University of KwaZulu-Natal,

Nelson R. Mandela School of Medicine,

Department of Radiology.

UTILIZATION OF COMPUTED TOMOGRAPHIC PULMONARY ANGIOGRAPHY IN CLINICALLY SUSPECTED ACUTE PULMONARY THROMBO-EMBOLISM AT INKOSI ALBERT LUTHULI CENTRAL HOSPITAL.

DR WONDER-BOY EUMANE MBATHA

(STUDENT NO: 983186748)

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Utilization of Computed Tomographic Pulmonary Angiography in clinically suspected Acute Pulmonary Thrombo-embolism at Inkosi Albert Luthuli Central Hospital.

by

Dr W.E Mbatha

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Supervisor: Dr J Maharajh

2014

DECLARATION

I, **Wonder-boy Eumane Mbatha**, declare that

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My wonderful wife Anele and my family for their support.

Dedicated to the memories of u-Baba, Rabi, Thoko and Mamkhulu.

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ABBREVIATIONS

PE: Pulmonary thrombo-embolism

CTPA: Computed Tomographic Pulmonary Angiography

IALCH: Inkosi Albert Luthuli Central Hospital

CXR: Chest x-ray

V/Q Scan: Ventilation-Perfusion scan

PIOPED I: Prospective investigation of Pulmonary Embolism Diagnosis I

PIOPED II: Prospective investigation of Pulmonary Embolism Diagnosis II

PISAPED: Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis

BREC: Biomedical Research and Ethics Committee

DVT: Deep Vein Thrombosis

CAD: Computer Aided Detection

FEU: Fibrinogen equivalent units

ABSTRACT

Background:

Computed Tomographic Pulmonary Angiography (CTPA) is now the primary imaging technique for patients with a high clinical suspicion of PE and in those with pre-existing pulmonary disease. A combination of pre-test probability assessment and D -dimer estimation leads to a more targeted approach to CTPA use.

Aim:

To evaluate the use of CTPA in clinically suspected pulmonary thrombo-embolism (PE) and to determine whether pre-test probability assessment and D-dimer estimation lead to a more targeted approach to CTPA use.

Materials and Methods:

Patients meeting the inclusion criteria were selected using a systematic sampling technique. Chart reviews were performed and Wells` scores were assigned and categorised into low, intermediate and high probability. CTPA results were categorised into PE confirmed, no abnormal radiological findings and alternate diagnoses. D-dimer test results were categorised into D-dimer positive, negative and unknown.

Results:

Of the 110 patients sampled, 29 examinations (26.4%) returned a positive result for acute PE, 52 examinations (47.3%) revealed no abnormal radiologic findings and 29 examinations revealed diagnoses other than PE. Well`s clinical probability scores were worked out and assigned. Seventy four patients (67.3%) were in the low probability category, 31 patients (28.2 %) were in the intermediate probability category and 5 patients (4.5%) were in the high probability category. In the low probability category 82.4% of the CTPA examinations were normal and revealed no PE and 17.6% of the examinations revealed pulmonary embolism. In the intermediate

category the majority of the cases, 60% revealed evidence of PE and 40% were negative for PE. In the high probability category all the patients (100%) had CTPA evidence of pulmonary embolism. Of the patients sampled, 26.4 % had D-dimer estimation and D-dimer test results were unknown in 73.6% of the patients. Of the patients that had D-dimer estimation, 55% were positive and 45% returned a negative result. Eighty percent (80%) of the patients with negative D-dimers had normal CTPA studies and PE was confirmed in 20% of them. Of the patients with positive D-dimer estimation, 46.2% were normal and PE was confirmed in 53, 8%. Patients in the low probability group, with negative D-dimer estimation, all returned negative CTPA results. Eighteen percent (18%) of intermediate probability category cases with negative D-dimers returned positive CTPA results.

In the study population, 46.4% of the patients had abnormal chest x-ray results, 9.1% had normal chest x-rays and chest x-ray results were unknown in 44.1% of the cases. Of the patients with normal CXRs, 85.7% had no abnormal radiologic findings at CTPA and 14.3% had confirmed PE. Of the patients with abnormal CXRs, 45.9% were negative for PE and PE was confirmed in 54.1% of them. In total, 13.6% of the patients had negative venous Doppler results, 9.1% were positive and results were unknown in 77.3% of the cases.

Of the patients with no current DVT, 72.3% returned normal CTPA results with 27.7% of the cases returning a positive PE result. Of the patients with current DVT, 73.3% returned positive CTPA results in relation to PE and 26.7% were normal.

Conclusion:

The results of the current study demonstrate that the majority of CTPA examinations performed at IALCH had low probability scores. The results seem to suggest that there has been over ordering of the test. The results raise serious concerns about the radiation dose delivered to patients which could have been avoided and further highlight the importance of correct patient selection prior to CTPA exam. The results further support the use of pre-test probability assessment in combination with D-dimer estimation prior to CTPA evaluation in the local setting.

APPENDICES

Appendix 1: Biomedical Research and Ethics Committee letter of approval.

Appendix 2: Institutional approval by Inkosi Albert Luthuli Central Hospital Management.

Appendix 3: Wells pre-test probabilities.

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CHAPTER 1: INTRODUCTION & BACKGROUND

BACKGROUND

Many institutions now use Computed Tomographic Pulmonary Angiography (CTPA) as the primary imaging technique in the assessment of patients with clinically suspected acute pulmonary thrombo -embolism (PE). Inkosi Albert Luthuli Central Hospital (IALCH) is no exception. CTPA imaging, with benefits from the rapid technologic advances, has replaced conventional pulmonary angiography as the reference standard for the diagnosis of PE [1]. It is the investigation of choice in patients with a high clinical suspicion of PE and in those with pre-existing pulmonary disease. Use of this modality however, without having established the pre-test probability of the disease, results in overuse of the test and an unjustified increase of cost and radiation burdens [2].

A steady increase in the number of CTPA requests at IALCH was observed which prompted the investigators to undertake an audit of the examinations performed. The results of the audit would be a key element in discussions with fellow radiologists and referring clinicians to develop or refine referral guidelines for suspected PE in the local setting.

The diagnosis of acute PE has always been a challenging one for the attending physician as the signs and symptoms of the disease are non-specific. Accurate and rapid identification of the patients who have PE is of great clinical relevance as PE is a potentially fatal condition, with a 3-month all-cause mortality rate of 6–11% in haemodynamically stable patients and 30% or higher in patients with PE presenting in haemodynamic instability [3]. In patients with a clinical suspicion of PE, between 15.4 and 37.4% of the studies performed return a positive result for PE and 56 % turn out to have an alternative diagnosis by CTPA according to published studies [4]. The present study aimed to evaluate the diagnostic yield of CTPA, in relation to PE and alternate diagnoses, in the local setting and to compare the findings to international standards, in an attempt to evaluate for the use of the modality in the local setting. The study also aimed to determine whether pre-test probability assessment and D-dimer estimation lead to a more targeted approach to CTPA use in the local setting.

CHAPTER 2: LITERATURE REVIEW

Acute pulmonary thrombo-embolism (PE), a medical emergency, is a common cardiovascular and cardiopulmonary illness with an incidence in the United States that exceeds 1 per 1000 and a mortality rate of 15% in the first 3 months after diagnosis. This renders PE possibly as deadly an illness as acute coronary syndromes and stroke [5]. The discussions on the aetiology of PE, in the contemporary set-up, have not only focused on acquired and inherited causes of hypercoagulability but also on an association between atherosclerotic disease and spontaneous venous thrombosis. Common reversible risk factors for PE include obesity, cigarette smoking and hypertension [5]. PE also occurs in the context of long-haul air travel, illness attributable to surgery, trauma, immobilization, cancer, oral contraceptives, pregnancy, and postmenopausal hormone replacement therapy, as well as medical conditions such as pneumonia and congestive heart failure [5]. Further predisposing factors include genetic predisposition to venous thrombosis, increased levels of clotting factors and deficiencies of anticoagulant factors [5].

The accurate diagnosis of PE remains a major challenge due to the non-specific findings of the clinical presentation and the limitations of radiographic imaging. CTPA has surpassed ventilation-perfusion (V/Q) scanning as the primary imaging modality in the investigation of patients with suspected PE due to its superior diagnostic accuracy. Multi-detector CTPA is increasingly being used in the evaluation of patients with clinically suspected PE, however, as a definitive diagnostic test CTPA may be limited by inadequate sensitivity, especially in instances of isolated sub-segmental emboli. A meta-analysis, looking at the outcomes in patients with suspected PE managed with CTPA, revealed that the rate of subsequent venous thrombo-embolism after negative results on CTPA is similar to that seen after negative results on conventional pulmonary angiography and that it appears to be safe to withhold anticoagulation after negative CTPA results [6].

The accuracy of diagnostic tests used in patients who are suspected of having PE varies greatly, but it is possible to estimate the range of pre-test probabilities over which each single test or series of tests in a diagnostic strategy can confirm or rule out the disease [7]. According to the Prospective investigation of Pulmonary Embolism

Diagnosis II (PIOPED II) investigators, the positive and negative predictive values of CTPA examinations are high with a concordant clinical assessment and additional testing is always necessary when the clinical probability is inconsistent with the imaging results [8] .Their results further revealed that, despite values of sensitivity and specificity of CTPA as high as 83% and 96% respectively, the positivity of the test results in a patient with low clinical probability indicated a chance of PE of 58% and negative results in a patient with high clinical probability indicated a chance of not being affected by PE of only 60% [8].

Recent technological advances have further increased the diagnostic accuracy of the CTPA technique and it is now believed to have fulfilled the requirements to replace conventional pulmonary angiography as the reference standard for the diagnosis of PE [1]. Most recent expert statements and international guidelines strongly recommend the assessment of pre-test clinical probability [1, 9-14] in the diagnostic evaluation of patients with clinically suspected PE.

Positive yield rates of less than 10% in CTPA studies in patients who were suspected of having PE have been reported in several recent reports which suggest possible overuse of the technique and probable poor patient selection [15-20] . It is noteworthy that the selection of patients who are suspected of having PE for undergoing testing has greatly changed since the advent of CTPA. Prospective diagnostic trials in the early 90's, which used pre-test clinical evaluation of symptoms followed by scintigraphy, showed the presence of disease in at least one-third of the patients examined [19, 20]. The mean age of patients was 64 and 56 years in Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISAPED) [21] and PIOPED I [19], respectively, whereas it was 51 years in the PIOPED II study [8].

