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The Frequency of Pleural Effusion and Additional Chest Findings in Patients Undergoing Computerised Tomographic Pulmonary Angiography for Suspected Pulmonary Embolism at a Level Four Academic Hospital in South Africa

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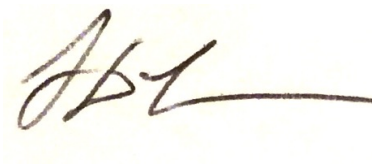
A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in Diagnostic Radiology

Johannesburg, 2016

DECLARATION

I, Shane Dorfman, declare that this research report is my own work. It is being submitted for the degree of MMed (RadD) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.



Dr Shane Dorfman

On this 15th Day of November, 2016.

PUBLICATIONS AND PRESENTATIONS

This work has never been published nor presented at any local or international congresses.

ABSTRACT

PURPOSE: The non-specific presentation of pulmonary embolism (PE) leads to a number of diagnostic challenges. Pleural effusions in particular are an under-recognised complication of PE with potentially lethal consequences. This study assessed the diagnostic yield of pulmonary embolism, frequency of pleural effusions, pulmonary hypertension and abnormal parenchymal findings in patients undergoing CTPA for suspected PTED.

METHOD: The CTPAs of 100 patients performed between September 2015 and January 2016 were analysed retrospectively. The presence/absence of the above-mentioned radiological abnormalities were documented.

RESULTS: PE was identified in 37% of cases. Pleural effusion was present in 37,8%, pulmonary hypertension in 66,7% and abnormal parenchymal findings in 59,5% of PE positive patients respectively. The only finding significantly associated with PE was peripheral wedge-shaped opacities (p=0,019).

CONCLUSIONS: There was a higher diagnostic yield of PE in this study when compared to similar studies conducted elsewhere. With the exception of peripheral wedge-shaped opacities, pleuro-parenchymal abnormalities are of limited value in diagnosing PE.

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NOMENCLATURE

In this research report, and as far as possible, unnecessary jargon and abbreviations have been avoided. There are, however, some abbreviations that are necessary due to their frequent use. The more commonly used abbreviations have been listed in alphabetical order below to assist the reader.

- CI - confidence interval
- CMJAH - Charlotte Maxeke Johannesburg Academic Hospital
- CTEPH - chronic thromboembolic pulmonary hypertension
- CTPA - computerised tomographic pulmonary angiography
- DVT - deep vein thrombosis
- HIS - hospital information system
- HIV - human immunodeficiency virus
- IQR - interquartile range
- PACS - picture archiving and communication system
- PE - pulmonary embolism
- PTED - pulmonary thromboembolic disease
- RIS - radiological information system
- SD - standard deviation
- TB – tuberculosis
- V/Q scan - ventilation/perfusion scan
- VTE- venous thromboembolic disease

PREFACE

My particular area of interest is respiratory radiology. During my daily practice as a radiologist at Charlotte Maxeke Johannesburg Academic Hospital, it became evident that a large number of Computerised tomographic pulmonary angiograms (CTPAs) for suspected pulmonary embolism (PE) are performed. Many of these CTPAs may not be indicated, and as radiologists, we are acutely aware of risks to the patient, particularly from ionising radiation and contrast-induced reactions. Of further note is the dearth of information on the referral form, particularly around clinical decision rules and previous imaging. My colleagues and I frequently have to request the chest radiograph, which often have various pleuro-parenchymal abnormalities. All of this raised a number of questions around yield and the association of these abnormalities with PE. This study aimed to answer these questions.

1. RATIONALE

Pulmonary thromboembolic disease (PTED) is a common clinical entity, with significant morbidity and mortality (1). While it is therefore imperative not to miss the diagnosis, the use of Computerised Tomographic Pulmonary Angiography (CTPA), a key investigation in diagnosing pulmonary embolism (PE), is not without risk to the patient. Of particular concern is ionising radiation exposure and the potential for contrast-related reactions (2). However, due to its relatively non-specific symptoms, pulmonary embolism remains a challenge to diagnose. This has led to an apparent increase in referrals for CTPA and a decreasing yield, raising concerns for patient safety (3).

South Africa is not immune to this problem, and in fact the high human immunodeficiency virus (HIV) and tuberculosis (TB) rates, which are independent risk factors for PTED (4), put the affected population at even greater risk of developing PE. There appears to be very little local literature regarding the yield rates of CTPAs performed in South Africa. There are, however, several studies documenting the frequency with which pulmonary embolism is detected on CTPA in the international literature (2, 5). Therefore, as a first objective, this study assessed the positive yield rate for PTED at Charlotte Maxeke Johannesburg hospital (CMJAH), which as a level four hospital, should be best placed to compare yield rates to a more developed settings.

Part of the diagnostic challenge alluded to above, is the myriad of causes of dyspnoea that may lead the clinician to suspect the possibility of PTED. One such cause is pleural effusion, which may occur alone, or in conjunction with pulmonary embolism. Despite

pleural effusions being a well-documented complication of PTED, with multiple studies showing the prevalence rates as high as one-third to one-half of cases (6, 7), PTED remains an under-recognised cause of pleural effusion (8). As prompt treatment of pulmonary embolism can reduce mortality rates from 30% to less than 10% (7), this delay in therapy may have dire consequences for the patient. Not only is there increased mortality, but postponing treatment of the pulmonary embolus may also result in the effusion becoming complicated, thereby increasing patient morbidity. Once again there is a dearth of literature assessing the prevalence of pleural effusion in patients with PTED in South Africa. This study, as an additional primary objective, assessed the prevalence of pleural effusion in patients with PE in the local setting.

Another significant complication of PTED is haemodynamic instability (1). The clinical impact of PE depends on the degree of pulmonary arterial impedance as well as the cardiovascular functional capacity of the patient (9). The higher the increase in pulmonary arterial pressure, the greater the risk of right ventricular failure and ultimately death (10). Similarly, the lower the cardiovascular reserve of the patient, the greater the impact (1). While acute pulmonary hypertension and right ventricular failure from massive PE will generally be clinically overt, often acute embolic events are missed and chronic thromboembolic pulmonary hypertension (CTEPH) may subsequently develop. While considered rare – estimated to be in the range of 1-4% (11), CTEPH carries significant morbidity and mortality. Consequently, radiological evidence of pulmonary hypertension in a patient may alter the clinician's treatment recommendations for the PE and also indicate to the clinician the need to implement the appropriate follow up investigations.

This study, as a third objective, evaluated the prevalence of pulmonary hypertension in the local setting. This was then compared to studies performed in other settings.

Lastly, as mentioned above, there are a number of conditions that may mimic the symptoms of PE. There have been a number of international studies that have assessed the occurrence of parenchymal abnormalities in patients with and without PE (7, 12). As a final objective, this study identified abnormal parenchymal findings in patients with or without PE on CTPA, and evaluated if there were any significant differences between the two groups. The findings in the local setting were then compared to the international literature.

2. LITERATURE REVIEW

2.1 Pulmonary Thromboembolic Disease

2.1.2 Definition

PTED refers to the lodgement of a clot in a pulmonary artery, with subsequent obstruction of the blood supply to the lung parenchyma. As PE commonly arise as a complication of deep vein thrombosis (DVT), the two are parts of the same process and better thought of together as venous thromboembolism (VTE) (13). PE occur in approximately one third of cases of DVT, while 70% of patients with pulmonary emboli show concomitant DVT (14).

2.1.3 Incidence and mortality rates

PTED is a common clinical entity with the overall prevalence estimated to be 60-70 per 100,000 population (1). This, however, is thought to be an underestimation, with asymptomatic PTED occurring in up to 40-50% of patients with underlying DVT (1). The prevalence rates are, however, risk dependent, with certain subsets of the population being at higher risk.

Although many cases are asymptomatic, PE can be fatal, with untreated acute PE mortality being approximately 33% (1). The number of deaths in Europe alone is estimated to be around 200,000 per year (15) while PE-related deaths in the USA are estimated at between 60,000 and 100,000 cases per year (16). There are no accurate,

current figures with respect to PE-related deaths in South Africa (personal communication, Professor Barry Jacobson, March 2016), although according to the South African Medical Research Council, there were 2111 deaths in 2000 from PE (17). This is far less per capita than that of the USA and talks to the inaccuracy of these statistics.

2.1.4 Pathophysiology of VTE and its relation to pulmonary hypertension

VTE is intrinsically linked to the interaction of the elements of Virchow's triad (hypercoagulability, stasis and endothelial damage) (18). Although the majority of DVT remain confined to the legs, as mentioned above, in up to 30% of cases, the clot will dislodge, resulting in PE. The resultant impact and manifestations of the PE depend on four major factors (9):

- **The size of the embolism** - and hence the resultant degree of occlusion of the pulmonary vascular tree.
- **The patient's pre-existing cardiopulmonary status**.
- **Chemical vasoconstriction** - due to serotonin and thromboxane from platelets adherent to the thrombus.
- **Reflex vasoconstriction** - as consequence of pulmonary artery dilatation.

The combination of these factors results in impedance to pulmonary arterial circulation, with resultant pulmonary hypertension. This increase in afterload, together with compensatory tachycardia, not only reduces right ventricular output (and ultimately cardiac output) but also increases strain on the right heart. This may result in right ventricular dilatation, and if severe enough, right ventricular failure. The right ventricular

enlargement also causes a compressive effect on the left ventricle, further decreasing left ventricular output (9). Furthermore, the redistribution of blood flow secondary to the clot results in ventilation-perfusion mismatching, further elevating pulmonary arterial pressure and exacerbating the hypoxaemia (19)

2.1.5 Risk factors

Risk factors for VTE can be divided into patient-related (predisposing risk) and procedure-related (exposure-related risks) (20). These risks can further characterised into high, moderate or low. This risk assessment is imperative as the guidelines for prophylaxis and treatment is risk class dependant (20). This risk assessment is expanded on in figures 2.1 and 2.2.

Risk assessment	
Predisposing risk factor	**Relative risk weighting**
Thrombophilia	High
History of VTE	High
Malignancy	High
Drugs, e.g. tuberculosis treatment, thalidomide	High
HIV infection	High
Auto-immune disease	High
Advanced age (>60 years)	Moderate
Chronic cardiac insufficiency	Moderate
Obesity (BMI >30 kg/m^2)	Moderate
Oestrogen therapy	Moderate
Pregnancy and the postpartum period	Low
Nephrotic syndrome	Low
Varicose veins	Low

Figure 2.1 Risk assessment for patient-related risk factors (20)

Source: Jacobson BF *et al*. Venous thromboembolism: prophylactic and therapeutic practice guideline. South African Medical Journal 2013; 103(4): 260-7. Appendix 1, Risk Assessment; p266

Subcategories of VTE risk in surgical patients[21]

	Surgical patients
Low VTE risk	• Surgery lasting <30 minutes • Injuries without or with only minor soft-tissue trauma • No or only minor additional predisposing risk factors
Moderate VTE risk	• Surgical procedures of longer duration • Immobilisation of lower limb with plaster cast • Lower limb arthroscopic procedures. • No or only minor additional predisposing risk factors
High VTE risk	• Major surgical procedures for malignancy • Multiple trauma or severe trauma of the spine, vertebra or lower limbs • Major orthopaedic surgery, e.g. hip or knee replacement • Major surgical procedure of cardiothoracic and pelvic regior

Figure 2.2 Risk assessment for procedure-related risk factors (20).

