GHANA COLLEGE OF PHYSICIANS AND SURGEONS

FACULTY OF RADIOLOGY

CORRELATION OF EMBOLIC BURDEN AND RIGHT HEART DYSFUNCTION PARAMETERS WITH SHORT-TERM MORTALITY IN ACUTE PULMONARY EMBOLISM USING COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAPHY

Submitted to Faculty of Radiology, in partial fulfilment of the requirements for the conferment of a Fellow of the Ghana College of Physicians (FGCP)

ASAMOAH, Nana Akua Konama

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DECLARATION

I, Dr. Nana Akua Konama Asamoah, hereby declare that this work is my dissertation submitted to the Ghana College of Physicians and Surgeons in part fulfilment of the College's requirements of its Fellowship award The results are of my own composition aside from other individual's work, which has been duly recognized in the reference area. This proposal has not been used for any other degrees or diplomas in the past.

Signature: NAAsamoah

Date: 15/10/2022

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We hereby certify that Dr. Nana Akua Konama Asamoah is a Senior resident currently in the Fellowship training in the Department of Radiology. In compliance with the Fellowship requirements, she is submitting this final dissertation titled "CORRELATION OF EMBOLIC BURDEN AND RIGHT HEART DYSFUNCTION PARAMETERS WITH MORTALITY IN ACUTE PULMONARY EMBOLISM USING COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAPHY" was supervised by us.

DR (MRS) A. BADU-PEPRAH
CONSULTANT (RADIOLOGY)
KOMFO ANOKYE TEACHING HOSP.
KUMASI

.....14/10/2022

Dr. Augustina Badu-Peprah (MBChB, FWACS, FGCP)

Supervisor

Consultant Radiologist, Komfo Anokye Teaching Hospital

.....

Dr. George Asafu- Adjaye Frimpong (FACHARZT RADIOLOGIE, Germany)

Supervisor

Senior Lecturer, Head of Radiology KNUST School of Medicine and Dentistry, Consultant Radiologist, KNUST Teaching Hospital

KOMFO ANOKYE
TEACHING HOSPITAL

P. O. Box 1934
KUMASI - GHANA
Tel: +233 - 3220 - 22301- 4
Fax: +233 - 3220 - 24654/24621
Website: www.kathhsp.org

Our Ref. No:.....

Your Ref. No:.....

CERTIFICATION BY HEAD OF DEPARTMENT, KOMFO ANOKYE TEACHING HOSPITAL

I hereby attest that Dr. Nana Akua Konama Asamoah is a senior resident currently in Fellowship training in the Department of Radiology. In compliance with the Fellowship requirements, she is submitting this final dissertation titled "CORRELATION OF EMBOLIC BURDEN AND RIGHT HEART DYSFUNCTION PARAMETERS WITH SHORT-TERM MORTALITY IN ACUTE PULMONARY EMBOLISM USING COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAPHY"

HEAD OF DEPARTMENT: Dr. Augustina Badu-Peprah ((MBChB; FWACS, FGCP)

DR. MRS. AUGUSTINA
BADU-PEPRAH
HEAD RADIOLOGY DIRECTORATE
KATH-KUMASI

fv Signature: .....

Date: 14/10/2022

Kwame Nkrumah
University of Science
and Technology, Kumasi

College of Health Sciences
SCHOOL OF MEDICINE AND DENTISTRY

DEPARTMENT OF RADIOLOGY

CERTIFICATION BY HEAD OF DEPARTMENT

I hereby certify that Dr. Nana Akua Asamoah is a Senior resident currently in Fellowship training in the Radiology Directorate at the Komfo Anokye Teaching Hospital. In compliance with her Fellowship requirements by the Ghana College of Physicians and Surgeons, she is submitting this dissertation proposal titled "CORRELATION OF EMBOLIC BURDEN AND RIGHT HEART DYSFUNCTION PARAMETERS WITH MORTALITY IN ACUTE PULMONARY EMBOLISM USING COMPUTED TOMOGRAPHY ANGIOGRAPHY" which was conducted at Spectra Health, a Radiodiagnostic & Interventional radiology center and an affiliate research site for the Kwame Nkrumah University of Science and Technology.

HEAD OF DEPARTMENT: DR. GEORGE ASAFU-ADJAYE FRIMPONG (MBChB, FACHARZT RADIOLOGIE, Germany Consultant Radiologist, KNUST Teaching Hospital).

SIGNATURE: .....

DATE: 14th OCTOBER, 2022

DEDICATION

I dedicate this work to my, loving husband Dr. Daniel Osei-Kwame and my darling twins, Kyle Osei-Kwame and Kyla Osei-Kwame. You guys are my reason…… Love you so much!

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ABSTRACT

Introduction: Various parameters, as identified on computed tomography pulmonary angiography (CTPA) in patients with acute pulmonary embolism (PE) are being used internationally to categorize patient into low or high risk to enhance choice of management by physicians. Data on Computed tomography (CT) pulmonary angiographic parameters as predictors of mortality in patients with acute pulmonary embolism and how they correlate with patient outcome in Ghana is minimal in comparison to developed countries.

Aim: The main aim of the study was to identify the most significant parameter on CTPA that predicts short-term mortality in patients with acute PE.

Material and Methods: The study was a prospective cross-sectional design assessing the right heart dysfunction parameters and clot/embolic burden as predictors of short-term mortality in patients with Acute pulmonary embolism. 60 patients presenting to spectra health with CTPA findings consistent with acute PE were Conveniently sampled. Additionally, Student t-test and logistics regression were conducted to compare and predict the best radiological parameter for mortality. A chi-square test was used in addition to Fisher's exact test at a 95% level of significance to test for the association of age and duration of death, age and outcome of patient.

Results: Sixty patient (60) patients, comprising 26 (43.3%) males and 34 (56.67%) females were enrolled in the study with a mean age of 58 years which ranges from 29 years to 89 years. Out of the 60 patients, 20 (33.33%) died, 40 (66.66%) survived. Of all the parameters evaluated on CTPA, the Rv/Lv ratio (P-value 0.001), Rv diameter (P-value 0.003), and clot load score (P-value 0.001), were highly associated with short term mortality on bi-variate analysis. However, on multivariate analysis of Rv/Lv ratio (P-value 0.118), Rv diameter (P-value 0.381), and clot load (P-value 0.03), the clot load score was found to be the most significant parameter for predicting short term mortality.

Conclusion: Right ventricular short axis diameter (Rv), Rv/Lv ratio (RV enlargement), and clot load score are significantly associated with short term mortality.

The results of this present study, hopefully serve as a baseline upon which future studies build to improve outcomes in patients with acute PE.

Key words: Computed tomography, Computed tomography pulmonary angiography, Embolus, Clot load.

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LIST OF ABBREVIATIONS

CTPA……Computed Tomography Pulmonary angiography

CT……. Computed tomography

DVT……. Deep vein thrombosis

ICOPER……International cooperative pulmonary embolism registry

IVC……Inferior vena cava

KNUST…….Kwame Nkrumah University of Science and Technology

Lv……..Left ventricle diameter

PA…… Pulmonary Artery

PA/Ao……Pulmonary artery/Aortic diameter ratio

PE……..Pulmonary Embolism

PIOPED……Prospective Investigation of pulmonary Embolism Diagnosis

SVC……..Superior vena cava

Rv……..Right ventricle diameter

Rv/Lv……Right ventricular/left ventricular diameter ratio

VTE……..Venous thromboembolism

CHAPTER ONE

INTRODUCTION

1.0 Background

Pulmonary embolism (PE) is a familiar ailment evidenced as blood clots partially or completely occluding the main pulmonary arteries or one or more of their more distal branches. The occlusion of the vascular lumen, be it partial or complete, results in the obstruction of blood flow to the lungs which can result in death from acute right heart failure. Overall mortality from acute pulmonary embolism (PE) is known to be high, and as such the need for urgent diagnosis and prompt treatment, to minimize the risk of PE associated morbidity and mortality. In Ghana, according to E. Aniteye et al, even with the use of thrombolysis, the mortality rates are still high in patients with massive PE[1]. Presentations of acute PE vary vastly among affected individuals. They may range from the patient being asymptomatic to death. In the work up of acute PE, clinicians employ clinical scoring systems, laboratory biomarker and imaging findings as guides.

Risk stratification based on these clinical scoring systems (e.g. Well's scores), laboratory biomarkers and imaging findings assist in determining and implementing the best treatment option for patients [2]. Pulmonary embolism, in the United States, according to Goldhaber et al is a common cardiopulmonary and cardiovascular illness with the mortality rate being 15% in the first 3 months of diagnosis, making it likely as lethal as acute myocardial infarction[3].

The thrombus/thrombi that results in a pulmonary embolism in most cases, arises from the deep venous system of the lower limbs. But in a few rare instances, the thrombus may arise from the right heart chambers, the veins of the upper extremities, the kidneys and the pelvis. The dislodged thrombus then makes its way to the lungs where it lodges itself at the point of bifurcation of the main pulmonary artery or at one or more of its lobar branches with consequent compromise of the hemodynamics of the right side of the heart and subsequently affecting gas exchange. Due to the high mortality associated with acute pulmonary embolism, the relevance of risk prediction and stratification to aid in adopting the most appropriate management or treatment options cannot be over emphasized[4].

Based on their severity, cases of acute PE may benefit from various modes of management. For example, those with high risk of mortality may benefit from management and treatment options such as close monitoring within the intensive care unit or thrombolytic treatment. Whereas for patients with lower risks, anticoagulation treatment may suffice with subsequent discharge[4] [5]. Clinical and laboratory indicators form the basis for most of the risk prediction rules currently available. In the evaluation of a patient with acute PE, added information could be obtained using diagnostic imaging.[6] [7]

In this regard, in the United States, computed tomography pulmonary angiography (CTPA) is now frequently used and is extensively accepted as the preferred diagnostic imaging modality in patients with suspected acute pulmonary embolism (PE). Reasons for this preference include shorter acquisition times, timely reports, lower incidence of inconclusive results, and the fact that it can detect additional pathologies which may be of diagnostic interest CTPA[8].

1.1 Rational for the study

This study sought to identify and evaluate how the various parameters of right heart strain and clot burden influence the outcome of patients with acute pulmonary embolism (PE). However, the primary purpose of this study was to determine which parameter/parameters was/were most relevant in predicting short term mortality, as pertains to our specific population; with short term mortality being defined as in-hospital death or death within a 30 day period following an account of acute PE computed tomography (CT) scan[9]. There are numerous parameters that influence patient outcome and short-term mortality. The identification and incorporation of the single most significant parameter into the radiological reports would serve as a guide to physicians, in choosing the optimum management or treatment option to improve patient outcome. For example, Apfalter et al indicated that pulmonary artery obstruction scores in patients with acute PE, could indicate the severity of an acute PE episode but was poor in its ability to predict death and also it took much more time to calculate in comparison with the calculation for vascular diameter measurements. Thus the routine assessment of obstructive indices in the light of an acute PE could not be justified[10]. Also, the parameters with less significant correlations could be weaned out of reports in an attempt to reduce reporting times, so as not to delay physicians in the selection of appropriate treatment.

In summary, the identification of the various parameters influencing short term mortality and the identification of the most significant parameter of severe acute PE associated with short-term mortality is of great relevance. It allows the adaptation of shorter, less time-consuming radiological reporting systems that provide nothing but relevant diagnostic information. The relevant information acquired from the identification of such parameter and their relation to mortality can influence patient management options, which hopefully will improve outcomes. In the end, the purpose of this research was to have a baseline for the development of a CTPA imaging-based risk stratification, or a simple prognostic module using CTPA. This CTPA imaging-based risk stratification could be built upon for implementation, within our local setting to guide management of patient with acute PE.

1.2 Problem statement

Worldwide, CTPA is being used as the first line imaging modality for acute for diagnosis PE[11] [12]. Various researches have been done by other authors to identify its usefulness as a prognostic imaging marker for better risk stratification in patients with acute PE[13]. This may serve as an aid to physicians, where prompt identification and initiation of the most appropriate treatment option is of a necessity.

Research done, in other centers have shown that various parameters are useful in assessing the severity and possible outcome of this and may therefore influence treatment options and overall outcome ailment[14] [15] Various parameters and their correlation with outcome have been assessed by various authors[9].

These parameters primarily include the signs of right heart strain, clot volume measurement and clot burden (load) measurements. The correlations of these parameters with patient outcome vary. The identification of which of these parameter/parameters correlates most significantly with the severity and patient outcome also vary[16]. Their incorporation into reports may assist physicians with choosing the most appropriate treatment option, thus timely treatment made available to patients. Venous thromboembolism (VTE) is a generally known precursor to PE. However, in Ghana, a postmortem-based study done, in a teaching hospital showed that venous thromboembolism (VTE) is a clinical diagnosis which was frequently missed by clinicians[17]. Unfortunately, in Ghana there is no known research that correlates the various parameters with mortality. This study seeks to fill in this gap by identifying the various parameters and to demonstrate exactly which parameter/parameters are most associated with short-term mortality in patients with acute PE using CTPA.

1.3 Hypothesis

Right Heart Dysfunction and Embolic Burden CTPA parameters are accurate predictors of short-term mortality in patients with acute PE.

1.4 Research Question

1. What are the demographic characteristics of patients with acute PE?
2. How accurate are the various CTPA parameters in predicting short-term mortality in acute PE?
3. What Rv/Lv ratio is associated with short-term mortality?
4. What clot load is associated with short-term mortality?
5. Which CTPA parameter is the most significant predictor of short-term mortality in acute PE?

1.5 Objectives of the study

1.5.1 Aim of the Study

The main aim of the study is to identify the most significant parameter(s), on CT pulmonary angiography that predicts short-term mortality in patients with Acute PE.

1.5.2 Specific objectives

1. To determine the demographic characteristics of patients with acute pulmonary embolism.
2. To identify the accuracy of the various radiological parameters for prediction of short-term mortality in acute PE on CTPA.
3. To determine the Rv/Lv ratio associated with short-term mortality using CTPA.
4. To determine clot load associated with short-term mortality using CTPA
5. To identify the parameter(s) which is/are the most significant predictor(s) of short-term mortality.

CHAPTER TWO

LITERATURE REVIEW

2.0 Introduction

Venous thromboembolism (VTE) has two clinical presentations. It may present as Pulmonary embolism (PE) or as Deep vein thrombosis (DVT); both of which share the same predisposing factors and similar associated co-morbidities[18]. In most instances, PE occurs secondary to DVT. Approximately 50% of patients with proximal DVT have an associated PE at a lung scan, but these DVTs are usually asymptomatic clinically[19]. When using diagnostic techniques with high sensitivities, DVT in the lower limbs can be found in about 70% of the patients with acute PE[20 21].

Inspite of the fact that PE and DVT are manifestations of a VTE, DVT and PE each have unique defining features. An initial acute episode or recurrence of PE is associated with an increased risk of death when compared to those presenting with DVT[22]. In one instance of a prospective cohort study showed that in acute PE the case fatality rate ranged from 7% - 11%[23]. In this same study PE related case fatalities were noted to exponentially increase with age, and it was higher in African-Americans than in Caucasians and between men and women, there was no difference seen in their case fatality rates[23]. In about 30% of patients if left untreated, acute PE is lethal, however this can be reduced to about 2% to 10% with prompt diagnosis and immediate treatment[3]. In Sub-Saharan Africa, a study by Tambe et al indicated a positivity rate of 32% for patients with acute PE which was higher than that recorded by the multicenter Prospective investigation of pulmonary embolism diagnosis (PIOPED) II study rate of 23%[24]. This chapter elaborates risk factors, pathophysiology, various parameters and their predictive value of short-term mortality in acute PE.

2.1 Risk Factors

Patients without any identifiable risk factors or predisposing factors may still present with acute PE, however, when carefully sought, usually one or more factors predisposing them to PE will be identified. According to the International Cooperative Pulmonary Embolism Registry (ICOPER), 20% of the patients had PE with no identifiable cause (idiopathic/unprovoked)[25].Some risk factors can be acquired and others may be hereditary. A combination of the two groups of risk factors may also be found in some patients.

2.1.2 Acquired risk factors

Sedentary life style, recent surgery (such as total hip replacement), trauma, obesity, increasing age, neurological disease, cigarette smoking and personal history of venous thromboembolic disease, prolonged air travel, physical immobility for long periods are some of the acquired conditions known to increase the risk of venous thromboembolism and consequently PE [26]. Other recognized acquired risk factors include the presence of spinal cord injuries and established malignancy. The antiphospholipid antibody syndrome is also noted as one of the causes of acquired hypercoagulable states. These are known to increase the risk of arterial thromboembolism and venous thromboembolism. Hyperhomocysteinemia, is usually caused by an acquired deficiency in folate, but in certain cases, it may be as a consequence of an inherited deficiency of the enzyme, methylenetetrahydrofolate reductase[26].

In women, pregnancy, the use of oral contraceptives and hormone replacement in post-menopausal women have also been known to increase the risk of hypercoagulable states and thus the risk of PE. In addition to the risk associated with hypercoagulable states, being it acquired or inherited, research show a correlation between atherosclerotic disease and spontaneous venous thrombosis[26 27].

2.1.3 Hereditary risk factors

Patients who present with recurring or unexplainable episodes of venous thromboembolism, females with repetitive spontaneous abortions, and various family members with venous thromboembolism are suspected to have inherited thrombophilias. These individuals are usually of a younger age group[26]. Various populations have various prevalence for these inherited thrombophilias. Significant among the thrombophilias are prothrombin gene mutation, deficiencies of protein C, protein S and Antithrombin III, as well as activated protein C resistance from Factor V Leiden[26].

2.2 Natural history of Acute Pulmonary embolism (APE).

Majority of PE's are usually as a result of DVT, thus, instead of considering DVT and PE as separate entities, the natural history of VTE should be evaluated as a whole to avoid overlooking significant findings that might otherwise be missed if they are considered as completely separate entities. History has it that studies on the natural history of VTE were initiated in the 1960s[28].

A report presented at that time showed that for 30% of the patients, DVT of the calf started at surgery and was noted to spontaneously resolve with a few days, but in approximately 25% of the patients, a proximal DVT and PE developed [18]

There is evidence that DVT occurs more frequently in orthopedic surgery than in the general population, the first two (2) weeks after surgery carry the highest post-op risk for DVT [20] [18].

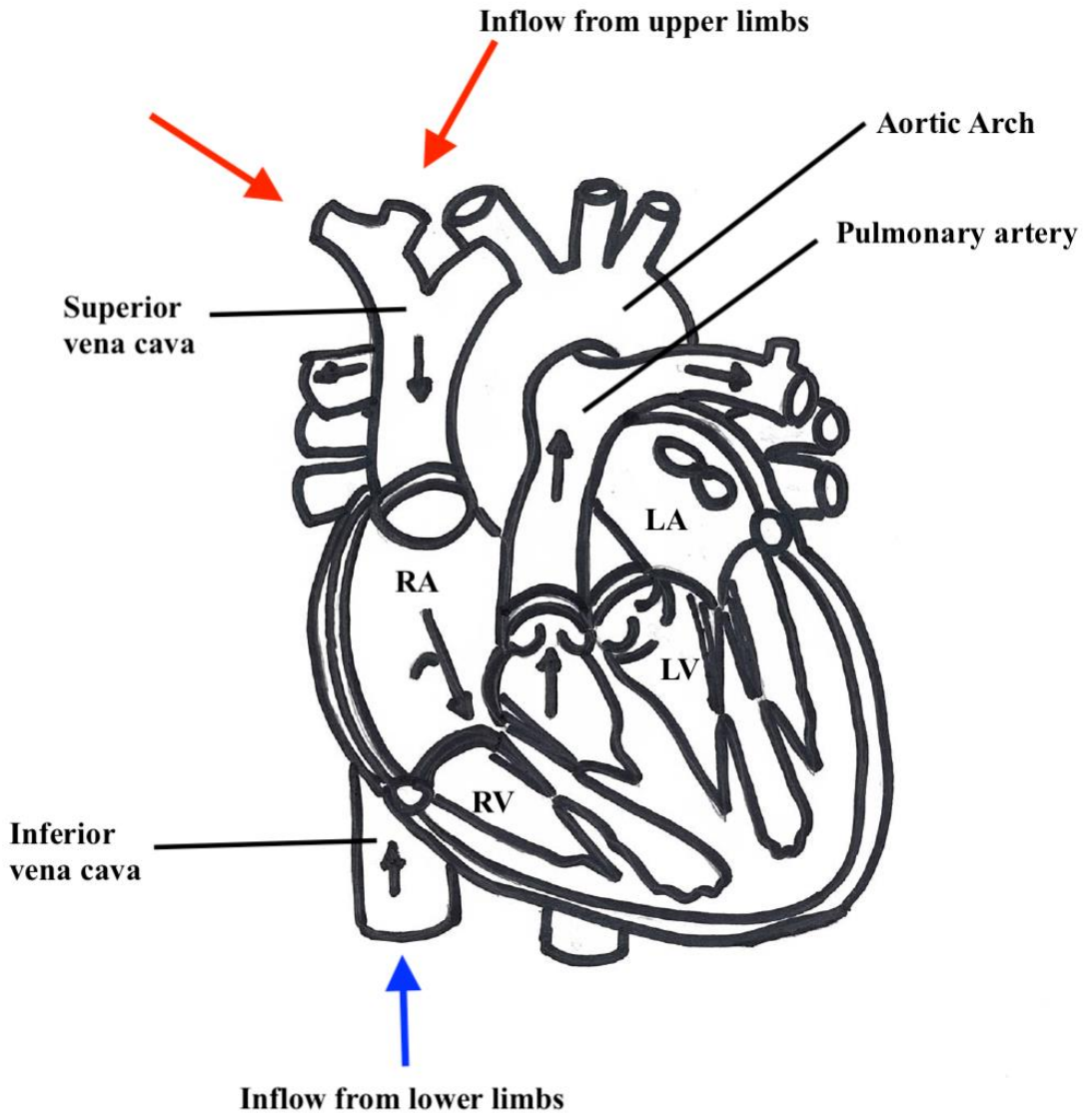
Commonly, within 3 to 7 days from onset of DVT is the period within which PE occurs and in approximately 10% of patients, it can be fatal within an hour from onset of symptoms with the diagnosis being unrecognized clinically in fatal cases. In 5% - 10% , PE presents with shock or hypotension, while up to 50% of the affected individuals present without shock, but with laboratory findings indicative of Right ventricular dysfunction (RVD), which tends to suggests a prognosis which is poorer [29] [30].

Complete resolution after PE occurs in about two-thirds of patients[31]. The majority (more than 90%) of PE related deaths occur in the untreated patients, most likely because they were not recognized [32]. In patients with PE that are treated, mortality is thought to occur in less than 10% of the cases. Pulmonary hypertension seen in patients with Chronic thromboembolic disease was noted in approximately 0.5 % – 5% in patients treated for PE[20] [18].

2.3 Pathophysiology

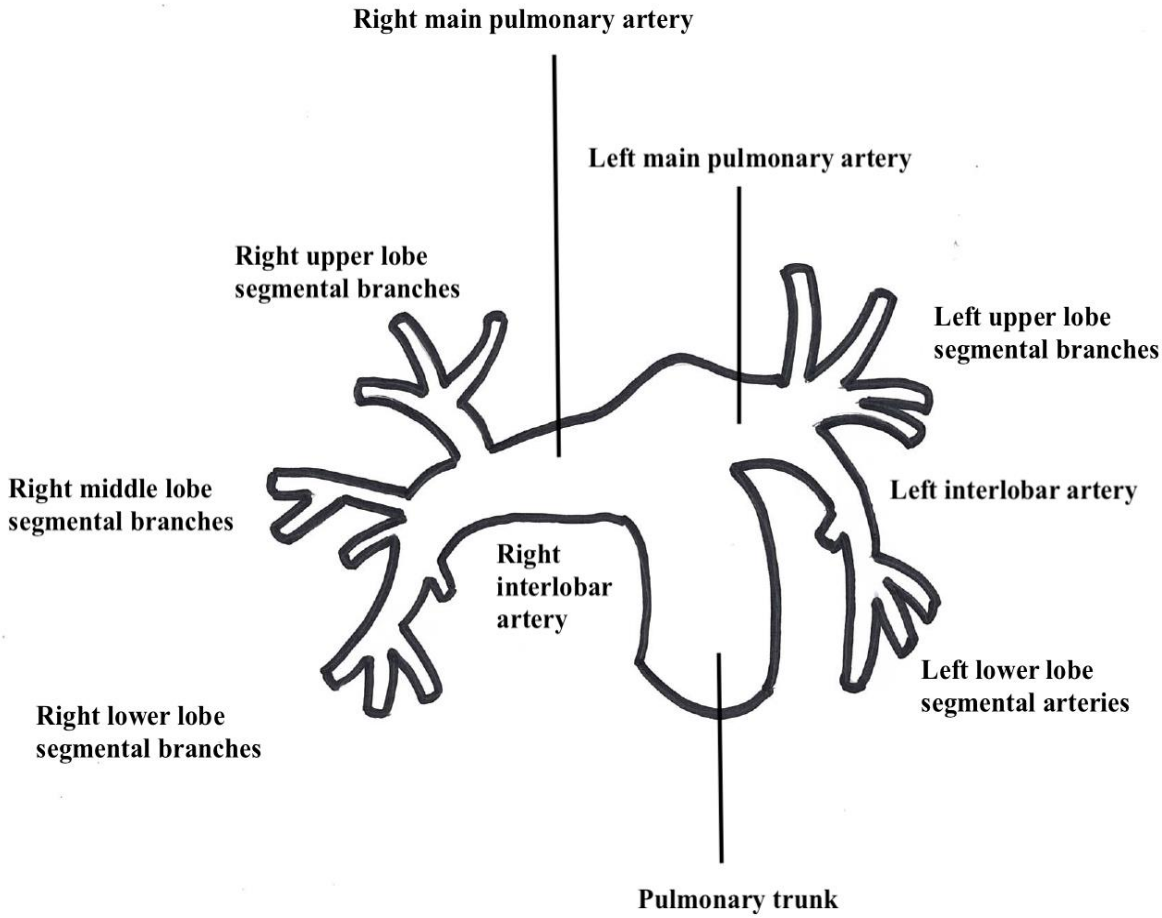
The outcomes of acute PE are mainly reflected in the hemodynamic state of the affected individuals. When more than 30 – 50% of the pulmonary arterial bed is occluded by a thromboembolism, hemodynamic manifestations of PE become apparent[33]. In VTE leading to PE, DVT of the lower extremities, the pelvis and rarely the upper extremities, are usually implicated. Dislodged thrombi from these deep veins of the lower limbs find their way in the caudocranial direction from the posterior tibial vein, to the popliteal vein, to the femoral vein, to the deep vein of the thigh (profunda femoris vein, to the external iliac vein, to the inferior vena cava) and then to the right side of the heart.

In the heart, it enters the right atrium (RA), the right ventricle (RV) and then the main pulmonary artery (Figure 1), the right main and/or left main pulmonary arteries or their branches (Figure 2) where it may become lodged in one or more of these vessels causing various degrees of obstruction with resultant disruption of the normal gaseous exchange processes and attendant changes in the hemodynamics of the affected individual.



Source: Author's construct

Figure 2. 1: Schematic diagram showing the flow direction of a dislodged pulmonary embolism within the heart from the upper limbs (red arrows) and lower limbs (blue arrow) into the pulmonary vasculature.