Confirming the recent trend toward a reduced prevalence of PE among patients suspected of having it, Mamlouk and colleagues, in their retrospective analysis of a large data set [22] reported that 90.2% (mean age, 50 years) of subjects referred because they were suspected of having PE had negative results and 6.4% had a positive finding at CTPA. The results from their series showed that, in the absence of risk factors for PE, the chance of a positive result at CTPA was less than 1%. Only 5% of their patients had D –dimer estimation and none of the patients with negative

results of the D -dimer test had a positive result at CTPA [22]. Their results further strongly suggest that, in the absence of risk factors for PE, notably with negative results of the D -dimer test, CTPA could be safely avoided and that in the emergency department setting, the combination of the absence of definite risk factors and negative D -dimer test results could be used to substantially decrease the number of CTPA examinations performed.

In another report [15], the researchers clearly showed that patients who were suspected of having PE often undergo CTPA without being appropriately stratified according to pre-test clinical probability and D -dimer level determination and, in some instances, even in the presence of low clinical probability and negative D -dimer test results. This approach is probably responsible for the observed steady increase in the total number of CT angiographic examinations performed and the concomitant reduced prevalence of positive results. Three scoring systems used to assess pre-test probability of PE have been tested prospectively and validated in large-scale clinical trials: the Wells score [24], the Pisa score [25], and the Geneva score [26]. The Wells and Geneva scores were developed for use in the emergency department, and the Pisa score is more optimized for use in hospitalized patients [12, 27]. All three scoring systems perform reasonably well at least to assess low clinical probability for PE and, consequently, they seem to be quite appropriate to reduce the number of unnecessary CTPA examinations, especially when combined with the D -dimer test [28, 2].

The increased use of CTPA and its well documented high radiation exposure has raised serious concerns about a possible related future increased incidence of cancer [29, 30]. The amount of radiation delivered to the mammary glands of women of reproductive age during CTPA examination puts them at high risk of developing breast cancer [31, 33]. This has prompted the proposal of several dose saving strategies for thoracic organs during CTPA for PE [34]. To further minimise the risk of radiation, experts suggest the use of lung scintigraphy as the first-line imaging test in women of reproductive age and patients with renal function impairment and contrast media allergy.

The article by Mamlouk and colleagues provides evidence that suggests that a substantial number of CTPAs could be avoided simply by adhering to the information

derived from clinical history and D-dimer test determination [22]. In an attempt to reduce the radiation exposure to patients suspected of having PE in the emergency department, Stein et al conducted collaborative educational seminars among the radiology, nuclear medicine, and emergency medicine departments over a period of time regarding the radiation dose and accuracies of V/Q scanning and CTPA for diagnosing PE [23]. To reduce radiation exposure, an imaging algorithm was introduced in which emergency department patients with a clinical suspicion of PE underwent chest radiography. If the chest radiograph was normal, V/Q scanning was recommended, otherwise CTPA was recommended. The practice patterns of physicians changed in response to an educational intervention, resulting in a reduction in radiation exposure to emergency department patients with suspected PE without compromising patient safety [23].

In a study conducted by Gupta and colleagues looking at the efficacy of clinical risk algorithms and a quantitative immunoturbidimetric D-dimer assay in the evaluation of patients undergoing CTPA for suspected acute PE, emergency department evaluations for clinically suspected PE were performed with the revised Geneva score, a quantitative D-dimer assay, and CTPA. The data appeared to support the use of a quantitative D-dimer assay as a first-line test in evaluation for PE when the clinical probability of the presence of PE is low or intermediate. The sensitivity and negative predictive value were 100% for these cases. The results further showed that more than 26% of CTPAs would have been avoided if the D-dimer assay had been used as a first-line test in the care of patients at low or intermediate risk [35].

The literature clearly suggests that the ideal diagnostic strategy for PE should include tests that prove accurate, safe, readily available, and cost effective. CTPA is an accurate and readily available diagnostic test for the diagnosis of PE. However, use of CTPA, without having established the pre-test probability of the disease and D-dimer estimation, will continue to result in overuse of the test and in an unjustified increase of costs and radiation load.

CHAPTER 3: OBJECTIVES, PATIENTS & METHODS

AIM OF STUDY:

To evaluate the use of CTPA in the diagnostic evaluation of adult patients with a clinical suspicion of acute PE at IALCH and to determine whether pre-test probability assessment and D-dimer estimation lead to a more targeted approach to CTPA use in the local setting.

OBJECTIVES:

- To determine the diagnostic yield of CTPA in the local setting.
- To evaluate the diagnostic yield of alternate diagnoses and to describe them.
- To describe the demographic and clinical profiles of patients diagnosed with PE.
- To compare the pre-test probability scores to the outcomes of the CTPA examinations.

PATIENTS AND METHODS

A. STUDY AREA:

The study was conducted at IALCH, a tertiary referral hospital in Durban, South Africa.

B. STUDY DESIGN:

Retrospective descriptive chart review.

C. STUDY POPULATION:

Patients referred to the radiology department for CTPA examination based on a clinical suspicion of acute PE. The study population included both inpatients and outpatients.

D. SAMPLE STRATEGY:

A systematic sampling technique was employed in the selection of the patients who satisfied the inclusion criteria. Every third patient was selected from the list of eligible patients following a random start.

E. INCLUSION CRITERIA:

Adult patients (>18 years) referred for CTPA examination on the basis of a clinical suspicion of PE, for the first time, in the period 01/01/2008 to 31/12/2011 at IALCH.

F. EXCLUSION CRITERIA:

- Studies performed in younger patients (< 18 years),
- Technically non-diagnostic or inadequate studies,
- Follow-up CTPAs performed on the same patients,
- CTPAs performed for indications other than PE.

STUDY PROTOCOL

ETHICAL AND MEDICO-LEGAL ASPECTS:

The study was a retrospective descriptive review of the charts for patients that were subjected to CTPA on the basis of a clinical suspicion of PE. There was no direct contact with the patients. A sheet containing patient hospital numbers was prepared. Each patient was allocated a study number that was linked with their hospital numbers. The information was kept in a separate data sheet which was locked away and access was restricted to the investigators. All patient data was generated from the new study numbers to protect patients' identity and possible linking of the patients to the study data. The study only commenced after full ethical approval was granted. It was reviewed and approved by the Biomedical Research and Ethics Committee (BREC) of the University of KwaZulu-Natal (Appendix 1) and Institutional approval

was granted by the Inkosi Albert Luthuli Central Hospital (IALCH) Management (Appendix 2).

CLINICAL PROBABILITY TESTING

Hospital identification numbers of the sampled cases were used to review the patient records which were searched for clinical parameters used to retrospectively work out Wells pre-test probabilities (Appendix 3). The investigator who allocated retrospective pre-test probability scores was blinded to the results of the CTPA examinations. Of the pre-test clinical probability scores available, the Wells test was chosen for its simplicity and the fact that its parameters were easy to obtain. Demographic profiles, including patients age and gender, were recorded. The charts were searched for records of symptoms and signs to suggest deep vein thrombosis (DVT) at or around the day of the examination. Symptoms looked for included upper or lower limb pain, swelling and discolouration. Signs included upper or lower limb tenderness, positive Homan`s sign, prominent superficial veins and skin discolouration. Patients were then grouped into those with clinically suspected or confirmed DVT, those with no evidence of DVT and a third category of unknown for the cases with insufficient data in relation to DVT. Patients were given 3.0 points for clinical evidence of DVT and an alternate diagnosis being less likely than PE.

Heart-rate recordings on the day of the CTPA examination were reviewed and patients were grouped into those with heart-rates of 100 per minute or more and those with heart-rates less than 100 per minute. Patients with heart-rates of at-least 100 per minute were given 1.5 points. Chart reviews also included recorded evidence of immobilisation such as travel history, surgery in the preceding month, etc. Patients with a history of immobilisation were allocated 1.5 points. Chart reviews included history of previous venous thrombo-embolic disease including DVT and PE. Patients with a positive history of previous venous thrombo-embolic disease were allocated 1.5 points. Recorded histories of haemoptysis were searched for and patients with a history of haemoptysis were allocated 1.0 point. Reviews further included history to suggest the presence of a recent malignancy or patients on palliative therapy. Patients with a positive history of malignancy were allocated 1.0 point. Points were tallied and patients who had scores more than 6 were allocated the high clinical probability

interpreted at the Syngo Multimodality Workstation with CAD, an automatic pulmonary embolus tool detection software. Findings in relation to PE were reported as either PE present or not and whether acute or chronic. Acute PE was defined as a partial or complete filling defect of the pulmonary arterial system (Figures 9, 10 and 11). Chronic PE was defined as the presence of direct pulmonary artery signs (complete or partial filling defect, the presence of an eccentric or calcified thrombus), signs related to pulmonary hypertension and/or signs of systemic collateral supply. CTPA results were reviewed and patients were grouped into confirmed PE, no abnormal radiologic findings and alternate diagnosis.

A total of 110 patients were selected from the study population using a systematic sampling technique following a random start. D-dimer results were reviewed and patients were categorised as positive, negative and unknown. The data was recorded in a Microsoft Excel spread sheet. Statistical analyses were performed using SPSS Statistics 19.

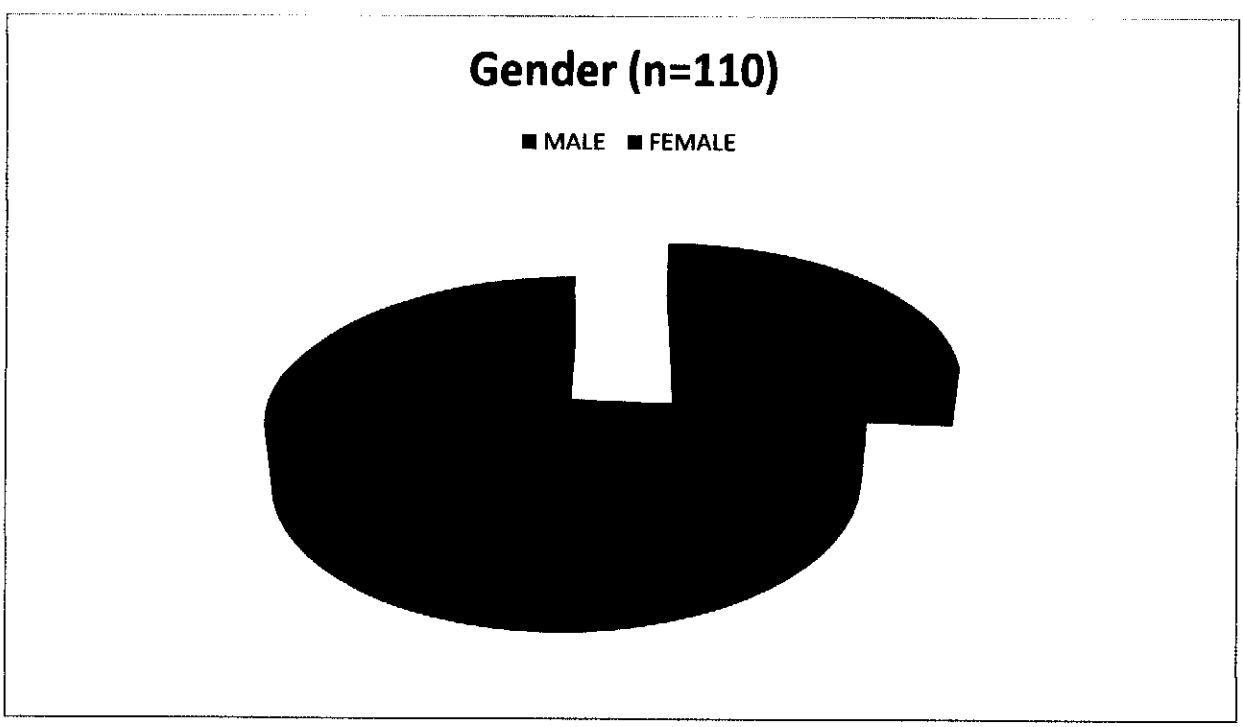
CHAPTER 4: RESULTS

The IALCH radiology database review revealed that a total of 1000 CTPA examinations were performed in the period 01/01/2008 to 31/12/2011with a notable increase in the number of examinations performed year on year. A total of 360 patients met the inclusion criteria. A systematic sampling strategy was employed, following a random start, and 110 patients were sampled. The patients sampled had a mean age of 43.10 with a standard deviation of 16.33. Of the sampled patients, 73.6% were female and males accounted for 26.4%.