Source: Jacobson B *et al.* Venous thromboembolism: prophylactic and therapeutic practice guideline. South African Medical Journal 2013; 103(4): 260-7. Appendix 1, Risk Assessment; p267

Figure 2.1 does require some qualification. Firstly, it must be noted that although malignancies have been lumped into a single risk factor, certain malignancies carry a higher risk for thrombotic disease, with pancreatic, ovarian and brain malignancies being associated with the most risk (21). Secondly, it should be noted that the risk of thrombotic events with thalidomide increases substantially when used in conjunction with dexamethasone (22). Thirdly, the table does not differentiate between hormonal replacement therapy and the oral contraceptive pill with respect to oestrogen therapy. However, they appear to have similar risk profiles, with the former having been shown to have a 2-6 fold increased risk of thrombotic events and the latter a 2-4 times increased risk (23).

2.1.5.1 Clinical Scoring Systems

A number of scoring systems exist, using clinical information and patient risk factors, as a means to estimate pre-test probability of a patient having a VTE event. Two such scores are the Geneva score and the Wells score. As the Wells score is typically used in the setting of the study population, it is described further. In 1997, Wells *et al*, developed a scoring system, using clinical information and risk factors to create a three level scoring system (24). This was later updated to a two-tier system (the 'modified' Wells score) in 2003 (25), which assigns scores to seven variables related to the patient's clinical findings as well as risk profile (25). Based on the score, a pre-test probability of the patient having a DVT or PE is assigned and a clinical decision rule (CDR) followed. This is expanded on in Figure 2.3.

Clinical feature	Points	Patient score
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3	
An alternative diagnosis is less likely than PE	3	
Heart rate > 100 beats per minute	1.5	
Immobilisation for more than 3 days or surgery in the previous 4 weeks	1.5	
Previous DVT/PE	1.5	
Haemoptysis	1	
Malignancy (on treatment, treated in the last 6 months, or palliative)	1	
Clinical probability simplified scores		
PE *likely*	More than 4 points	
PE *unlikely*	4 points or less	

Figure 2.3 Wells clinical decision (26)

Source: National Institute for Health and Clinical Excellence. Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing 2012 [cited 2016 27th February]. Available from: www.nice.org.uk/guidance/CG144.

This scoring system has been further simplified to a two-tier scoring system – less than or equal to 4 points and more than 4 points, indicating an 'unlikely' or 'likely' probability, respectively (25)

2.1.6 Clinical presentation of pulmonary embolism

Part of the issue related to the increasing CTPA referral and dropping yield rate is the non-specific signs and symptoms related to PE. According to the Prospective Investigation of Pulmonary Embolism Diagnosis II (PIOPED II) trial the most frequent presenting symptom of acute pulmonary embolism is new dyspnoea at rest or on exertion (79% of patients) (27). Other frequent symptoms included pleuritic chest pain (59%), cough (39%) and orthopnoea (35%) (27). Less common symptoms include wheeze, calf or thigh swelling, and non-specific chest pain.

Signs also present a diagnostic challenge with tachypnoea, a non-specific finding, being present in nearly half of the patients (27). Other signs include tachycardia, abnormal findings on chest examination, such as crackles, wheezes and decreased breath sounds, and signs of DVT (27). Rarely patients presented with cyanosis, pyrexia or diaphoresis.

It therefore becomes apparent from the above, that the most common signs and symptoms may have a multitude of causes. This, without combining it with a clinical decision rule such as a Wells score, could account for the excessive referral and decreased yield of CTPA for suspected PE.

2.1.7 Pleural effusions in PTED

PTED remains an under-recognised cause of pleural effusion (8). Pleural effusions occur in around half of patients with pulmonary embolism (6). According to international studies, this prevalence is higher than in patients without pulmonary emboli (28).

The exact pathogenesis of pleural effusions arising from PE remains unknown. However, it is thought to be related to increased vascular permeability in the lungs secondary to ischaemia or the release of vasoactive cytokines (29). Another proposed mechanism is that it relates to increased hydrostatic pressure due to increased pulmonary pressure, which results in an increase of systemic venous pressure at the parietal pleural surface (7). Irrespective, there is excessive interstitial fluid, which traverses the visceral pleura and enters the pleural space.

From a clinical perspective, pleuritic chest pain in patients with pleural effusion is highly suggestive of underlying PE (8). Biochemically, the vast majority pleural effusions, if not all, are exudative (6). The effusion itself tends to be small (less than one-third of the hemithorax) and unilateral in more than 75% of patients (6). According to Yap *et al* the majority (86%) of the effusions tend to be on the same side as the emboli, however, the location and the number of arteries involved do not predict the presence of the pleural effusion (28).

Although typically the pleural effusion remains small and therefore does not alter the clinical management (28), there are complications related to pleural effusion which may require action. Left unchecked, the effusion may become loculated, with loculations seen

on CTPA as frequently as 20% of the time (6). Other complications include increasing size, or contra-lateral effusion, which, particularly after the initiation of anti-coagulation therapy, likely represent recurrent emboli, haemothorax or pleural infection (6). A further rare complication that may develop is Dressler's syndrome, which is characterised by pericardial effusion, fever and increased white cell count (6).

2.1.8 Diagnosis

As mentioned above, pre-test clinical assessment such as a modified Wells score, helps triage patients into those likely to have a pulmonary embolus and avoids unnecessary testing. However, there are additional investigations, both non-imaging, as well as imaging-related, where the findings may support a diagnosis of pulmonary embolism.

2.1.8.1 Non-imaging

Non-imaging investigations include:

- **Biochemical** – in the past decade, D-dimer measurements have become fundamental to the evaluation of patients with suspected acute pulmonary embolism (30). This test measures fibrinogen degradation products associated with endogenous fibrinolysis and in a low risk setting has a high sensitivity for VTE (approaching 100%) (31). However, this test has a low specificity as it may be elevated in a number of inflammatory diseases, in cardiac and renal failure, in malignancies, after trauma, post-surgery (31), and in pregnancy (30). It therefore becomes apparent once again, that mimickers of PE clinically may also be

associated with elevated D-dimer levels, further affecting referral patterns and yield rates.

- **Electrocardiography (ECG)** – ECG changes can range from an isolated finding of tachycardia in minor PE, to evidence of right ventricular strain, including a right bundle branch block and/or evidence a prominent S wave in lead I and a Q wave and inverted T wave in lead III in a patient with a large pulmonary embolus (so called S1,Q3,T3 pattern) (31). Therefore, in minor PE, where tachycardia is the only presentation on ECG, there is once again low specificity, contributing to the diagnostic dilemma associated with PE.
- **Arterial blood gases** – characteristic findings are a reduced PaO_2 and normal to reduced $PaCO_2$ (31). However, PaO_2 may be normal in smaller PE and there are many causes of hypoxaemia which may result in reduced PaO_2 (31). As such, this test has a low discriminatory value when used in isolation.

2.1.8.2 Diagnostic imaging

While CTPA remains the mainstay of diagnostic imaging, and will be discussed in detail in section 2.2, it is not the only useful test in diagnosing pulmonary embolism. Other investigations that may contribute to the diagnosis of PE include:

- **Chest radiograph** - radiographic findings are non-specific and chest radiographs are often normal in PE (32). Findings that may be present include peripheral wedge-shaped opacities signifying pulmonary infarction (Hampton's hump), oligaemia in areas of the lung affected by pulmonary emboli (Westermark's sign), atelectasis and pleural effusions (31). Chest radiographs may also show enlarged pulmonary arteries and right-sided chamber cardiac enlargement (32) in keeping

with cor pulmonale. It therefore becomes apparent, that while non-specific, chest radiographs may be useful in finding indirect signs of PE, discovering associated findings, as well as identifying complications of pulmonary embolism.

Chest radiographs are also useful to exclude mimickers of PE. These include left-sided heart-failure, pneumothorax and rib fractures (31). Moreover, a chest radiograph is necessary for correct interpretation of a Ventilation/Perfusion (V/Q) scan.

- **Ventilation/Perfusion scan -** as V/Q scans fall under the ambit of the nuclear medicine specialist, rather than radiologist, and have largely been replaced by CTPA. Thus an in-depth analysis of V/Q scans falls beyond the scope of this research. Nevertheless, V/Q scans do play a complimentary role in the diagnosis of PE and may be the preferred choice of investigation in certain settings. These include patients with renal dysfunction that prohibit the use of contrast agents, young female patients where there is concern over breast radiation and where the diagnostic quality of CTPA may be poor. Examples of poor/non-diagnostic scans include those with significant motion artefact and low signal to noise ratio in morbidly obese patients (33).

  In contrast to CTPA, which can directly visualise the embolus, V/Q scans measure the consequent perfusion defect resulting from the PE (31). However, unlike many of the mimickers of PE, there are no associated ventilation defects, creating a 'mismatch'. The probability that the mismatch is due to PE is then stratified into high, medium or low risk, based on the abnormality visualised on the scan. Based

on this, an informed decision on further management or diagnostic investigation can be made.

- **Pulmonary angiography - f**ormal angiography has largely been replaced by CTPA and should only be considered when other investigations are inconclusive as they carry a higher risk of mortality (31). It is also invasive and tends to be less readily available. This procedure requires the injection of contrast agent through a pigtail catheter introduced into the pulmonary artery. A diagnosis is made by visualising abrupt cut-off of a pulmonary vessel or a filling defect noted within the pulmonary artery.
- **Magnetic Resonance Pulmonary Angiography (MRPA)** - one of the primary concerns surrounding CTPA is the cancer risk associated with ionising radiation, particularly in young patients. MRPA may provide a safer alternative to CTPA but is still currently beset with issues such as low sensitivity, long scanning times, uncertainty over which is the optimal sequence and high technical failure rate (34). These factors currently limit its use, however, it may become more beneficial as techniques improve.

2.2 Computerised Tomographic Pulmonary Angiography (CTPA)

Due to its high sensitivity, ready availability and quick scan time, CTPA has become the pre-eminent imaging investigation in patients with suspected pulmonary embolism (15). This has resulted in substantially increased referral rates over the last decade. However, the concomitant drop in positive yield has raised concern for patient safety. As

mentioned above, this concern revolves predominantly around ionising radiation exposure and contrast-related risks, in particular nephrotoxicity (2).