Source: Author's construct

Figure 2. 2: Schematic diagram showing the pulmonary artery and its branches

2.3.1 Hemodynamic Effects

In a PE episode, the key consequences are typically hemodynamic[29]. Various factors are known to influence the hemodynamic response to pulmonary embolism. These factors include the presence of concomitant cardiopulmonary disease, size of embolus and neurohumoral reactions in response to the pulmonary artery embolic process. Physical obstruction to blood flow by the physical presence of the embolus, though a contributor, is not the solely responsible for the hemodynamic decompensation that occurs in acute PE. Thus, the PE, is not entirely liable for the observed hemodynamic decompensation that occurs. Other factors, such as the release of humoral factors, namely thrombin from plasma, serotonin from platelets and histamine from injured tissues all contribute to the hemodynamic decompensatory process [34].

Also, in addition to the physical obstruction, PE also tends to cause consequent hypoxemia and the release of vasoconstrictors, which cause narrowing of the already compromised pulmonary artery lumen, consequently increasing the resistance in the pulmonary vasculature and hence the afterload in the right ventricle. Right ventricular dilation, hypokinesis, tricuspid regurgitation and ultimately right ventricular failure may ensue as a result of the sudden increase in the right ventricular afterload. Systemic hypotension and cardiac arrest may ensue rapidly[26].

Eventually systemic hypotension and cardiac arrest may rapidly occur in patients with right heart failure from the increased right ventricular afterload. When the right ventricular chamber is overloaded, the pressure changes can result in flattening of the interventricular septum and its deviation towards the left ventricle in diastole. This deviation, towards the left ventricle in diastole will result in impaired left ventricular function due to the fact that the interventricular deviation distorts the normal circular architecture of the left ventricular cavity with reduced left ventricular distensibility resulting in an impaired left ventricular filling in diastole. Also, this causes the left atrium to contract more than usual in contributing to the filling of the left ventricle. Additionally, the increase in the right ventricular pressure from the overload will subsequently increase the stress on the walls of the heart thus increasing its myocardial oxygen demand, amid the already limited supply and subsequently resulting in myocardial ischemia.

The myocardial ischemia is mainly said to be the direct result of mass effect or pressure on the right coronary artery, reducing subendocardial perfusion thus, limiting oxygen available to myocardium[35]. Some researchers suggest that the role that humoral pulmonary vasoconstriction or reflex plays is of less relevance in humans[36]

2.3.2 Gaseous Exchange

Efficient transfer of oxygen and carbon dioxide in the lungs are impaired in acute PE. The most common gas exchange abnormalities detected in acute PE consists of an increment in the alveolar-arterial oxygen tension gradient and hypoxemia (decreased arterial partial pressures of oxygen, $P0_2$). There is a resultant increase in the total dead space, and subsequently, a ventilation and perfusion mismatch occur with the blood from the obstructed arteries being re-routed to other gas exchanging units. Also shunting of venous blood into the systemic circulation may ensue[26]. The anatomic dead space of the lung and inspired air that enters the respiratory bronchioles, alveolar ducts, and alveolar sacs (i.e., the gaseous exchange units) are the constituents of normal tidal volume.

The ratio of ventilation to perfusion are well matched in normal lungs with the ratio being about 1.0. There is a disruption of the normal ventilation perfusion ratio when there is a reduction in alveolar ventilation to pulmonary capillaries relative to blood flow (low V/Q units). This results in impaired transfer of oxygen with the ratio of ventilation to perfusion falling to less than 1.0. When there is no ventilation to perfused lung units or when venous blood bypasses the lungs and enters the systemic circulation right-to-left shunting is said to occur[26].

Oxygen transfer involves a sequence of events which consists of gas flowing from a high-pressure source; namely the atmosphere, to a lower pressure source; namely the mitochondria. As the gas moves from the atmosphere to the alveoli, to arteries and then to the tissues, finally, the partial pressure of oxygen decreases. The initial decrease in the oxygen pressure occurs in the upper airways. This happens when air enters the humid upper airways in which the water vapor molecules reduce the partial pressure of air. Furthermore, the alveolar oxygen pressure is decreased when carbon dioxide from the capillaries diffuses into the gaseous exchange units. An alveolar to arterial tension gradient indicates the inefficiency of oxygen transfer across the lungs and this is usually as a result of a decreased ratio of ventilation relative to perfusion within the gaseous exchange units of the lungs [26].

2.3.3 Hypoxemia

In acute pulmonary embolism, there are a multitude of processes that elucidate the presence of hypoxemia. The impaired pulmonary oxygen transfer is most commonly caused by a ventilation-perfusion mismatch[37]. In PE, there is redistribution of blood flow such that some lung units have high ventilation perfusion ratios, while others have low ventilation perfusion ratios and this is contradictory to what occurs in normal lungs where ventilation and blood flow are well matched. Venous (deoxygenated) blood flow in the gas exchange units of the lung occurs when the ratio of the available airspaces responsible for ventilation are reduced in comparison to the available capillary flow thus blood is poorly oxygenated. This is called arterial hypoxemia; Low ventilation-perfusion ratios are further caused by atelectasis and this also contributes to arterial hypoxemia resulting from loss of surfactant and alveolar hemorrhage. When there is right ventricular failure in Pulmonary Embolism, arterial hypoxemia is also compounded by the low oxygen pressure in venous blood[26].

A reduction in the cardiac output causes a concomitant reduction of the oxygen in venous blood because of tissue usage. When there is a reduction in the cardiac output, the oxygen in venous blood is reduced because the tissues extract increased proportions of oxygen. As venous blood passes through gas exchange units of the lung to the systemic circulation, abnormally low partial pressure of oxygen in venous blood magnifies the effect of low ventilation-perfusion ratios. However, on the contrary, when the lungs are normal, low venous oxygen has no effect on the arterial oxygen content, hence the ventilation to perfusion ratios remain normal[26].

Patients that manage to overcome and survive an acute episode of PE, despite the occurrence of associated right ventricular failure, do so as a result of the activation of the sympathetic systems by systemic sensors, which initiate in response the Frank-Starling mechanism, chronotropic and inotropic mechanisms. These pathways consequently increase the pressures in the pulmonary arterial systems which assists in restoring the resting pulmonary circulation, filling of the left ventricle and left ventricular output. These compensatory responses alongside systemic vasoconstriction may result in the stabilization of the systemic blood pressures in patients presenting with acute PE ref

2.4 Clinical Evaluation of acute PE

It is recommended that severity of PE should not be assessed on the bases of the physical/anatomical burden, distribution and the size of the emboli, but rather it should be considered on the bases of its association with short term mortality. As such, recent guidelines discourage the use of phrases like massive, sub-massive and non-massive in the estimation of the level of risk of PE-related early mortality. Clinically, PE can be stratified according to the various levels of risk of short-term or early mortality (defined as in hospital death or death with 30 days of the episode) based on the presence of various risk markers such as shock, hypotension and/or RVD parameters[38].

2.4.1 Diagnosis

Clinically, being able to evaluate suspected patients for a possibility of PE based on their clinical presentation is of great importance in interpretating test results and selecting the most relevant diagnostic plan of action[38].

2.4.2 Clinical presentation

In the majority of cases, a single clinical symptom or a combination of symptoms such as chest pain or discomfort, syncope, tachypnoea and/or dyspnea are present[39] [40]. Syncope though rarely occurring, is a significant presentation of pulmonary embolism. It may be an indicator of a significantly low hemodynamic reserve. The severe cases of PE may present with arterial hypotension and shock. Pleuritic chest pain is another common manifestation of PE. It may present alone or with dyspnoea. The pleurisy as a result of irritation of the pleura due to an embolus in the subsegmental vessel with resultant pulmonary infarction. There may be alveolar hemorrhage accompanied by hemoptysis[38]. Individual clinical signs are usually non-specific and not sensitive. Usually, chest X-rays show abnormal findings in the setting of acute PE. These changes are that of pleural effusions, plate-like atelectasis and elevation of the diaphragm. The findings on chest X-ray are usually non-specific[41].

In recent times, degradation product of crossed-linked fibrin called Plasma D-dimer has been studied. In acute PE, the levels of D-dimer are noted to increase due the fibrinolysis and coagulation pathways simultaneously. Therefore, it can be inferred that if D-dimer levels are low, the probability of the patient having a PE is very low. That is to say, a D-dimer that is within normal range renders a diagnosis of DVT or PE unlikely, making the negative predictive value of D-dimer high. D-dimer is produced in other clinical conditions

such as cancer, inflammation, aortic dissection, infection, inflammation and necrosis; as these conditions are also associated with fibrin production. This renders the positive predictive value of D-dimer low there for rendering it a poor assessor of PE and not useful in confirming PE[42].

Hypoxemia is a common association with PE, however, in patients with PE, up to approximately 20% of the patients presenting with PE will have both arterial oxygen pressure (PaO2) and alveolar-arterial oxygen gradients that are normal. Other findings on an electrocardiogram may point to the development of PE. These may include: T wave inversion in the leads V1–V4, the classic S1Q3T3 presentation, lead VI QR pattern, and a complete or an incomplete right bundle-branch block (RBBB). These findings represent signs of RV strain on an electrocardiogram (ECG), and when the onset of PE is acute, it may be helpful in clinical evaluation. However, these changes are non-specific and may also be identified in right ventricular strain patterns of other aetiologies other than PE. However, its association with a suspected PE may generally indicate a more severe form of the condition. It must be emphasized therefore that these routine laboratory tests, the presenting symptoms and the elucidated clinical signs are only able to heighten the clinicians index of suspicion but they are not able to confidently exclude or confirm the presence of acute PE[38].

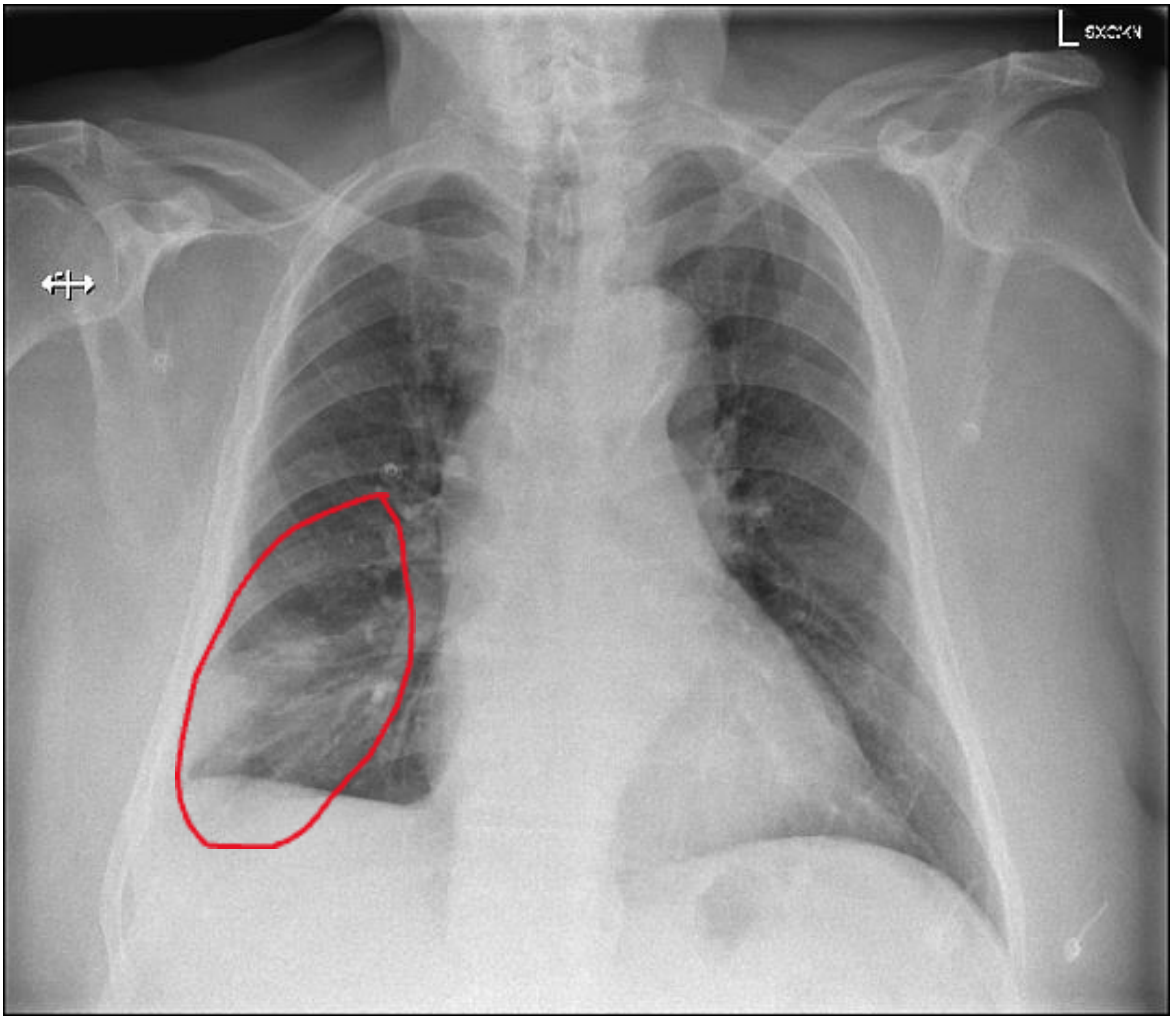
2.4.3 Imaging in the evaluation of PE

A multitude of imaging modalities are used in evaluating patient with acute PE. Among these are Chest X-ray/radiographs, CTPA, CT venography (CTV), Magnetic resonance Pulmonary angiography (MRPA) ventilation/perfusion (V/P) scans, venous ultrasound and echocardiography.

2.4.3.1 Chest Radiographs

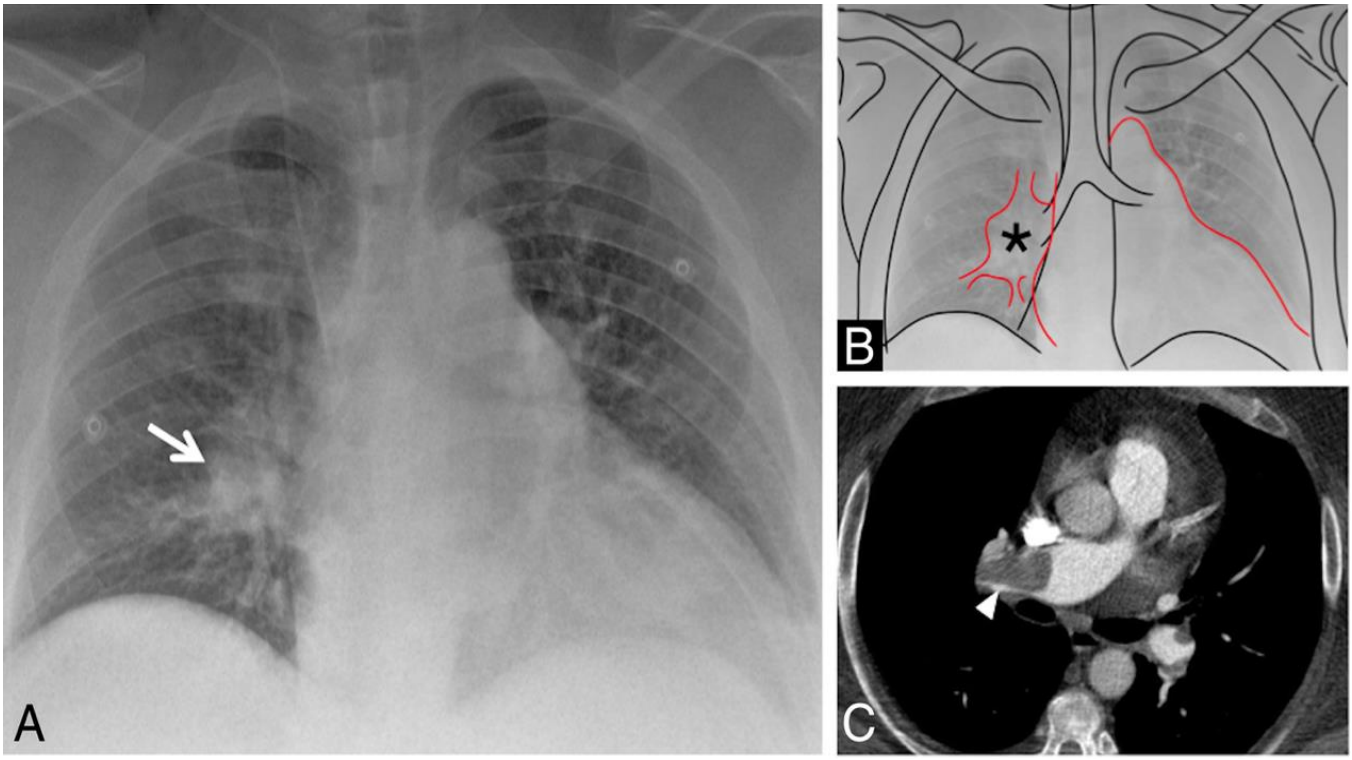
Chest radiographs are not particularly useful in the specific diagnosis of PE; however, it can be used to exclude other possible causes of certain disease processes that cause acute chest pain such as pneumothorax, pneumonia or pulmonary oedema. Inspite of this, chest radiographs still show some particular radiographic changes that may be seen in patient with acute PE.

These include the Fleischner sign (Fig 2.4), the Westermark sign (Figure 2.5) and the Hampton's hump sign (Figure 2.3). Fleischner sign (Figure 2.4) is used to describe a dilated or enlarged pulmonary artery. The occurrence of the Fleischner sign is a consequence of an intraluminal pulmonary artery embolus which distends the lumen of the vessel or it may be due to pulmonary hypertension. When there is regional oligemia in the setting of PE, it is called the Westermark sign. In the diagnosis of PE, the Westermark sign has a specificity of 92%, and sensitivity of 14%, a negative predictive value (NPV) of 76% and a positive predictive value (PPV) of 38%. The Hampton's hump is a wedge-shaped peripheral opacity which results as consequence of pulmonary infarction (Figure 6). Other non-specific chest findings on a radiograph of a patient with acute PE are elevated diaphragm, vascular redistribution and pleural effusion[43].



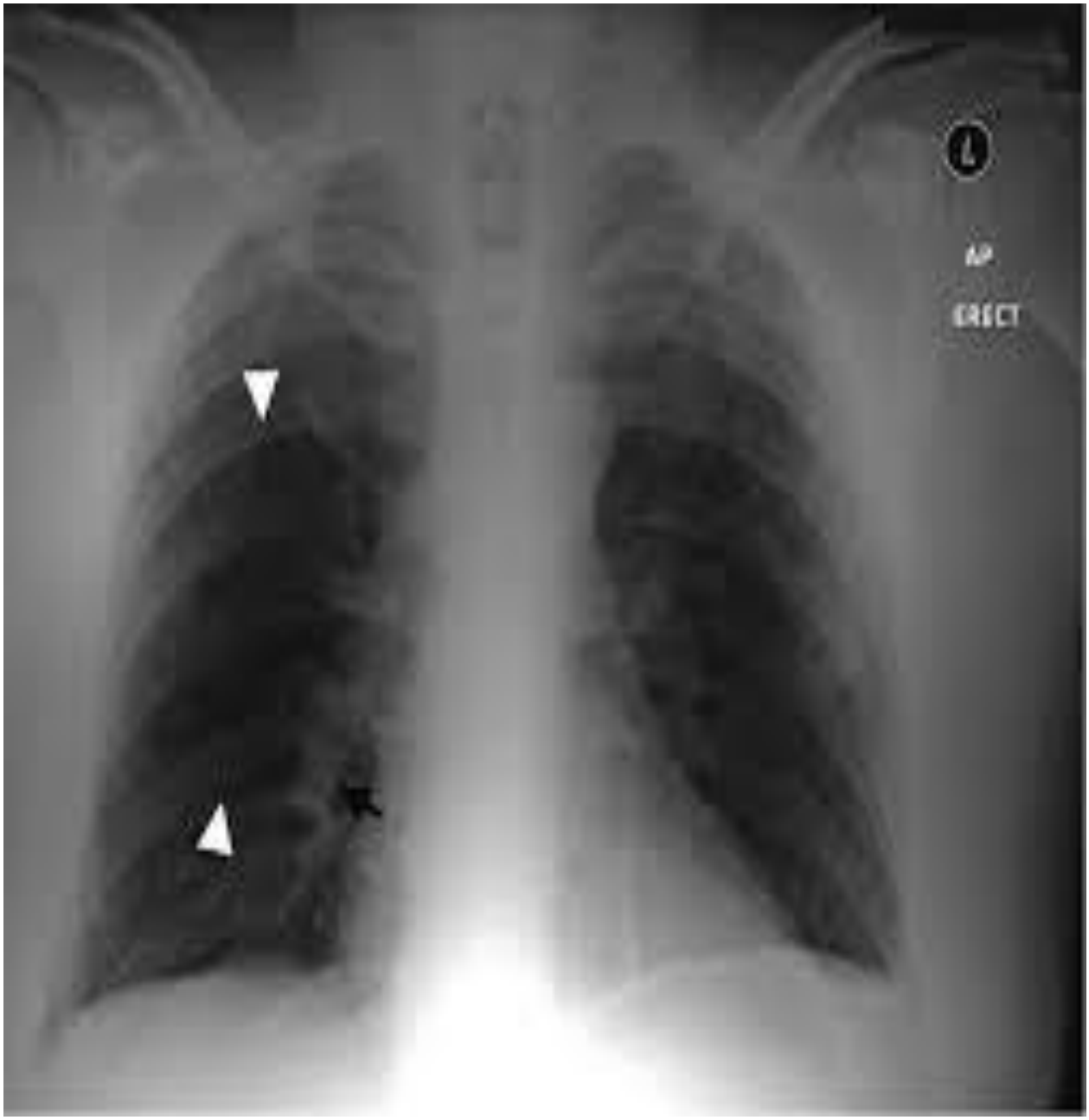
Source: radiopedia.org

Figure 2. 3: Frontal radiograph of the chest showing a peripheral wedge-shaped peripheral opacity in the setting of an Acute pulmonary embolic episode would be due to an infarcted lung (Hamptons hump). Differential diagnosis include hemorrhage or focus of infection



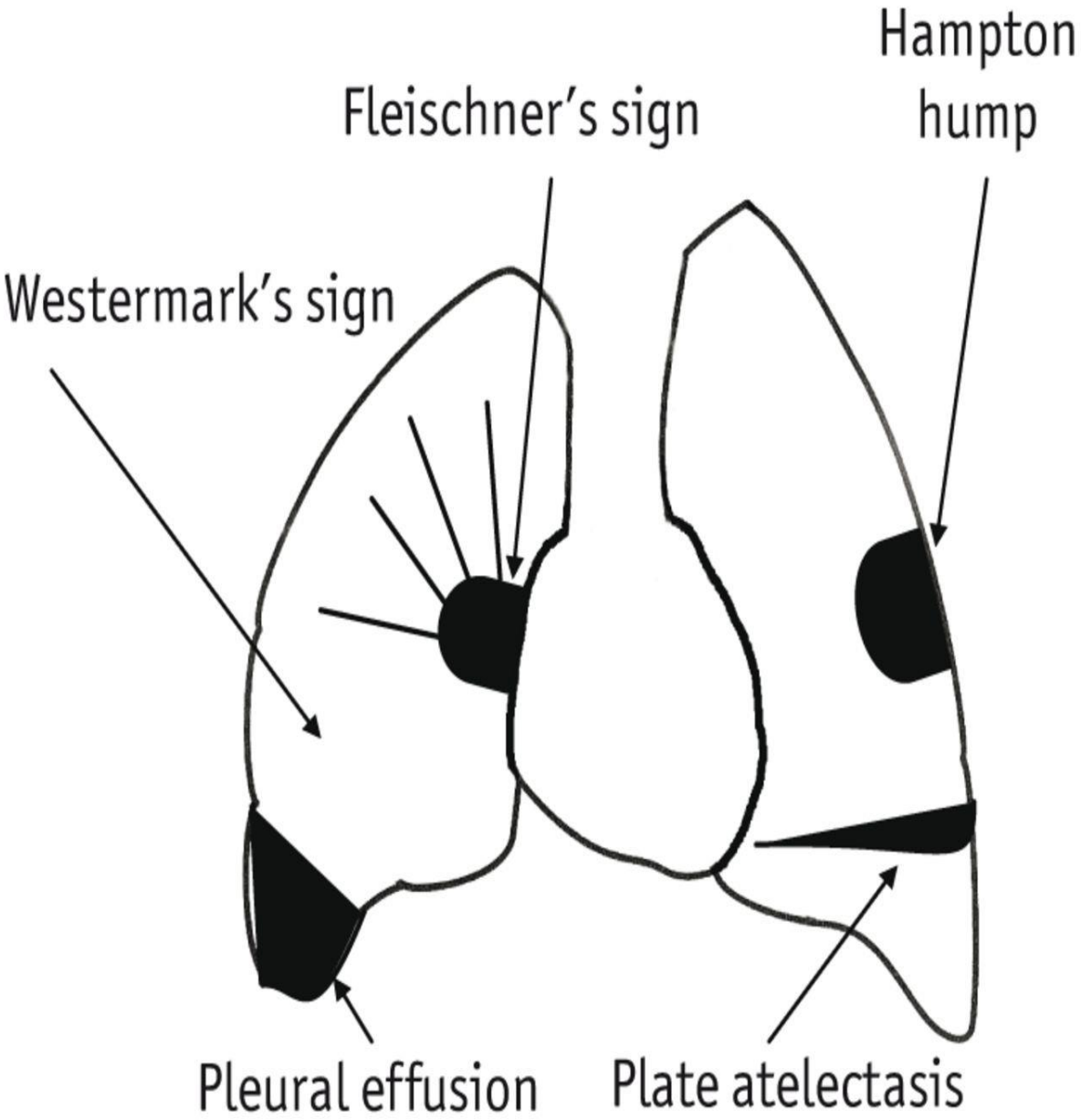
Source: https://insightsimaging.springeropen.com/articles/

Figure 2.4: Shows enlargement of both pulmonary arteries "Fleishcner sign", especially on the right in a patient with acute PE which is seen as a filling defect in the right main pulmonary



Source: https://litfl.com/westermark-sign/

Figure 2. 5: Shows a focal relatively lucent area of oligemia (Westermark sign) in the middle zone of the right lung in a patient with acute PE

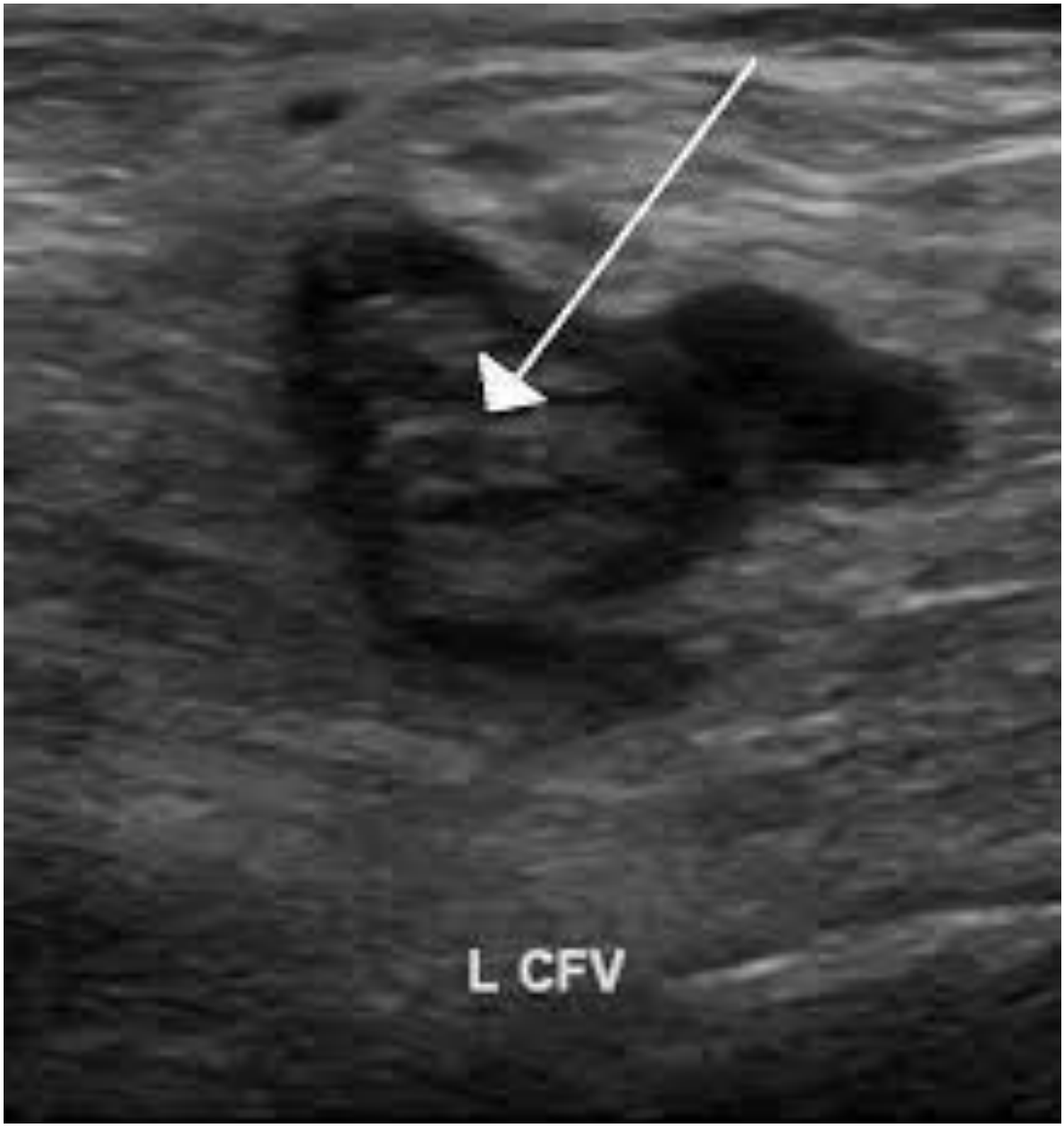


Source: breathe.ersjournals.com

Figure 2. 6: Schematic representation of Chest radiograph findings in acute PE.