TABLE 1: TABLE SHOWING PATIENT AGE DISTRIBUTION

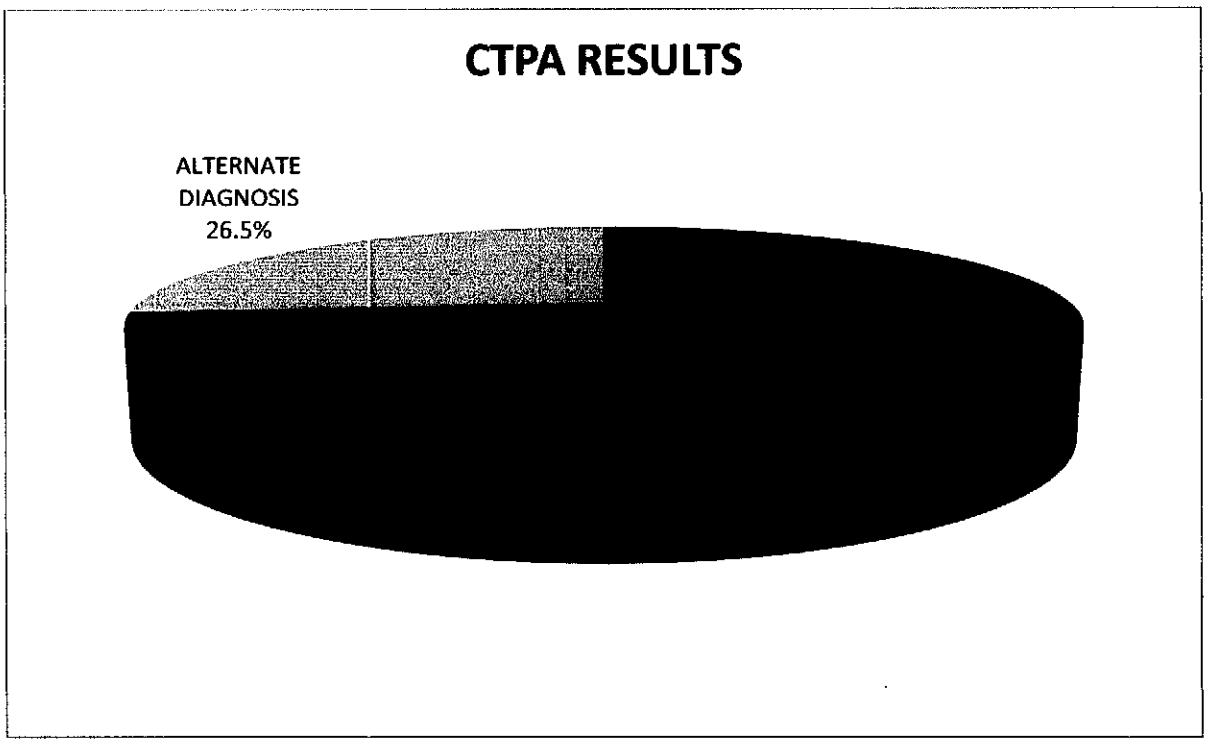
	N	Minimum	Maximum	Mean	Std. Deviation
Age	110	18	84	43.10	16.329
Valid N	110				

FIGURE 1: PIE CHART SHOWING PATIENT GENDER DISTRIBUTION



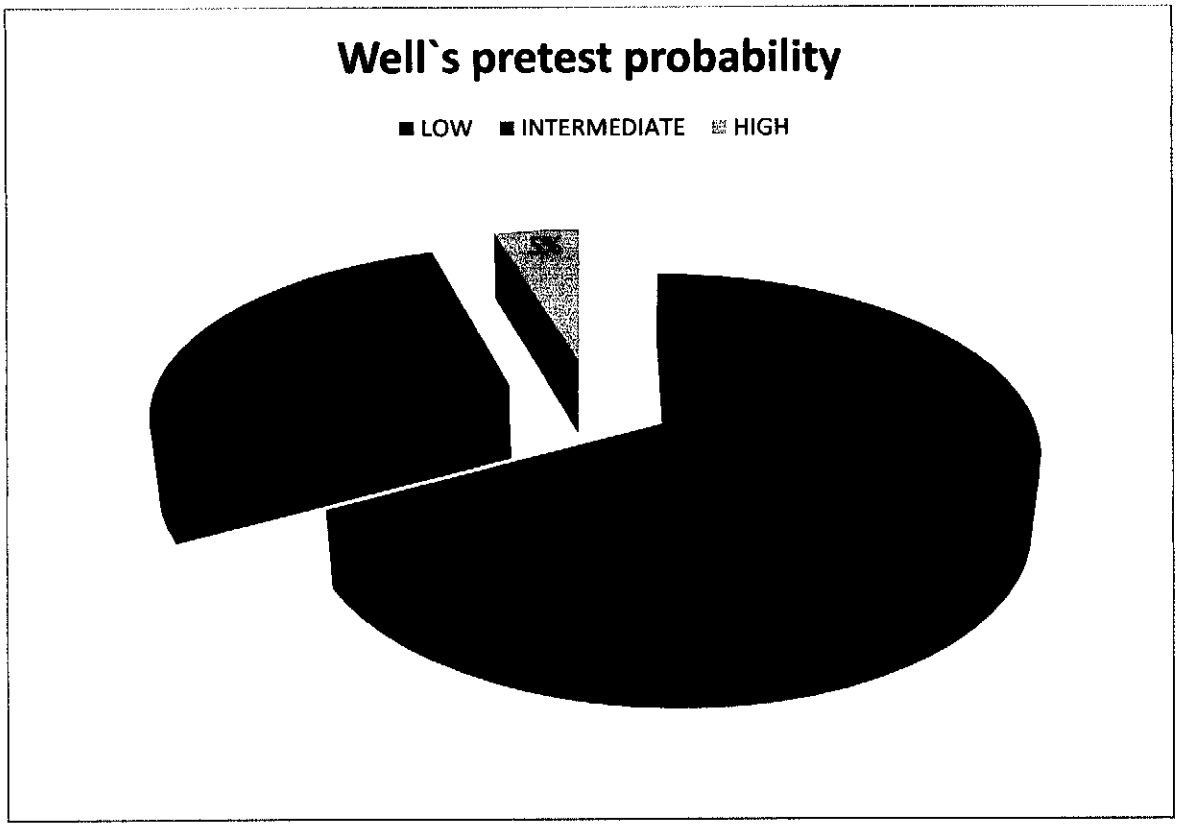
Of the 110 patients sampled, 29 examinations (26.5%) returned a positive result for acute PE, 52 examinations (47%) revealed no abnormal radiologic findings and 29 examinations (26.5%) revealed diagnoses other than PE.

FIGURE 2: PIE CHART SHOWING CTPA RESULTS



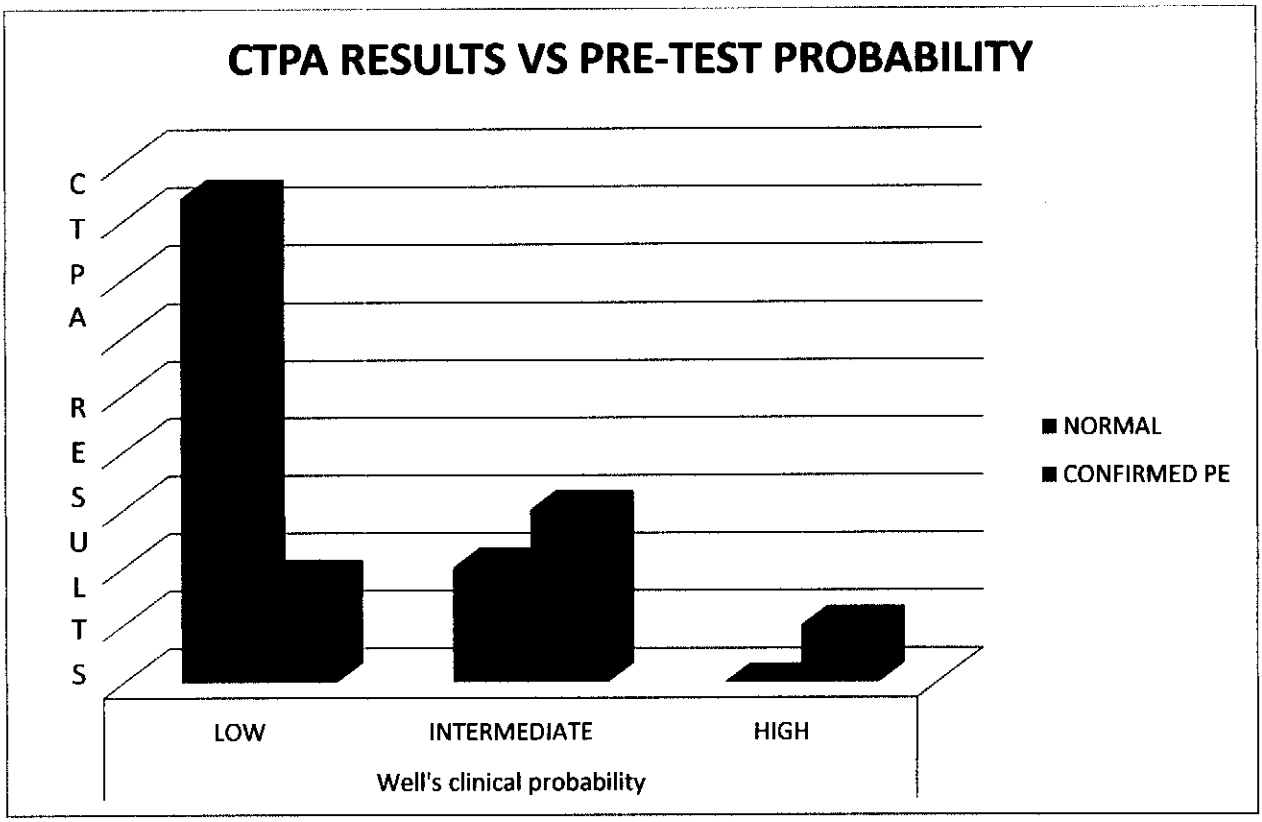
Well's clinical probability scores were worked out and assigned. Seventy four patients (67.3%) were in the low probability category, 31 patients (28.2 %) were in the intermediate probability category and 5 patients (4.5%) were in the high probability category.