A number of studies have looked at yield rates for PE on CTPA, with the PIOPED II study, according to Devaraj *et al*, reporting emboli in 22.6% of cases (15). More recent studies have reflected even lower yield with a number of studies showing prevalence rates in the region of 9%-16% (5,35,36). This trend has led to the creation of pre-test probability scores with a view to improving positive yield. One such score is the Wells score, which was discussed in detail above. It has been shown that, for example, a negative D-dimer assay in a low or intermediate risk patient, obviates the need for further investigation (2).

Referral patterns are not the only issue with respect to CTPA. Despite technical advances, non-diagnostic scans remain a problem. While rates may vary from centre to centre, non-diagnostic scans are thought to be in the order of 5%-10% (15). This poor quality may relate *inter alia* to patient and/or technical factors (33), the more common of which are explored further below.

2.2.1 Non-diagnostic scans

A number of technical advances have been made with a view to enhancing scan quality. Of fundamental importance is the contrast enhancement in the main pulmonary arteries. This is indicated by the attenuation level, which is measured in Hounsefield units (HU). A Hounsefield unit less than 200 in the pulmonary trunk is considered non-diagnostic (37). Maximising peak attenuation levels is not only related to the concentration and volume of

iodine administered, but also to the timing of the scan, such that it coincides with peak attenuation in the pulmonary arteries (38). One way of achieving this is to bolus track (as do the CT scanners at Charlotte Maxeke Johannesburg Academic Hospital), by triggering the scan a short time after a threshold Hounsefield value is reached in the region of interest (37) (in this case the pulmonary trunk).

A second commonly encountered technical issue is streak artefact, caused by dense contrast within the superior vena cava (SVC). This causes obscuration of the right pulmonary artery and upper lobe arteries. This artefact can be reduced by flushing the SVC with a saline chaser (15).

Patient factors may also result in sub-optimal scan. One of the more common causes is overweight patients which results in a decreased signal to noise ratio. In our centre, this is typically countered by increasing the intensity of the x-ray beam by increasing the milliampere seconds (mAs). A second commonly encountered patient-related issue is motion artefact from respiration. This artefact renders pulmonary embolism at this anatomic level indeterminate (33). Higher multi-slice scanners have reduced this issue as they scan faster, reducing breath-hold time required by the patient.

2.2.2 Radiological findings

The CTPA may provide both direct and indirect evidence of pulmonary emboli. Moreover, based on the radiological appearance, pulmonary emboli can be further categorised into acute or chronic. Location (pulmonary trunk, main pulmonary arteries, lobar, segmental

and sub-segmental) and by association, size, as well as degree of occlusion may also be ascertained and are relevant to clinical impact (1) and management decisions. The respective radiological features of acute and chronic emboli are expanded on below:

2.2.2.1 Acute pulmonary embolism

Direct signs of acute pulmonary embolism include:

- **Complete filling defect** – complete occlusion of the pulmonary artery with failure to opacify the vessel lumen. The diameter of the vessel at the site of the thrombus may be increased due to impacted thrombus (39).
- **Partial filling defect** – the thrombus may be central or eccentric and forms an acute angle with the vessel wall (33). When central, the thrombus is surrounded by contrast on either side forming a 'polo mint' sign when seen in short axis and 'railway sign' when seen in long axis (39).

Indirect radiological findings of acute pulmonary embolism include:

1. **Oligaemia** – while more commonly seen on formal angiography, occasionally a decrease in vessel calibre (as measured against adjacent bronchi) distal to the thrombus may be seen (39).
2. **Mosaicism** - non-uniform arterial perfusion can manifest as a patchwork of regions of differing attenuation on CT, known as mosaicism (40).

2.2.2.2 Chronic pulmonary embolism

As for acute pulmonary emboli, there are both direct as well as indirect radiological findings related to chronic emboli:

Direct findings include:

- **Complete filling defect** – complete occlusion of the vessel, which is smaller than adjacent vessels (33). This is therefore in contradistinction to a complete occlusion from an acute embolus, whereby the affected vessel may be increased in diameter.
- **Partial filling defect** – these tend to be eccentric and crescent-shaped and form obtuse angles with the vessel wall (33). Again this is in contradistinction to acute emboli, which may be central or eccentric and form acute angles with the vessel wall. Once organised, the thrombus may also cause intimal irregularities, bands, abrupt vessel narrowing and webs (41).

Indirect findings include:

- **Post-stenotic dilatation** - post-stenotic aneurysmal formation is a common manifestation of chronic PE (39).
- **Calcification -** within thrombi (41).
- **Signs of systemic collateral supp**ly – collateral supply arises from the bronchial vessels with concomitant increase in their size and calibre (39).
- **Mosaicism** – as for acute pulmonary emboli.

While the above provides information with respect to diagnosing pulmonary embolism, the role of the radiologist extends beyond just identifying and further characterising the disease. Pivotal to the further management of the patient is the presence of complications. This research addresses, *inter alia,* two key complications – pleural effusion and pulmonary hypertension, which are reviewed below.

2.2.2.3 Pleural effusions in pulmonary thromboembolic disease

A pleural effusion is a general term for fluid within the pleural space and radiologically one cannot differentiate between exudative and transudative effusions. CT is sensitive for the detection of small amounts of fluid and is therefore useful in pleural effusions secondary to PE, as they tend to cover less than one-third of the hemithorax (6). These effusions are unilateral in more than 75% of patients (6), with the majority (86%), ipsilateral to the emboli.

While, typically, effusions remain small, the effusion may become complicated. If the PE remains untreated, the effusion may become loculated. These loculations are seen on CTPA as frequently as 20% of cases (6). The effusion may also increase in size, or be found on the contra-lateral side, which, particularly after the initiation of anti-coagulation therapy, may represent recurrent emboli, haemothorax or pleural infection (6).

2.2.2.4 Pulmonary hypertension in pulmonary thromboembolic disease

Pulmonary hypertension is defined as a mean pulmonary arterial pressure greater than or equal to 25mm Hg (42). Pulmonary arterial pressure cannot be directly measured radiologically, and trans-oesophageal echocardiography (TEE) and right-heart catheterisation remain the first-line and definitive diagnostic tools for assessing pulmonary arterial pressures respectively. Nevertheless, imaging does have a role to play, with both chest radiography and CTPA portraying findings indicative of pulmonary hypertension.

On CTPA, a main pulmonary artery diameter of 29mm or more, measured at the level of the bifurcation, represents pulmonary hypertension (43). While a diameter of less than 29mm does not necessarily exclude pulmonary hypertension, this value has been shown to have a positive predictive value of 97% (43). Other vascular signs of pulmonary hypertension include a segmental artery to bronchus ratio of more than 1:1 in three of four lobes; and an aorta to main pulmonary artery ratio of less than 1:1 in patients under the age of 50 years (43).

2.2.2.5 Abnormal parenchymal findings on CTPA

CTPA is also useful to identify additional and/or alternate parenchymal findings that may clinically mimic PE or be found in conjunction with PE. A study by Liu *et al* identified a number of parenchymal abnormalities, including wedge-shaped opacities, masses, nodules and consolidation (7). All of these findings were found to be more common in patients with PE than in those without. A second similar study, however, only showed wedge-shaped opacities and consolidation to be significantly associated with PE (12).

3.0 AIMS AND OBJECTIVES

3.1 Aims

This aim of this study was to assess the diagnostic yield in patients at Charlotte Maxeke Johannesburg Academic Hospital undergoing CTPA for suspected PTED and to document the prevalence of pleural effusion, pulmonary hypertension and abnormal parenchymal chest findings in patients with and without documented PTED.

3.2 Study Objectives

The primary study objectives were:

1. To assess the positive yield rate of PTED in cases undergoing CTPA for suspected PTED at Charlotte Maxeke Johannesburg Academic Hospital.
2. To assess the frequency of pleural effusions in PE positive and PE negative CTPA investigations.

The secondary objectives were:

1. To assess the frequency of pulmonary hypertension in PE positive and PE negative CTPA investigations.
2. To document the frequency of abnormal parenchymal CT findings in PE positive and PE negative scans.
3. To compare the frequency of pleural effusion, pulmonary hypertension, and the frequency and nature of abnormal parenchymal chest findings in patients with PE positive and PE negative scans.

4.0 RESEARCH METHODOLOGY

4.1 Research Paradigm

This research was a retrospective quantitative cross-sectional study of CTPA reports in a population of subjects who underwent CTPA for suspected PTED at Charlotte Maxeke Johannesburg Academic Hospital.

4.2 Sample

The study population comprised adult patients who had undergone a CTPA at CMJAH for suspected pulmonary embolus, starting in January 2016, and moving in reverse chronological order until a sample size of 100 was reached. This resulted in the study extending back to September 2015.

For this study, the sample size was calculated by estimating the proportion of pleural effusions in the study group at 0.5. Motulsky regards this as "a worst-case assumption that may overestimate the needed sample size." (44). Two other assumptions were a confidence Interval of 95% and a precision (margin of error) of 10%, which is considered reasonable (Personal communication, Professor Peter Cleaton-Jones, February 2016).

Sample size for prevalence was determined using the formula (45):

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where;

n = sample size,

Z = Z-statistic for the chosen level of confidence,

P = expected prevalence or proportion

d = precision

Once the equation is rearranged: $N = \frac{4.\ 0.5\ (0.5)}{0.1^2} = 100$

This sample size was then checked to ensure that it was adequate to analyse the secondary objective of testing for differences between groups with and without pulmonary embolism. As this comparative analysis generally required a test of association for 2x2 tables, a Fisher's exact test was mainly used. The sample size needed for a Fisher's exact test was calculated by a Power analysis using G*Power analysis programme (46). For the detection of small, medium, or large effect sizes, with 80% power at the 5% significance level, sample sizes of 785, 87 and 31, respectively, were required. As studies typically aim for the detection of at least a medium effect size (Personal communication, Dr Petra Gaylard, April 2016), should it exist (which would require a sample size of 87), the sample size of 100 chosen for this study was also adequate for this secondary objective.

4.2.1 Inclusion criteria

All patients, 18 years of age and older, at CMJAH in whom CTPA was performed for suspicion of pulmonary embolism during the time period specified in 5.2 above.

4.2.2 Exclusion criteria

1. Patients with missing radiological reports.
2. Patients in whom the reporter could not ascertain whether there were pulmonary emboli due to non-diagnostic scans or similar technical issues.

4.3 Materials and Methods

Ethics approval was obtained from the Human Ethics Research Council (Medical) (see Appendix A). The existing database of all patients that have undergone CTPA at CMJAH was accessed. The reports conforming to the inclusion criteria were retrieved, and the relevant data, where available (as per Appendix B: Data collection sheet), was captured by the author onto an excel spreadsheet. Studies that met the exclusion criteria were excluded and substituted with an additional CTPA study in order to keep the sample size at 100. The patient data was anonymised by ascribing a random code to each patient. The key to this code is only available to the researcher and supervisors.