2.4.3. Compressive ultrasonography (CUS)

Compressive ultrasonography (CUS) has a positive yield of about 20 %when used to search for a proximal DVT in a patient with acute PE. It may be used in certain cases as a backup procedure to reduce the overall false-negative rate when a single-detector CT is used or in cases where patients who are positive for PE have other contra-indications to the use of contrast or ionizing radiation[38]. The presence of a DVT will be seen an intraluminal filling defect which partially or completely occludes the lumen of the affected vein. This renders the vein in compressible and prevent the vein from collapsing was to wall on CUS (Figure 2.7)



Source: https://en.wikipedia.org/wiki/Ultrasonography_of_deep_vein_thrombosis

Figure 2.7: An ultrasound image that soft tissue and it shows as and an intraluminal mixed density.

2.4.3.3 Lung Scintigraphy (LS)/VQ scanning

PE can be safely excluded when the results of a perfusion scan are normal. In a patient whose clinical probability of having a PE is low, a nondiagnostic VQ scan may be merged with the fact that the patient is low-risk for PE and this can be used as an acceptable exclusion criterion. This has however not been validated[38] (Figure 2.8)

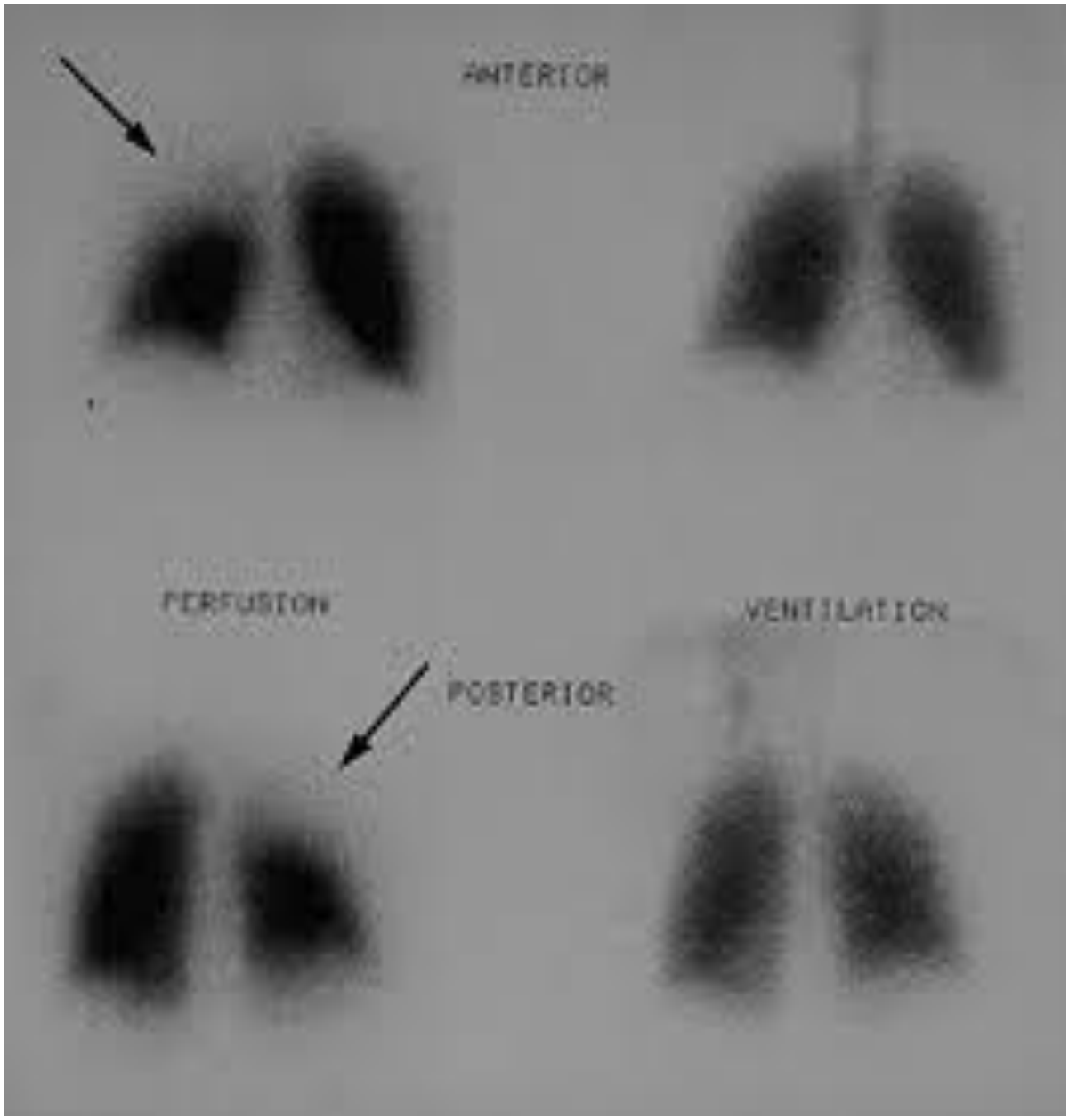


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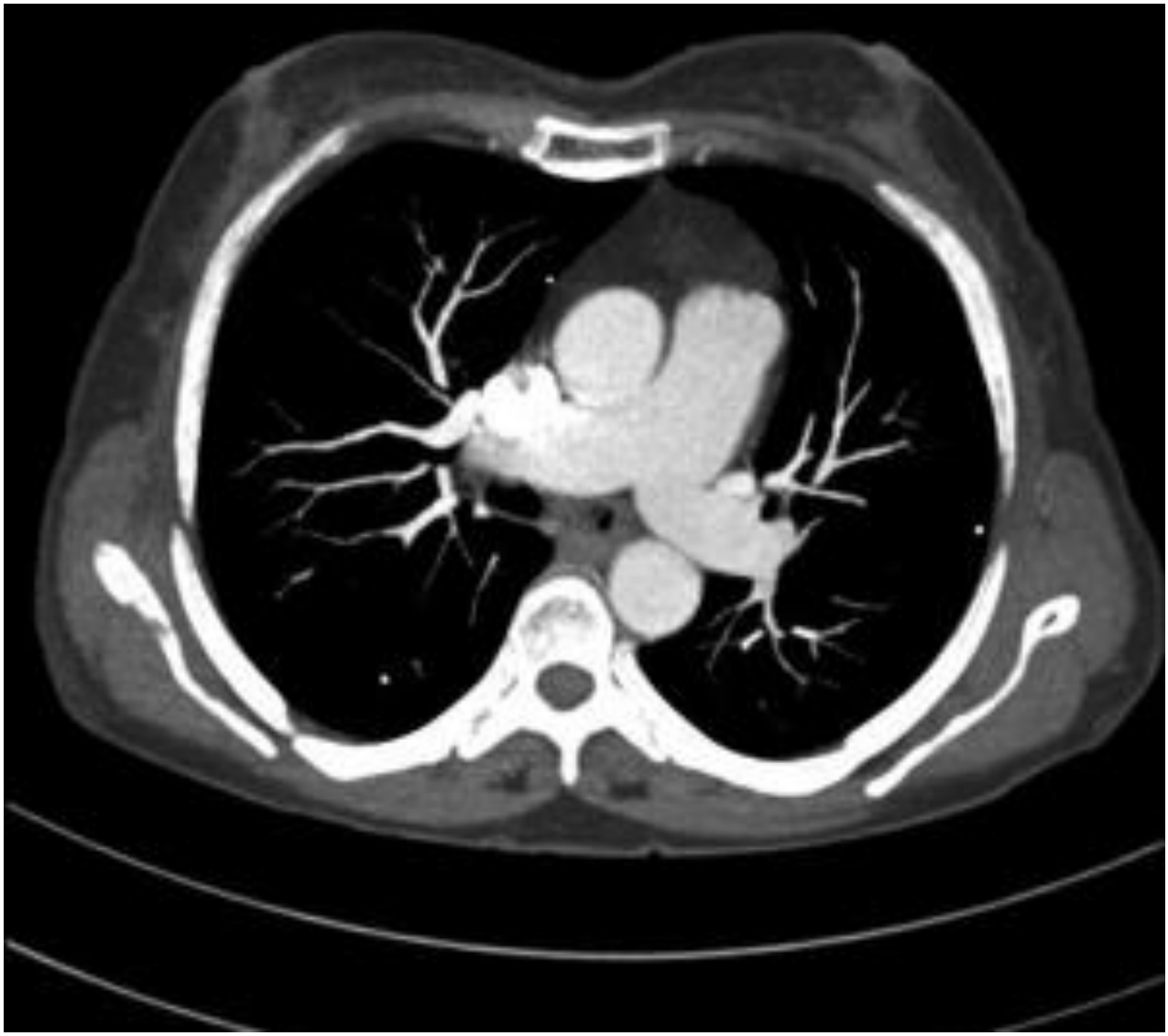
Figure 2. 8: Shows a ventilation/perfusion lung scan perfusion which shows a perfusion defect in the right upper lobe.

2.4.3.4 CT Pulmonary Angiography

CTPA (Figure 2.9) has become the preferred imaging modality for the workup of patients with suspected acute PE It is a critical component in clinical diagnostic algorithms[44] . CTPA is noted to have a high sensitivity and specificity. A sensitivity of 83% and a specificity of 96% noted in the PIOPED II trial [45]. Among its notable attributes, are the fact that it has short image acquisition time and is minimally invasive. CTPA imaging allows for evaluation of other structures and identification of other pathological process that may have similar presentations of chest pain and dyspnea seen in acute PE. An example of such a disease process is pneumonia[46]. However, inspite of its usefulness, there are concern of its use of ionizing radiation. However this is addressed by the used the creation and implementation of ionization-reducing protocols[43].

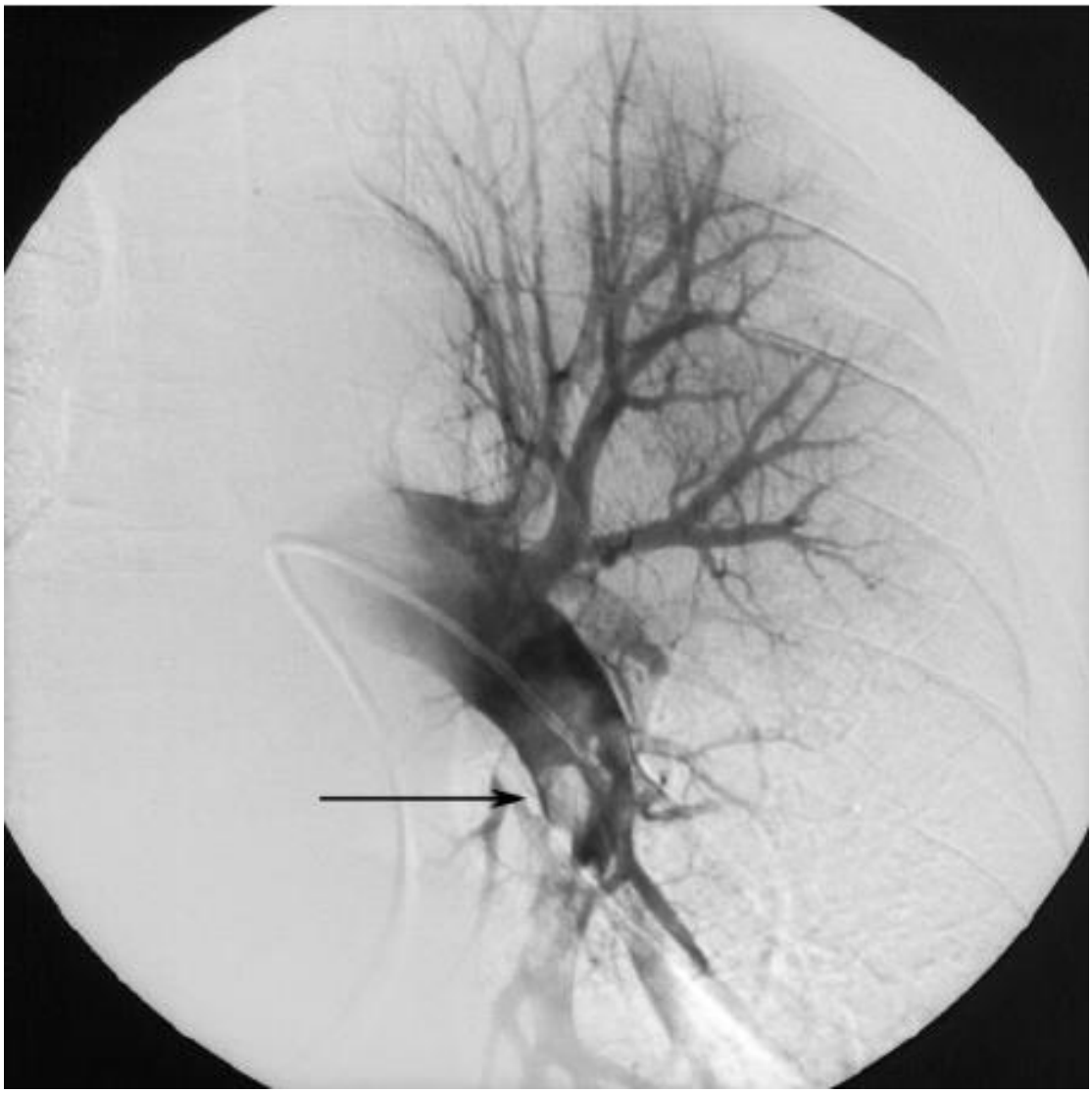


Source: qims.amegroups.com

Figure 2.9: Axial: CTPA of the chest demonstrating that the lumen of the Pulmonary arteries completely outlined with contrast.

2.4.3.5 Pulmonary Angiography

Pulmonary angiography, though reliable, in known to be an invasive test. It however useful when non-invasive imaging results are equivocal[38] (Figure 2.10).

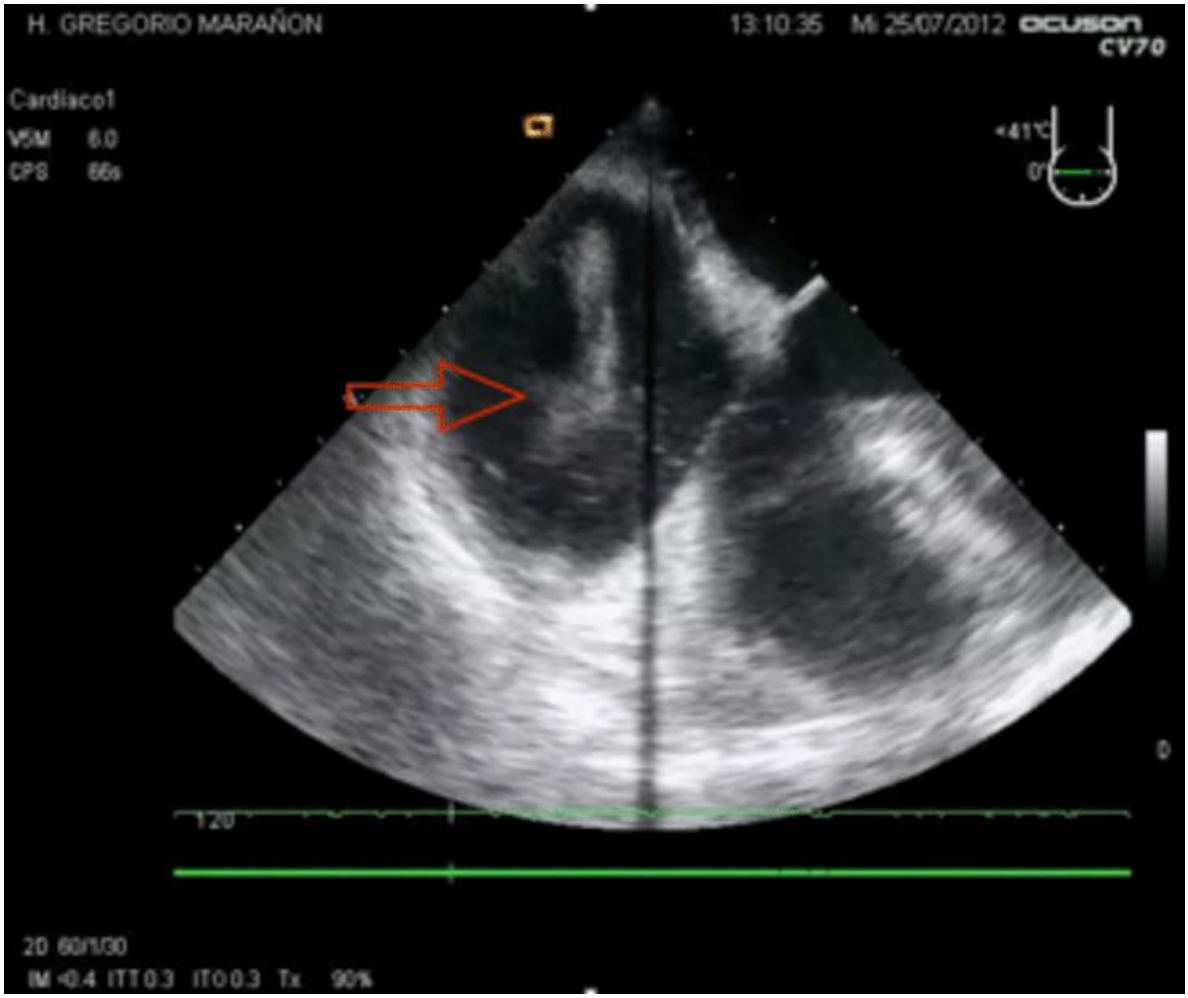


Source: researchgate.net

Figure 2.10: shows an intraluminal filling defect, consistent with an embolus in the right lower lobe pulmonary artery on digital subtraction angiography.

2.4.3.6 Echocardiography

Echocardiography (Figure 2.11) is useful in the bedside evaluation of critically ill-patients who are suspected of have PE. Bedside echocardiography is particularly useful when emergency management decisions need to be made. In patient that present with shock or hypotension, if signs of right ventricular dysfunction or overload usually eliminates PE as the cause of the hemodynamic compromise Echocardiography is most useful in non-high risk PE where it can be used to further stratify non-high risk into low or intermediate risk PE groupings[38].



Source: qims.amegroups.com

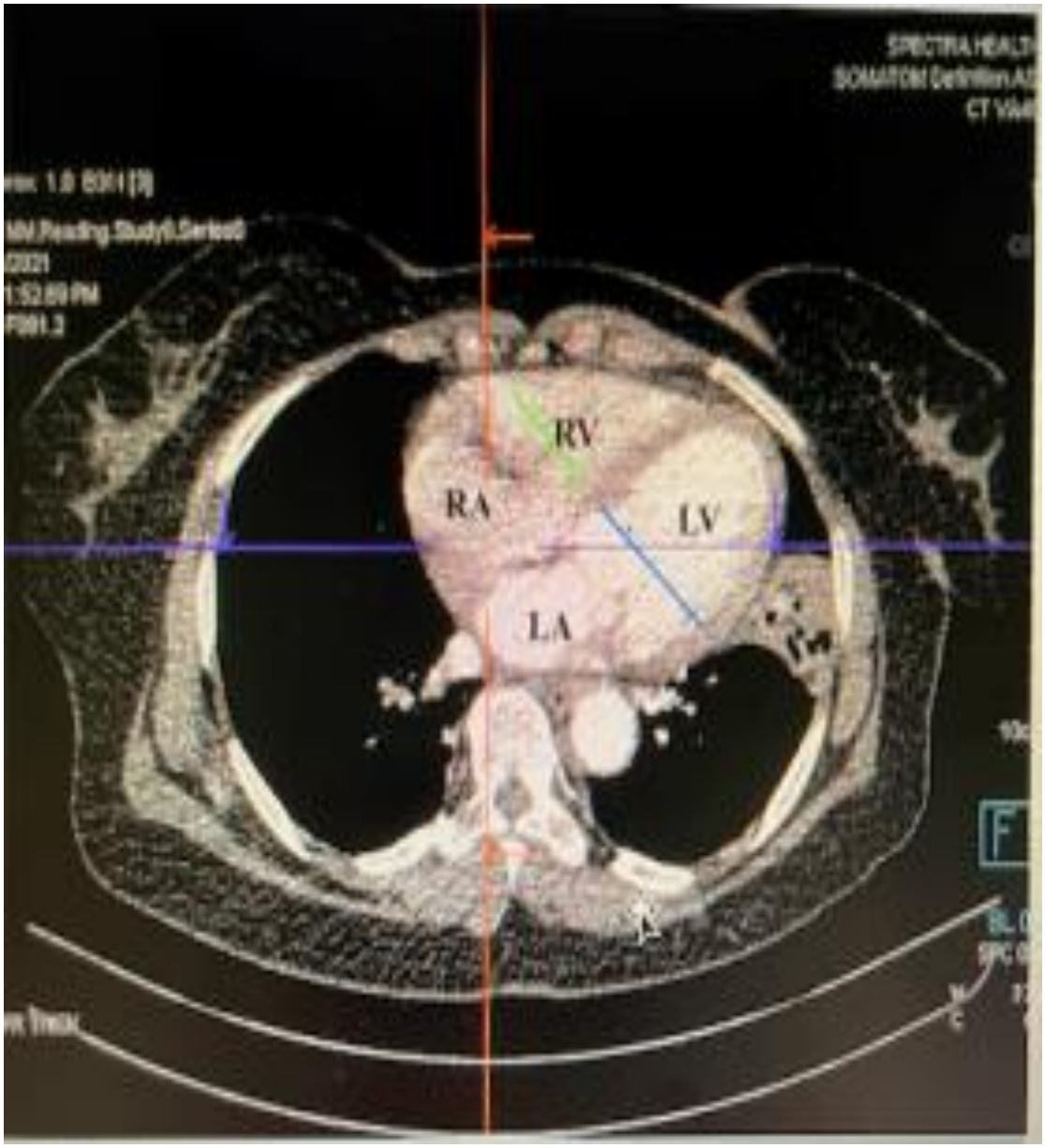
Figure 2.11: Image is an Echocardiogram with evidence of an echogenic intraluminal filing defect within the heart chamber.

2.5 Predictors Short-term mortality on CTPA

2.5.1 RV short axis, LV short axis and RV/LV short axis ratio.

RV short axis and more significantly the RV/LV diameter ratio (also known as RV enlargement) (Figure 2.12) acquired from four chamber view axial CT scan images of the heart describe positive associations with the severity of PE episodes[47] or possible fatal outcome[48] Conversely, the LV measurement acquired in its short axis plane show a negative association with the severity of PE episodes[47] or with fatal outcomes[13].