FIGURE 3: PIE CHART SHOWING WELL`S PRE-TEST PROBABILITIES



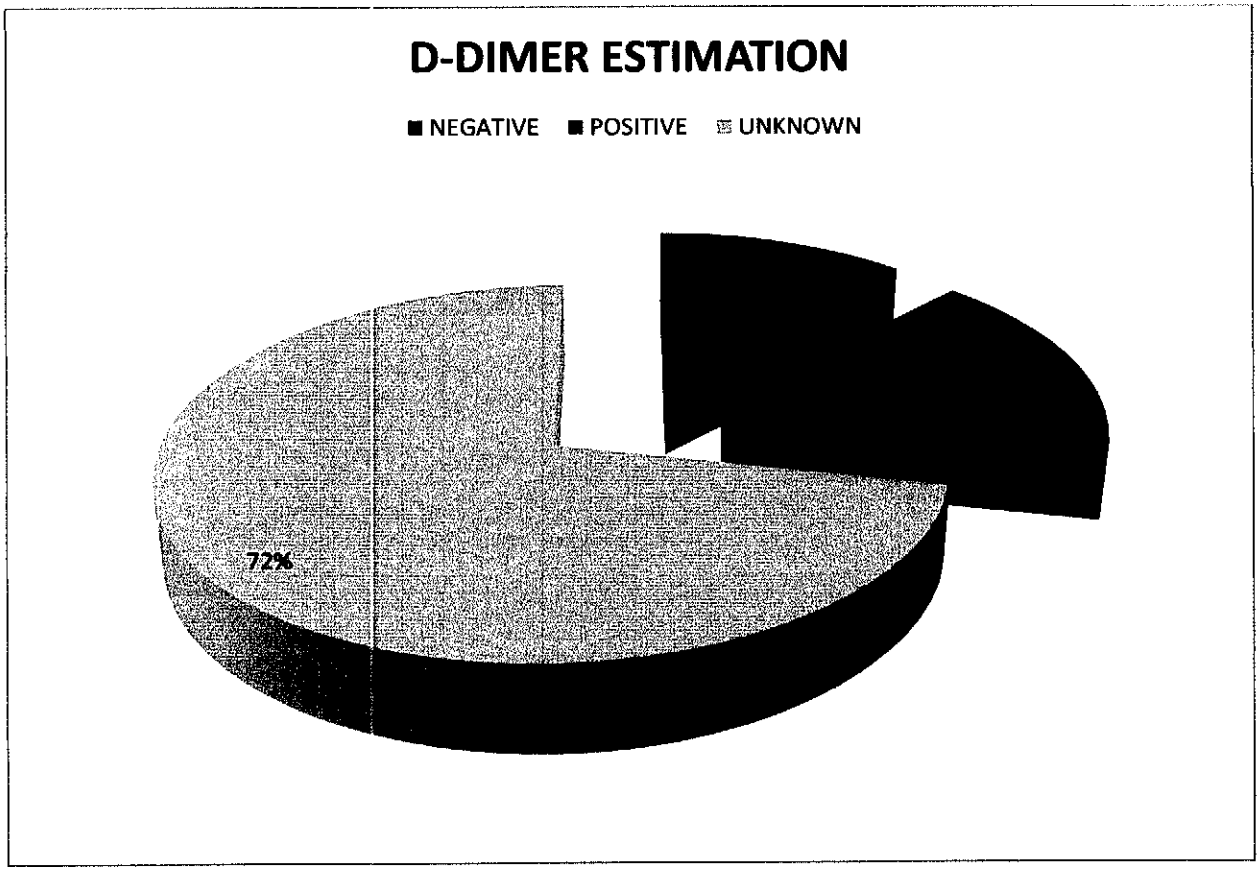
In the low probability category 82.4% of the CTPA examinations were normal and revealed no PE and 17.6% of the examinations revealed pulmonary embolism. In the intermediate category, the majority of the cases (60%) revealed evidence of PE and 40% were negative for PE. In the high probability category all the patients (100%) had CTPA evidence of pulmonary embolism.

FIGURE 4: BAR DIAGRAM SHOWING CTPA RESULTS VS PRE-TEST PROBABILITY



Of the sampled patients, 26.4% had D-dimer estimation performed and D-dimer test results were unknown in 73.6%. Of the patients that had D-dimer tests performed 55% were positive and 45% returned were negative.

FIGURE 5: PIE CHART SHOWING D-DIMER RESULTS



Eighty percent of the patients with negative D-dimers had normal CTPA studies and PE was confirmed in 20%. Of the patients with positive D-dimer test results, 46.2% were normal with PE being confirmed in 53, 8%.

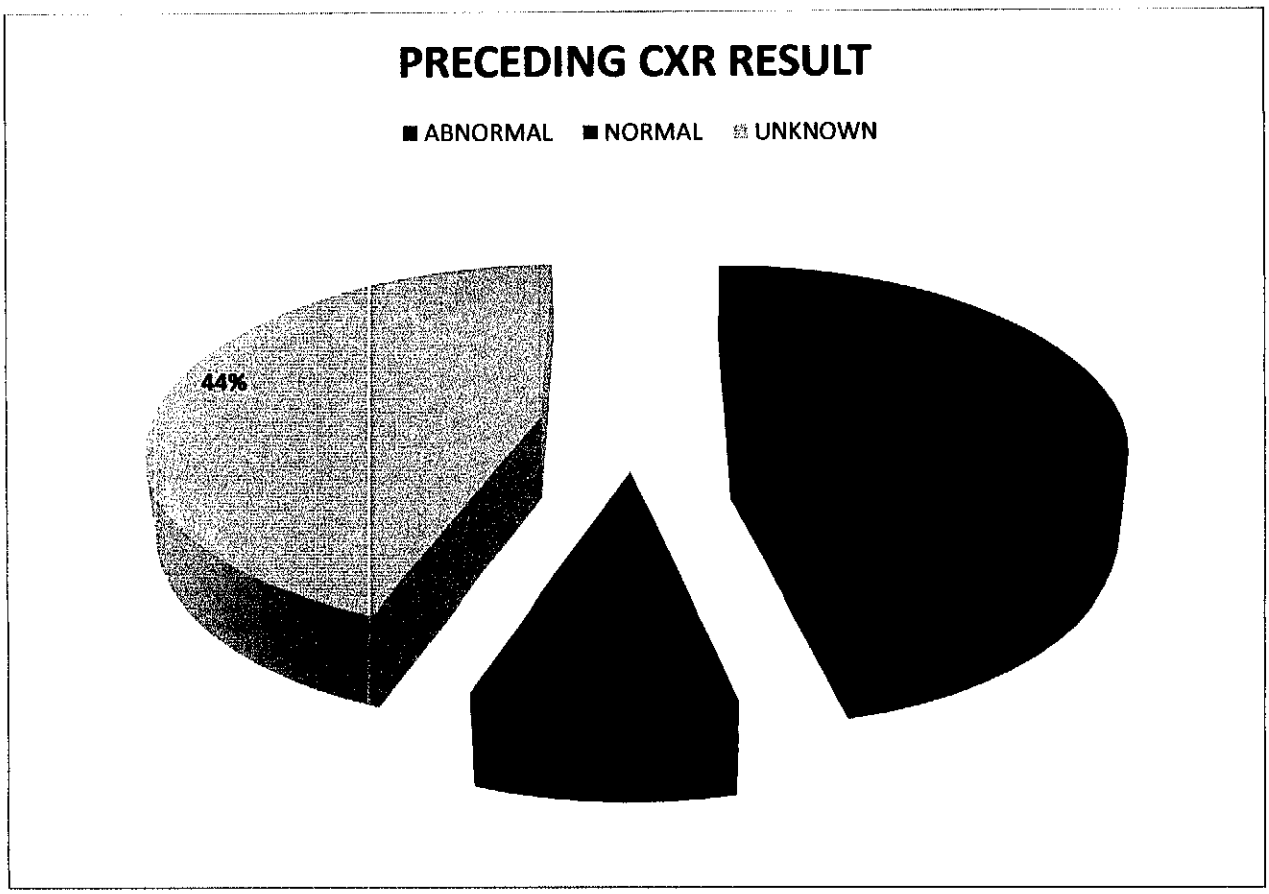
TABLE 2: D-DIMER TEST RESULT VS CTPA RESULT CROSS-TABULATION

		CTPA result			Total
		NORMAL	CONFIRMED PE	ALTERNATE DIAGNOSIS	
D-dimer test result	NEGATIVE	8	2	1	11
	POSITIVE	6	7	5	18
Total		14	9	6	29

Patients in the low probability group, with negative D-dimer estimation, all returned negative CTPA results. Eighteen percent (18%) of intermediate probability category cases with negative D-dimers returned positive CTPA results.