The CTPA studies included were done on either the 64-slice or 128-slice Multi Detector Computerized Tomography, Phillips imaging system at Charlotte Maxeke Johannesburg Academic Hospital. The technical parameters are as follows:

- **128-Slice scanner** - The iodinated contrast material, Jopamiron (iodine concentration of 370mg per millilitre) is injected at a rate of 3 – 3.5ml/s with no bolus tracking. The region of interest is applied at the centre of the pulmonary trunk. A tube voltage of 120kV with a baseline tube current of 200mAs (this is

increased in patients with higher body mass indices), pitch of 0.891, slice thickness of 1mm and detector collimation of 0.625mm was used. The rotation speed is 0.5s.

- **64-Slice scanner** - The iodinated contrast material, Jopamiron (iodine concentration of 370mg per millilitre) is injected at a rate of 3 – 3.5ml/s with no bolus tracking. The region of interest is applied at the centre of the pulmonary trunk. A tube voltage of 100kV with a baseline tube current of 10mAs (this is increased in patients with higher body mass indices), pitch of 0.798, slice thickness of 1mm and detector collimation of 0.625mm was used. The rotation speed is 0.5s.

4.4 Data Collection

The CTPA reports of the study group had the following data collected as per the attached data collection sheet (see appendix A):

- Presence or absence of pulmonary emboli.
- Presence or absence of pleural effusions.
- Presence or absence of radiological evidence of pulmonary hypertension (as indicated by a main pulmonary artery measurement of 29mm or greater at its bifurcation).
- Presence or absence of abnormal parenchymal findings, specified under the following headings:
    - Wedge-shaped opacification (likely indicative of a pulmonary infarct)
    - Consolidation/Ground-glass opacification

- Atelectasis
- Mass

In order to provide a more comprehensive study, the following data were also captured, where available:

- Pleural effusion characteristics, including laterality and size
- Age and gender
- Risk factors (as per Wells score criteria)
- Wells score
- Presence or absence of a raised D-dimer level
- Human immunodeficiency virus (HIV) status

4.5 Reliability and Validity

CTPAs have both a high sensitivity and specificity for detecting PE (38). Virtually all CTPAs at CMJAH are performed with standard technical parameters that enhance the reliability of these studies.

4.6 Bias and Assumptions

South Africa not only has a higher prevalence of HIV infection, which will results in a two- to ten-fold increased risk of VTE (4), but also presents with an array of pathology that can mimic PE. This may result in a decrease in external validity in a setting with lower HIV infection rates.

There is also inter-observer variability associated with diagnosing PE. In order to reduce this inter-observer variability, only the consultant radiologist's report, or review of the registrar report (if done on call after hours), was used. It is assumed for the purposes of this research that the consultant radiologist's findings were correct.

Furthermore, as data was collected, it became apparent that missing information resulted in certain limitations. Therefore assumptions needed to be made and criteria followed for certain variables as necessary. These included:

- **Pulmonary embolus** – pulmonary emboli were considered present if assessed as such in the report, irrespective whether central or peripheral.
- **Pleural effusion** - if the presence of a pleural effusion was not mentioned, it was assumed to be absent as it is an easily identified finding and unlikely to be omitted in the report if present.
- **Pulmonary hypertension** - In contradistinction, the diagnosis of pulmonary hypertension requires active measurement, which is typically performed (as evidenced by 88% of CTPA reports from the sample documenting a measurement even when less than 29mm, with a further 8% of reports at least documenting the presence or absence of pulmonary hypertension). As such, if no mention was made of the size of the pulmonary artery trunk and/or the presence or absence of pulmonary hypertension was not mentioned, it was assumed to be missing data.
- **Abnormal parenchymal findings**:
    - **Atelectasis** – during the course of data collection, it became apparent that different types of atelectasis were mentioned, including 'passive' (secondary to pleural effusion), 'dependant' and 'segmental'. For

completeness sake, all forms of atelectasis were included under the general heading of 'atelectasis'.

- **Mass –** nomenclature with respect to nodule versus mass needed to be addressed. The strict radiological definition of a mass is a lesion greater than 3cm, with lesions less than this being termed nodules (40). This was strictly adhered to. Therefore, if there was at least one mass lesion that measured 3cm or more, it was included as a mass, even if termed a nodule in the report. If there was no measurement given, it was taken at face-value that a 'mass' was a mass and a 'nodule' (irrespective if solitary or multiple) was a nodule.

- **Risk factors** – the Wells scoring system only accounts for 'previous DVT/PE' or 'clinical signs of DVT'. There were cases with a current proven DVT/PE which were included as a risk factor under 'previous DVT/PE' as the Wells scoring system does not have a specific line item for proven, currently existing PE.

4.7 Data Analysis

Descriptive analysis of the data was carried out as follows:

- **Categorical variables -** were summarised by frequency and percentage tabulation, and illustrated by means of bar charts.
- **Continuous variables –** were described by the mean, standard deviation, median, interquartile range, and by histograms.

Fisher's exact test was used to assess the relationships between categorical variables and the presence/absence of PE. The strength of the associations was measured by the phi coefficient, using the following scale of interpretation:

- **0.50 and above** - high/strong association
- **0.30 to 0.49** - moderate association
- **0.10 to 0.29** - weak association
- **Less than 0.10** – little, if any association

The relationship between continuous variables and the presence/absence of PE was assessed by the Student's t-test where the data were normally distributed. Where the data were not normally distributed, a non-parametric alternative, the Wilcoxon rank sum test was used. The strength of the associations was measured by the Cohen's d for parametric tests, whilst the r-value was used for the non-parametric tests. The following scale of interpretation was used:

- **0.80 and above** - large effect
- **0.50 to 0.79** - moderate effect
- **0.20 to 0.49** - small effect
- **Less than 0.20** - near zero effect

Data analysis was carried out using SAS version 9.4 for Windows. A 5% level of significance ($p<0.05$) was used throughout.

5.0 RESEARCH RESULTS

5.1 Sample Population

A sample of 100 CTPAs meeting the inclusion criteria (and not meeting the exclusion criteria) was used. During the data collection process, four CTPAs were excluded due to missing age data (therefore it could not be verified that these patients met the inclusion criteria for age), two were excluded as the patients were under 18 years of age, and one was excluded as it was called non-diagnostic (no reason was documented). These seven excluded scans were replaced with CTPA's that met the inclusion criteria and did not conform to the exclusion criteria.

5.2 Demographics

Of the 100 patients analysed, 75 were female (75%), 24 (24%) were male, and in 1 patient the gender was unknown due to missing data. Although age in this study group follows a non-normal distribution and therefore the median and IQR is more relevant, in order to compare to other studies that have quoted only the mean and SD, both have been included. The mean age of the group was 49 years (SD 17). The median age of the group was 49 years (IQR 31,5 to 62 years). This age distribution is shown in figure 5.1.

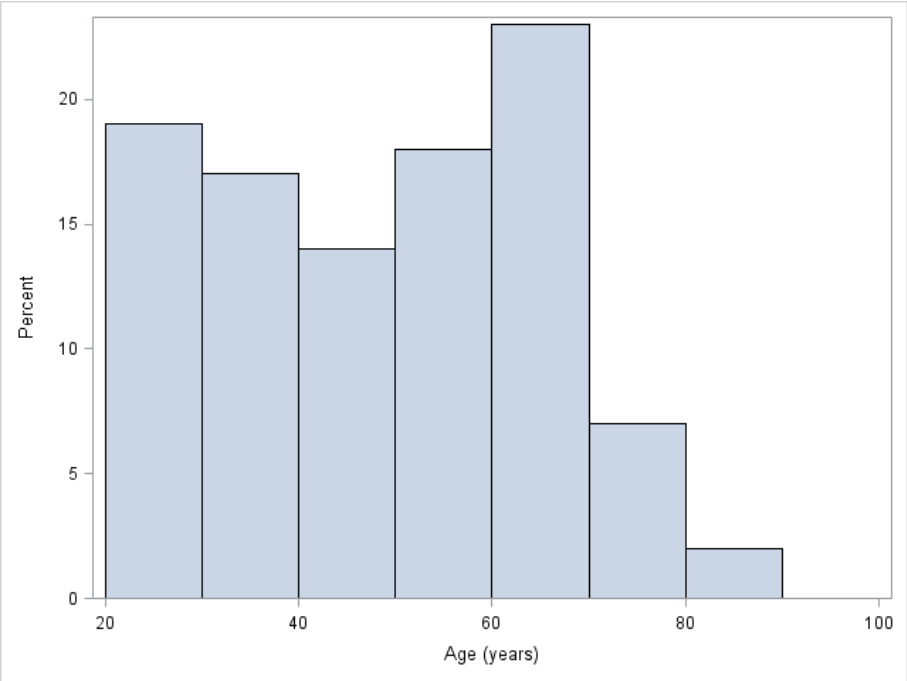


Figure 5.1 Age distribution of study group

5.3 Diagnosis of Pulmonary Embolus

5.3.1 Yield

A diagnosis of pulmonary embolism was confirmed in 37 cases (37%) (95% Confidence interval: 27,6%-47,2%). There was no evidence of pulmonary embolism in 60 cases (60%), while 3 cases (3%) were equivocal (no definitive diagnosis of PE was made, but the reporter stated that he/she could not exclude PE, for reasons other than non-diagnostic scans).

5.3.2 Diagnosis of pulmonary embolism by gender

Two female and one male scans were equivocal for PE, while one scan did not document gender. Of the remaining 96 scans, 37 were PE positive, of which 28 (77,8%) were female and 8 (22,8%) male. As shown in table 5.1, as a proportion per gender, 38,3% of females and 34,8% of males were PE positive. There was no statistically significant difference between genders for those with and without PE (p=0.81).

Table 5.1 Diagnosis of pulmonary embolism by gender

Gender	Female		Male	
N	73		23	
PE negative	45	61,6%	15	65,2%
PE positive	28	38,4%	8	34,8%

5.3.3 Diagnosis of pulmonary embolism by age

There was no statistically significant difference in the age of those with and without pulmonary embolism (p=0,49). The mean age for the positive group was 49,2 years (SD 17,1 years) and the negative group 46,1 years (SD 16,8 years). The median age was 52,5 years (IQR 31-62,5 years) and 47 years (IQR 32-62 years) for the positive and negative groups respectively. This is reflected in Table 5.2.