According to Araoz, RV/LV ratio is not a significant predictor of PE related mortality but rather a predictor of less severe morbidity such as ICU admission. Van der Meer [13]et al on the other hand found a notable relationship between RV/LV ratios and PE associated mortality. Schoepf et al showed a 78.2% sensitivity, 38% specificity, 15.6% positive predictive value and 92.3% negative predictive value to be associated with the RV enlargement in predicting 30-day mortality[49]



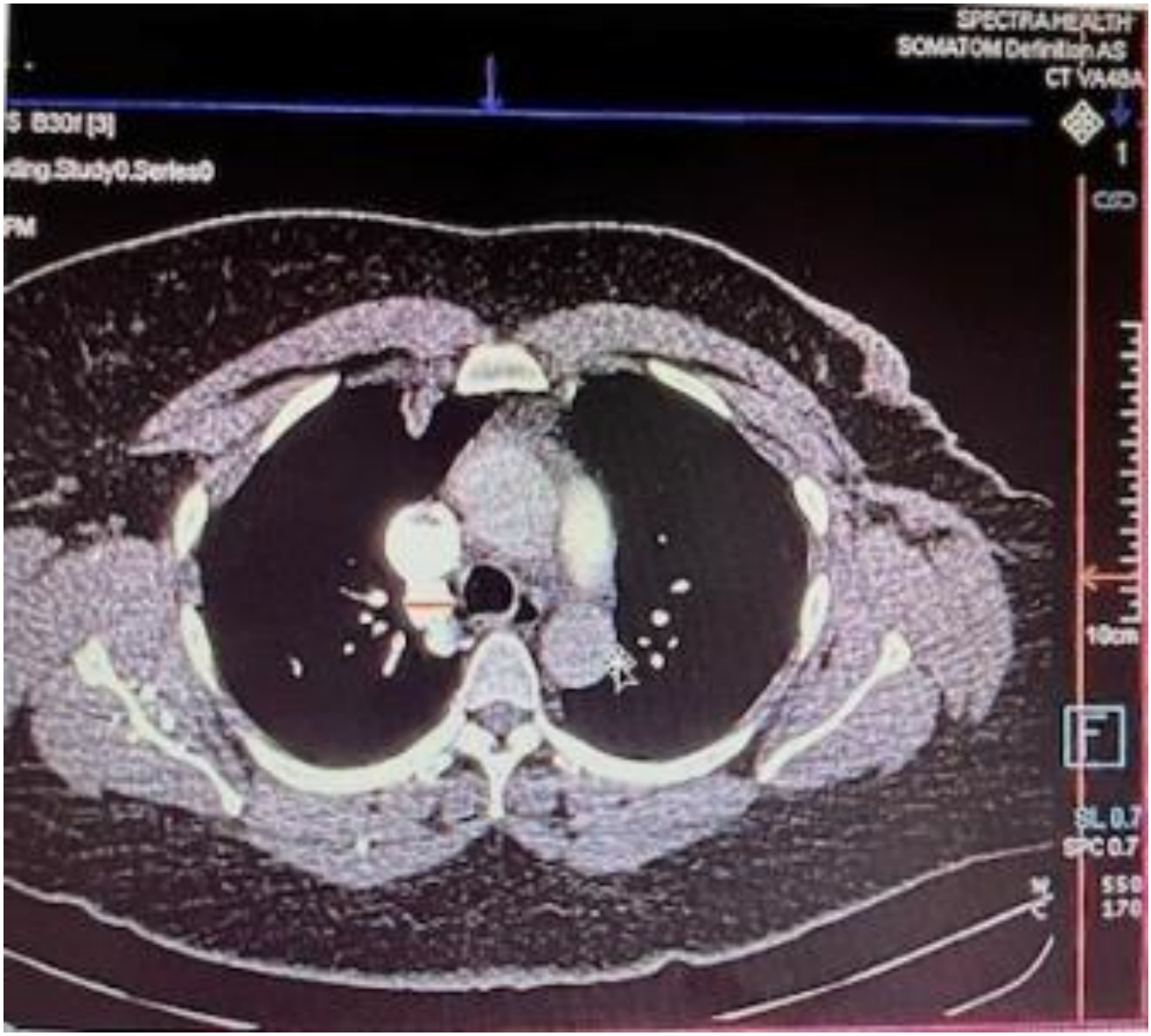
Source: Author's own image

Figure 2.12: Axial CT scan image of the heart showing the right ventricle short axis diameter (green line) and the left ventricle short axis diameter (blue line). (Courtesy KNUST affiliate site, Spectra Health and Imaging Limited, Kumasi, Ghana.

2.5.2 Diameters of the Superior vena Cava (SVC) and Azygos vein.

As pressure builds up on the right side of the heart, it may result in a pooling of blood within the more proximal venous structures That is to say that pressure build-up on the right side of the heart, is directly proportional to pressure build up in the more proximal venous structures, such as the Superior vena cava and Azygos vein (Fig. 2.13). This was demonstrated in a study done by Collomb et al, where the superior vena cava showed significant variance in diameters for patients who had had an episode of severe acute pulmonary embolism and those with non-severe pulmonary embolic episodes[47]. Ghuysen et al also indicated that there was a significant correlation between the mortality and imaging parameters of which include the proximal SVC diameter and Azygos diameters.

Others studies also showed a statistically significant difference in the diameters of patient who survived acute PE episodes and those that did not[14]. But even though there were discrepancies between patients with severe and non-severe diseases none conclusively indicated SVC diameters to be a good predictor of short-term mortality. Ghaye et al rather cited Azygos diameter as a good predictor of short-term mortality[50].

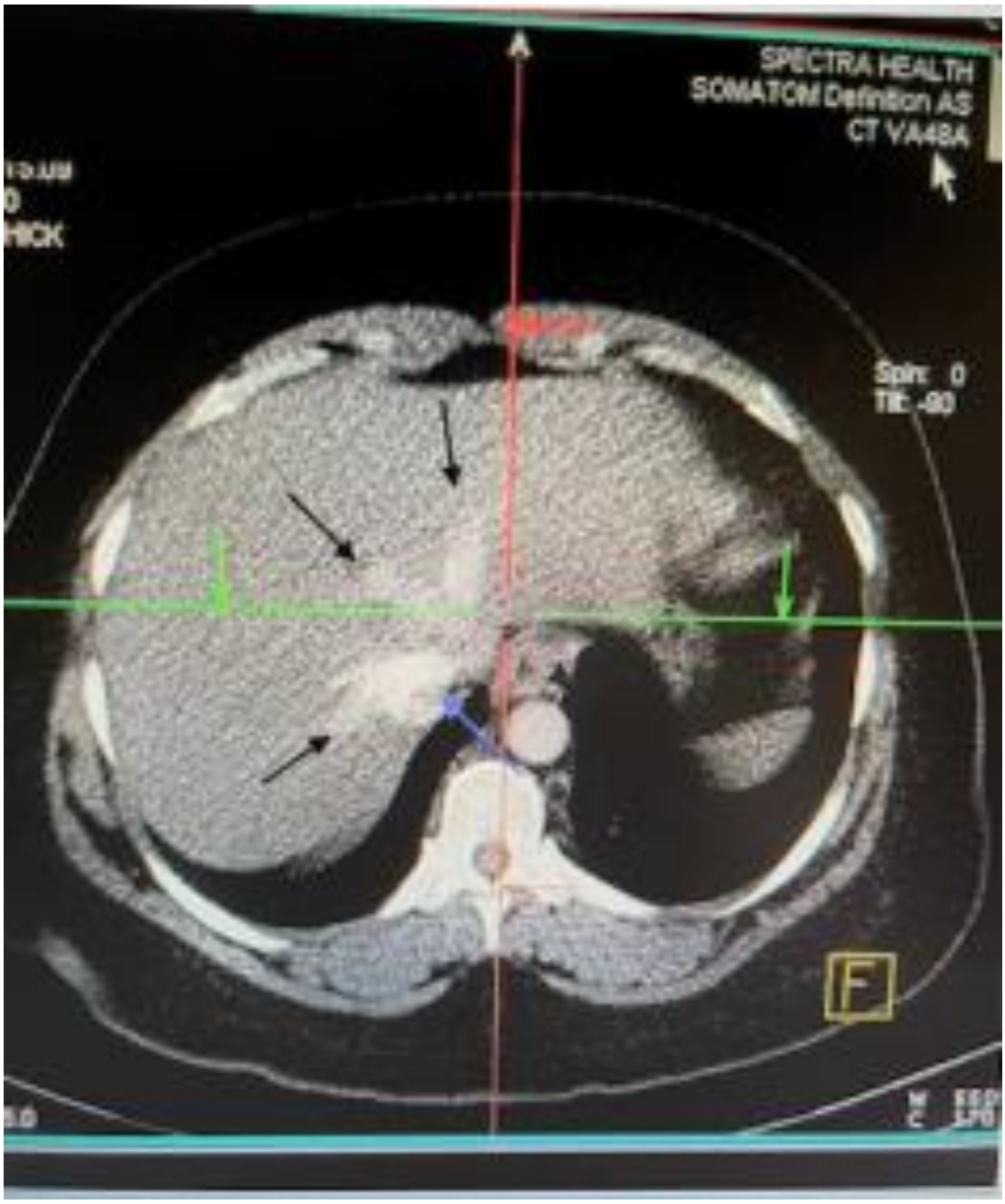


Source Author's own image

Figure 2.13: Azygos vein dilation in a patient with Acute pulmonary embolism (red line). The Superior vena cava is the circular contrast filled structure anterior to the Azygos vein (red line) (Courtesy KNUST affiliate site, Spectra Health and Imaging Limited, Kumasi

2.5.3 Contrast reflux into Inferior vena cava (IVC)

Another more proximal manifestation of acute right heart failure is the reflux of contrast medium into the IVC (Fig 2.14). According to Furlan et al reflux of contrast in to the IVC was one of the right heart dysfunction parameters that had a strong association with short term mortality [51] and this was similar to Ghuysen et al's study which suggested a significant correlation between mortality and reflux into the IVC [52]. However, Collomb et al's findings were of the contrary, in that, he found no significant differences in patients with severe and non-severe PE[53]

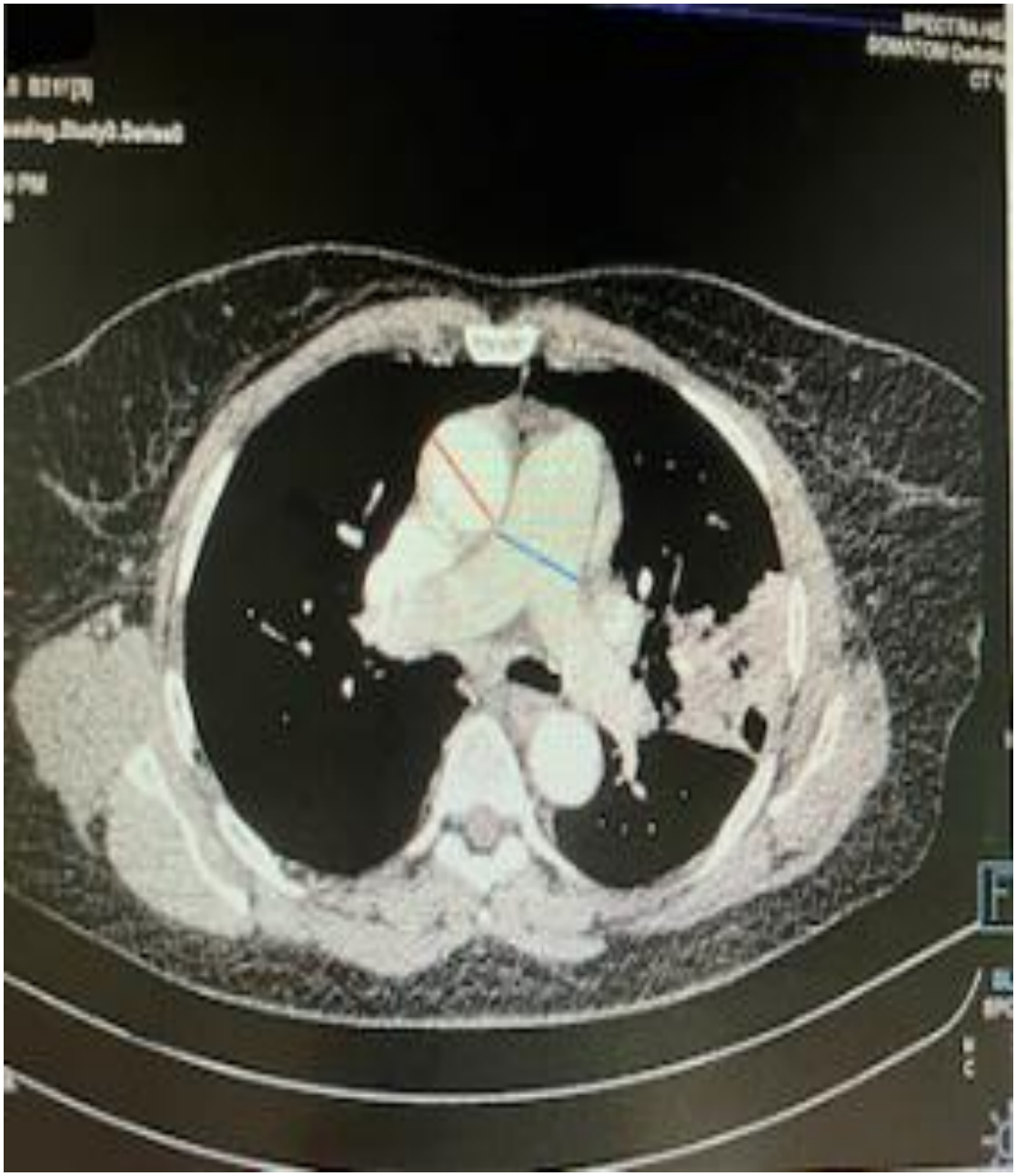


Source: Author's image

Figure 2.14: CT showing contrast reflux into the IVC (blue arrow) and hepatic veins (black arrows) in a patient with PE and right-ventricular dysfunction. (Courtesy KNUST affiliate site, Spectra Health and Imaging Limited, Kumasi, Ghana

2.5.13 Pulmonary artery and ascending Aorta ratio

The ratio PA diameter to ascending aorta diameter (Figure 2.15) was not useful as a prognostic factor for acute PE by Van der Meer et al[48] as he could not find a significant association between this parameter and mortality. None of the other known studies could establish relationship between the pulmonary artery and ascending aorta diameter ratio and mortality in PE.

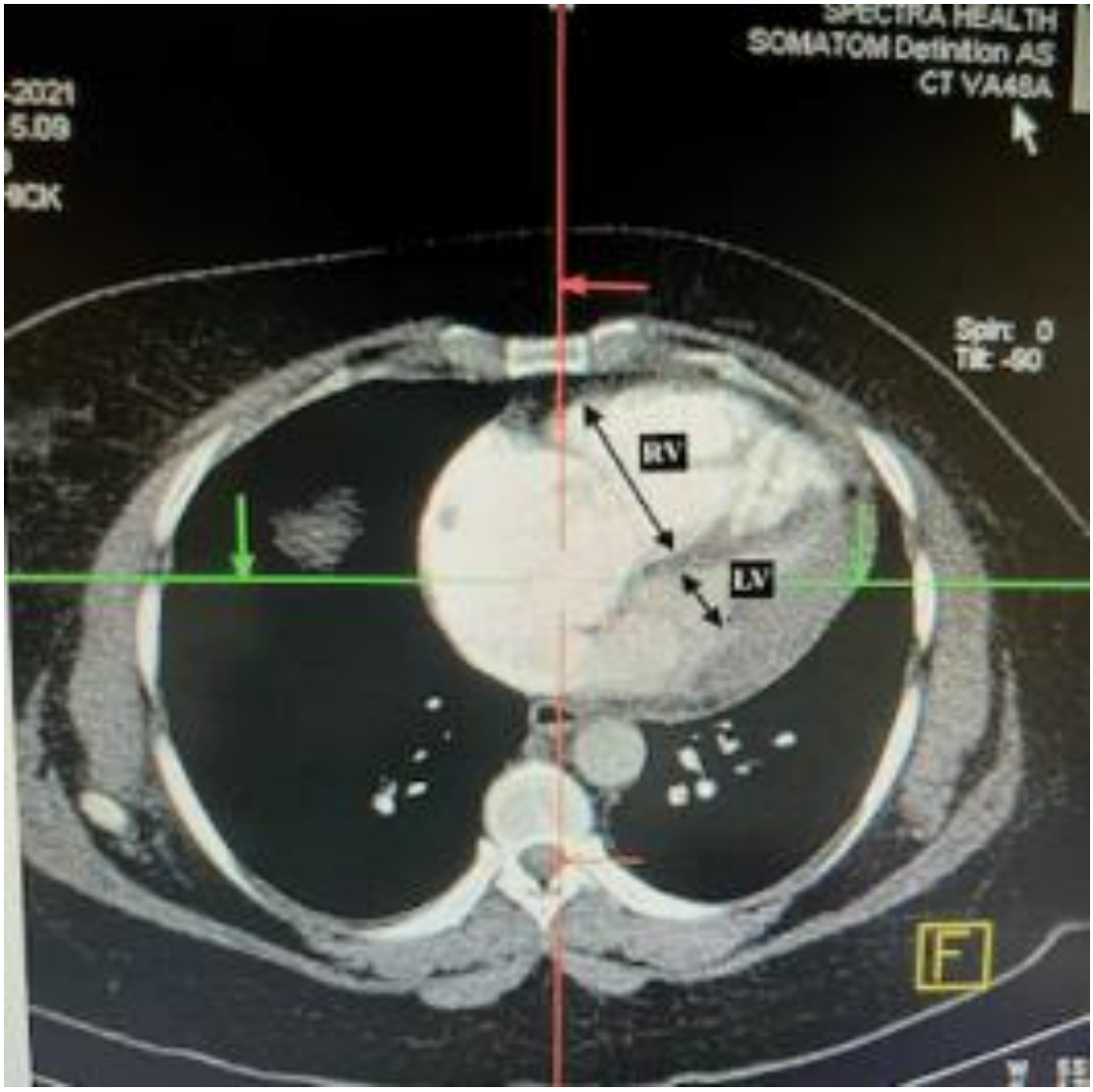


Source: Author's image

Figure 2.15: Axial CTPA showing pulmonary artery (blue line) and adjacent ascending aorta diameters (red line) in the measurement of Pa/Ao diameter ratio. (Courtesy KNUST affiliate site, Spectra Health and Imaging Limited, Kumasi, Ghana)

2.5.5 Interventricular septum deviation

According to Van der Meer et al, interventricular septum deviation (Figure 2.16) had no predictive value as far as the outcome of PE was concerned[54]. This was contrary to studies done Ghuysen et al, which indicated



Source: Author's image

Figure 2. 16: CTPA showing the heart in the four-chamber view showing the Leftward septal deviation (red arrow). (Courtesy KNUST affiliate site, Spectra Health and Imaging Limited, Kumasi, Ghana.)

2.5.6 Clot Load Score

According to Collomb et al, the clot load scores (Figure 2.17) (fairly useful in providing information on how severe a recent episode of PE may be, but limited in predicting the possible of the outcome in affected patients[47]. This is contrary to the findings of the study done by Wu et al, which showed the clot load scores to be a notable predictor of outcome of patients with PE[15]. Van der Meer et al's finding[54] concur with Wu et al in that, they both agreed that clot load scores are a relevant predictor of patient outcome. However, in Wu et al's study, Clot load was not compared to other parameters. It was evaluated as a parameter on its on with no comparison to others. Araoz et al, indicated PA clot scores as a poor parameter in predicting outcome in patients with acute PE[55]

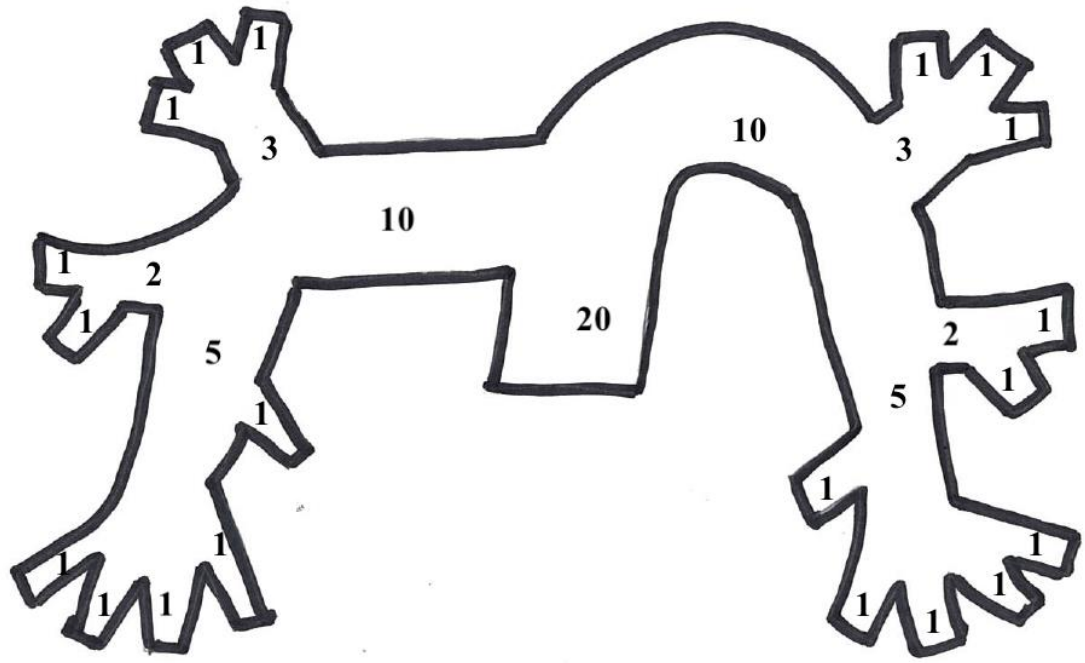
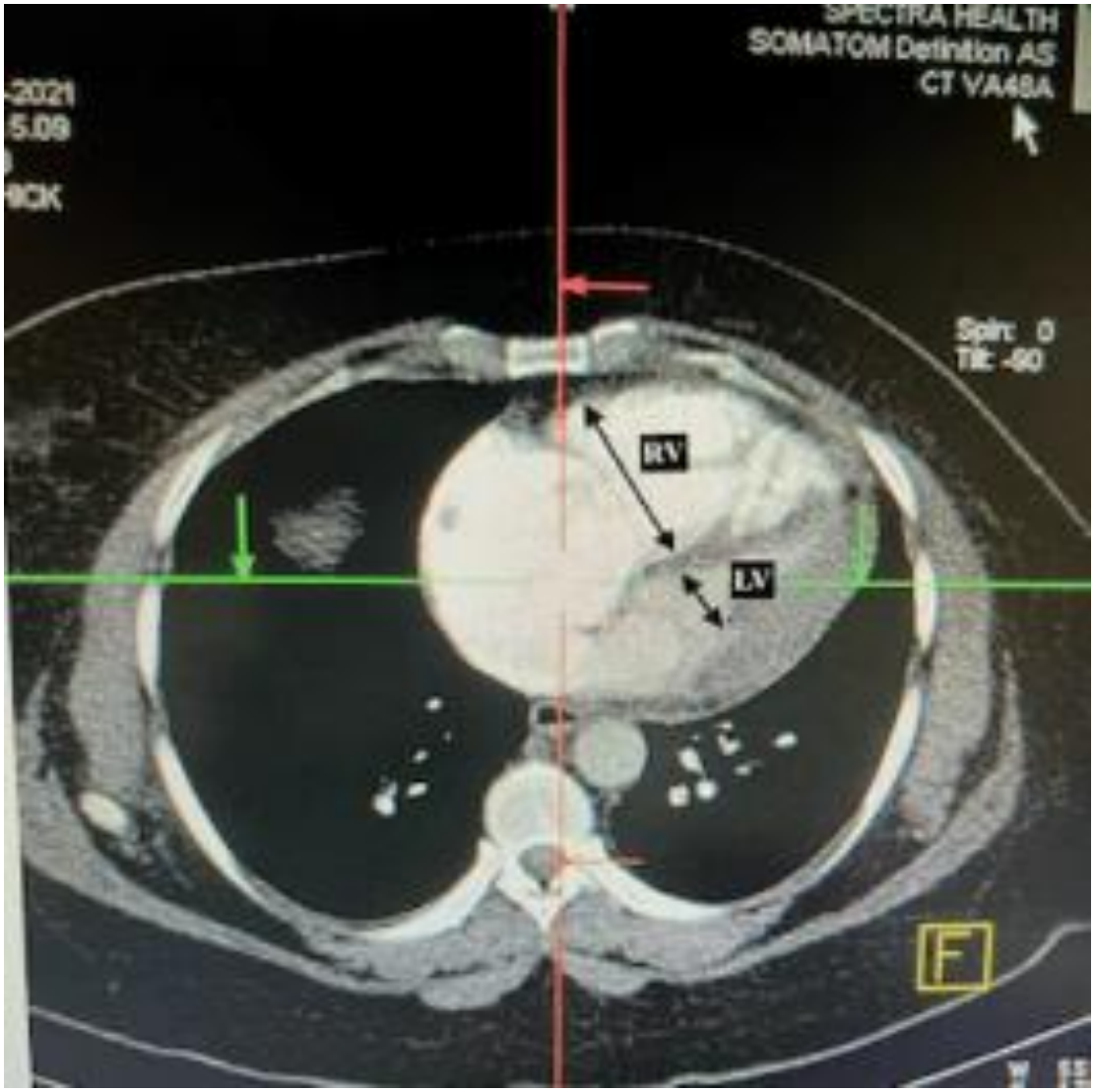


Figure 2.17: Schematic representation of the arterial tree of the lung and the showing how the various branches are scored according to Qanadli scoring system.

2.6 RV/LV Ratio associated with short term mortality.

According to Van der Meer et al, patients with an RV/LV ratio of >1.0 (Fig 2.18) have a 10.1% chance of dying within a 3-month period. Conversely, those with an RV/LV ratio of 1 or less had almost no chance of PE-related death (negative predictive value of 100%). According to Quiroz et al[56] when the RV/LV diameter ratio was calculated in the four chamber view, a ratio of more than 0.9 had the ability to predict the occurrence of adverse clinical occurrences. Adverse clinical occurrences being defined as 30-day mortality, the requirement of cardiopulmonary resuscitation, mechanical ventilation, vasopressors, thrombolysis or embolectomy. They also demonstrated patients with Rv/Lv diameter ratios of 0.9 or less on the four chamber view to have lower mortality rates[57].



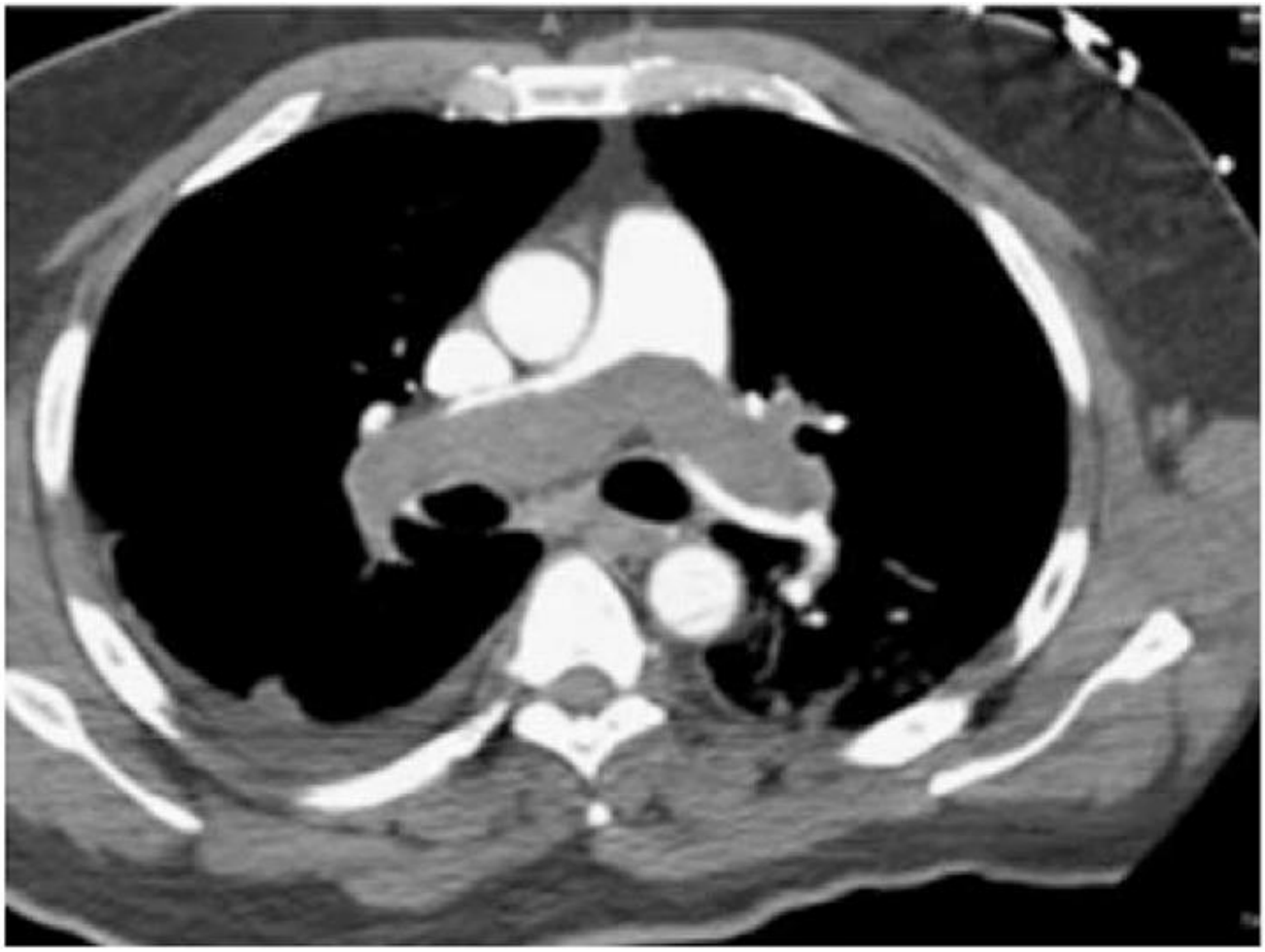
Source; Author's image

Figure 2.18: CTPA showing the heart in the four-chamber view with dilation of the right ventricular lumen (RV) and narrowing of the left ventricular lumen (LV) with resultant increment in the RV/LV ratio indicative of a right heart strain (Courtesy KNUST affiliate site, Spectra Health and Imaging Limited, Kumasi, Ghana.)