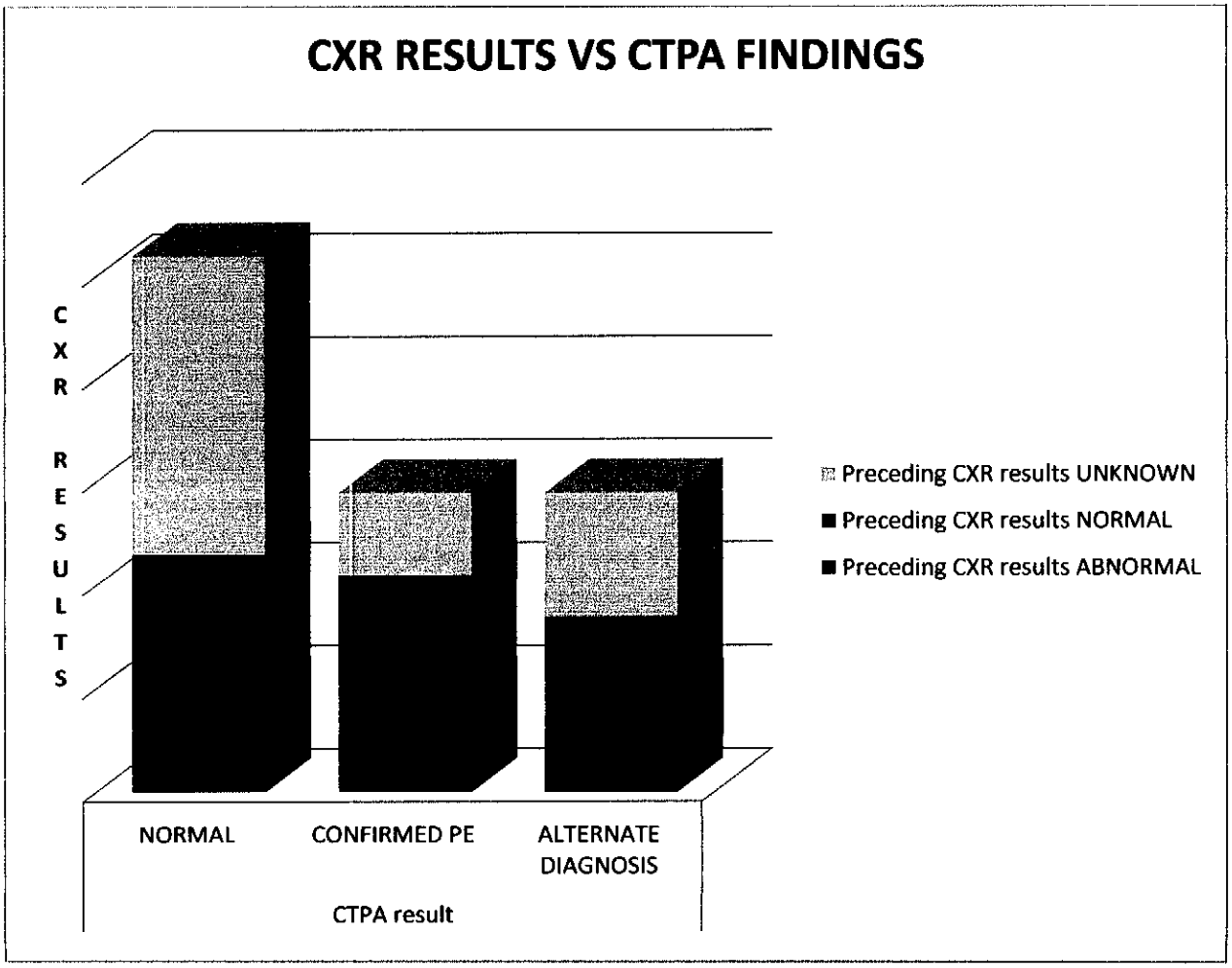
A total of 46.4% of the sampled patients had abnormal chest x-rays, 9.1% had normal chest x-rays and chest x-ray results were unknown in 44.1% of the cases.

FIGURE 6: PIE CHART SHOWING CXR RESULTS



Of the patients with normal CXRs, 85.7% had no abnormal radiologic findings at CTPA and 14.3% had confirmed PE. Of the patients with abnormal CXRs, 45.9% were negative for PE and PE was confirmed in 54.1%.

FIGURE 7: CXR RESULTS VS CTPA FINDINGS



Venous Doppler results were negative in 13.6% of the patients, 9.1% were positive and results were unknown in 77.3% of the cases. Of the patients with no current DVT, 72.3% returned normal CTPA results with 27.7% of these cases returning a positive PE result. In total, 73.3% of the patients with current DVT returned positive CTPA results in relation to PE and 26.7% were normal.

FIGURE 8: PIE CHART SHOWING DISTRIBUTION OF ALTERNATE DIAGNOSES

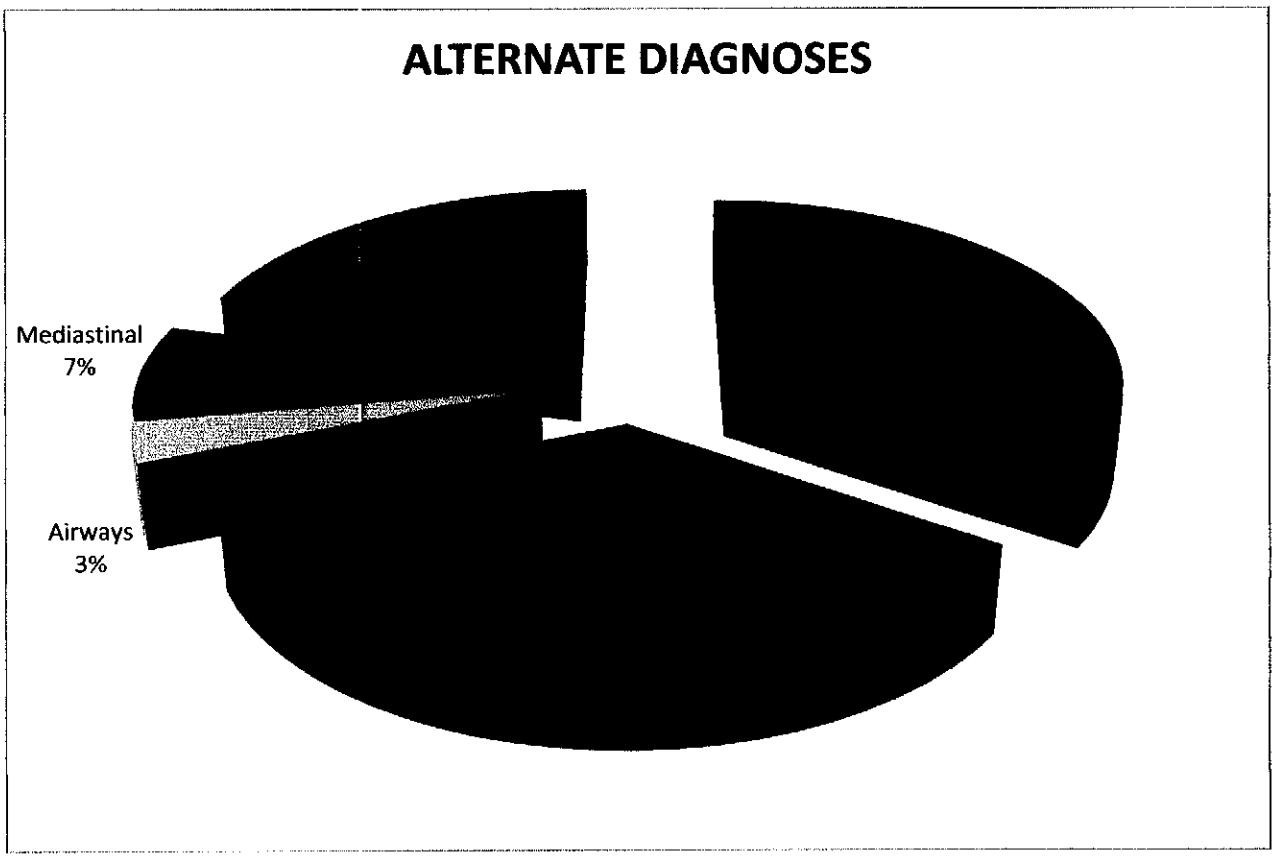


FIGURE 9: CTPA SHOWING A FILLING DEFECT IN THE RIGHT PULMONARY ARTERY.

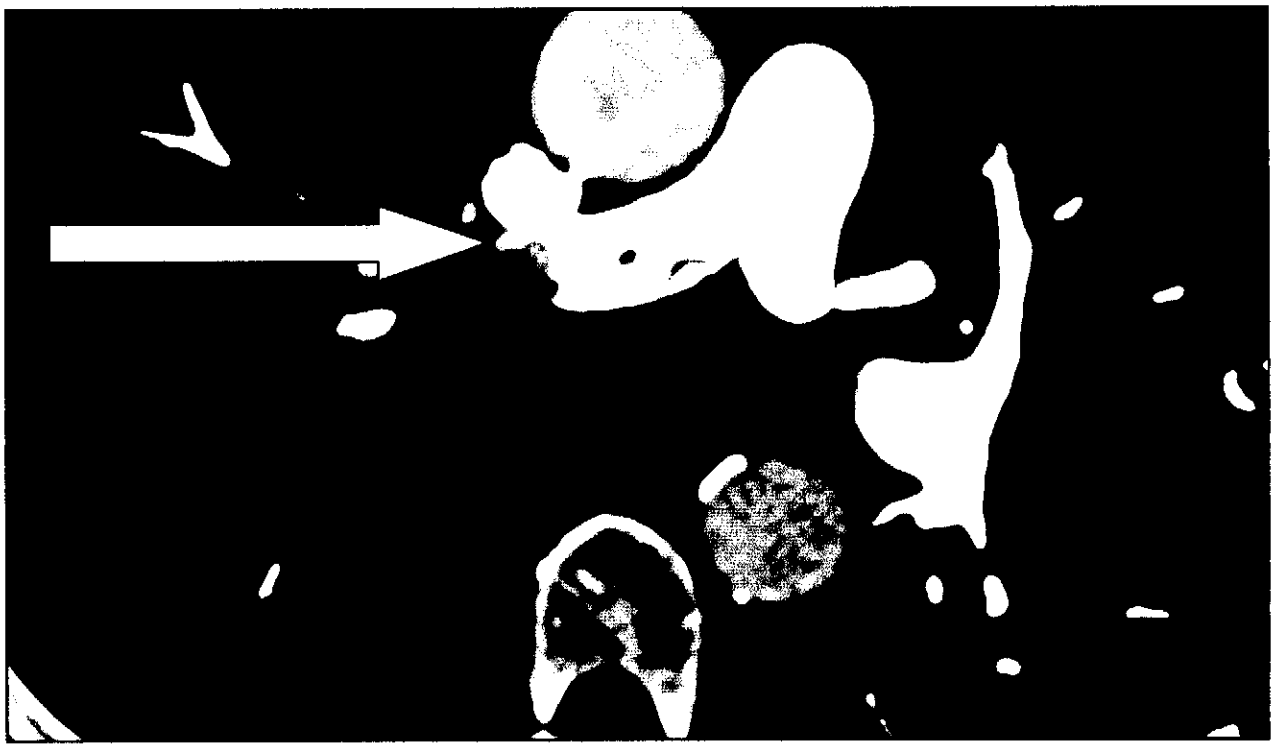


FIGURE 10: CTPA, SAGITTAL REFORMAT, SHOWING A FILLING DEFECT IN THE PULMONARY ARTERY.

