanning. *AJR Am J Roentgenol* 2000;**174**:1041-7.

9. van Rossum AB, Pattynama PM, Mallens WM, *et al*. Can helical CT replace scintigraphy in the diagnostic process in suspected pulmonary embolism? A retrolective-prolective cohort study focusing on total diagnostic yield. *Eur Radiol* 1998;**8**:90-96.

10. van Erkel AR, van Rossum AB, Bloem JL, *et al*. Spiral CT angiography for suspected pulmonary embolism: a cost-effectiveness analysis. *Radiology* 1996;**201**:29-36.

11. Raptopoulos V, Boiselle PM. Multi-detector row spiral CT pulmonary angiography: comparison with single-detector row spiral CT. *Radiology* 2001;**221**:606-613.

12. Ghaye B, Szapiro D, Mastora I, *et al*. Peripheral pulmonary arteries: how far in the lung does multi-detector row spiral CT allow analysis? *Radiology* 2001;**219**:629-636.

13. Remy-Jardin M, Mastora I, Remy J. Pulmonary embolus imaging with multislice CT. *Radiol Clin North Am* 2003;**41**:507-519.

14. Washington L, Gulsun M. CT for thromboembolic disease. *Curr Probl Diagn Radiol* 2003;**32**:105-126.

15. Schoepf UJ, Kessler MA, Rieger CT, *et al*. Multislice CT imaging of pulmonary embolism. *Eur Radiol* 2001;**11**:2278-2286.

16. Patel S, Kazerooni EA, Cascade PN. Pulmonary embolism: optimization of small pulmonary artery visualization at multi-detector row CT. *Radiology* 2003;**227**:455-460.

17. Stein PD, Hull RD, Kayali F, Ghali *et al*. Venous thrombo-embolism according to age: the impact of an aging population. *Arch Intern Med* 2004;**164**:2260-2265.

18. Anderson FA, Jr., Wheeler HB, Goldberg RJ, *et al*. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism. The Worcester DVT Study. *Arch Intern Med* 1991;**151**:933-938.

19. Stein PD, Henry JW. Prevalence of acute pulmonary embolism among patients in a general hospital and at autopsy. *Chest* 1995;**108**:978-981.

20. Murchison JT, Wylie L, Stockton DL. Excess risk of cancer in patients with primary venous thromboembolism: a national, population-based cohort study. *Br J Cancer* 2004;**91**:92-95.