2.7 Clot Load scores associated with short term mortality.

Wu et al demonstrated that patients with clot load scores (Figure 2.19) of more than 60% ended up with acute PE related mortality. This was evident in his study when 83%, representing 5 out of 6 patients with a score of more that 60% or above passed, but 1.9%, representing 1 out of 53 patients died for those with a clot score less than 60%. Of those with a clot score greater than 60%, the single survivor managed to pull through after receiving thrombolytic therapy. The single death amongst those with a clot score of less than 60% was not PE related but due to end-stage malignancy. Both Wu et al and Rutger et al's, findings indicated that clot load scores are a relevant predictor of mortality.

But the cut off for clot load score associated with negative clinical outcome used by Rutger et al, was similar to that recommended by Qanadli et al[58] which set it lower than that of Wu et al. Rutger et al said a Clot load score of more than 40% is to be associated with negative clinical outcomes[59]. According to Rutger, patients with an obstructive index greater than 40% had 11.2 times increase risk of PE related mortality within 3 months. Araoz et al on the other hand, indicated PA clot scores as a poor parameter in predicting outcome in patients with acute PE[60].



Source: Researchgate.net

Figure 2. 19: CTPA showing and intraluminal filling defect that fills the main right (completely) and the left (partially). A right pleural effusion is also demonstrated.

2.8 Evaluation of parameter with the most significant correlation with short term mortality

According to Ghaye et al the RV/LV ratio and the Azygos vein diameter, are useful parameters in predicting mortality in patients with PE[14]. Wu et al in his study, sought to ascertain whether the quantification of pulmonary embolus (clot load) on CTPA was a good predictor of outcome, which it was[61]. No research was found that indicated that one parameter was better compared to the other in predicting short term mortality.

CHAPTER THREE

MATERIALS AND METHODS

3.1 Introduction

This chapter discusses the study site, the materials and methods that were used for this study. These included the study site, the study population, methods of data collection and analysis, as well as ethical considerations

3.2 Study design

The study was a prospective cross-sectional design assessing the right heart dysfunction parameters and clot/embolic burden as predictors of short-term mortality in patients with Acute pulmonary embolism.

3.3 Study site

The study was carried out at an affiliate radiological facility of the Kwame Nkrumah University of Science and Technology, namely Spectra Health Ltd. It was established in June 2011. Spectra Health Ltd has been tasked with training and research in the field of Radiology and Radiological interventional procedures. Spectra Health Ltd. is an imaging and interventional radiology center with headquarters at Patasi, Kumasi The main areas of operations include: Diagnostic Imaging, Interventional Radiology, Specialist Ambulatory Clinics, Research and Training and Medical Tourism

Spectra health currently has equipment including a mammography machine, a 4D ultrasound machine capable of Doppler as well as cardiac imaging, a diode laser equipment, 64 slice CT scanner with an advanced software, a 1.5 Tesla MRI Scanner, Cath lab (Artis Zee Multipurpose Suite). Spectra health has a catchment area of Kumasi and beyond with patients coming from as far as the Ivory Coast and Togo to undergo highly specialized interventional procedures such as tumor embolization for uterine fibroids amongst others. As part of the diagnostic imaging service provided by Spectra health, they perform, averagely 800 CT pulmonary angiograms annually to serve the patient populations of hospitals like the Komfo Anokye Teaching Hospital, the Kwame Nkrumah University of Science and Technology hospital, South Suntreso hospital, the Kumasi South (Regional) hospital as well as many other prominent hospitals within Kumasi and the Ashanti region.

3.3 Study Population

This study consisted of patients with CTPA confirmed Pulmonary embolism who presented at Spectra health. This study will constitute images of all patients 18 years and above presenting to Spectra health within the study period with CTPA-diagnosed acute PE.

3.3.1 Inclusion Criteria

1. All stable patients 18 years and above with a CTPA report positive for Acute pulmonary embolism. These patients must be conscious, able to communicate and agree to allow their images to be used for the purpose of the study.
2. All Unstable patients 18 years and above with a CTPA report positive for Acute pulmonary embolism with legally authorized representative consents to allow patients images to be used for the purpose of the study.

3.3.2 Exclusion Criteria

1. Patient who had the diagnosis of acute pulmonary embolism made by any other means other than CT pulmonary angiography
2. Patients who did not give consent to allow their images to be used.
3. Patients below the age of 18 years who had CTPA positive for Acute PE

3.4 Sample size

Spectra Health takes a lot of CT imaging daily including routine CT scan examinations of the Head, Spine abdomen and pelvis, CT urography, virtual colonoscopy amongst others, Averagely, 800 CT pulmonary angiogram scans are done annually, of which only about 128 were positive for acute pulmonary embolism. Within a data collection period of six (6) months it is expected that about 72 cases of acute pulmonary embolism will be seen at the center.

Hence, the sample size was calculated using the Cochrane's correct formula for finite population:

$$n = S / 1 + ((S-1) / Pop)$$

$$S = \frac{z^2 * p (1-p),}{d^2}$$

Where

S = initial sample size

z^2 = the table value of chi-square for 1 degree of freedom at the desired confidence level 0.05(3.841)

p = the population proportion (assumed to be 0.50 since this would provide the maximum sample size)

d = margin of error set at 5%, thus 0.05

n = sample size required

Pop = target population (72 patients with confirmed acute pulmonary embolism within the year)

$$S=\frac{3.841*0.5*(1-0.5)}{(0.05)^2}$$

$$S=\frac{0.9604}{0.0025}$$

S=384.16 ~384

Hence, the sample size is

n = 384 / 1+ ((384−1) / 72)

= 384 / 1 + 5.31944

= 384 / 6.31944

= 60.76

~ 61

Allowing for a 5% error rate, the sample size is 63.

3.5 Sampling Method

Convenient sampling technique was used. All CT pulmonary angiograms scan images of patients 18 years and above who underwent CTPA on account of suspected acute pulmonary embolism and are diagnosed by the reporting radiologist at Spectra health as having an acute pulmonary embolism will have their images retrieved by the principal investigator and the various parameters or right dysfunction and clot burden evaluated.

3. 6 Data Collection Procedures

Data was collected by administering structured questionnaires to the patient/caregiver reporting to the radiological facility with positive CTPA results, who meet the inclusion criteria.

The questionnaire was in sections. Certain sections that had to do with assessment and measurements of technical parameters were filled by radiologists while patient demographic and information on follow-up were filled by the trained research assistants.

The trained research assistants administered the consent forms in a language understandable to the patient. Data was recorded from respondents, electronically using tablets and smart phones.

Two research assistants were recruited and trained within a week on how to collect the demographic data and follow up on patients. The images were de-identified. The images demographics and clinical data were given anonymous identification numbers. The results of the images of all patients with a diagnosis of acute pulmonary embolism made by the resident radiologist were recorded. The images were then reviewed by a radiologist with at least five years working experience in interpretating CTPAs. A specific section of the questionnaire which focuses on the relevant parameters to be assessed radiologically were filled by the radiologist. The research assistants called to follow up on the recruited patients by way of telephone call at the end of 30 days; which started from the day of imaging[9].

3.6.1 Protocol for acquisition of CT pulmonary angiograms

CT pulmonary angiograms were acquired using a 64-slice CT scanner (Figure 3.1). (Somatom Definition AS 64 slice CT scanner from Siemens, Germany. Model number 08098555. Date of manufacture was October 2009). Prior to the performance of the CTPA, conscious patients were taught to hold their breath for 10 – 40 seconds in full inspiration while lying in the supine position (Figure 3.3). For patients who were on mechanical ventilation, ventilation was suspended manually, in deep inspiration. Patients who were short of breath were scanned while they breathed shallowly.

A helical craniocaudal acquisition of images was used. Collimations of 1mm to 6mm and a pitch of 1.4 was used depending on the patient's condition and their ability to tolerate breath-holding. The time for acquisition was about 0.5 second per rotation, using a tube current which was be modulated inherently by the machine using the CareDose 4D software, which is automatically adjusts the tube current based on the patient's body habitus. Peak voltage of 140kVp was used. Image reconstruction was done using a soft tissue kernel with an increment of 1 - 3mm and a 512 x 512 matrix size. To enable proper visualization of the heart, the main pulmonary arteries and the subsegmental arteries, and also to identify other relevant findings, the scanning range will start from the lung apices to 2cm below the diaphragm.

To achieve optimum contrast enhancement of the thoracic vessels, 140mls of iodinated contrast (Omnipaque 300mg of iodine/ml by GE healthcare, Norway) was given 10 seconds prior to acquisition via an antecubital access using a Imaxeon single barrel injector (Figure 3.2). The rate of flow of contrast was set at 4ml/sec. The results of the CTPA were then transferred to the resident radiologist for reporting. Patients whose images are positive of acute pulmonary embolism were then interviewed and their consent sought for the use of their clinical information and imaging findings in the study.

Source Author's image

Figure 3. 1: Image of the CT scanner: Somatom Definition AS 64 slice CT scanner from Siemens, Germany. Model number 08098555. Date of manufacture was October 2009 was used for CTPA. It comes with ECG-gating that ensure the images are acquired in diastole, as required by set protocol

Source Author's image.

Figure 3. 2: image of Single Barrel Contrast injector which is used for bolus contrast administration to at appropriate volume to achieve optimal enhancement of the pulmonary arteries in Acute PE.

Source: Author's image

Figure 3. 3: Image show positioning of patient for CTPA. This patient was pregnant, therefore fetal shielding was employed to minimize radiation to fetus.

3.6.2 Interpretation of CT Pulmonary angiograms

Images of patients who consented to having their images used were uploaded to an Eizo workstation. The software, Syngo via by Siemens (Figure 3.4) was used for the reading of the images. For optimal visualization of the pulmonary arteries and its branches, the images were interpreted using a standard mediastinal window with the ability to change window setting to the one that best suit the interpretation needs of the radiologist. The images were read by a radiologist with at least 5 years of experience in reviewing CT Pulmonary angiograms.

The reader filled a structured questionnaire, which constitutes assessment of various cardiovascular parameters, PA clot load parameters and qualitative parameters as defined by the questionnaire (Appendix 1). With exception of the diagnosis of acute PE the reader was blinded from the clinical information and the outcomes of the patients, as well as any form of prior imaging findings of the patient.

Source: Source:facebook.com

Figure 3. 4: Image acquisition room at Spectra Health (Courtesy KNUST affiliate site, Spectra Health and Imaging Limited, Kumasi, Ghana

3.6.3 Interpretation of Acute Pulmonary embolism

3.6.3.1 Clot scores:

In this study, the criteria recommended by Ghaye et al[11] was be used as the basis for the diagnosis of acute pulmonary embolism on Imaging.

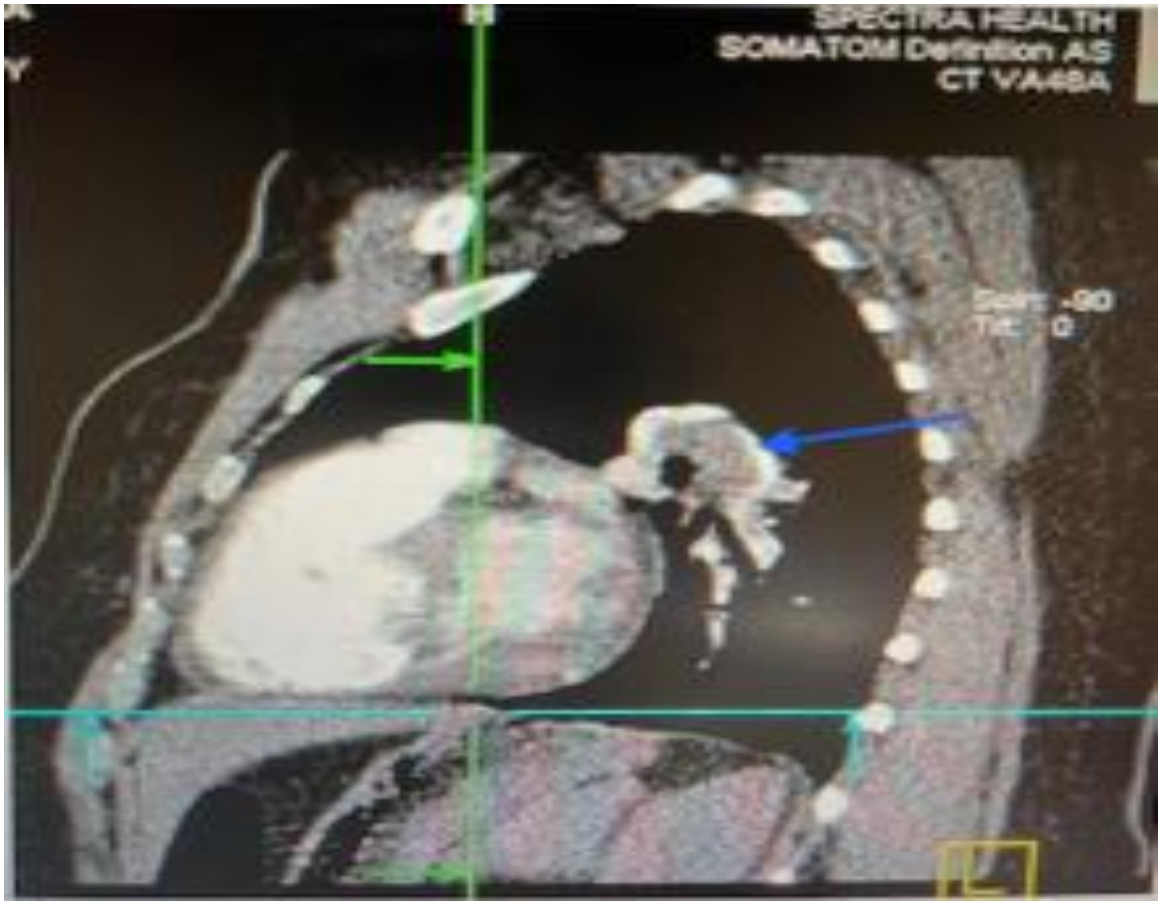
On imaging acute Pulmonary embolism was identified as

- An intraluminal filling defect that was central and partially occluded (Figure 3.5, 3.6 and 3.7) the lumen and was surrounded by contrast, described as the "railway sign" when seen parallel to the long axis of the lumen or as the "polo mint sign (Figure 3.6 below) when viewed perpendicular to the long axis of the vessel lumen.
- A mural filling defect which is surrounded by contrast and had an acute angle to the vessel wall or a filling defect which was eccentric and partially occluded the lumen of the vessel.
- A filling defect that occupied/filled the entire lumen and was not surrounded by contrast and there is associated dilation of the artery compared to the contralateral side.

A diagram of the Pulmonary artery vasculature was provided as part of the questionnaire and the sites of filling defects marked on a schematic diagram. (Figure 3.8 below). Both lungs were considered as having 10 segmental arteries each. The clot score was calculated based on the amount and location of the clot on CTPA, according to Qanadli[58]. The clot score was calculated as the product of N (the value of the proximal clot site which was equal to the number of segmental branches arising distally) x D (the degree of obstruction with a value of 1 describing partial obstruction and a value of 2 for complete obstruction).

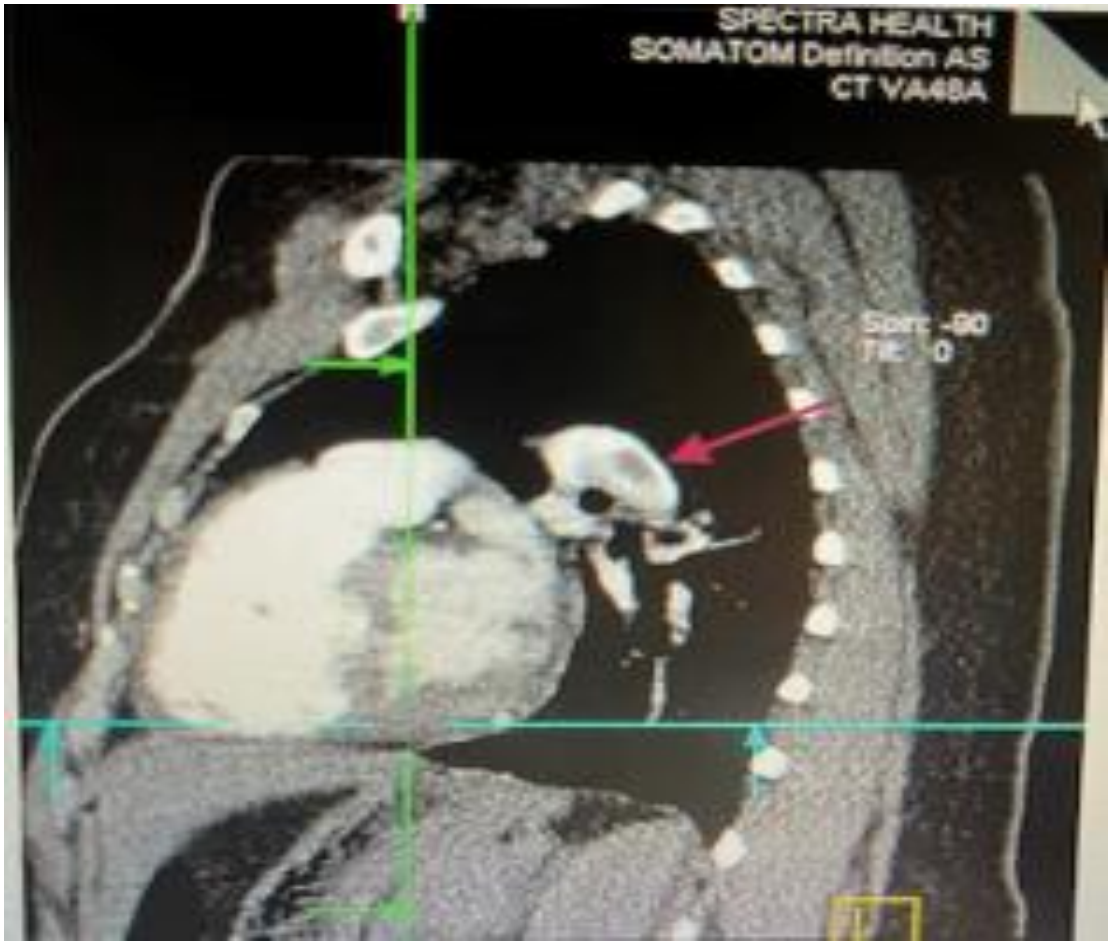
N x D = Clot load score

A clot partially occluding the lumen, D = 1 was defined as the clot occupying greater than 0% and less than 100% of the lumen of the vessel. A clot completely occluding the lumen, D = 2 is defined as the clot occupying 100% of the lumen. The fraction of the lumen filled by thrombus (the width of the thrombus divided by the diameter of the vessels lumen) was not considered. The maximum obstructive score attainable was 40 (each lung had a maximum of 20). This score was then calculated as a percentage.



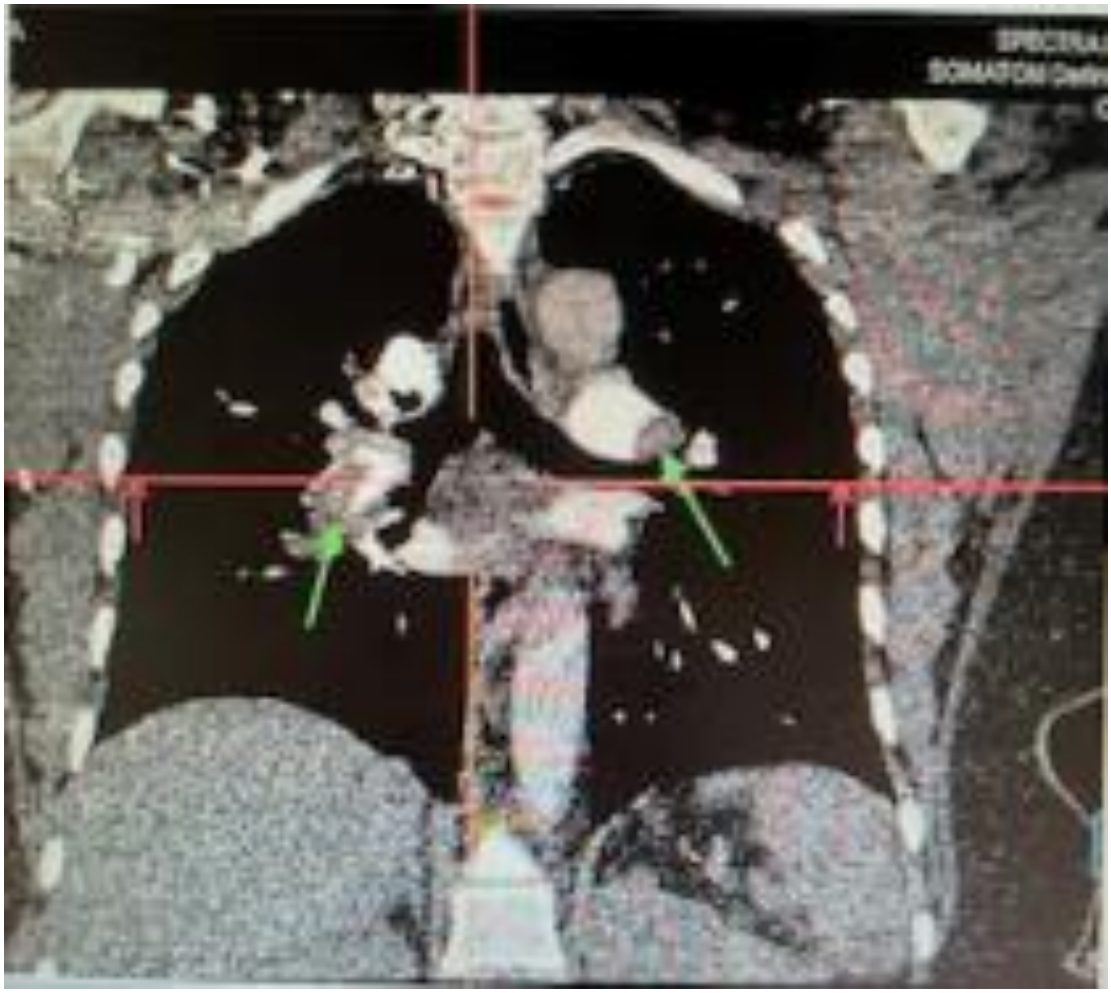
Source: author's images.

Figure 3. 5 : Sagittal reconstructed CTPA images of the chest with intraluminal filling defects that partially (Blue arrow) occludes the lumen. (Courtesy KNUST affiliate site, Spectra Health and Imaging Limited, Kumasi, Ghana.)



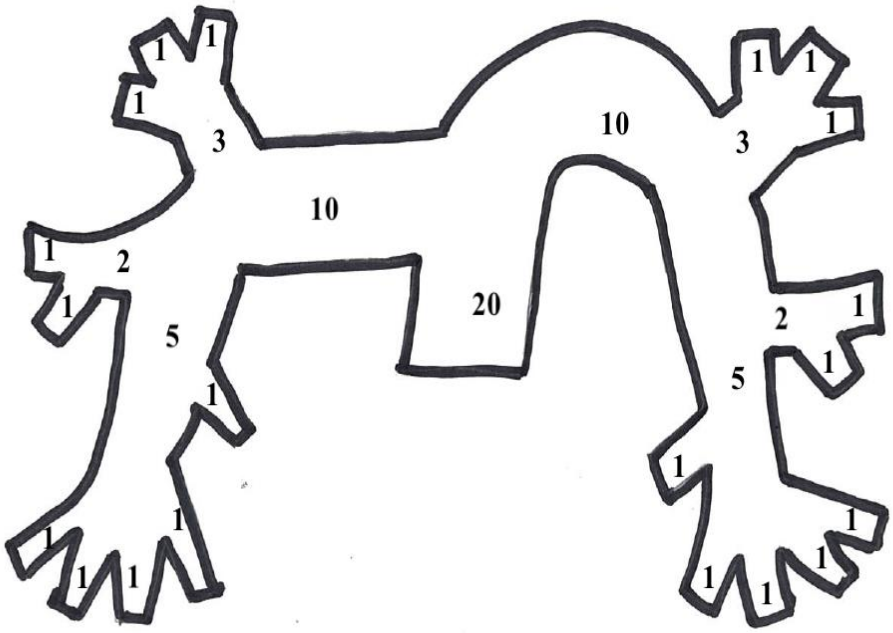
Source: author's images

Figure 3. 6 : Sagittal reconstructed CTPA images of the chest with intraluminal filling defects completely (red arrow on the right) surrounded by contrast. When completely surrounded by contrast it is described as the "polo mint sign. (Courtesy KNUST affiliate site, Spectra Health and Imaging Limited, Kumasi, Ghana.)