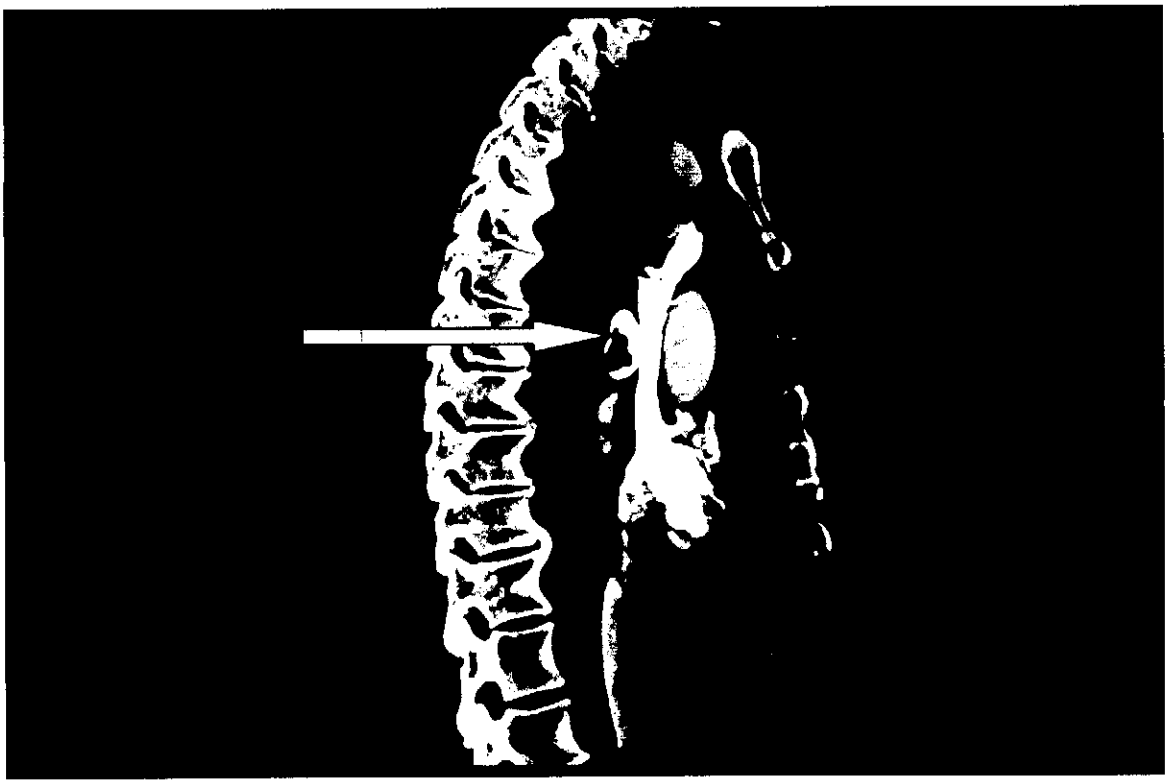
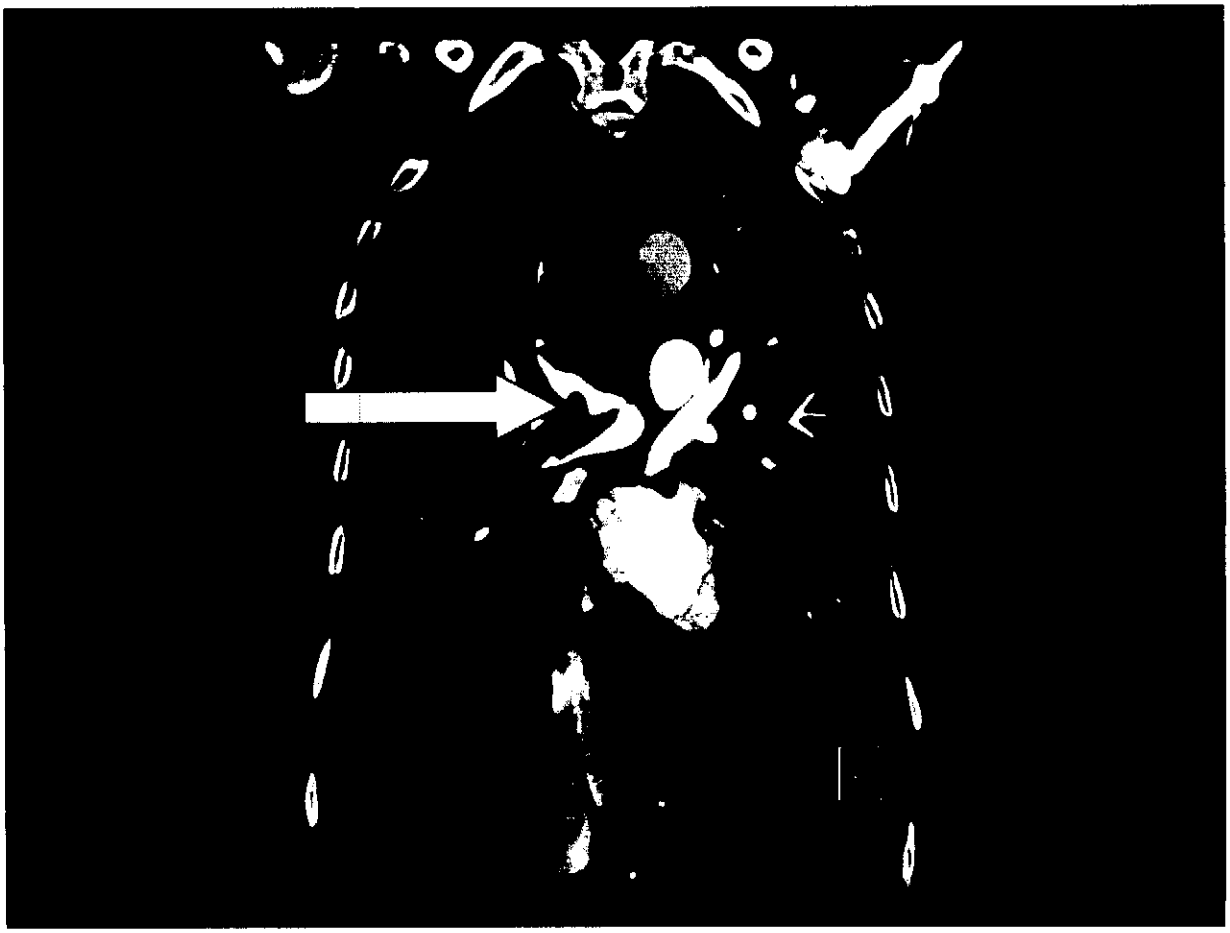


FIGURE 11: CTPA, CORONAL REFORMAT, SHOWING A FILLING DEFECT IN THE PULMONARY ARTERY.



CHAPTER 5: DISCUSSION

CTPA is the investigation of choice in patients with a high clinical suspicion of PE and in those with pre-existing pulmonary disease. Several recent reports have shown positive yield rates less than 10% in CTPA studies in patients who were suspected of having PE [15-18] . Prospective diagnostic trials which used pre-test clinical evaluation of symptoms followed by V/Q scans, showed the presence of disease in at least one-third of the patients examined [19,20] . These data indicate that the selection of patients who are suspected of having PE for undergoing testing has greatly changed since the advent of CTPA. Mamlouk and colleagues [22] reported that 90.2% of patients referred because they were suspected of having PE had negative results of CTPAs with only (6.4%) of patients referred from the emergency department having a positive finding at CTPA. The results from the study by Mamlouk seem to suggest that, in the absence of risk factors for PE, notably with negative results of the D -dimer test, CTPA could be safely avoided in many cases.

Results from the current study showed that 67% of the CTPA examinations performed at IALCH were in the low probability pre-test category. These results suggest overuse of the technique and, possibly, poor choice in the selection of patients undergoing the examination. Of the sampled cases, 28.2 % were in the intermediate probability category and 4.5% were in the high probability category (Figure 3). In the low probability category 82.4% of the CTPA examinations were normal and revealed no PE and 17.6% of the examinations revealed pulmonary embolism. In the intermediate category the majority of the cases i.e 60%, revealed evidence of PE and 40% were negative for PE. In the high probability category all the patients (100%) had CTPA evidence of pulmonary embolism (Figure 4).

In total, 26.4% of the examinations performed were positive for PE (Figure 2) which is fairly comparable to international standards (15.4 - 37.4%). A total of 47.2% of the studies revealed no radiologic abnormality and a further 26.4% of the examinations revealed alternate diagnoses. The low percentage of alternate diagnoses underlines the fact that a more targeted approach is necessary in the evaluation of these patients and that possible pick-up of an alternate diagnosis cannot justify CTPA use in low probability cases.

The examinations that revealed alternate diagnoses showed cardiac disease in 35% of the cases. Congestive cardiac failure was the most common cardiac condition followed by right sided heart failure. Pulmonary disease was present in 34% of the examinations that revealed alternate diagnoses. Pneumonia, pulmonary tuberculosis and interstitial lung disease were the most common lung parenchymal diseases picked-up. Pleural disease accounted for 21% of the alternate diagnoses and pleural effusion was the most common finding. Mediastinal disease accounted for 7% and airways disease for 3% of the alternate diagnoses (Figure 8).

D-dimer levels are elevated in plasma in the presence of an acute clot because of simultaneous activation of coagulation and fibrinolysis. A normal D-dimer level renders acute PE or DVT unlikely. Although D-dimer is very specific for fibrin, the specificity of fibrin for VTE is poor because fibrin is produced in a wide variety of conditions, such as cancer, inflammation, infection, necrosis, dissection of the aorta, and therefore, D-dimer is not useful for confirming PE. Data from a study conducted by Gupta and colleagues, looking at the efficacy of clinical risk algorithms and a quantitative D-dimer assay in the evaluation of patients undergoing CTPA for suspected acute PE, appeared to support the use of a quantitative D-dimer assay as a first-line test in evaluation for PE when the clinical probability of the presence of PE is low or intermediate [35].

Mamlouk and colleagues [22] clearly described the results of the most commonly adopted strategy to evaluate patients who are clinically suspected of having PE which show that the combination of the absence of definite risk factors and negative D - dimer test results could be used to substantially decrease the number of CTPA examinations performed in an emergency department. In the current study, 26.4% of the patients had D-dimer estimation and results were unknown in 73.6% (Figure 5). Of the patients that had D-dimer tests performed, 62.1% were positive and 37.9% returned negative results (Table 2).

Patients in the low probability group with negative D-dimer estimation all returned negative CTPA results. Eighteen percent of intermediate probability category cases with negative D-dimers returned positive CTPA results. The use of alternate interpretation of the Well`s criteria, where scores of 4 or less are considered PE

unlikely and more than 4, PE likely, suggests that CTPA`s can be safely withheld in the PE unlikely cases (Appendix 3).