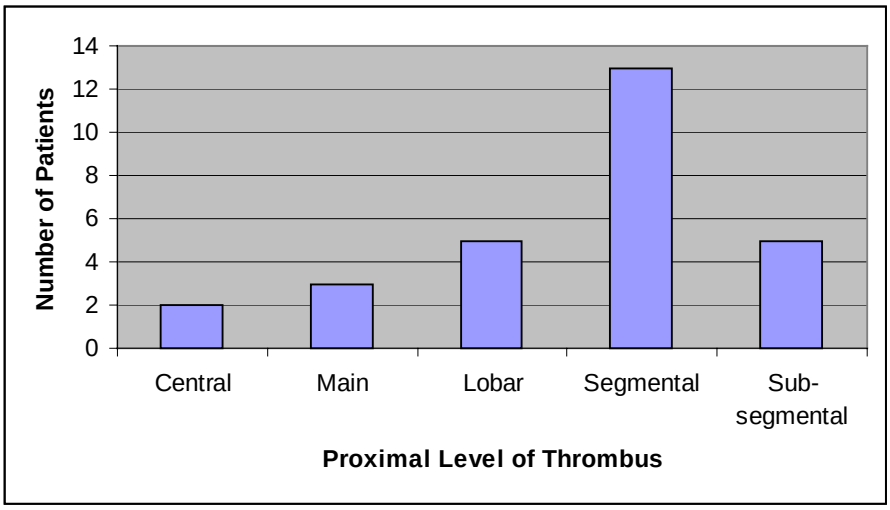

Figure I: Proximal Extent of Thrombus

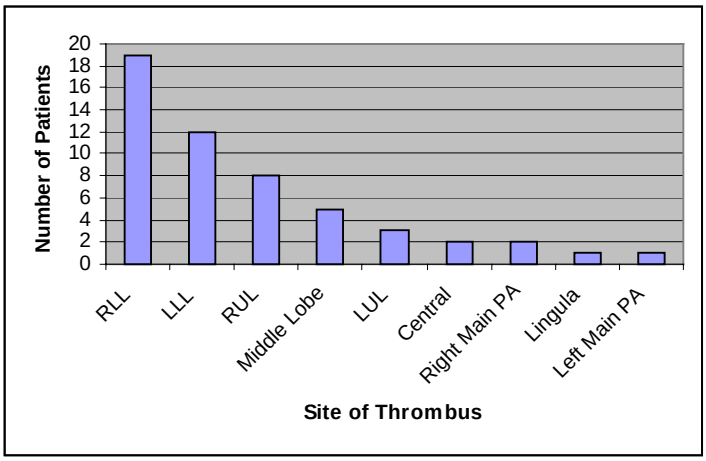

Figure II: Site of Thrombus

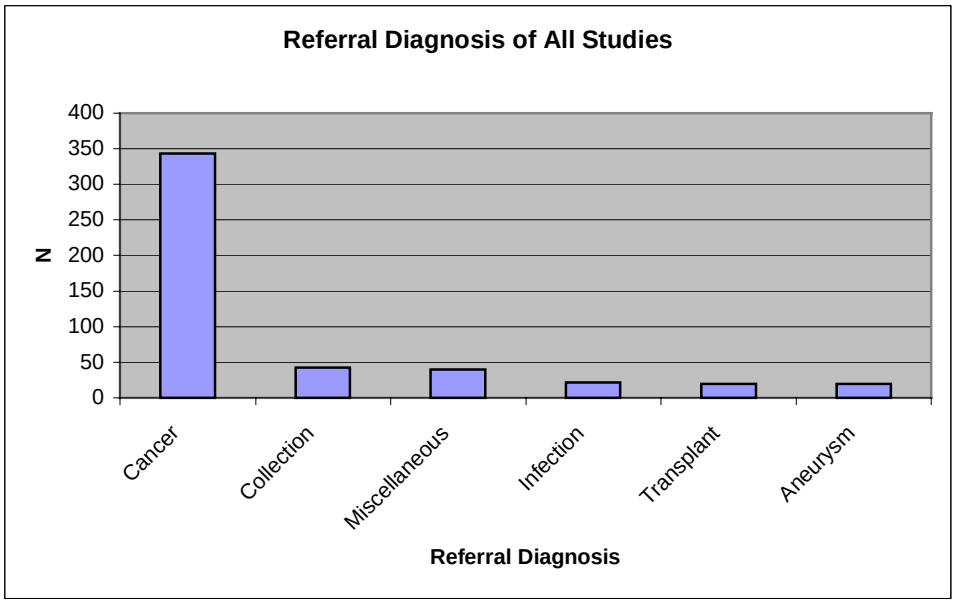

Figure III: Presumptive Diagnosis at Referral

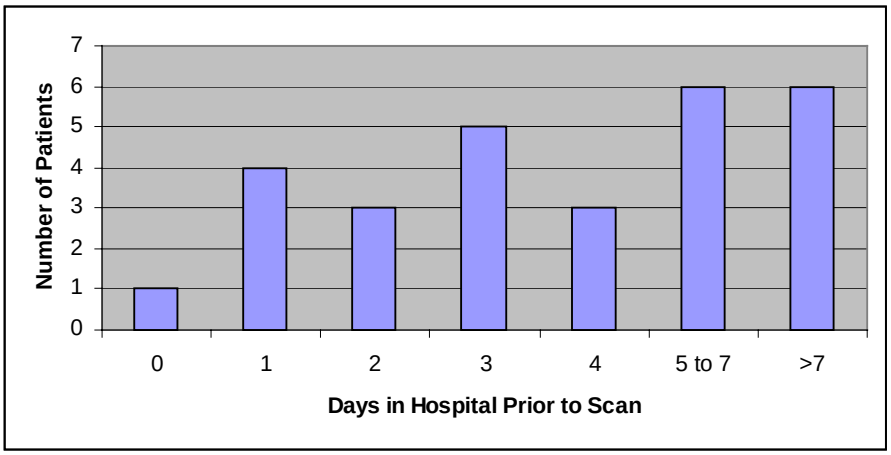

Figure IV: Days in Hospital prior to Diagnosis of PE