Table 5.2 Diagnosis of pulmonary embolism by age

Pulmonary Embolism	PE negative		PE positive	
N	60		37	
Mean/SD	49,2	17,5	46,1	16,8
Median/IQR	52,5	31 to 62.5	47	32 to 62

5.4 Pleural Effusion and Pulmonary Embolism

Overall 40 patients (40%) had an identifiable pleural effusion on CTPA. Of the 60 patients with no pulmonary embolism, 26 (43,3%) had pleural effusions. A total of 14 patients out of 40 patients (37,8%) with PE had pleural effusions. There were no significant differences between the frequency of pleural effusion in those with and without pulmonary embolism (p =0,67). These findings are reflected in table 5.3.

Table 5.3 Pleural effusion and pulmonary embolism

Pleural Effusion		**Overall**		**PE negative**		**PE positive**	
N		100		60		37	
Yes	n / %	40	40,0%	26	43,3%	14	37,8%
No	n / %	60	60,0%	34	56,7%	23	62,2%

Of the 14 PE positive pleural effusions, it was documented that seven were bilateral and seven were right-sided. Of the seven right-sided effusions, three were contralateral to the side of the PE, two were ipsilateral, one had PE evident bilaterally and one scan report had no documentation of the side of the PE. Six of the 14 PE positive effusions were small, three were documented as large and five scan reports did not comment on size.

5.5 Pulmonary Hypertension and Pulmonary Embolism

A total of 54 patients (54%) had evidence of pulmonary hypertension (main pulmonary artery of greater than 29mm), 42 patients (42%) showed no radiological evidence of pulmonary hypertension, and in 4% the data were missing. The main pulmonary artery (PA) measured more than 29mm in 32 out of 60 PE negative patients (53,3%) and 22 out

of 37 PE positive patients (66,7%). While the percentage appeared higher in PE positive patients, the difference was not significant (p=0,27). These findings are indicated in Table 5.4.

Table 5.4 Pulmonary hypertension and pulmonary embolism

Pulmonary hypertension		Overall		PE negative		PE positive	
N		100		60		37	
Yes	n / %	54	54,0%	32	53,3%	22	66,7%
No	n / %	42	42,0%	28	46,7%	11	33,3%

5.5.1 Main pulmonary artery size

The main pulmonary artery size distribution followed a non-normal distribution, and as such, the median and interquartile range were reported. The overall median size of the main pulmonary artery was 30 mm (IQR 27 to 35,4 mm). The median size of the main PA was 30mm (IQR 26,4-34,6) and 30,3mm (IQR 27,5-37) in the PE negative and positive groups respectively. These differences were not significant (p=0,30). The distribution of the data is shown in Figure 5.2.

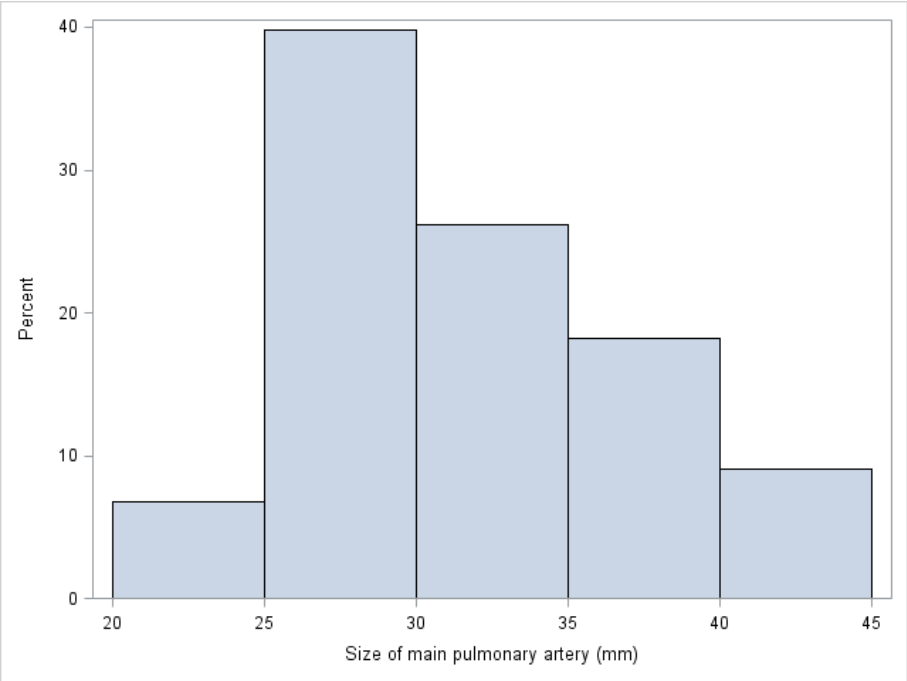


Figure 5.2 Distribution of the size of the main pulmonary artery

5.6 Abnormal Parenchymal Findings

At least one parenchymal CT abnormality, as per the data points, was detected in 59% of cases. The most common parenchymal finding was consolidation/ground-glass opacification (41%), followed by atelectasis (19%). Wedge-shaped opacification and masses both had a prevalence of 4%. This is illustrated in figure 5.3.

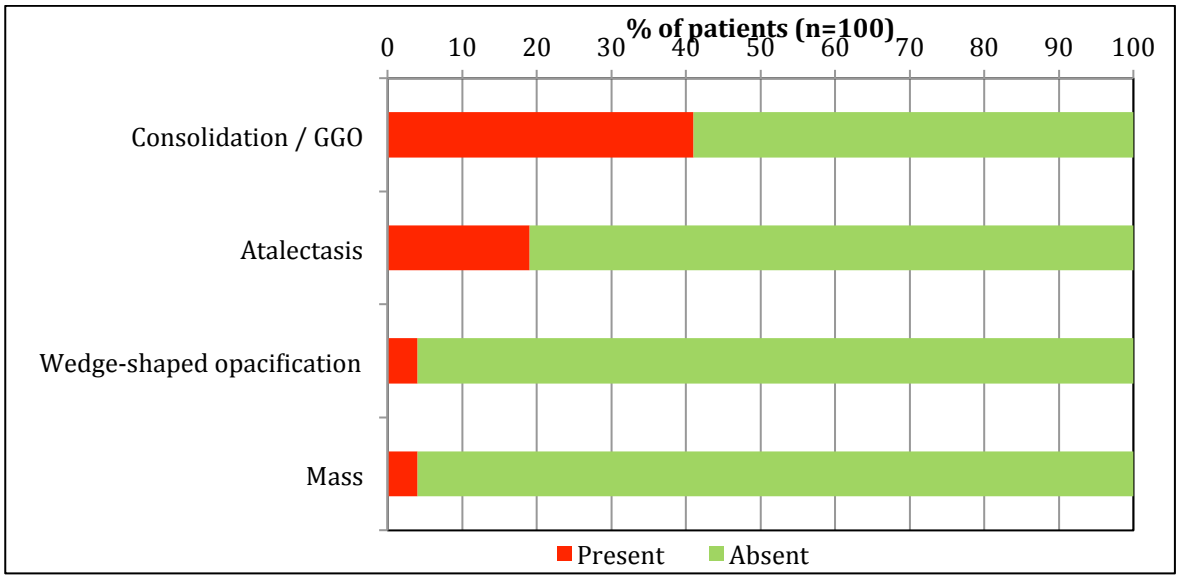


Figure 5.3 Prevalence of parenchymal abnormalities

Overall, 58,3% of PE positive and 59,5% of PE negative patients showed parenchymal abnormalities, which was not significantly different (p=>0,99). When these parenchymal abnormalities were looked at independently, only peripheral wedge-shaped opacities were more common in the PE group compared with the non-PE group (four vs. zero; p=0,019; phi = 0,26). While consolidation/Ground-glass Opacification and atelectasis appeared to be more common in the PE positive group (45,9% versus 38,3% and 18,9% versus 18,3% respectively) and masses were ostensibly more common in the non PE group (5% versus 0%), none of these findings were shown to be significantly different. These findings are indicated in Table 5.5*.

Table 5.5 Abnormal parenchymal findings and pulmonary embolism

Variable*	Category		PE negative		PE positive	
N			60		37	
At least one parenchymal abnormality			35	58,3%	22	59,5%
Wedge-shaped opacification	Yes	n / %	0	0,0%	4	10,8%
	No	n / %	60	100,0%	33	89,2%
Consolidation/ GGO	Yes	n / %	23	38,3%	17	45,9%
	No	n / %	37	61,7%	20	54,1%
Atelectasis	Yes	n / %	11	18,3%	7	18,9%
	No	n / %	49	81,7%	30	81,1%
Mass	Yes	n / %	3	5,0%	0	0,0%
	No	n / %	57	95,0%	37	100,0%

*With the exception of peripheral wedge-shaped opacities (p=0,019), there were no significant differences.

5.7 Risk Factors, Wells score, D-Dimer levels and HIV Status

While not defined as objectives, the researcher collected individual risk factors (as per the Wells score), overall Wells score, D-dimer values, and HIV status, where available. In terms of risk factors (as per Wells scoring system), 5 cases had clinical evidence of DVT, there was a tachycardia in 16 cases (although it was mostly unspecified if the heart rate was above 100 beats/min as per Wells score) and a history of recent surgery/immobilisation was given in 21 of the 100 cases. There was a previous DVT/PE or current proven DVT/PE in 9 cases, malignancy was mentioned in 15 of the 100 cases and haemoptysis was documented once. The remaining cases contained missing data and therefore this did not allow for any meaningful statistical analysis.

The overall Wells score was only documented in 10% of patients, and ranged from 3,5 to 7,5. Three of these cases had pulmonary emboli and had Wells scores of 3, 7 and 7 respectively. The marked absent data precluded any meaningful analysis.

The D-dimer level was raised in 30 out of the 100 patients, with the vast majority of the remaining cases having no recorded D-dimer level, nor indication as to whether it was elevated or not. Of these 30 patients, 11 had concomitant PE. Once again the lack of data did not allow for further consequential analysis.

In terms of combining the D-Dimer with Wells score, as would be done when following clinical decision rules, only 3 cases had both a documented raised D-dimer level and Wells score. Of these, one had pulmonary embolism (Wells score 3,5). The remaining two patients, although reported as PE negative, did have significant risk factors for PE as evidenced by wells scores of 6 and 7,5 respectively.

The HIV status was given as positive in 19 cases and negative in two cases. Of the 19 HIV positive patients, 9 had pulmonary emboli, while one of the two documented HIV negative patients had a PE. The rest failed to mention HIV status. Therefore similarly, the absent data precluded any further analysis.

5.8 Overall CTPA Findings

Eighty-eight scans (88%) had at least one CTPA abnormality. Pulmonary hypertension was the most common finding (54%), followed by consolidation and/or ground-glass opacification (41%). The third most common finding was pleural effusion (40%), followed by pulmonary embolism (37%). Atelectasis (19%), masses (4%) and wedge-shaped opacifications (4%) were less commonly seen. The prevalence of each abnormal finding is indicated Figure 5. 4*.