The patients sampled had a mean age of 43.1 with a standard deviation of 16.3 and ranged from 18 to 84 (Table 1). Of the sampled patients, 73.6% were female and males accounted for 26.4% (Figure 1). Of the female patients, 50.9% were in the reproductive age group.As a result of the increased clinical use of CTPA, and its well documented high radiation exposure, serious concerns have been raised about the possibility of increased incidence of cancers in the future. That is why it is important to select patients for CTPA correctly [29, 30].

The article by Mamlouk and colleagues provides evidence that suggests that a substantial number of CTPAs could be avoided simply by adhering to the information derived from clinical history and D-dimer test determination [22] . In the current study, only 26.4% of the sampled patients had D-dimer estimation performed. The combination of negative D-dimers and a low probability category returned no PE positive CT examinations. This highlights the value of D-dimer estimation in the work up of these patients and the fact that more than 73% of the sampled cases did not have D-dimers performed clearly suggests that clinicians should be encouraged to use this test more in the triage of patients for CTPA evaluation.

The current study was a retrospective chart review and limitations of retrospective studies did apply to this study as well. Pre-test probability scores were worked out based on chart entries which were, at times, incomplete. The study was a single centre study conducted at an institution with good quality equipment which could have introduced an element of bias. The study population was heterogeneous, as it included in- and outpatients, and chart entries prior to CTPA were of varying quality between these groups. The CT scans were reported by different observers of varying experience and this also served as a limiting factor.

CHAPTER 6: CONCLUSION

PE remains a very challenging disease to diagnose. The myriad of alternate diagnoses clearly highlights the magnitude of the challenge clinicians are faced with in the clinical evaluation of the patients suspected of having PE. The results of the current study demonstrate that the majority of CTPA examinations performed at IALCH had low probability scores. These results suggest overuse of the technique and, possibly, poor choice in the selection of patients undergoing the examination. The results raise serious concerns about the radiation dose delivered to patients, which could have been avoided, and further highlight the importance of correct patient selection prior to CTPA examination. The results further support the use of pre-test probability assessment in combination with D-dimer estimation prior to CTPA evaluation in the local setting. CTPA is an accurate and readily available diagnostic test for the diagnosis or exclusion of PE. However, use of CTPA, without having established the pre-test probability of the disease, will continue to result in overuse of the test and in an unjustified increase of costs and radiation load.

BIBLIOGRAPHY:

1. Remy-Jardin M, Pistolesi M, Goodman LR , et al. Management of suspected acute pulmonary embolism in the era of CT angiography: a statement from the Fleischner Society. Radiology 2007; 245 (2): 315 – 329.
2. van Belle A, Buller HR, Huisman MV, Huisman PM, Kaasjager K, Kamphuisen PW, Kruip MJ, Kwakkel-van Erp JM, Leebeek FW, Nijkeuter M, Prins MH, Sohne M, Tick LW; Christopher Study Investigators. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. JAMA 2006; 295: 172–9.
3. Wood KE. Major Pulmonary Embolism. Chest 2002; 121: 877–905.
4. Duncan K, Warwick R; Royal College of Radiologists. Appropriateness of usage of computed tomography pulmonary angiography investigation of pulmonary angiography. Available from : http://www.rcr.ac.uk/audittemplate.aspx [Accessed 10 August 2012]
5. Goldhaber SZ, Elliot CG. Acute Pulmonary Embolism: Part I: Epidemiology, Pathophysiology, and Diagnosis. Circulation 2003, 108:2726-2729
6. Moores LK, Jackson WL Jr, Shorr AF, Jackson JL. Meta-analysis:outcomes in patients with suspected pulmonary embolism managed with computed tomographic pulmonary angiography. Ann Intern Med. 2004 Dec 7; 141(11):866-74.
7. Roy PM , Colombet I , Durieux P , Chatellier G , Sors H , Meyer G . Systematic review and meta-analysis of strategies for the diagnosis of suspected pulmonary embolism. BMJ 2005 ; 331 (7511): 259 – 263
8. Stein PD, Fowler SE, Goodman LR, et al. Multidetector computed tomography for acute pulmonary embolism. N Engl J Med 2006; 354 (22): 2317 – 2327 .
9. Stein PD, Woodard PK, Weg JG, et al. Diagnostic pathways in acute pulmonary embolism: recommendations of the PIOPED II Investigators. Radiology 2007; 242 (1): 15 – 21.
10. Qaseem A, Snow V, Barry P, et al. Current diagnosis of venous thromboembolism in primary care: a clinical practice guideline from the

American Academy of Family Physicians and the American College of Physicians . Ann Intern Med 2007; 146 (6): 454 – 458.

11. Torbicki A, Perrier A, Konstantinides S, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) . Eur Heart J 2008; 29 (18): 2276 – 2315.
12. Stein PD, Sostman HD, Bounameaux H, et al. Challenges in the diagnosis of acute pulmonary embolism. Am J Med 2008; 121 (7): 565 – 571.
13. Reid JH, Coche EE, Inoue T, et al. Is the lung scan alive and well? Facts and controversiesin defining the role of lung scintigraphy for the diagnosis of pulmonary embolism in the era of MDCT. Eur J Nucl Med Mol Imaging 2009; 36 (3): 505 – 521.
14. Bajc M , Neilly JB , Miniati M , Schuemichen C , Meignan M , Jonson B . EANM guidelines for ventilation/perfusion scintigraphy. II. Algorithms and clinical considerations for diagnosis of pulmonary emboli with V/P (SPECT) and MDCT. Eur J Nucl Med Mol Imaging 2009; 36 (9): 1528 – 1538.
15. Costantino MM, Randall G, Gosselin M, Brandt M, Spinning K, Vegas CD. CT angiography in the evaluation of acute pulmonary embolus. AJR Am J Roentgenol 2008; 191 (2): 471 – 474.
16. Hall WB, Truitt SG, Scheunemann LP, et al. The prevalence of clinically relevant incidental findings on chest computed tomographic angiograms ordered to diagnose pulmonary embolism. Arch Intern Med 2009; 169 (21): 1961 – 1965.
17. Kline JA, Courtney DM, Beam DM, King MC, Steuerwald M. Incidence and predictors of repeated computed tomographic pulmonary angiography in emergency department patients. Ann Emerg Med 2009; 54 (1): 41 – 48.
18. Weir ID, Drescher F, Cousin D, et al. Trends in use and yield of chest computed tomography with angiography for diagnosis of pulmonary embolism in a Connecticut hospital emergency department . Conn Med 2010; 74 (1): 5 – 9.
19. The PIOPED investigators. Value of the ventilation/ perfusion scan in acute pulmonary embolism: results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA 1990; 263 (20): 2753 – 2759.

20. Miniati M, Pistolesi M, Marini C, et al. Value of perfusion lung scan in the diagnosis of pulmonary embolism: results of the Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISA-PED) .Am J Respir Crit Care Med 1996 ; 154 (5): 1387 – 1393 .
21. Ranji SR, Shojania KG, Trowbridge RL, Auerbach AD. Impact of reliance on CT pulmonary angiography on diagnosis of pulmonary embolism: a Bayesian analysis. J Hosp Med 2006; 1 (2): 81 – 87.
22. Mamlouk MD, vanSonnenberg E, Gosalia R, et al. Pulmonary embolism at CT angiography: implications for appropriateness, cost, and radiation exposure in 2003 patients. Radiology 2010; 256 (2): 625 – 632.
23. Stein EG , Haramati LB , Chamarthy M , Sprayregen S , Davitt MM , Freeman LM . Success of a safe and simple algorithm to reduce use of CT pulmonary angiography in the emergency department. AJR Am J Roentgenol 2010; 194 (2): 392 – 397.
24. Wells PS, Ginsberg JS, Anderson DR, et al. Use of a clinical model for safe management of patients with suspected pulmonary embolism. Ann Intern Med 1998; 129 (12): 997 – 1005.
25. Miniati M, Prediletto R, Formichi B, et al. Accuracy of clinical assessment in the diagnosis of pulmonary embolism. Am J Respir Crit Care Med 1999; 159 (3): 864 – 871 .
26. Wicki J, Perneger TV, Junod AF, Bounameaux H, Perrier A. Assessing clinical probability of pulmonary embolism in the emergency ward: a simple score. Arch Intern Med 2001; 161 (1): 92 – 97.
27. Eisner MD. Before diagnostic testing for pulmonary embolism: estimating the prior probability of disease. Am J Med 2003; 114 (3): 232 – 234.
28. Perrier A, Roy PM, Sanchez O, et al. Multidetector-row computed tomography in suspected pulmonary embolism. N Engl J Med 2005; 352 (17): 1760 – 1768.
29. Brenner DJ, Hall EJ. Computed tomography -an increasing source of radiation exposure. N Engl J Med 2007; 357 (22): 2277 – 2284.
30. Amis ES Jr, Butler PF, Applegate KE, et al. American College of Radiology white paper on radiation dose in medicine. J Am Coll Radiol 2007; 4 (5): 272 – 284.

31. Parker MS, Hui FK, Camacho MA, Chung JK, Broga DW, Sethi NN. Female breast radiation exposure during CT pulmonary angiography. AJR Am J Roentgenol 2005; 185 (5): 1228 – 1233.
32. Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography. JAMA 2007; 298 (3): 317 – 323.
33. Milne EN. Female breast radiation exposure. AJR Am J Roentgenol 2006; 186 (6): E24.
34. Hurwitz LM, Yoshizumi TT, Goodman PC, et al. Radiation dose savings for adult pulmonary embolus 64-MDCT using bismuth breast shields, lower peak kilovoltage, and automatic tube current modulation . AJR Am J Roentgenol 2009; 192 (1): 244 – 253.
35. Gupta RT, Kakarla RK, Kirshenbaum K, Tapson VF. D-dimers and Efficacy of Clinical Risk Estimation Algorithms: Sensitivity in Evaluation of Acute Pulmonary Embolism. AJR 2009; 193:425 430.
36. www.pathology.med.umich.edu/handbook/Tables/DDIMER_INNOVANCE.pdf. [Accessed 10 October 2013]

APPENDIX 2

The Wells score:

- clinically suspected DVT - 3.0 points
- alternative diagnosis is less likely than PE - 3.0 points
- tachycardia - 1.5 points
- immobilization/surgery in previous four weeks - 1.5 points
- history of DVT or PE - 1.5 points
- haemoptysis - 1.0 points
- malignancy (treatment for within 6 months, palliative) - 1.0 points

Traditional interpretation

- Score >6.0 - High (probability 59% based on pooled data)
- Score 2.0 to 6.0 - Moderate (probability 29% based on pooled data)
- Score <2.0 - Low (probability 15% based on pooled data)

Alternate interpretation

- Score > 4 - PE likely. Consider diagnostic imaging.
- Score 4 or less - PE unlikely. Consider D-dimer to rule out PE.