Source: author's images

Figure 3. 7: Coronal reconstructed CTPA images of the chest showing intraluminal filling defects in the main pulmonary arteries and their branches bilaterally (Green arrows) in a patient with acute PE. (Courtesy KNUST affiliate site, Spectra Health and Imaging Limited, Kumasi, Ghana



Source: Author's own construct

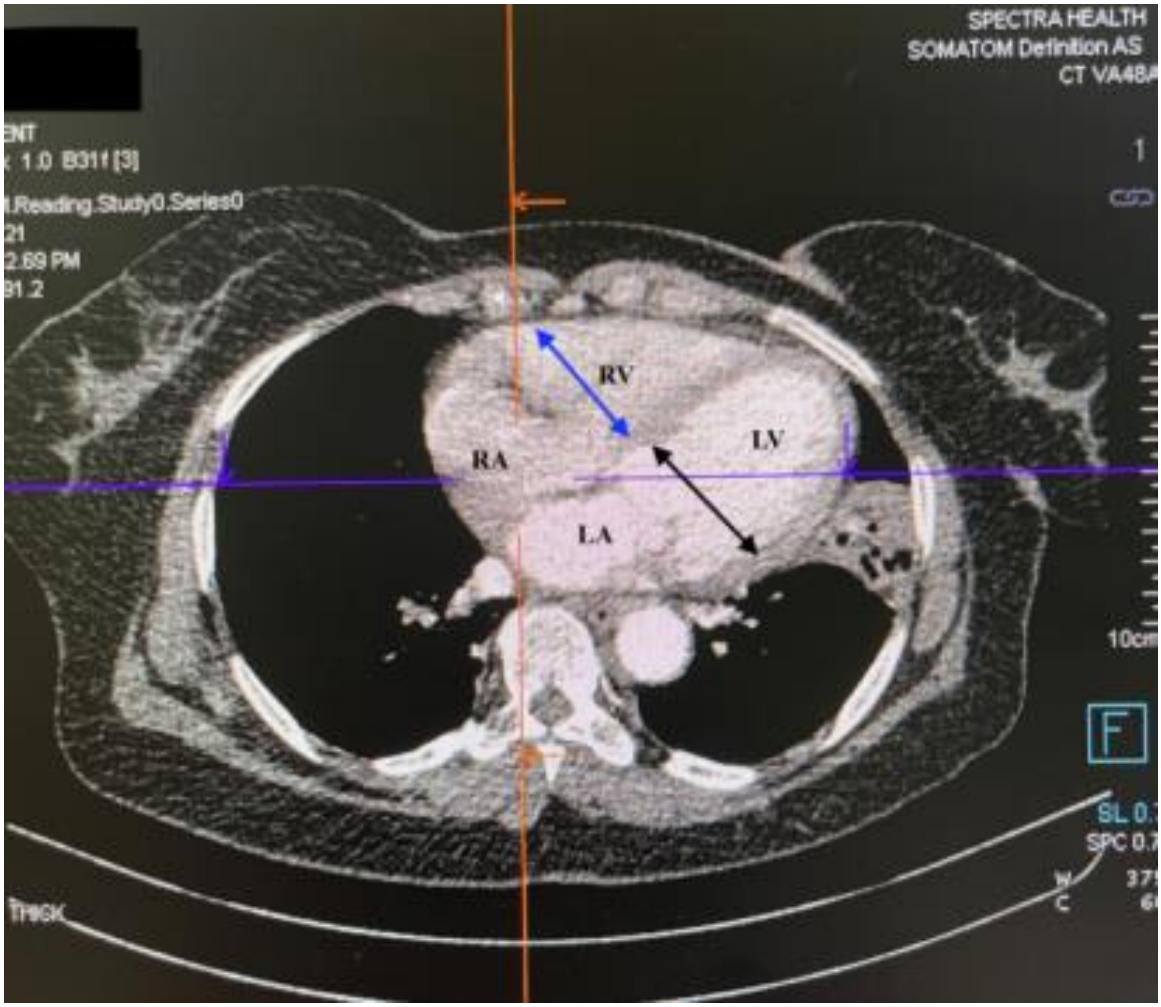
Figure 3. 8: Schematic representation of the arterial tree of the lung and the showing how the various branches are scored according to Qanadli scoring system.

3.6.3.2. Right ventricular short axis, left ventricular short axis and Rv/Lv ratio

Parameters such as the right ventricle short axis and the left ventricle short axis have been proven to have a correlation with the severity[47] and fatal outcomes[13 14]. The heart was be rotated to show a four-chamber view (Figure 3.9) in which the short axis of the right ventricle (blue arrow) and the short axis of the left ventricle (black arrow) were measured in diastole within the time of a single transverse scan.

This was ensured by synchronizing an electrocardiogram for ECG triggering. This scan was acquired perpendicular to the long axis of the heart. The widest distance between the inner aspects of the free walls of the ventricles and the interventricular septum[13 62 55 56] were measured and these measurements used to calculate the RV/LV ratio.

The cause of death in patients with severe acute pulmonary embolism is commonly known to be due to circulatory collapse from right-sided heart failure. On CTPA, measuring the various dimensions of the right heart chambers and the venous structures which are more proximal, like the azygos vein and the inferior vena cava was used is evaluating acute right heart failure.



Source: author's image

Figure 3. 9: RV/LV Measurement on an axial CT image: Axial CT scan of the Heart in the four-chamber view in a patient with suspected pulmonary embolism. Measurements were taken at the upper third of the ventricle below the valves at level of maximum ventricular diameter.

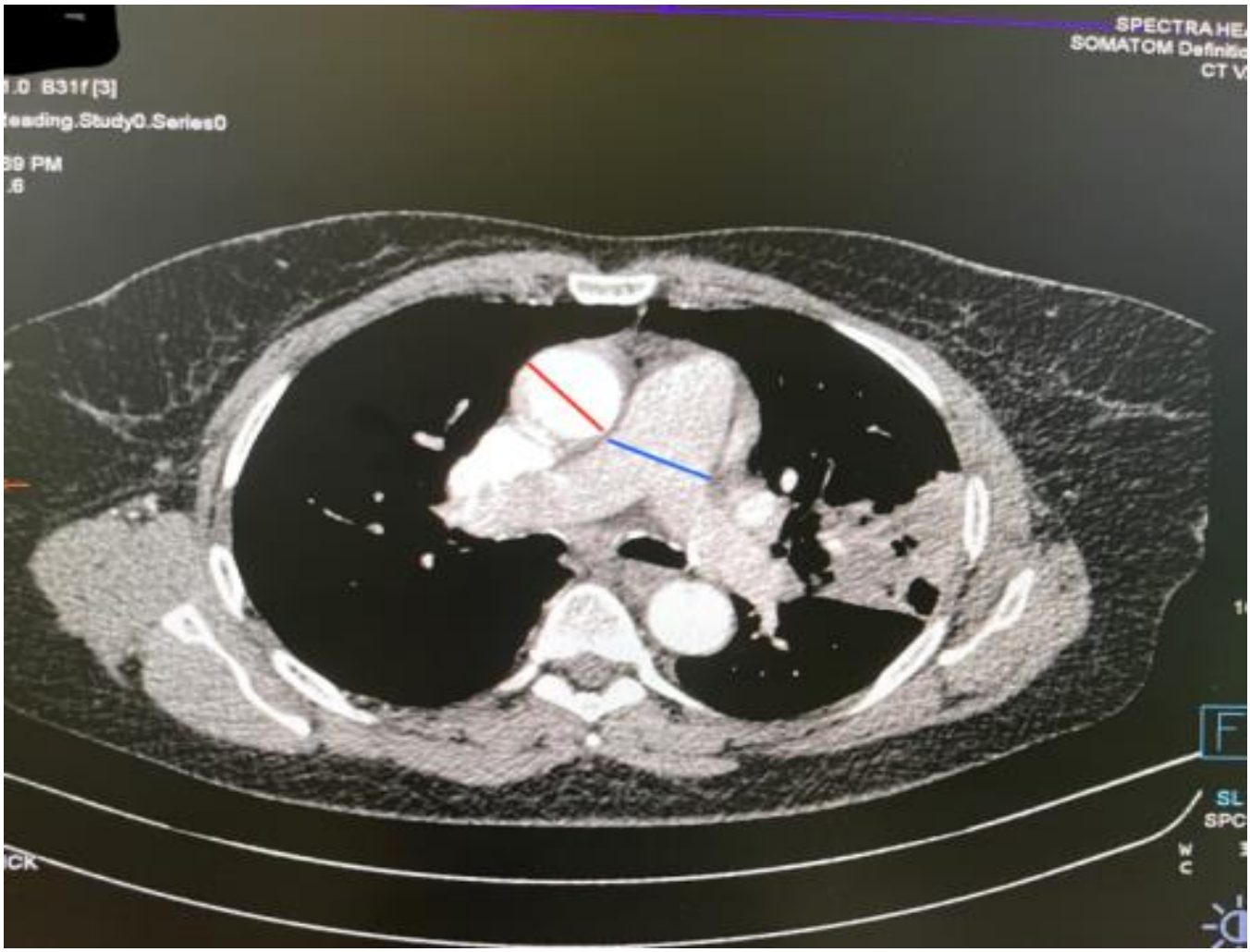
3.6.3.3 Pulmonary artery/Aortic diameter ratio (PA/Ao diameter)

The main pulmonary artery lumen and the ascending aorta diameters (Figure 3.10) were acquired by the use of electronic calipers and it will form the bases on which the Main pulmonary artery diameter and aortic diameter ratio will be calculated.

The vascular measurements will also include the diameter of the Azygos vein and the Superior vena cava. Again, electronic calipers will be used to do these measurements on images that are adjusted and re-formatted in a plane 90 degree to the long axis of the vessel being evaluated.

The diameter of the main pulmonary artery was obtained just proximal to its bifurcation into its branches, the Aortic diameter was obtained in the middle third portion of its ascending component, the diameter of the Azygos vein was obtained in its region that faces the right tracheal wall and the superior vena cava, at the level of the Azygos arch.

Qualitative parameters that were evaluated and documented as being present or absent will include leftward bowing of the interventricular septum, the presence of refluxed contrast medium into the inferior vena cava.



Source: Author's image

Figure 3. 10: To Obtain the artery-aorta (PA/Ao) ratio measurements were taken at the widest transverse diameter of the PA (Blue line) and the corresponding transverse diameter of the ascending aorta (Red line). (Image courtesy KNUST affiliate site, Spectra Health and Imaging

3.7 Data Collection Techniques and tools

The report for each CTPA were reviewed from the database by a single author and the images of the positive tests selected. Images of all patients with a diagnosis of Acute pulmonary embolism made by the resident radiologist were recruited if their consent is given. The trained research assistants administered the consent forms in a language they understand. The images demographics and clinical data were given anonymous identification numbers. Clinical information and demographics were taken by two trained research assistants. The research assistants followed up on the recruited patient by way of telephone call at the end of 30 days from the onset of symptom. The images were then reviewed by a radiologist with at least five years working experience. He will fill a structured questionnaire which focuses on specified parameters.

3.8 Data Management and Analysis

Data collected from the facility each day was uploaded to the cloud server, which was password-protected to prevent access by unauthorised persons. Only the principal investigator had the password and could access the cloud server. Data was then exported to Microsoft Excel (Redmond, Washington). All analysis was carried out using STATA version 17 (College Station, Texas) statistical software. The study employed both descriptive and inferential statistics in analysing the data.

The key variables used were socio-demographic characteristics (sex, age, educational status and occupational status), clinical findings, risk factors, clinical management imaging findings, total cloth score and outcome of patient. Social and demographic information of the respondents was presented using percentages, frequencies, means, standard deviations, pie charts and tables.

Student t-test and logistics regression were conducted to compare and predict the best radiological parameter for mortality. A chi-square test was used in addition to Fisher's exact test at a 95% level of significance to test for the association of age and duration of death, age and outcome of patient. To obtain predictors of mortality, bivariate and multivariate analyses were conducted between radiological parameters (right ventricular, left ventricular, Rv/Lv ratio, Pulmonary artery diameter, aortic diameter, pulmonary aortic diameter, azygos diameter, reflux IVC and left ward bowing of interventricular septum) and mortality.

All analyses in this report were narrowed to cases that were reported during the study period. Statistical significance for all testing was set at a p-value of 0.05 with a 95% confidence interval.

3.9 Data Handling

The safety of data collected was guaranteed by ensuring proper handling and maintaining data from getting misplaced or the material from getting destroyed. All electronic records were password protected and will be stored for 10 years. All paper records will be stored for three years. During this period, anonymity of respondents will be guaranteed. Data collected were checked for completeness and correctness and entered in MICROSOFT EXCEL^{TM}. Data analysis was done using STATA 17 for windows. Data analyzed was presented graphically and frequencies tabulated.

There was the use of parametric testing and inferential statistics including chi-square and students t-tests to for associations. The level of significance will be set using 95% confidence intervals.

3.10 Ethical and Legal Considerations

After approval by the Ghana College of Physicians and Surgeons, after which permission was sought from the study site; which was Spectra Health, an affiliate diagnostic and research center under the Kwame Nkrumah University of Science and Technology for the research to be conducted. The study was registered, ethical clearance was sought and a certificate issued by the Committee on Human Research and Publication Ethics (CHRPE), at the School of Medical Sciences at the Kwame Nkrumah University of Science and Technology (KNUST), Kumasi. This body directs and records all research that takes place at KNUST or any of its affiliate sites, of which Spectra Health is one. All necessary protocols were reviewed and approved by the committee.

The study's purpose and goal were explained to the identified patients or the relative of the patient with the desired imaging findings. Those who agreed were recruited. Before recruitment, detailed issues of protection of their confidentiality were discussed with them or their accompanying relative relatives. Patients who agreed or patients whose legally authorized representative agreed to allow the patient part in this research were interviewed in a private space. Their images were deidentified. All ethical requirement and principles were adhered to throughout the period of the study.

CHAPTER FOUR

RESULTS

4.0 Introduction

This chapter presents the results of this research as obtained using graphs and tables. The results are presented in tables and figures preceded by a narration. The proposed sample size was sixty-three (63) participants; however, a total of sixty-four (64) participants were recruited for this study all of which had image findings positive for acute PE. Out of this total, four (4) patients were excluded from the study on account of poor image quality that was suboptimal as a result of excessive motion artifacts. So even though these images were diagnostic of PE, the poor image quality made quantification of clot burden and measurement of other vascular parameters unachievable. Consequently, a patient population of 60, in total were included in the final study.

4.1 Demographic status of Participants

Table 4.1 represents the demographics of the participants and consisted of patient age, gender, occupational status and educational levels and is represented graphically in Fig 4.1. Out of the 60 participants recruited in this study, 26 (43.33%) were males and 34 (56.67) were females. The age distribution of participants ranged from 29 – 89 years with the average age of the participants being 58 years. The majority, 26 (43.44%) of the participants that presented with acute PE were between the ages of 51 - 70 (43.4%), with the lowest number of participants being found within the 21 – 30 years age category. Majority, 24 (40%) of the patients had basic education and the minority, 13 (21.67%) having achieved tertiary education. The majority, 35 (58.33%) of the participants in this study were employed with very few 3 (5%) of the participants being professionals. 20 (33.33%) participants died within the 30 – period.

Table 4. 1: Demographics of patients with acute PE

Variable	Frequency (N=60)	Percentage
Age group		
21-30 years	1	1.67
31-40 years	8	13.33
41-50 years	11	18.33
51-60 years	13	21.67
61 -70years	13	21.67
71-80 years	8	13.33
81-90 years	6	10.00
Gender		
Male	26	43.33
Female	34	56.67
Educational status		
None	12	20.00
Basic	24	40.00
SHS	11	18.33
Tertiary	13	21.67
Occupational status		
Unemployed	25	41.67
Farmers	8	13.33
Professional	3	5.00
Skilled worker	6	10.00
Traders	18	30.00

Source: Field Data, 2021

Table 4. 2 represents the demographic pattern of Patients Outcome of the study population. Out of the 20 (33.3%), patients with short term mortality, 5 (25%) occurred among patients between the ages of 41 – 50 and 5 (25%) also occurred between the ages of 51- 60. Cumulatively, half of the deaths occurred among patients between the ages 41 – 60 years. The majority 13 (65%) of deaths within the 30-day period occurred among females. Mortality was lowest among participants that had tertiary education, 3 (15%) and was not note to occur in workers with a professional background (0). No association was seen between the listed demographic parameters and short-term mortality.

Table 4. 2: Distribution of Demographics and outcome of participants

Socio-demographic characteristics	Alive	Dead	P-value	X^2
Age			**0.77**	**3.24**
21-30 years	**1**	**0**		
31-40 years	**6**	**2**		
41-50 years	**6**	**5**		
51-60 years	**8**	**5**		
61 -70years	**10**	**3**		
71-80 years	**6**	**2**		
81-90 years	**3**	**3**		
Age			**0.335**	**0.84**
Male	**19**	**7**		
Female	**21**	**13**		
Educational status			**0.59**	**1.90**
None	**7**	**5**		
Basic	**17**	**7**		
SHS	**6**	**5**		
Tertiary	**10**	**3**		
Occupational status			**6.75**	**0.15**
Unemployed	**20**	**5**		
Farmers	**4**	**4**		
Professional	**3**	**0**		
Skilled worker	**4**	**2**		
Traders	**9**	**9**		

Source: Field Data, 2021

4.3 Risk Factors

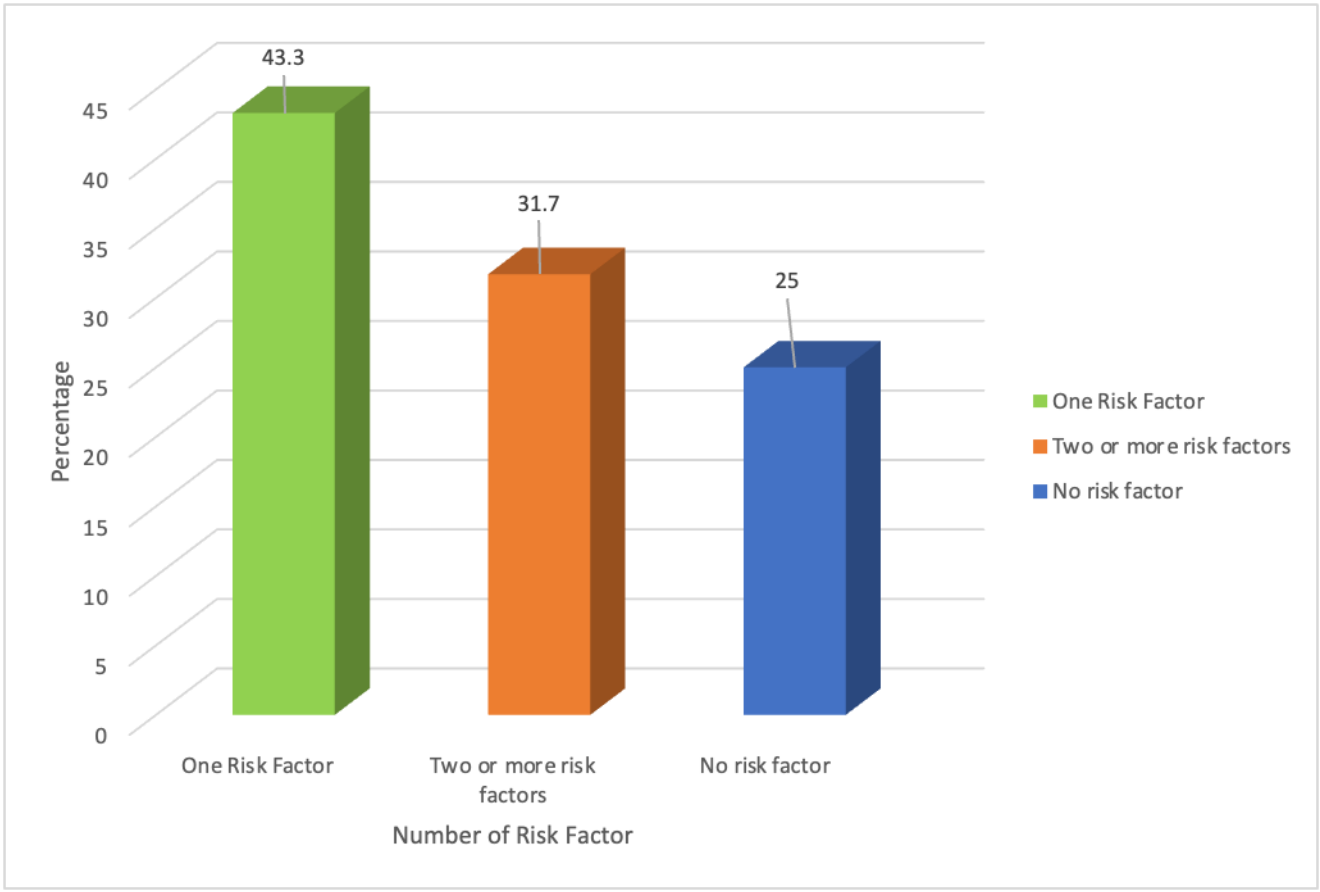
Table 4.3 represents the distribution pattern of the Risk Factors in the study population. The five commonest risk factors associated with acute PE were Hypertension 27 (45%), which was followed by Diabetes mellitus 15 (25%), recent surgery 7 (11.67%), clotting abnormalities 6 (10%) and the lowest was COVID-19 pneumonia 5 (8.33%) and Fig 4.2. is a graphical representation of the Range of average numbers of risk factors in participants with acute PE. The majority 45 (75%) of the participants had at least one risk factor with the minority 15 (25%) having unprovoked/idiopathic PE.

Table 4. 3: Distribution of risk factors for PE identified among participants

RISK FACTORS	FREQUENCY	PERCENTAGE
Hypertension	27	45.00%
Diabetes Mellitus	15	25.00%
Clotting Abnormalities	6	10.00%
Recent Surgery	7	11.67%
History of Recent Travel	2	3.33%
Immobilization	2	3.33%
Asthma	3	5.00%
Covid 19 Pneumonia	5	8.33%
End stage renal disease	2	3.33%
Heart Failure	2	3.33%
DVT	2	3.34%
Obesity	1	1.67%
Renal Malignancy	1	1.67%
Right Tibia Fracture	1	1.67%
Recurrent PE	1	1.67%

Source: Field Data, 2021

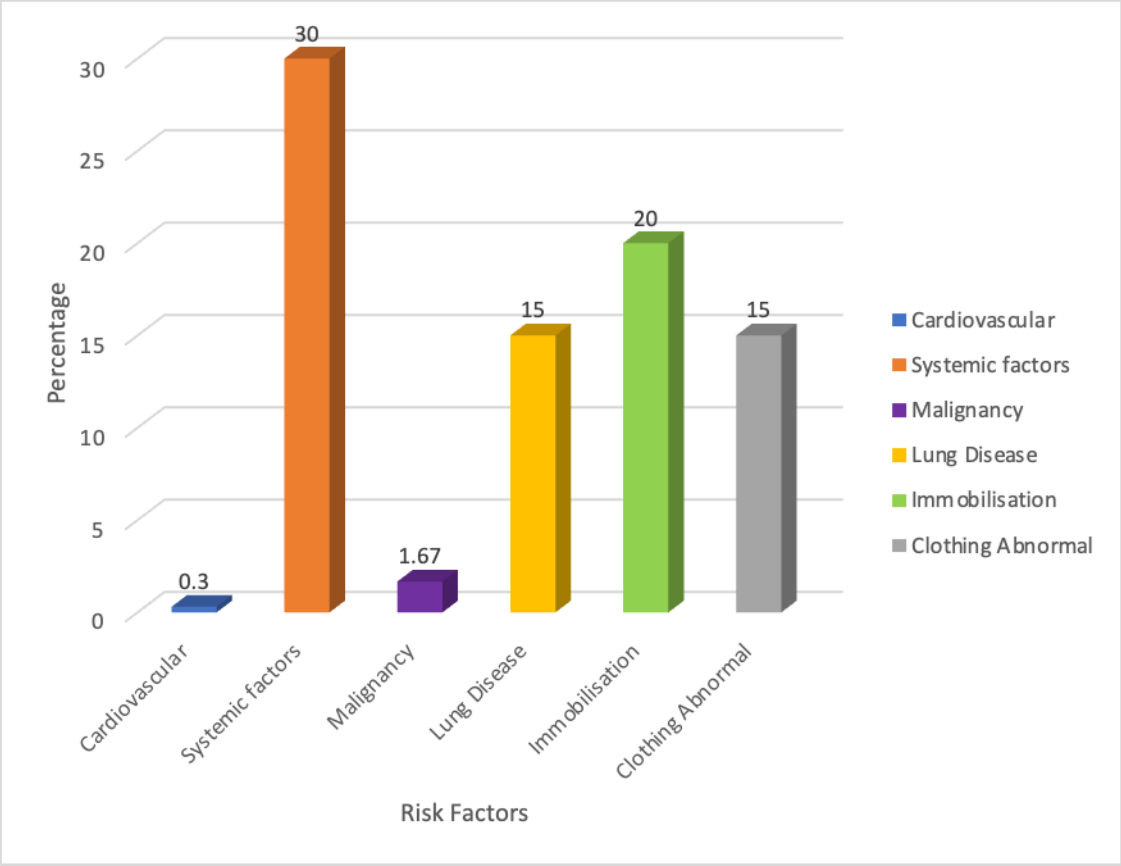
Figure 4.1 is a graphical representation of the average number of risk factors that the participants had. It is noted that the majority, 45 (75%) of patients had at least one risk factor. 14 (25%) had no identifiable or known risk factor.



Source: Field Data, 2021

Figure 4. 1: Range of average numbers of risk factors in participants with acute PE

Fig 4. 2 is the graphical representation of Categories of Risk factors of the participants. A lot of risk factors are associated with PE. For the sake of simplicity, they were grouped under various heading; namely Cardiovascular, Systemic, Malignancy, Lung disease, Immobilisation, and Clotting abnormalities as risk factors. The cardiovascular factors consisted of hypertension, and heart failure. The systemic factors consisted of diabetes mellitus, renal failure and obesity. Clotting abnormalities consisted of patients with a history of DVT or recurrent PE. The Immobilization category constituted patient who had had recent surgery, tibial fractures and history recent travel. Lung diseases included Asthma and COVID 19 pneumonia.



Source: Field Data, 2021

Figure 4. 2: Categorized Risk Factors of acute PE in recruited patient population

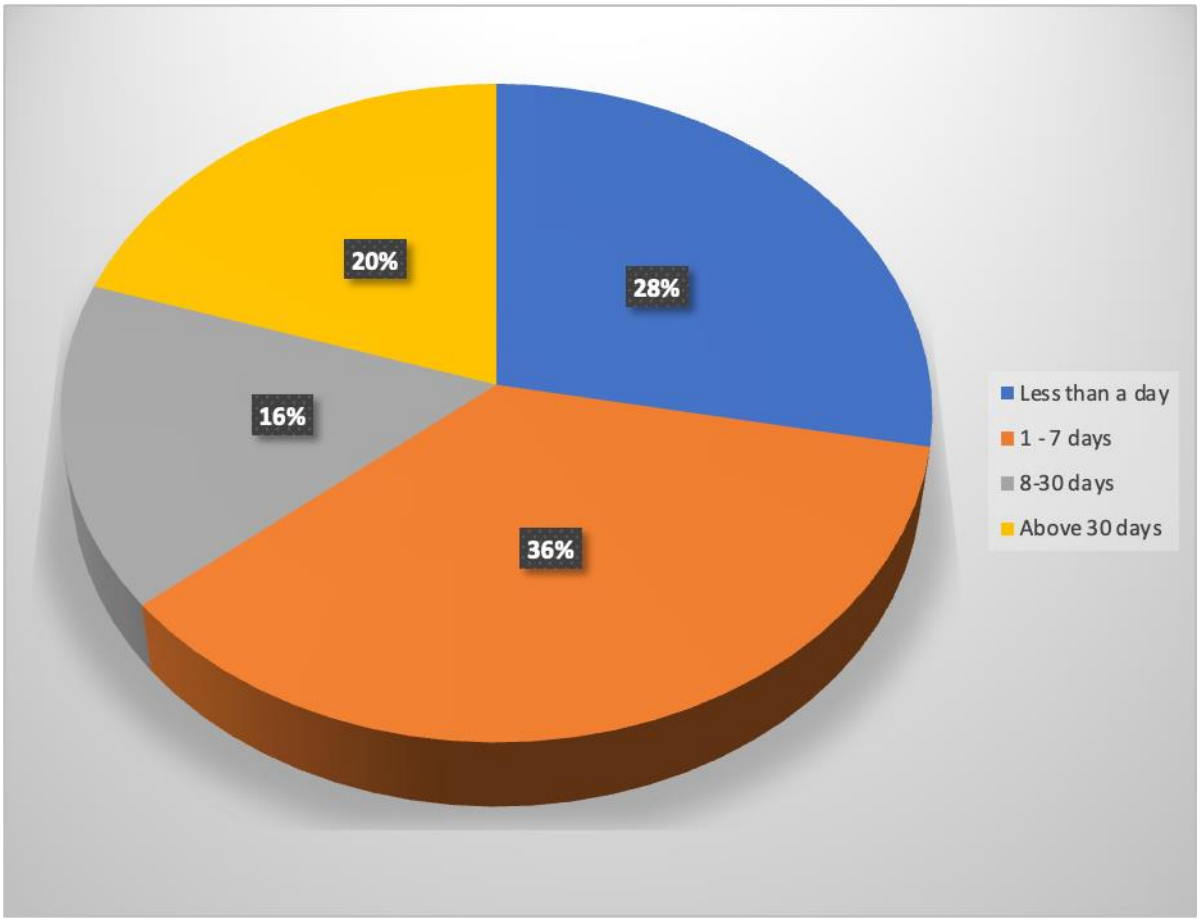
Table 4.4 represents the distribution pattern of the symptoms that the participants presented with. The majority of the participants 36 (60%) presented with breathlessness. Chest pain/discomfort was the second commonest 18 (30%) symptom. Shock was the least occurring presentation, with only 1 (1.67%) participant presenting so.