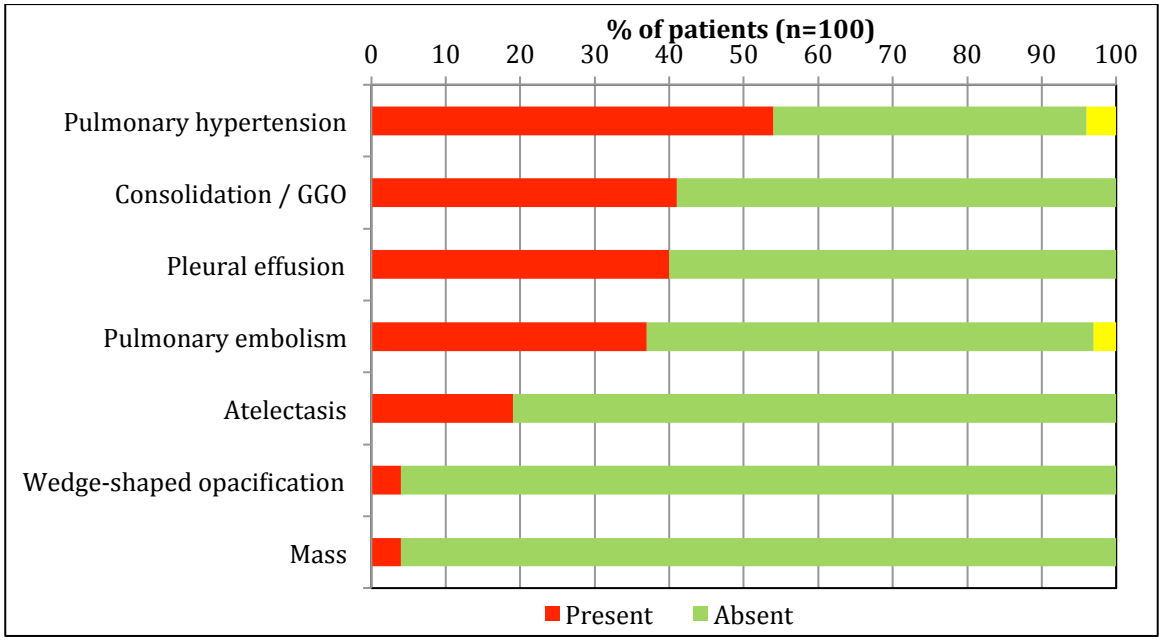


Figure 5.4 Prevalence of CTPA findings

* Missing data with respect to PE represents equivocal scans

In terms of the PE positive group, 81,7% had at least one CTPA abnormality (excluding PE). This figure was 81,1% in the PE negative group. There was no significant difference between the two groups (p=>0,99).

6.0 DISCUSSION

Computerised tomographic pulmonary angiography (CTPA) has become the pre-eminent investigation for diagnosing pulmonary embolism (PE). However, it is not without risk to the patient and increasing referral rates and decreasing yields have raised cause for concern. Part of the reason for this increasing referral is the diagnostic challenge presented by a myriad of conditions that may mimic pulmonary embolism. CTPA, however, is not only useful in diagnosing pulmonary embolism but is also helpful in identifying additional and/or alternate findings. These findings encompass pleural and vascular abnormalities such as pleural effusions and pulmonary hypertension, as well as parenchymal findings. The latter include *inter alia* masses, consolidation and/or ground-glass opacification, wedge-shaped opacifications and atelectasis.

This study looked at the above elements. Each section of the results chapter above is analysed in this chapter with a view to comparing it to current existing literature. Interpretation was facilitated by insights gained and knowledge garnered from the literature review, as well as the day-to-day knowledge of the researcher.

6.1 Demographics

The female to male ratio of the current study population referred for CTPA was 3:1. Although this could be attributed to females having a higher prevalence of PE than males, studies, including this one, have shown no gender bias with respect to pulmonary embolism (47). Therefore other reasons should be sought.

As referral is predominantly based on clinical presentation, exploration of any possible gender differences in clinical presentation is warranted. The International Cooperative Pulmonary Embolism Registry (ICOPER), showed dyspnoea to be more common in women, while haemoptysis and chest pain were more common in men (47). A similar study by Ebadi *et al* also found dyspnoea to be more common in women. As dyspnoea is the most common presenting symptom of pulmonary embolism (27), which in itself is fairly non-specific, this may account for the higher referral rates in females.

As previously mentioned, due to age following a non-normal distribution, the median and interquartile range are more appropriate measures than the mean and standard deviation. However, in order to compare the findings to other studies, which typically quote mean and standard deviation, the latter has also been included in this study.

The mean age of the group was 49 years (SD 17 years). The median age of the group was 49 years (IQR 31,5 to 62 years). This was somewhat lower than international studies where the mean age was approximately 60 years with a similar standard deviation to this study (7, 47). This may relate to differences in risk factors, such as a higher rate of HIV and TB infection in South Africa, which are independent risk factors for PTED (4) and will typically present in younger patients. This appears to be substantiated by a study by Bibas *et al*, which showed the mean age for VTE in HIV positive patients to be approximately 40 years old, which is 20 years earlier than those without HIV infection (4). However, this could not be confirmed in the current study, as the data regarding risk factors for PE in the current study group, and in particular that related to HIV infection, was scanty.

Further analysis of the age distribution shows more patients to be in the 60 to 70 year range than any other decade, despite a lower overall group mean/median. There is evidence to suggest that incidence increases with age (48). Although there are fewer people in the 70 years and above age groups in this study, this is likely a result of there being fewer people, in general, in these age groups, rather than a lower prevalence rate. This increased frequency of this older group may then reflect a peak in a population group which more closely follows the demographics of those in international literature where the HIV/AIDS prevalence is lower. Thus we possibly have a bimodal type distribution, with different age values in HIV positive and negative groups. This once again affords an opportunity for further research where the HIV status and prevalence can be analysed according to age in the local setting.

6.2 Diagnosis of Pulmonary Embolus

6.2.1 Yield

A diagnosis of pulmonary embolism was confirmed in 37 cases (37%). This yield rate measures favourably with a number of studies performed elsewhere, where yield rates are in the 9%-16% range (5,35,36). Even when compared to the PIOPED study, which has a higher yield rate of 23% (15), this study compares positively. While this may relate to better clinical assessment, with the lack of D-dimer values and Wells scores on the referral letters merely a documentation omission, it may also indicate that clinical decision rules are not being followed. Therefore this higher yield may be due to other reasons, which warrant further consideration.

One possibility is that the increased risk factors, particularly HIV infection and TB may contribute to a higher prevalence of concomitant PE in patients presenting with alternate findings, which would typically not be present in HIV negative patients. Another possible reason for this increased yield may relate to overcalling by the radiologists. A future application then of this study could look at inter-observer variability among radiologists when reading CTPA's.

6.2.2 Diagnosis of pulmonary embolism by gender

Although 75% of the PE positive patients were female, this was merely a function of three times as many females than males being referred for CTPA's, rather than any true difference in prevalence. When analysed separately, there was no significant difference in frequency by gender, with 28 out of 75 females (37%) and 8 out of 24 males (33%) being PE positive. This is in line with other studies, which have shown the incidence of VTE is gender neutral (47).

6.2.3 Diagnosis of pulmonary embolism by age

There were no significant differences in the age of those with and without pulmonary embolism. There is a dearth of literature comparing age in those with and without PE, however, the lack of statistical difference between the PE positive and negative groups in the current study is concordant with a study by Liu *et al*, albeit the mean age in the current study, is approximately a decade younger (7).

6.3 Pleural Effusion and Pulmonary Embolism

Pleural effusion was present in 37,8% of the PE positive group. A number of studies have shown the frequency of pleural effusions to be approximately 50% (6, 49). While the prevalence of pleural effusion has shown to be higher in the post-operative setting, of the eight patients with pulmonary embolism that cited immobilisation/surgery as a risk factor, only two had pleural effusions. While this figure is likely inaccurate due to significant missing data, it does suggest that there may be other reasons for this lower prevalence rate.

One reason may be the relatively small sample size of this study and a larger study may therefore yield different results. A second possibility is ethnicity. The previously mentioned studies were performed in a first world setting, where the demographics are likely different to the local setting. Ethnicity has been shown to have a bearing on prevalence rates of pleural effusions in patients with PE, with a study performed in the USA showing Asians to have a lower prevalence, when compared to Caucasian patients (50). This hypothesis is further borne out by the fact that a study performed on a Chinese population also showed a markedly lower frequency, in the order of 19% (7).

Some studies have shown pleural effusions associated with pulmonary emboli are typically small, unilateral and ipsilateral to the PE (6, 28). The findings of this study are quite different, showing an equal number of bilateral and unilateral effusions and a contralateral to ipsilateral ratio of 3:2 in those that were unilateral. The size findings conformed more to the international literature, with six of the 14 PE positive effusions being documented as small, and only three as large (size was not commented on in the

remainder). The small numbers may account for these differences but the greater bilaterality should be noted and may merely reflect the lack of sensitivity of CTPA in identifying sub-segmental pulmonary emboli (6).

As a secondary objective this study also compared the prevalence of pleural effusions in those with and without PE. Although there appeared to be more patients with effusions in the PE negative group versus the PE positive group (60% versus 40%), this was not significantly different. This was in keeping with international literature (7, 12).

6.4 Pulmonary Hypertension and Pulmonary Embolism

A total of 54 patients (54%) had radiological evidence of pulmonary hypertension (as indicated by a main pulmonary artery of greater than 29mm). Of these, 32 were PE negative and 22 PE positive. This translated to a 66,7% prevalence of pulmonary hypertension (PH) in those with PE (22 out of 37). While this study did not differentiate between acute and chronic pulmonary hypertension, this is still substantially higher than would be expected from combining the prevalence of both. The literature estimates the prevalence of chronic thromboembolic pulmonary hypertension to be in the region of 1-4% (11, 51) and acute pulmonary hypertension from massive PE to be approximately 10% (52).

However, that this is not a like for like comparison as these other studies excluded all those with known previous confirmed diseases leading to PH. The higher prevalence in this study is therefore likely accounted for by the confounding variables of concomitant

PH predisposing pathology, which is clearly high in the sample population. This is evidenced by the fact that even in those patients without PE, 32 out of 54 (53,3%) had radiological evidence of pulmonary hypertension.

While the frequency of pulmonary hypertension was ostensibly approximately 13% higher in the PE positive group as noted above, this was not significantly different. Moreover, as discussed, the possibility of pre-exiting pulmonary hypertension from non-PE related causes, has likely elevated the prevalence of PH in the PE positive group, making this apparent increased prevalence even more spurious.