APPENDICES:

APPENDIX 1

Data Collection Sheet:

Patient study number	:		
Age	:		
Gender	□ Male	□ Female	
Signs and symptoms of DVT:			
Upper/lower limb pain	□ Yes	□ No	□ Unknown
Tenderness	□ Yes	□ No	□Unknown
Upper/lower limb swelling	□ Yes	□ No	□ Unknown
Skin discolouration	□ Yes	□ No	□ Unknown
Prominent superficial veins	□ Yes	□ No	□ Unknown
Clinical response	□ Favourable	□ Unfavourable	□ Unknown
Heart rate	□ > 100	□ < 100	
History of immobilization	□ Yes	□ No	□ Unknown
Previous DVT	□ Yes	□ No	□ Unknown
Previous PE	□ Yes	□ No	□ Unknown
History of haemoptysis	□ Yes	□ No	□ Unknown
History of cancer	□ Yes	□ No	□ Unknown
Homan's sign	□ Positive	□ Negative	□ Unknown
D-dimer test result	□ Positive	□ Negative	□ Unknown

Preceding CXR result	□ Normal	□ Abnormal	□ Unknown
Venous Doppler result	□ Positive	□ Negative	□ Unknown
Wells clinical probability	□ Low	□ Intermediate	□ High
CTPA result	□ Confirmed PE	□ Alternate diagnosis	
	□ No abnormal radiologic diagnosis		

UNIVERSITY OF
KWAZULU-NATAL

INYUVESI
YAKWAZULU-NATALI

21 May 2012

Dr J Maharajh
Department of Radiology
School of Clinical Medicine

Dear Dr Maharajh

PROTOCOL: "Utilization of Computed Tomographic Pulmonary Angiography in clinically suspected Acute Pulmonary Thrombe-embolism at Inkosi Albert Luthuli Central Hosptial.." Student: W Mbatha, student number: 983186748. (Radiology)

I am pleased to inform you that the abovementioned study has been approved.

Please note:

- The Academic Leader: Research must review any changes made to this study.
- The study may not begin without the approval of the Biomedical Research Ethics Committee.

May I take this opportunity to wish the student every success with the study.

Yours sincerely

pp: Professor R Hift
Dean: School of Clinical Medicine

CC. Dr W Mbatha

Biomedical Research Ethics Committee
Westville Campus

Postgraduate, Higher Degrees & Research
School of Clinical Medicine, NRMSM Campus
Postal Address: P/Bag X3, Congella, Durban, 4013, South Africa
Telephone: +27 (0) 31 260 4745 **Facsimile:** +27 (0) 31 260 4723 **Email:** janfjes@ukzn.ac.za **Website:** www.ukzn.ac.za

health

Department:
Health
PROVINCE OF KWAZULU-NATAL

Health Research & Knowledge Management sub-component
10 – 103 Natalia Building, 330 Langalibalele Street
Private Bag x9051
Pietermaritzburg
3200
Tel.: 033 – 3953189
Fax.: 033 – 394 3782
Email.: hrkm@kznhealth.gov.za
www.kznhealth.gov.za

Reference : HRKM 71/14
Enquiries : Mr X Xaba
Tel : 033 – 395 2805

Dear Mr Dr WE Mbatha

Subject: Approval of a Research Proposal

1. The research proposal titled **'Utilisation of Computed Tomographic Pulmonary Angiography (CTPA) in clinically suspected acute pulmonary thromb-embolism at Inkosi Albert Luthuli Central Hospital'** was reviewed by the KwaZulu-Natal Department of Health.

   The proposal is hereby **approved** for research to be undertaken at Inkosi Albert Luthuli Central Hospital.

2. You are requested to take note of the following:
   a. Make the necessary arrangement with the identified facility before commencing with your research project.
   b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.

3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Mr X. Xaba on 033-395 2805.

Yours Sincerely

Dr E Lutge
Chairperson, Health Research Committee
Date: 5/08/2014.

health

Department:
Health
PROVINCE OF KWAZULU-NATAL

Inkosi Albert Luthuli Central Hospital
Ethekwini Health District
Office of the Medical Manager
Private Bag X 03, Mayville, 4058
800 Bellair Road, Mayville, 4058
Tel.: 031 240 1059,
Fax.: 031 240 1050
Email.:ursulanun@ialch.co.za
www.kznhealth.gov.za

17 March 2014

Dr W E Mbatha
Department of Radiology
IALCH

Dear Dr Mbatha

Re: Ref No: BE 228/11: Utilization of Computed Tomographic Pulmonary Angiography in clinically suspected Acute Pulmonary Thrombo- embolism at Inkosi Albert Luthuli Central Hospital.

As per the policy of the Provincial Health Research Committee (PHRC), you are hereby granted permission to conduct the above mentioned research once all relevant documentation has been submitted to PHRC inclusive of Full Ethical Approval.

Kindly note the following.

1. The research should adhere to all policies, procedures, protocols and guidelines of the KwaZulu-Natal Department of Health.
2. Research will only commence once the PHRC has granted approval to the researcher.
3. The researcher must ensure that the Medical Manager is informed before the commencement of the research by means of the approval letter by the chairperson of the PHRC.
4. The Medical Manager expects to be provided feedback on the findings of the research.
5. Kindly submit your research to:

   The Secretariat
   Health Research & Knowledge Management
   330 Langaliballe Street, Pietermaritzburg, 3200
   Private Bag X9501, Pietermaritzburg , 3201
   Tel: 033395-3123, Fax 033394-3782

Yours faithfully

Dr P Ramdas
Medical Manager

health

Department:
Health
PROVINCE OF KWAZULU-NATAL

Inkosi Albert Luthuli Central Hospital
Ethekwini Health District
Office of the Medical Manager
Private Bag X 03, Mayville, 4058
800 Bellair Road, Mayville, 4058
Tel.: 031 240 1059,
Fax.: 031 240 1050
Email.:ursulanun@ialch.co.za
www.kznhealth.gov.za

Reference: BE228/11
Enquiries: Medical Management

17 March 2014

Dr W E Mbatha
Department of Radiology
IALCH

Dear Dr Mbatha

RE: PERMISSION TO CONDUCT RESEARCH AT IALCH

I have pleasure in informing you that permission has been granted to you by the Medical Manager to conduct research on: **Utilization of Computed Tomographic Pulmonary Angiography in clinically suspected Acute Pulmonary Thrombo- embolism at Inkosi Albert Luthuli Central Hospital.**

Kindly take note of the following information before you continue:

1. Please ensure that you adhere to all the policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. This research will only commence once this office has received confirmation from the Provincial Health Research Committee in the KZN Department of Health.
3. Kindly ensure that this office is informed before you commence your research.
4. The hospital will not provide any resources for this research.
5. You will be expected to provide feedback once your research is complete to the Medical Manager.

Yours faithfully

Dr P Ramdas
Medical Manager

PERMISSION TO CONDUCT A RESEARCH STUDY/TRIAL

This must be completed and submitted to the Medical Superintendent/s / Hospital Manager/s for signature.

For **King Edward VIII Hospital (KEH) and Inkosi Albert Luthuli Central Hospital (IALCH)** studies please submit the document together with the following:

1. Research proposal and protocol.
2. Letter giving provisional ethical approval.
3. Details of other research presently being performed by yourself if in the employ of KEH, (individually or as a collaborator).
4. Declaration of all funding applications / grants, please supply substantiating documentation.
5. Complete the attached KEH Form - *"Research Details"*

Once the document has been signed it should be returned to **Mrs Patricia Ngwenya:** Biomedical Research Ethics Administrator, Room N40, Govan Mbeki Building, Westville Campus, University of KwaZulu-Natal.

To: Chief Medical Superintendent / Hospital Manager

Permission is requested to conduct the above research study at the hospital/s indicated below:

Site 1 address:
IALCH

Investigator/s:
Principal: DR W.E. Mbatha
Co-investigator:
Co-Investigator:

Signature of Chief Medical Superintendent/Hospital Manager:
P.D Reinolds

Date: 17/08/2014

Site 2 address:

Investigator/s
Principal:
Co-investigator:
Co-Investigator:

Signature of Chief Medical Superintendent / Hospital Manager:

Date:

NB: Medical Superintendent/s / Hospital Manager/s to send a copy of this document to Natalia

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INYUVESI
YAKWAZULU-NATALI

RESEARCH OFFICE
BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 260-4609
Email: BREC@ukzn.ac.za
Website: http://research.ukzn.ac.za/ResearchEthics/BiomedicalResearchEthics.aspx

21 December 2011

Dr. WE Mbatha
Department of Radiology
Nelson R Mandela School of Medicine
University of KwaZulu- Natal

Dear Dr Mbatha

PROTOCOL: Utilization of Computed Tomographic Pulmonary Angiography in clinically suspected Acute Pulmonary Thrombo-embolism at Inkosi Albert Luthuli Central Hospital.
REF: BE228/11

PROVISIONAL APPROVAL

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 01 November 2011.

The study is given **PROVISIONAL APPROVAL** pending receipt of:

1. Permission from the Hospital Manager (IALCH).
2. Postgraduate Education Committee Approval.
3. The main application forms are very poorly completed with important points left out (e.g. section 3.1 to 3.3 in the main form and point 8 in expedited form).
4. There was no hypothesis stated in the application form.

Please refer to attached document "Permission to Conduct a Research Study/Trial". This must be completed and submitted to the Hospital Manager for signature. For King Edward VIII Hospital (KEH) and Inkosi Albert Luthuli Central Hospital (IALCH) studies please submit the document **together with items 1 to 5 as outlined on the form.**

Once the document has been signed it should be returned to this office.

Only when full ethical approval is given, may the study begin. **Full ethics approval has not been given at this stage.**

PLEASE NOTE: Provisional approval is valid for 6 months only - should we not hear from you during this time - the study will be closed and reapplication will need to be made.

health

Department:
Health
PROVINCE OF KWAZULU-NATAL

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Tel.: 031 240 1059,
Fax.: 031 240 1050
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17 March 2014

Dr W E Mbatha
Department of Radiology
IALCH

Dear Dr Mbatha

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Kindly note the following.

1. The research should adhere to all policies, procedures, protocols and guidelines of the KwaZulu-Natal Department of Health.
2. Research will only commence once the PHRC has granted approval to the researcher.
3. The researcher must ensure that the Medical Manager is informed before the commencement of the research by means of the approval letter by the chairperson of the PHRC.
4. The Medical Manager expects to be provided feedback on the findings of the research.
5. Kindly submit your research to:

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   Tel: 033395-3123, Fax 033394-3782

Yours faithfully

Dr P Ramdas
Medical Manager