Table 4. 4: Distribution of the symptoms of participants.

SYMPTOMS	FREQUENCY	PERCENT
Chest pain or discomfort	18	30.00%
Breathlessness	36	60.00%
Malaise	10	16.67%
Lower limb swelling	11	18.33%
Shock	1	1.67%
Cough	5	8.33%
Dizziness	3	5.00%
Easy Fatiguability	3	5.00%
Hemoptysis	2	3.33%

Source: Field Data, 2021

Fig 4.3 is a graphical representation of Duration of illness from time of diagnosis on CTPA to death of patients in the study population. 20 (33.3%) patients out of 60 (66.7%) patients died within the 30 - day period indicating that majority of the patient survived beyond 30 days. Of those who died within the 30-day period, the majority of deaths 36% occurred between the days 1-7 and the second highest number of deaths 28% occurred within 24 hours. That is to say that more than half (64%) of deaths occurred within the first 7 days from diagnosis of acute PE.



Source: Field Data, 2021

Figure 4. 3: Distribution of Duration between diagnosis and Death patients with short term mortality for PE.

Table 4.5 represents the outcome of patients among the various age categories. The majority of survivors, 10 (25%) were found between the ages of 61 – 70 with the highest occurrence of short-term mortality 10 (25%) occurring between the ages of 41 – 60. However, there was no statistical evidence to prove that there exists an association between age group of patients and patient outcome. (P-Value = 0.943).

Table 4. 5: Age distribution of participants with acute PE versus outcome of patients

AGE GROUP	Alive	Dead	Total	P-VALUE
21 – 30	1	0	1	0.943
31 – 40	6	2	8	
41 – 50	6	5	11	
51 – 60	8	5	13	
61 – 70	10	3	13	
71 – 80	6	2	8	
81 – 90	3	3	6	
TOTAL	40	20	60	

Source: Field Data, 2021

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Table 4.6: represents the distribution pattern of mortality within the 30-day period among the various age categories and it was found that for age categories 41 years and above, the majority 16 (80%) of their mortality occurred within the first 7 days and for those 40 years and below all their mortalities, 4 (20%) occurred between days 8 -30. Significantly, there was no evidence to prove any association Age, duration between date of diagnosis and date of mortality in patients with short term mortality (P- Value = 0.453) in patients with APE.

Table 4. 6: AGE, DURATION BETWEEN DATE OF DIAGNOSIS AND DATE OF MORTALITY IN PATIENTS WITH SHORT TERM MORTALITY

AGE	**Less than a day**	**1-7 days**	**8-30 days**	**Total**	**P - VALUE**
21 - 30	0	0	0	0	0.453
31 - 40	0	0	2	2	
41 - 50	3	2	0	5	
51 - 60	0	4	1	5	
61 - 70	1	2	0	3	
71 - 80	1	0	1	2	
81 - 90	2	1	0	3	
TOTAL	7	9	4	20	

Source: Field Data, 2021

Fig 4.4 is a graphical representation of the number pf participants in the study population who had reflux of contrast medium in the Inferior vena cava due to increased right heart pressures. The majority of the participants 55% showed evidence of reflux of contrast medium into the inferior vena.

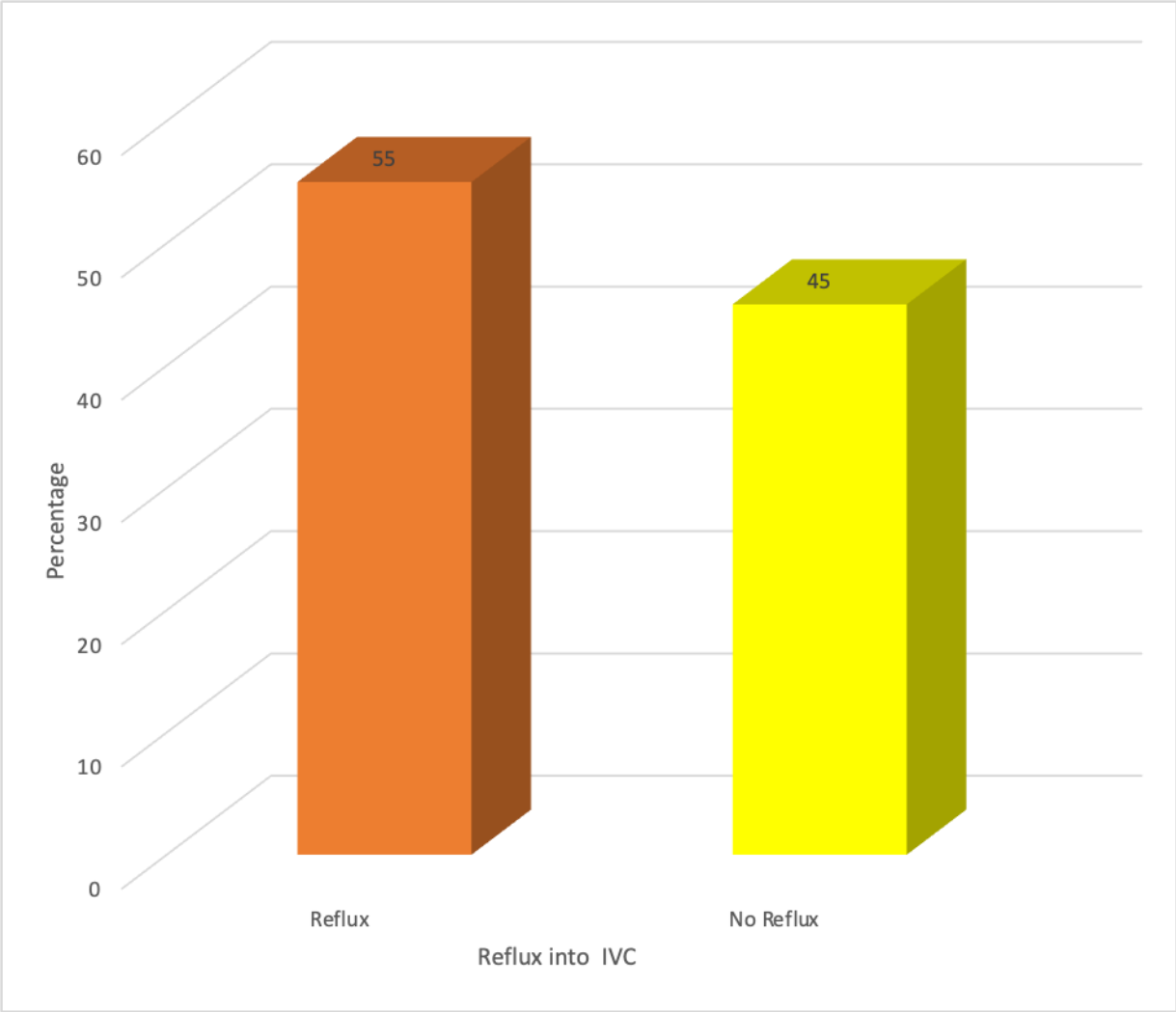


Figure 4. 4: Distribution of Reflux into IVC with Short term Mortality

Fig 4.5 is a graphical representation of the number pf participants in the study population who had leftward intraventricular septal bowing due to increased pressures on the right side of the heart. The majority of the participants 75% showed evidence of reflux of contrast medium into the inferior vena.

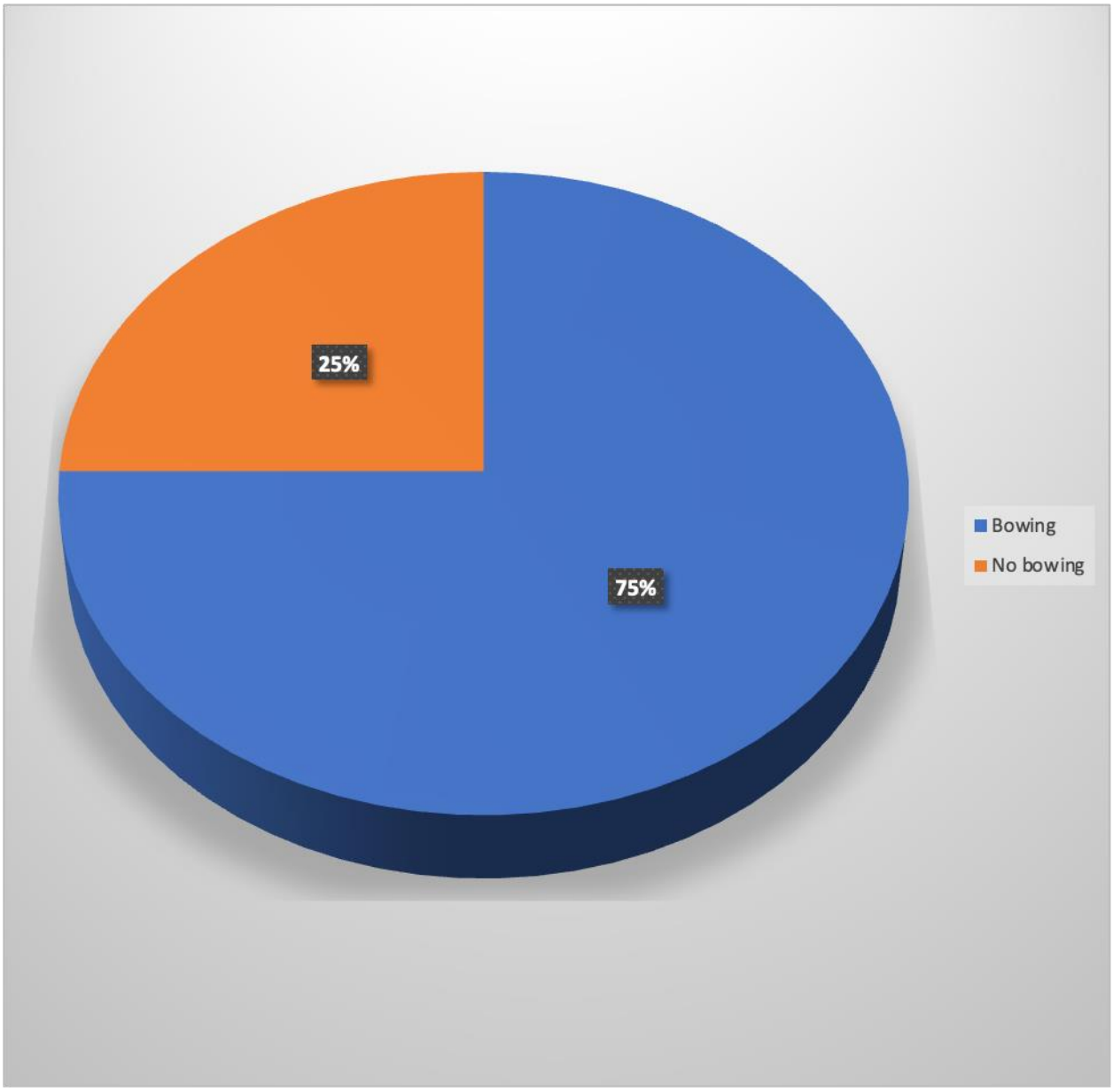


Figure 4. 5: Distribution of leftward interventricular septal bowing with short term mortality

Table 4. 7 represents the ranges for the various Radiological Parameters of right Heart Dysfunction and cloth load scores in Acute PE found in this study. The Pulmonary Artery Aortic Diameter Ratio recorded an average of 2.63 and a minimum of 0.59 as shown in table 4.0. The ranges for the Rv/Lv ratio in the study population was from 0.7 – 2.63 (Mean; 1.43) he least presenting. The ranges for the total clot score recorded was 5% - 75% (Mean; 45.58)

Table 4. 7: SUMMARY OF RADIOLOGICAL PARAMETERS OF RIGHT HEART DYSFUNCTION AND CLOT LOAD SCORES IN ACUTE PE.

	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
Age	29	89	58.07	15.30
Rv/Lv Ratio	0.7	2.63	1.43	0.41
Pulmonary Artery Diameter	2	4.60	2.98	0.57
SVC Diameter	1.72	4.42	2.41	0.49
Right Ventricular Diameter	2.33	6.80	4.23	0.98
Left Ventricular Diameter	1.95	5.10	3.07	0.77
Aortic Diameter	2.22	5.80	3.16	0.65
Pulmonary Artery Aortic Diameter Ratio	0.59	98	2.63	12.53
Azygos Diameter	0.57	5	1.12	0.57
Total Clot Score	2	30	18.23	8.35
Total Clot Score Percent	5	75	45.58	20.88

Source: Field Data, 2021

Table 4. 8, 4.9 and 4.10represent the list of the various radiological parameters of Right heart dysfunction and clot load score among survivors and non-survivors (continuous variables), leftward bowing and reflux into the IVC (non-continuous variables) and their accuracy in predicting short term mortality. From this table, using univariate analysis, the continuous variables which were found to be accurate predictors of short-term mortality consisted of the RV diameter (P-value = 0.003), Rv/Lv ratio (P-value = 0.001) and the clot score (P-value < 0.001) and leftward bowing (P-value = 0.04) was the non-continuous variable which was found to be an accurate predictor of short-term mortality.

Table 4. 8: RADIOLOGICAL PARAMETERS (CONTINUOUS VARIABLES) AND THEIR ACCURACY IN THE PREDICTION OF SHORT-TERM MORTALITY IN ACUTE PE.

Variable	OR	95% CI	P - Value	Coefficient	Chi2
Rv diameter	2.85	11.43 – 5.66	0.003*	1.04	11.31
					2.28
Lv diameter	0.55	0.2– 1.23		- 0.58	
Rv/Lv Ratio	39.04	4.92 – 309.93	0.001*	3.66	19.22
PAD	1.89	0.72 – 4.97	0.19	0.63	1.74
Azygos diameter	0.96	0.36 – 2.53	0.94	- 0.03	0.00
Clot score (%)	1.07	1.03 – 1.11	<0.001*	0.06	1
SVC diameter	3.08	0.93 – 10.23	0.06	1.12	3.83

*** Statistically significant at α= 0.05**

Source: Field Data, 2021

Table 4. 9: SUMMARY OF RADIOLOGICAL PARAMETERS (CONTINIOUS VARIABLES) OF RIGHT HEART DYSFUNCTION AND CLOT LOAD SCORES IN ACUTE PE WITH SHORT TERM MORTALITY

	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
Age	35	89	58.15	15.61
Rv/Lv Ratio	1.1	2.63	1.73	0.45
Pulmonary Artery Diameter	2.56	4.60	3.11	0.51
SVC Diameter	1.74	3.1	2.59	0.37
Right Ventricular Diameter	3.06	6.80	4.81	0.90
Left Ventricular Diameter	2.1	5.1	2.87	0.67
Aortic Diameter	2.33	5.8	3.22	0.80
PA/Ao Diameter Ratio	0.58	1.44	1.00	0.23
Azygos Diameter	0.76	1.72	1.11	0.27
Total Clot Score	5	30	24.25	6.58
Total Clot Score Percent	12.5	75	60.62	16.46

Source: Field Data, 2021

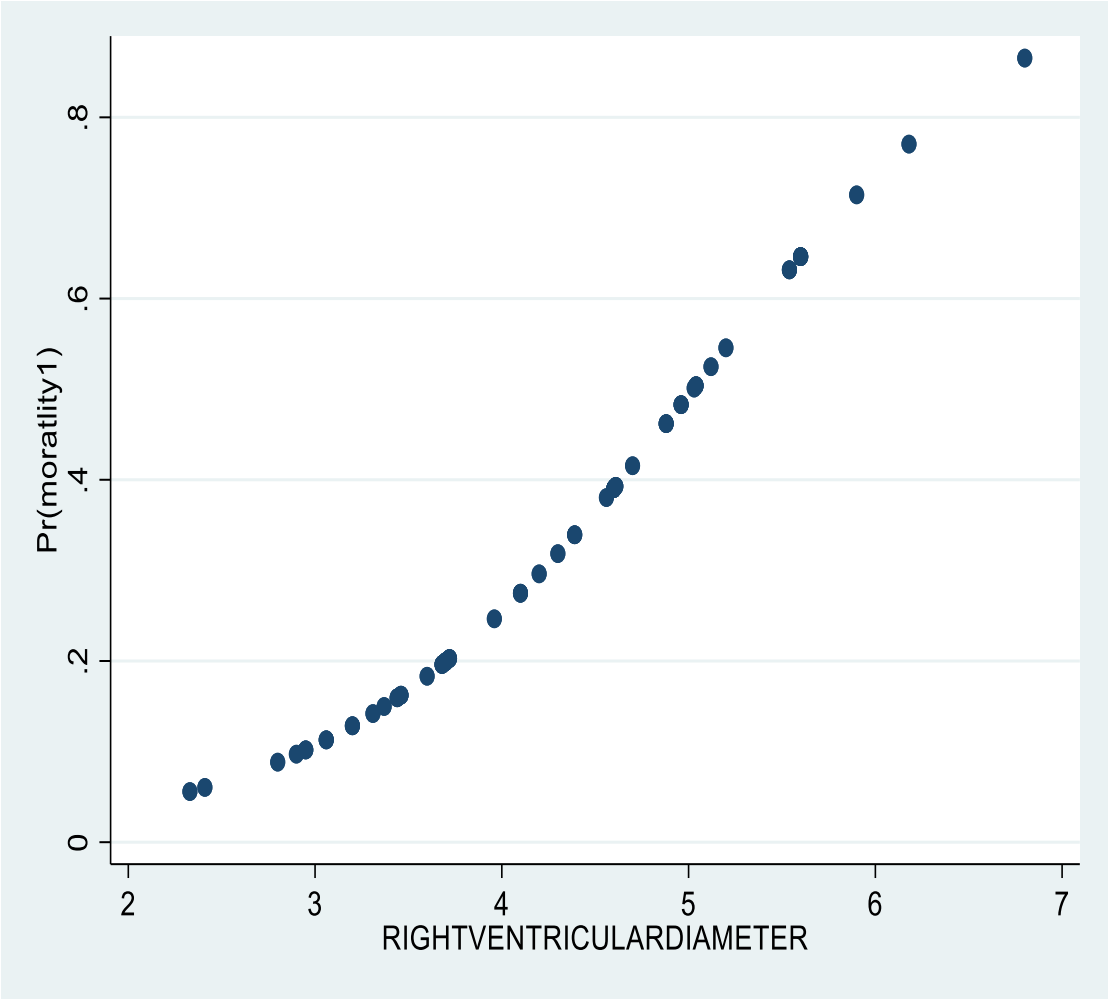
Table 4. 10: RADIOLOGICAL PARAMETERS (CATEGORISED VARIABLES) AND THEIR ACCURACY IN THE PREDICTION OF SHORT-TERM MORTALITY IN ACUTE PE

	Left ward bowing		Chi square	P value
Mortality	No	Yes	4.10	0. 04*
Alive	21 (80.77)	19 (55.88)		
Dead	5 (19.23)	15 (44.12)		
	Reflux into IVC		0.13	0.71
Alive	20 (68.97)	20 (64.52)		
Dead	9 (31.03)	11 (35.48)		

4.5 Radiological Parameters and their Accuracy in the Prediction of Short-Term Mortality in Acute PE.

The Figures 4.16, 4.17, 4.18. 4.19, 4.20 and 4.21 show graphically the relationship between the various radiological parameters and short-term mortality and their various statistical distributions.

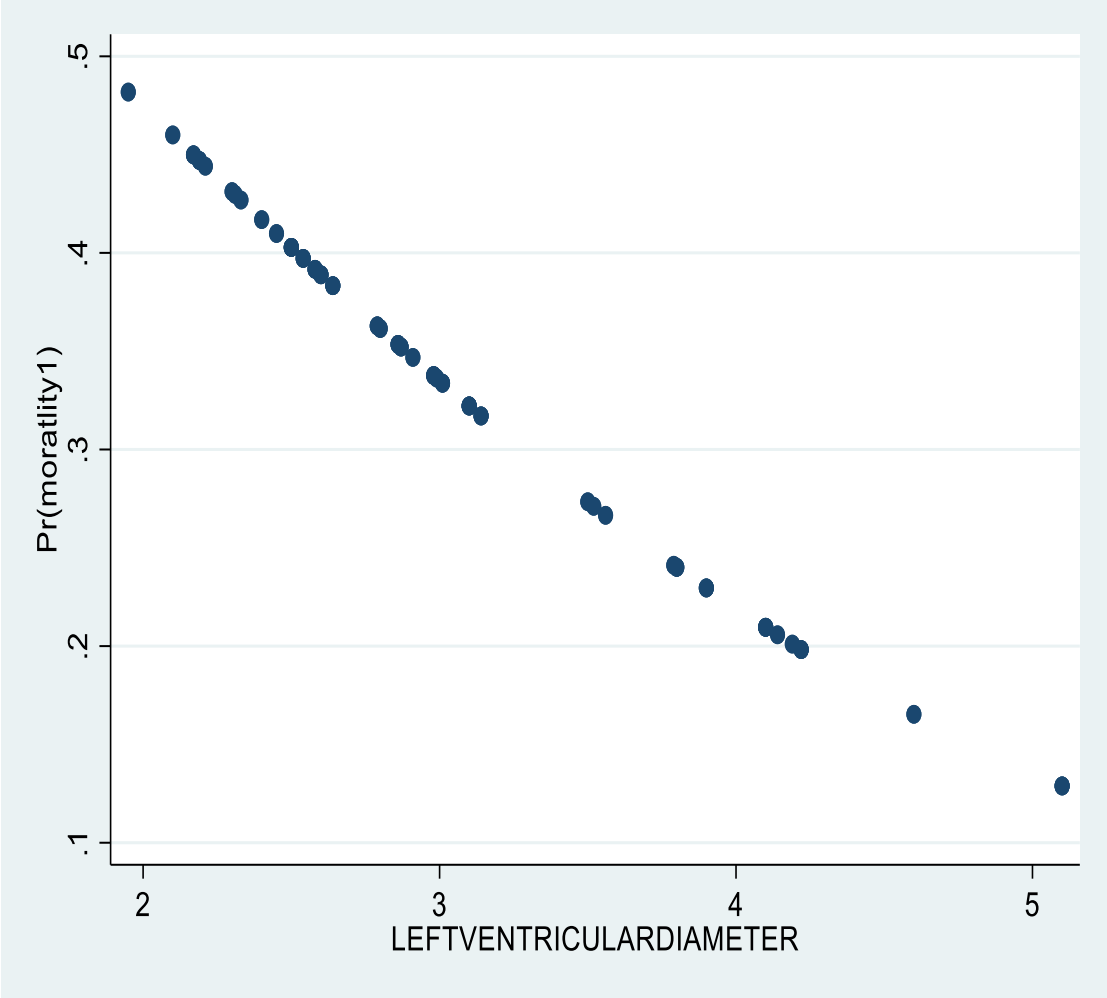
The parameters that were good predictors of mortality on univariate analysis were RV diameter, Rv/Lv ratio and Clot load score



Source: Field Data, 2021

Figure 4. 6: Distribution of Right ventricular Diameter and Mortality

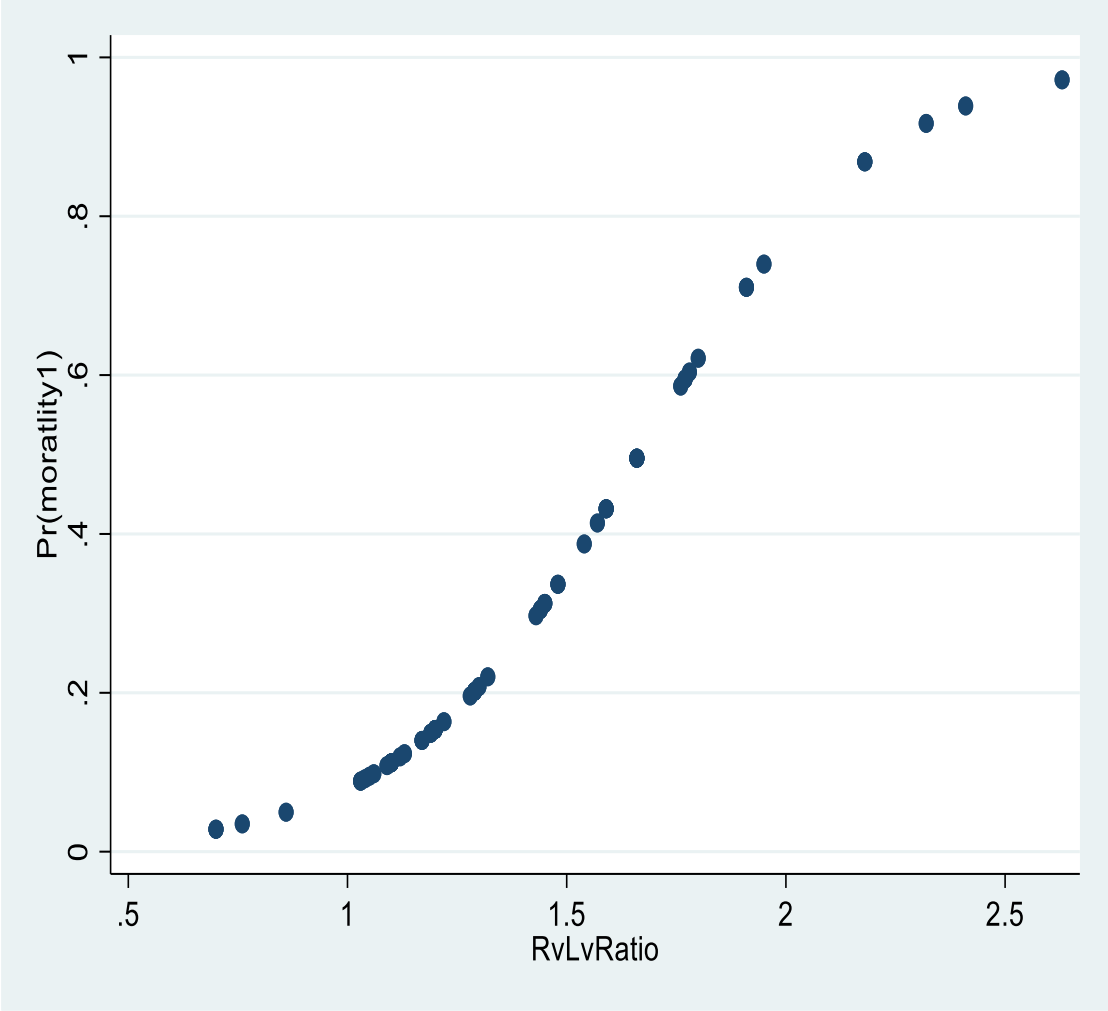
The graph above demonstrates that as the right ventricular short axis increase, mortality also increases.