6.5 Abnormal Parenchymal Findings

CTPA is not only useful in diagnosing PE, but is also helpful in identifying parenchymal findings that may be associated with, or be sequelae of pulmonary embolism. Furthermore, it can also identify alternate pathologies that may mimic pulmonary embolism. These abnormal parenchymal findings were categorised into four groups: peripheral wedge-shaped opacifications (likely indicative of pulmonary infarcts), consolidation and/or ground-glass opacification, atelectasis and masses.

The overall frequency of parenchymal abnormalities was 59%. The PE positive and negative groups were virtually identical in terms of prevalence of parenchymal findings. Although the overall figure is lower than that seen in similar studies, which were closer to 85%-87% range (12, 53), this is easily explained as these other studies, in contradistinction to this one, included ‘nodules’, which are a common finding.

In terms of individual parenchymal findings, a study by Karabulut showed only consolidation and wedge-shaped opacities to be significantly associated with PE (12). In a second study, by Liu *et al*, all of these CT abnormalities appeared to be more common in PE positive patients, but none were found to have a statistically significant relationship with PE (7). A third study by Shah *et al* (53) only showed a statistically significant association with peripheral wedge-shaped opacities and PE.

This study also only found peripheral wedge-shaped opacities to have a statistically significant association, albeit weak, with PE. While consolidation/GGO and atelectasis were ostensibly more common in the PE positive group and masses appeared to be more common in the non PE group, none of these findings were found to be significantly different.

While the association of peripheral wedge-shaped opacities (likely indicative of pulmonary infarct) is anticipated, as it is a direct complication of pulmonary embolus, the other findings may be found in a number of other conditions and their lack of association to PE in various studies is therefore not surprising. It can thus be concluded that parenchymal abnormalities, other than peripheral wedge-shaped opacities, are not particularly helpful in differentiating patients with and without pulmonary embolism.

6.6 Risk Factors, Wells scores, D-Dimer levels and HIV Status

There was substantial data missing for risk factors, overall Wells scores, and D-dimer levels. This precluded the use of comparative statistics. While recent surgery/immobilisation (21% cases), and malignancy (15%) were the two most commonly cited individual risk factors (as per Wells score), the lack of data did not allow for any meaningful interpretation.

A Wells score was only calculated in 10 of the 100 patients. Of these, three had PTED. While two of the three had high probability Wells scores i.e. greater than four, the small sample size did not allow for analysis of whether a higher Wells score was significantly associated with the presence of PE.

A total of 30 patients were reported to have raised D-dimers. Only 11 of the 30 were found to have PE. This is not surprising as D-dimers have a low specificity for PE and are raised in a number of conditions, including those which might mimic a PE such as cardiac failure (31).

As clinical decision rules make use of both D-dimers and Wells score, it is relevant to analyse their concomitant documentation as it relates to PE. Only 3 reports had both a documented Wells score and a raised D-dimer level. It is interesting to note that the two that had a high probability of PE, as per Wells score, did not have a PE and vice-versa. In light of the lack of data, however, not much store should be placed on this finding. What this may suggest, however, is that clinical decision rules are not routinely followed in the study setting. This would likely result in higher referral rates and lower yields than is

optimal. Alternatively, this data may just not be included by the clinicians on the referral forms.

Data on HIV status was similarly absent, with only 21 referral forms documenting HIV status. As HIV is in itself an important risk factor to PE and given that the local setting has amongst the highest prevalence rates of HIV worldwide (54), it is of particular relevance. This, however, likely relates more to the clinician not relaying the information on the referral form, rather than HIV status being unknown, as it is commonly tested for in the local setting.

6.7 Overall CTPA Findings

The vast majority of scans (88%) showed some form of CT abnormality as per the data collected, which is in keeping with similar studies (12, 53). Of these, the most common finding was pulmonary hypertension (54%), followed by consolidation/ground-glass opacification (41%) and then by pleural effusions (40%). Pulmonary embolism was present in 37% of scans. Atelectasis (19%), masses (4%) and wedge-shaped opacifications (4%) were less commonly found.

The substantially higher frequency of pulmonary hypertension is easily explained in that similar studies excluded patients with known pathology predisposing to pulmonary hypertension. The prevalence of parenchymal abnormalities, however, was in contrast to studies by Shah *et al* and Karabulut *et al* which both found atelectasis to be the most common parenchymal finding (present in 66% and 44% of patients respectively) (12, 53).

The lower frequency of atelectasis in this study is surprising as mimickers of PE are frequently associated with some form of atelectasis (55), including pleural effusions, which was in itself a common finding. Pleural effusions were evident in 56% in the study by Shah *et al* and in and 43% of patients in the study by Karubulut *et al*(12), which was more in keeping with the findings of this study.

As already discussed, only wedge-shaped opacities showed a significant association with PE in the current study. It is therefore apparent that pleuro-parenchymal abnormalities, with the exception of these wedge-shaped peripheral opacities, are of limited value when assessing for PE on CTPA. The same remains true for radiological evidence of pulmonary hypertension.

6.8 Possible Limitations of the Study

The study had a number of possible limitations:

- **Lack of data** - being retrospective in design, not all the data that the researcher wished to collect was available. This was particularly true for Wells score, D-dimer levels and HIV status.
- **Missing data** – as per 4.6 certain assumptions needed to be made with respect to missing data. Of particular note is the assumption that if the presence of pleural effusions were not mentioned in the report, it was deemed to be absent. This was based on the fact that this finding is easily identified and generally noted. However, as the researcher did not review the reports himself, there is room for error.
- **Interobservor variability** - the completeness and accuracy of the radiological reports may vary depending on the level of expertise and experience of the reporting radiologist. While the researcher attempted to minimise this issue by

only using consultant radiologist reports, even among consultants, some variability may exist.

- **Lack of external validity** – as this is a single centre study, the results and findings may not be generalizable to the population at large.

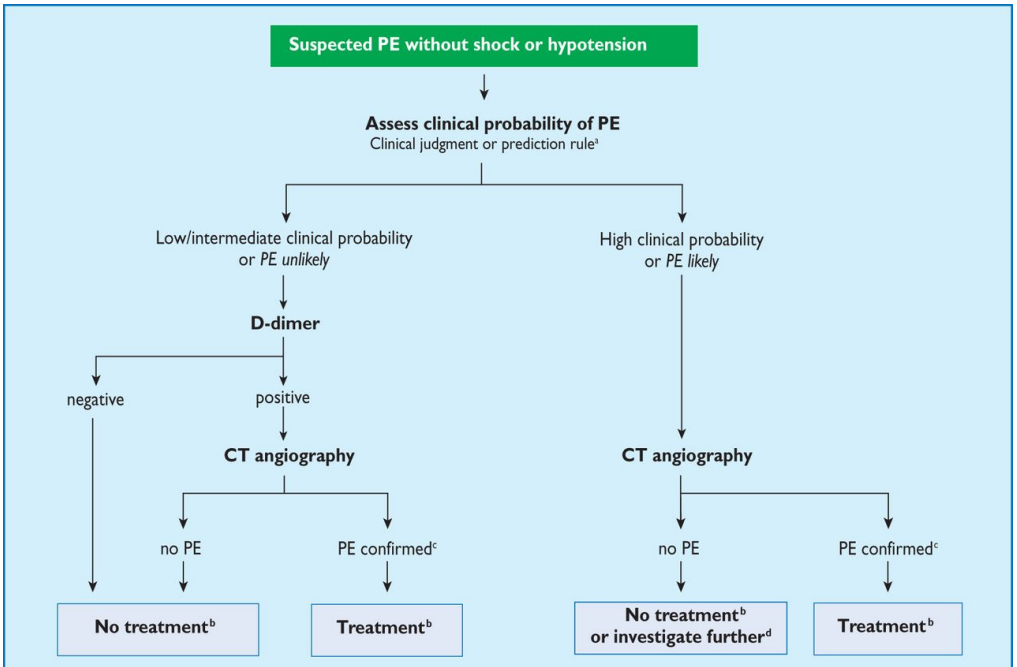
6.9 Future Applications

6.9.1 Referral template and radiological care pathway

It is apparent from this study that there is a lack of information, particularly with respect to Wells score, D-dimer level and HIV status. This, in turn, may suggest a low usage of clinical decision rules, which will inevitably result in unnecessary referrals for CTPA and increased patient risk. Moreover, unnecessary investigations further burden an already over-utilised and under-resourced public health sector.

This has led the researcher to create a referral template (See Appendix C), with a view to alleviating the above-mentioned issues. This template outlines the necessary inputs that the clinician should specify. The referral template expands on the conventional patient information sticker, which typically only contains patient name, demographic details such as age and gender, and the hospital number. The template also incorporates D-dimer levels and Wells score, features of clinical presentation and provides space to enter other relevant information. This includes specifying other known risk factors, which may not be included in Wells score, such as connective tissue diseases and clotting abnormalities. Moreover, information with respect to relevant previous imaging, which is of paramount importance, is also provided for.

The timing of this application is fortuitous, as the department of radiology at CMJAH has just gone live with a Picture Archiving and Communication System (PACS), which will be linked to the Radiological Information System (RIS) and ultimately to the Hospital Information System (HIS). While a lengthy explanation of what PACS, RIS and HIS are, is beyond the scope of this research, the point is that the implementation of this technology will allow for control of both inputs and outputs. Furthermore, previous imaging (along with reports) can easily be accessed. In terms of inputs, the patient sticker information, Wells score and D-dimer values can be made mandatory, while other pertinent information such as HIV status, clinical presentation and other risk factors can have the option for data inputs where available. This information can then feed a pre-designed clinical decision rule, which algorithmically determines the radiological (and even management) pathway. An example of such an algorithm is provided in Figure 6.1.



CT = computed tomographic; PE = pulmonary embolism.
[a]Two alternative classification schemes may be used for clinical probability assessment, i.e. a three-level scheme (clinical probability defined as low, intermediate, or high) or a two-level scheme (PE unlikely or PE likely). When using a moderately sensitive assay, D-dimer measurement should be restricted to patients with low clinical probability or a PE-unlikely classification, while highly sensitive assays may also be used in patients with intermediate clinical probability of PE. Note that plasma D-dimer measurement is of limited use in suspected PE occurring in hospitalized patients.
[b]Treatment refers to anticoagulation treatment for PE.
[c]CT angiogram is considered to be diagnostic of PE if it shows PE at the segmental or more proximal level.
[d]In case of a negative CT angiogram in patients with high clinical probability, further investigation may be considered before withholding PE-specific treatment.

Figure 6.1 2014 European Society of Cardiology guidelines on the diagnosis and management of acute pulmonary embolism(56)

The above algorithm can be further modified to suggest chest radiography as a first-line investigation. While chest radiographs are relatively insensitive to the diagnosis of PE (57), they are useful in identifying mimickers of PE as well as in aiding the interpretation of V/Q scans. Furthermore, chest radiographs have lower radiation, lower cost and increased ease and convenience of use when compared to a CT scan.

Similarly the pathway can incorporate suggesting V/Q scans as an alternative investigation in appropriate settings. These include patients with renal dysfunction that prohibit the use of contrast agents and young female patients where there is concern over breast radiation. It is also useful as an alternate investigation in non-diagnostic CTPAs.

6.9.2 Reporting Template

CTPA reports are not standardised, which results in inconsistent and at times absent data. This not only impacts the quality of the report and by association service delivery to the clinician, but also reduces the ability to perform research. As such, the researcher has created a reporting template (See Appendix D), which provides the radiologist with a quick, easy to use checklist. It can similarly be embedded into the PACS and RIS system, so that it is automatically generated once the report dictation is initiated.

While its design and content is fed by existing templates such as the Radiological Society of North America (RSNA) CTPE template (58), it has been substantially enhanced and modified. These changes not only incorporate relevant elements derived from the literature review and this study, but also from the day-to-day experience and knowledge of the author who is a Fellow of the College of Radiologists of South Africa.

The checklist covers salient information with respect to the PE itself, as well as complications and associated and/or alternate findings. It breaks it systematically into information around the embolus itself, then into the key vascular complications, viz. pulmonary arterial hypertension and by extension right ventricular strain. It then moves on to pleural complications/findings followed by parenchymal findings and then progresses to the general findings a reader needs to look at when reviewing a CT chest of any nature. It does assume some baseline radiological knowledge for e.g. that the pulmonary artery trunk is measured at the bifurcation, and that the reader understands how to characterise a mass, but is extensive enough to provide a fairly full checklist to guide a junior registrar and to remind a more senior interpreter.

6.9.3 Future research

This study, both through its limitations and findings gives rise to a number of future research opportunities, particularly around the first 3 objectives. These include:

- **Yield –** relating to the higher yield rate of PE positive patients in this study when compared to the international literature. It was postulated that *inter alia* this

might relate to higher frequency due to increased HIV/TB prevalence. Another possible causative factor could be overcalling by the radiologist. This lends itself to the following research opportunities:

- Comparative analysis of the prevalence of PE in South Africa in HIV and/or TB infected and non-infected patients respectively
- Interobservor variability in assessing PE on CTPA

- **Pleural effusions** - relating to lower prevalence and different characteristics of pleural effusions in the PE positive group in this study, which show stark differences with respect to the international literature. An opportunity exists to analyse the following:
  - Ethnic differences in the prevalence of pleural effusion in the local setting
  - Characteristics of pleural effusions in PE positive patients
- **Pulmonary hypertension –** the significantly higher frequency of pulmonary hypertension in this study, compared to other similar studies, likely relates to not excluding patients with known conditions predisposing to pulmonary hypertension (PH). A study using this exclusion criteria could be performed in order to compare like with like:
  - Frequency of pulmonary hypertension in patients with no known predisposing factors for PH, undergoing CTPA suspected for pulmonary embolism

7.0 CONCLUSION

Pulmonary thromboembolic disease (PTED) is a common clinical entity, with significant morbidity and mortality. However, due to its relatively non-specific symptoms, pulmonary embolism remains a challenge to diagnose. This has led to apparent increasing referrals for CTPA and decreasing yield rates raising concern for patient safety.

Part of the diagnostic challenge alluded to above, is the myriad of causes of symptoms that may mimic pulmonary embolism (PE). There are a number of pleuro-parenchymal abnormalities that may be visualised on CTPA that could account for these symptoms. Of particular interest, is pleural effusion. Pulmonary embolism is an under-recognised cause of pleural effusion, and delay in therapy may cause an increase in morbidity and mortality. Pleural effusions as mentioned, however, are not the only abnormal finding, and this led the researcher to further interrogate the frequency and association, if any, that these findings may have with PE.

In light of the above, this study assessed the diagnostic yield in patients at Charlotte Maxeke Johannesburg Academic Hospital undergoing CTPA for suspected PTED and documented the occurrence of pleural effusion, pulmonary hypertension and abnormal parenchymal chest findings in patients with and without documented PTED. It also sought to capture relevant clinical and biochemical parameters such as risk factors, Wells Score, D-dimer levels and HIV status.

While similar studies have been done internationally, there is a dearth of literature in the local setting. South Africa provides a markedly different environment, including *inter alia* higher HIV/AIDS and TB prevalence (both of which are independent risk factors for PTED), distinctive demographic profile and in many cases, a more constrained and over-burdened public sector. It is therefore the hope of the researcher that the findings of this research provides information which will assist the clinician in his referral process, enhance the quality of the radiological service provided and streamline the process in general.

As an in-depth discussion of results is provided in chapter six, only the key findings are mentioned here. There were two primary objectives: yield rate and frequency of pleural effusions.

- **Yield** - A diagnosis of pulmonary embolism was confirmed in 37 cases (37%). The yield rate compared favourably with other studies, and while this may be due to better clinical assessment, other causes that could contribute to this, include *inter alia* higher HIV/AIDS and TB prevalence, and possible overcalling by the radiologist.
- **The frequency of pleural effusions** - Overall 40 patients (40%) had an identifiable pleural effusion on CTPA. Of the 60 patients with no pulmonary embolism, 26 (43,3%) had pleural effusions. A total of 14 patients out of 40 patients (37,8%) with PE had pleural effusions. . There was no significant differences in frequency in those with and without PTED. The frequency of pleural effusions was lower than that quoted in other studies and showed somewhat different characteristics to those typically documented. The frequency disparity may relate to ethnic differences (substantiated

by the literature) and the characteristics may merely be as a result of the small amount of available data in this regard.

In terms of the secondary objectives, pulmonary hypertension was present in 54% of cases with no significant difference between the PE positive and negative groups. This was a far greater proportion of cases when compared to other studies. However, other studies excluded patients with pre-existing conditions that may cause pulmonary hypertension, which would account for the difference. Abnormal parenchymal findings were a common finding, with 59% of cases showing at least one parenchymal abnormality. This was not unanticipated due to the number of PE mimickers discussed. The most common parenchymal finding was consolidation/ground-glass opacification (41%), followed by atelectasis (19%). Wedge-shaped opacification and masses both had a prevalence of 4%. Overall, only peripheral wedge-shaped opacities had an association with pulmonary emboli. This finding is not without merit, as the other abnormalities are commonly found in a number of other conditions, whereas peripheral wedge-shaped opacities in this case likely indicate pulmonary infarct, the most common cause of which is PE.

While not a defined objective, it was also clear that the referral form seldom provided information with respect to individual risk factors (as per Wells score), overall Wells score, D-dimer levels and HIV status. While these may merely be omissions on the form, it may also imply that clinical decision rules and risk factors are not properly assessed.

It can therefore be concluded that pleuro-parenchymal abnormalities, with the exception of peripheral wedge-shaped opacities, as well as evidence of pulmonary hypertension are of limited value when assessing for PE on CTPA.

As with most research, the findings themselves are not the only benefit of the study, but much is also gained through the analyses and interpretation of the results. Moreover, the further questions it catalyses and future research opportunities it presents, is what drives growth of the current knowledge base. This study was no different.

The researcher used the findings to not only identify further research opportunities but also to create a referral and reporting template that will hopefully alter the entire radiological care pathway, pro-actively assisting both the clinician in his/her referral patterns for CTPA and similarly giving guidance to the radiologist, thereby improving his/her service delivery.

It is clear that diagnosis of pulmonary embolism is fraught with difficulty starting with clinical diagnosis, through to determining the appropriate investigations and then interpreting the many additional or alternate radiological findings. It is the researcher's wish that this study will in some way contribute to creating a more efficient and effective radiological pathway for suspected pulmonary embolism, that not only improves patient care, but also catalyses further research.

APPENDIX A: ETHICS CLEARANCE CERTIFICATE

R14/49 Dr Shane Dorfman

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160391

NAME: (Principal Investigator)	Dr Shane Dorfman
DEPARTMENT:	Diagnostic Radiology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	The Frequency of Pleural Effusion and Additional Chest Findings in Patients Undergoing Computerised Tomographic Pulmonary Angiography for Suspected Pulmonary Embolism at a Level Four Academic Hospital in South Africa
DATE CONSIDERED:	Adhoc
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof Charles Feldman and Dr Grace Rubin
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	23/03/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004, 10th floor, Senate House/2nd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.**

Principal Investigator Signature

Date 4/4/16

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX B: DATA COLLECTION SHEET

Num-ber	Anony-mised patient Code	Age (years)	Gender	Risk Factors* (as per Wells)	Wells score	D-dimer Level	HIV Status	Pulmon-ary Embolus	Pleural Effusion	Pulmon-ary Hyper-tension	Size PA (mm)	Wedge-shaped Opacific ation	Consolid ation/ GGO	Atelec-tasis	Mass
1															
2															
3															
4															
5															
6															
7															
8															
9															
10															
11															
12															
13															
14															
15															
…															
…															
100															

* Each risk factor was individually captured

APPENDIX C: REFERRAL TEMPLATE

REFERRAL TEMPLATE: CTPA

Patient Sticker

D-dimer Value:

Wells Score:

HIV status:

Clinical presentation:……

……

Other relevant information including risk factors:……

……

……

Previous imaging: Investigation/Date/Findings

1.

2.

3.

APPENDIX D: REPORTING TEMPLATE

REPORTING TEMPLATE: CTPA

1. Pulmonary Embolism: N ☐ Y ☐ Site(s)/Acute &/or chronic/

2. Pulmonary HT: N ☐ Y ☐ Pulmonary Artery Caliber (Trunk/L/R main)

3. RV Strain: N ☐ Y ☐ RV:LV/Septal bulge/IVC reflux

4. Pleural Effusion: N ☐ Y ☐ Side(s)/Size (S/M/L)/△size/Loculations

5. Parenchymal Abn:

- **Consolidation:** N ☐ Y ☐ Location(s)
- **GGO*:** N ☐ Y ☐ Location(s)
- **Nodules:** N ☐ Y ☐ Single vs Multiple/Type/Size/Site(s)
- **Masses:** N ☐ Y ☐ Characteristics/Size/Site(s)/Adj. structures
- **Atelectasis:** N ☐ Y ☐ Type/Extent/Site(s)/Cause (if visualised)
- **PWO**:** N ☐ Y ☐ Location(s)

*GGO =Ground-glass opacification; **PWO = Peripheral wedge-shaped opacifications

6. Lymphadenopathy: N ☐ Y ☐ Location(s)/Size/Characteristics

7. Heart & Vasculature: NL ☐ ABN ☐ Abnormality?

8. Thyroid: NL ☐ ABN ☐ Abnormality?

9. Visualised Abdomen: NL ☐ ABN ☐ Abnormality?

10. Visualised Bones: NL ☐ ABN ☐ Abnormality?

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