Source: Field Data, 2021

Figure 4. 7: Distribution of Left ventricular Diameter and Mortality

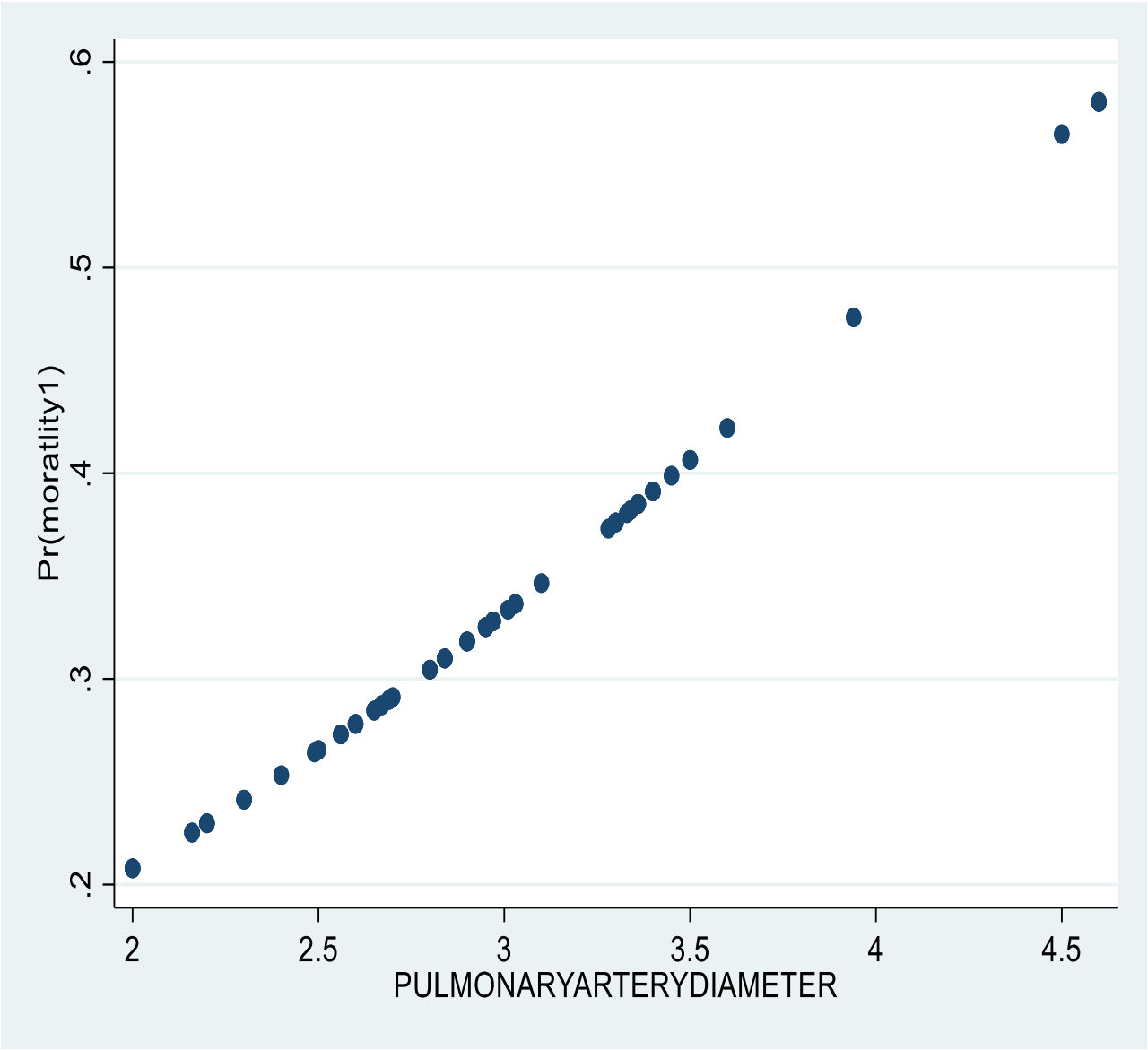
The graph above demonstrates that as left ventricular diameter decreases mortality increases. This shaped curve resembles no statistical distributions.



Source: Field Data, 2021

Figure 4. 8: Distribution of Rv/Lv Ratio and Mortality

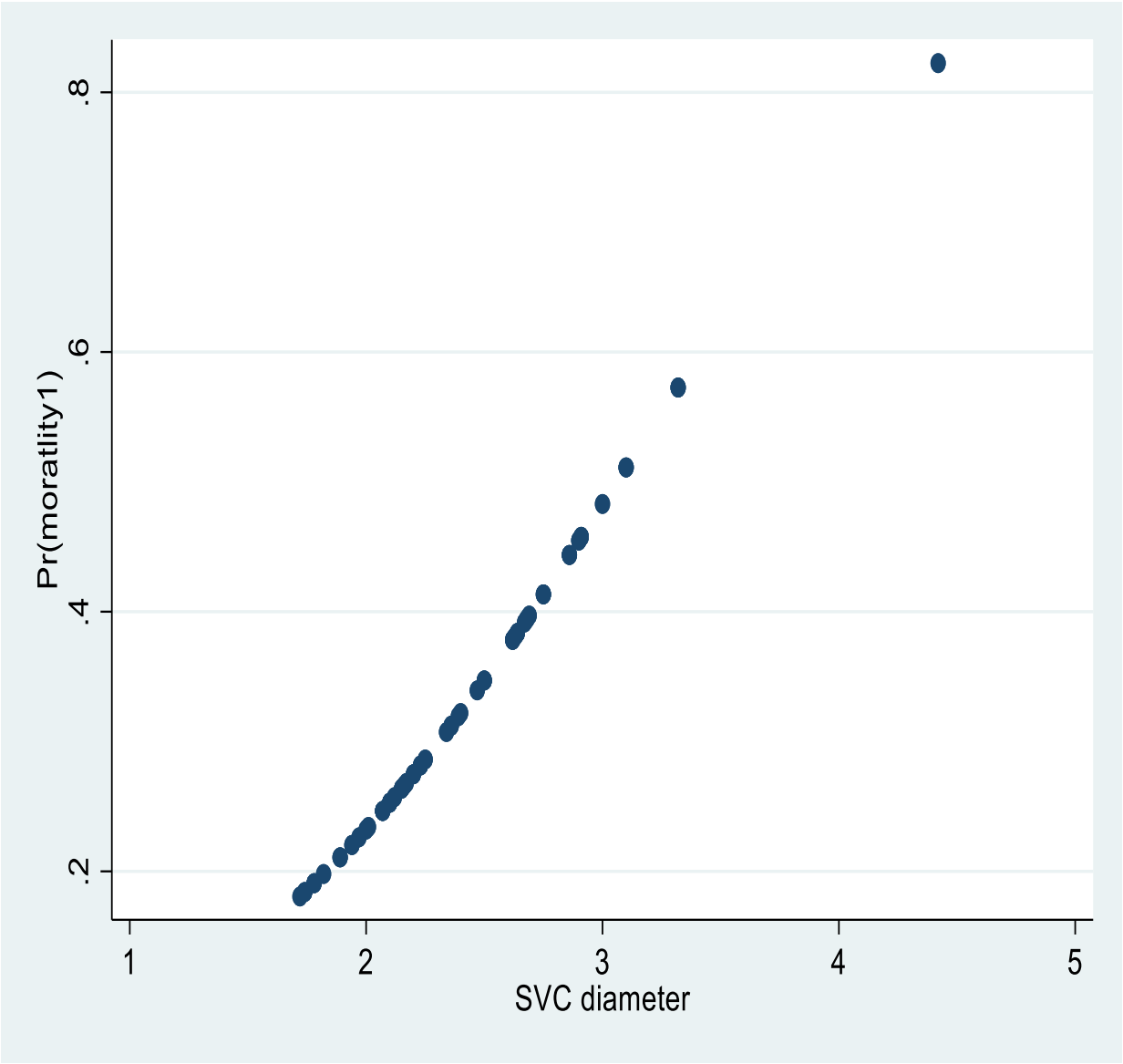
The graph above demonstrates that as Rv/Lv ratio increase, mortality also increases. This s-shaped curve resembles some statistical distributions.



Source: Field Data, 2021

Figure 4. 9: Distribution of Pulmonary Artery Diameter and Mortality

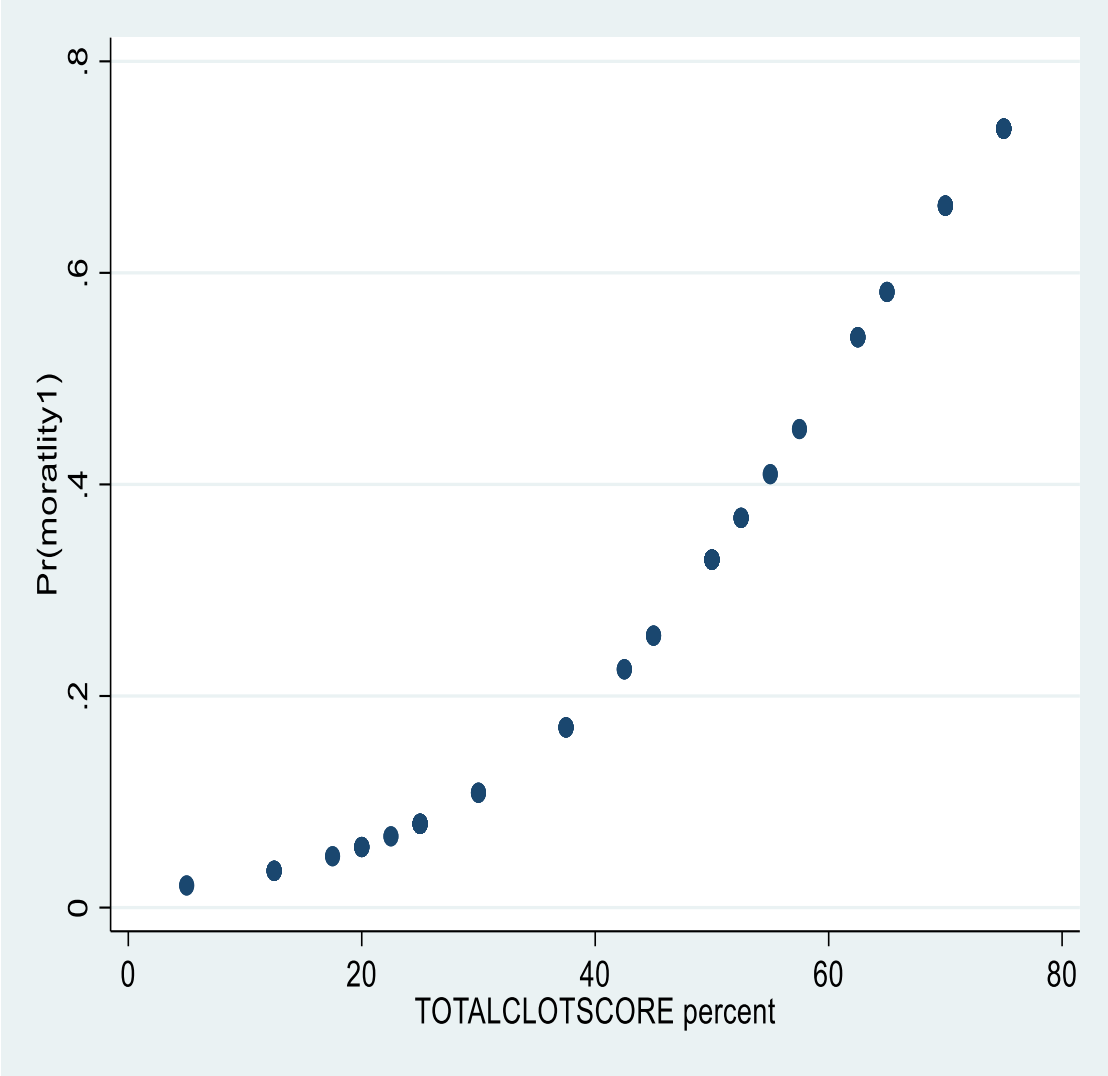
The graph above shows that as Pulmonary artery (PA) diameter increases, mortality also increase. There is no statistical relationship between PAD and mortality. The odds however are an increasing odd, (Table 4.8).



Source: Field Data, 2021

Figure 4. 10: Distribution of SVC Diameter and Mortality

The graph above shows that as SVC diameter increases mortality also increases. There is no statistical relationship between SVC diameter and mortality (Table 4.8)



Source: Field Data, 2021

Figure 4. 11: Distribution of Total Clot Score and Mortality

The graph above shows that as total clot score, increases mortality also increases This s-shaped curve resembles some statistical distribution.

Table 4.11 represents the ranges and means of the Rv/Lv ratios among patients with acute PE in general, and patients with acute PE that died within the 30-day period.

The mean Rv/Lv ratio among all the participants was 1.42 and the mean Rv/Lv ratio among those who died (1.73). That is to say that those with who died averagely, had higher Rv/Lv ratios compared to the general participant population.

Table 4. 11: Distribution of means of Rv/Lv Ratio among participants with Acute PE and those with short-term Mortality

Variable	Mean (SD±)	Min -Max	Confident Interval
Rv/Lv Ratio for patients with APE	**1.42 (0.41)**	**0.7 – 2.63**	**1.31 – 1.53**
Rv/Lv ratio for patient with short-term mortality	**1.73 (0.45)**	**1.1 – 2.63**	**1.52 – 1.94**

Source: Field Data, 2021

The average Rv/Lv ratio associated with mortality was 1.73 (SD± 0.45)

Table 4.12 shows majority 56 (93.3%) had Rv/Lv ratios of greater than 1.0. None of the patient with an Rv/Lv ratio of less than 1.0 died, but the minority 20 (35.7%) of patients with an Rv/Lv ratio of greater than 1.0 died. However, using the cut off of 1.0 for Rv/Lv showed no statistical significance (P-value = 0.14).

Table 4. 12: Distribution of the Rv/Lv ratio (< 1.0 and >1.0) associated with short – term mortality

Clinical Parameters	Alive	Dead	P-value	X^2
Rv/Lv ratio			**0.14**	**2.14**
Less than 1.0	**4**	**0**		
1.0 and above	**36**	**20**		

Table 4.13 shows that with an Rv/Lv ratio cut off of 1.5, 13 (65%) were seen to have died within the 30-day period and this value of 1.5 as a showed statistical significance (P-value = 0.001) compared to 1.0 (P-value = 0.14) as seen in table 4.11 in predicting short-term mortality.

Table 4. 13: Distribution of the Rv/Lv ratio (< 1.5 and >1.5) associated with short – term mortality.

Clinical Parameters	Alive	Dead	P-value	X^2
Rv/Lv ratio			**0.001***	**10.37**
Less than 1.5	**31**	**7**		
1.5 and above	**9**	**13**		

Table 4.14 represents the averages values of total clot load scores among the general population of participants with acute PE (45.58) and those with acute PE that died within the 30-day period (60.62).

Table 4. 14: Distribution of means of Total clot score and Mortality

Variable	Mean (SD±)	Min -Max	Confident Interval
Total clot score in patients with Acute PE	**45.58 (20.87)**	**5 – 75**	**40.19 – 50.97**
Total clot score for PE- related mortality	**60.62 (16.46)**	**12.5 - 75**	**52.92 – 68.32**

Source: Field Data, 2021

The average clot load score associated with mortality was 60.62 (SD± 16.46)

Table 4.15 show that the majority 42 (70%) of participants had a clot load score of more than 60 and the majority of deaths 13 (65%) occurred among those with Clot scores of more than 60. The cut of clot load score set at 60 show statistical significance for mortality (P – Value = 0.001).

Table 4. 15: Distribution of the Clot load (< 60% and >60%) associated with short – term mortality

Clinical Parameters	Alive	Dead	P-value	X^2
Cloth Load Score			**0.001***	**17.50**
Less than 60%	**35**	**7**		
60% and above	**5**	**13**		

Table 4.16 show that the majority 37 (61.7%) of participants had a clot load score of more than 40 and the majority of deaths 18 (90%) occurred among those with Clot scores of more than 40. The cut of clot load score set at 40 show statistical significance for mortality (P – Value = 0.001) and this was similar in terms of statistical significance when compared to cut of values of 60 (P-value 0.001) for predicting short-term mortality (Table 4.14).

Table 4. 16: Distribution of the Clot load (< 40% and >40%) associated with short – term mortality

Clinical Parameters	Alive	Dead	P-value	X^2
Cloth Load Score			**0.001***	**10.188**
Less than 40%	**21**	**2**		
40% and above	**19**	**18**		

Table 4.17 represents evidence that using Multivariate analysis, the Clot load score is the overall best predictor of short-term mortality (P-value = 0.034) when compared to other significant predictors of short-term mortality as identified on univariate analysis of all the parameters (Tables 4.8, 4.9 and 4.10).

Table 4. 17: Determination of the radiological parameter which is the most significant predictor of short-term mortality in patient with Acute PE

Variable	OR	95% CI	P - Value	Coefficient
Right ventricular	1.49	0.60 – 3.66	0.381	0.40
Rv/Lv ratio	6.88	0.61 – 77.20	0.118	1.92
Clot load	1.04	1.00 – 1.09	0.034	0.04

Figures 4.5, 4.6, 4.7, 4.8, 4.9, 4.10, 4.11, 4.12: Normality curve distribution for the various Radiological parameters (Continuous variables)

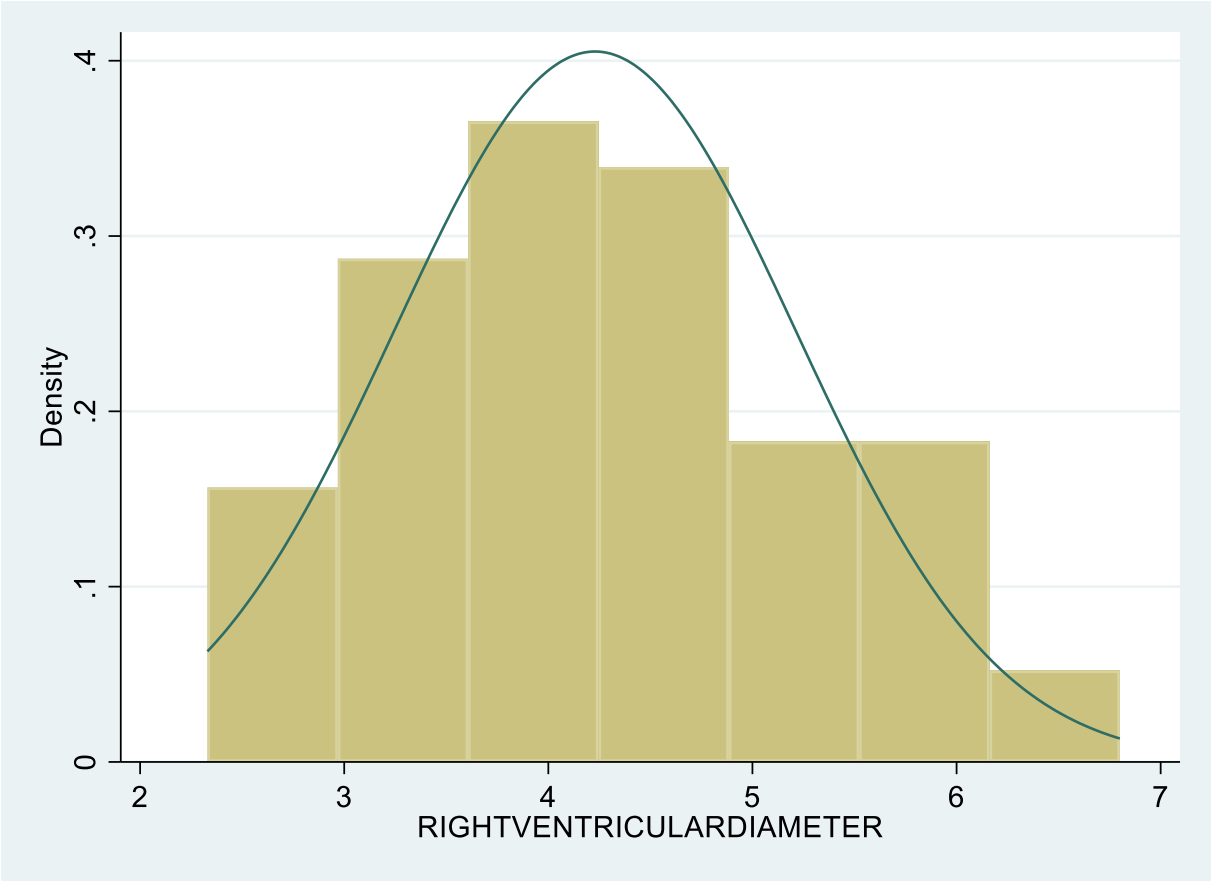


Figure 4. 12: Distribution of Normality of Right ventricular Diameter

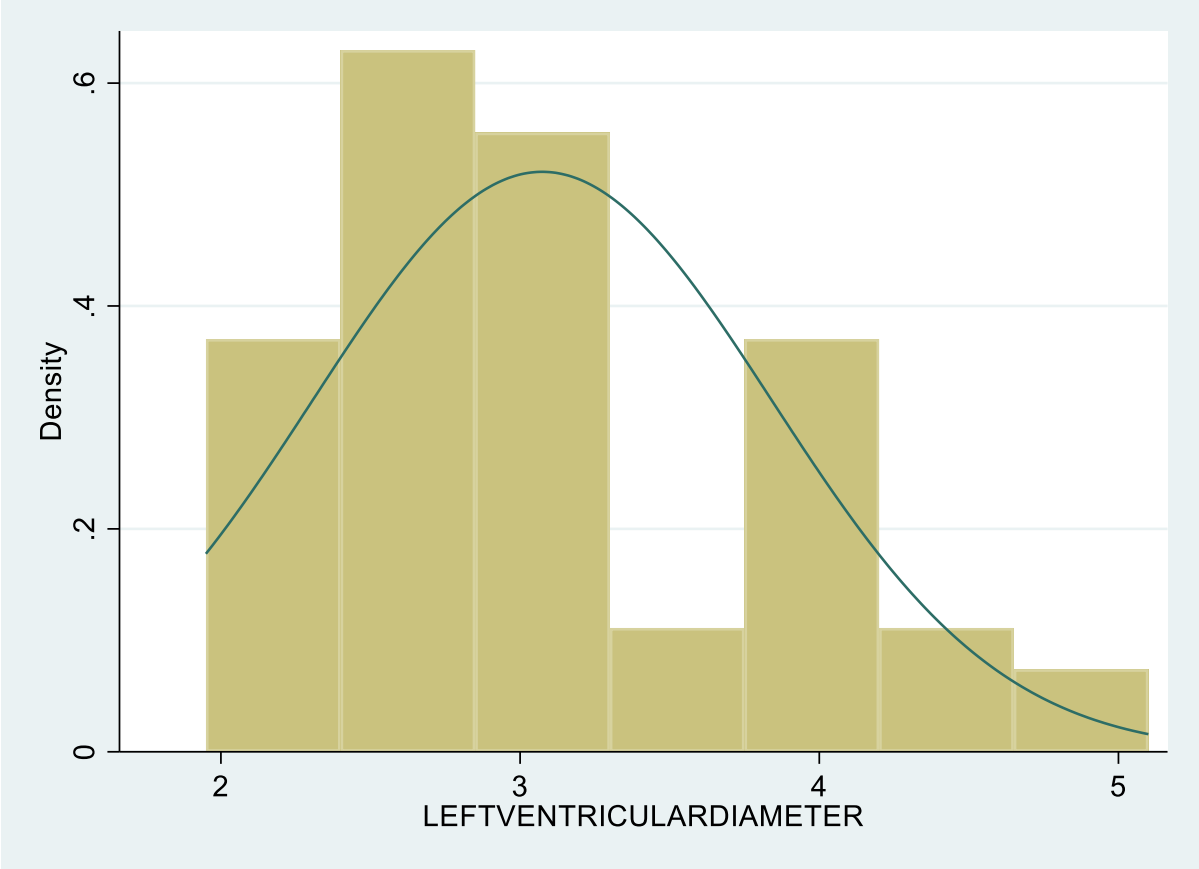


Figure 4. 13: Distribution of Normality of left ventricular Diameter

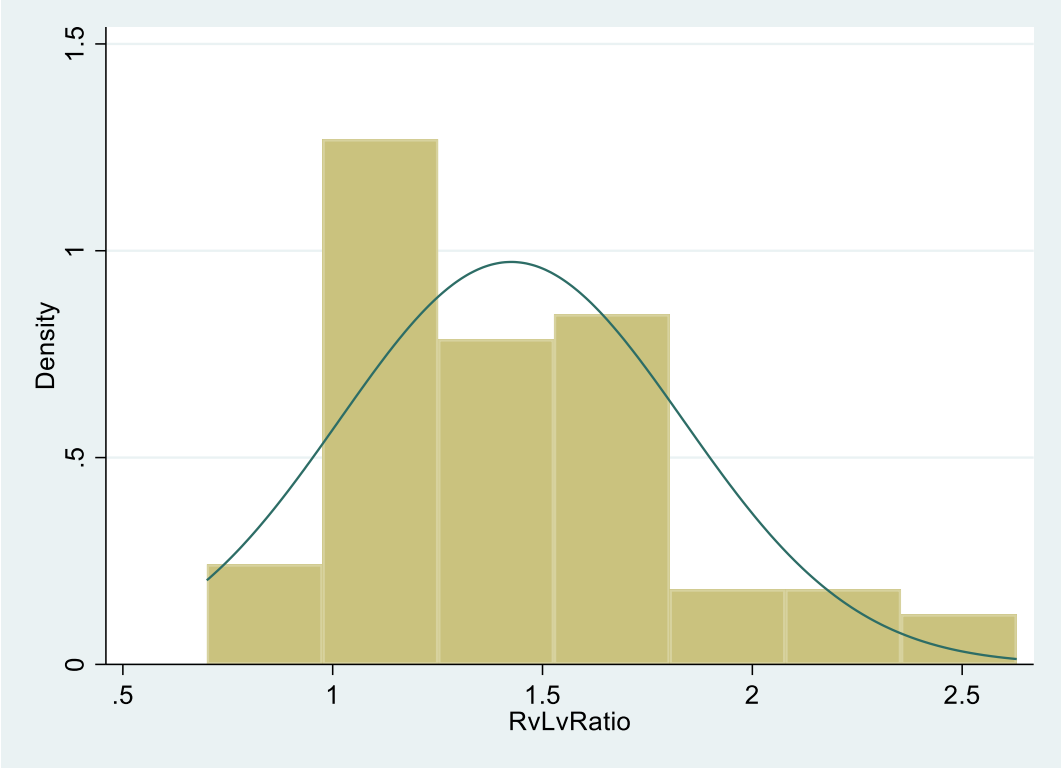


Figure 4. 14: Distribution of Normality of Rv/Lv Ratio

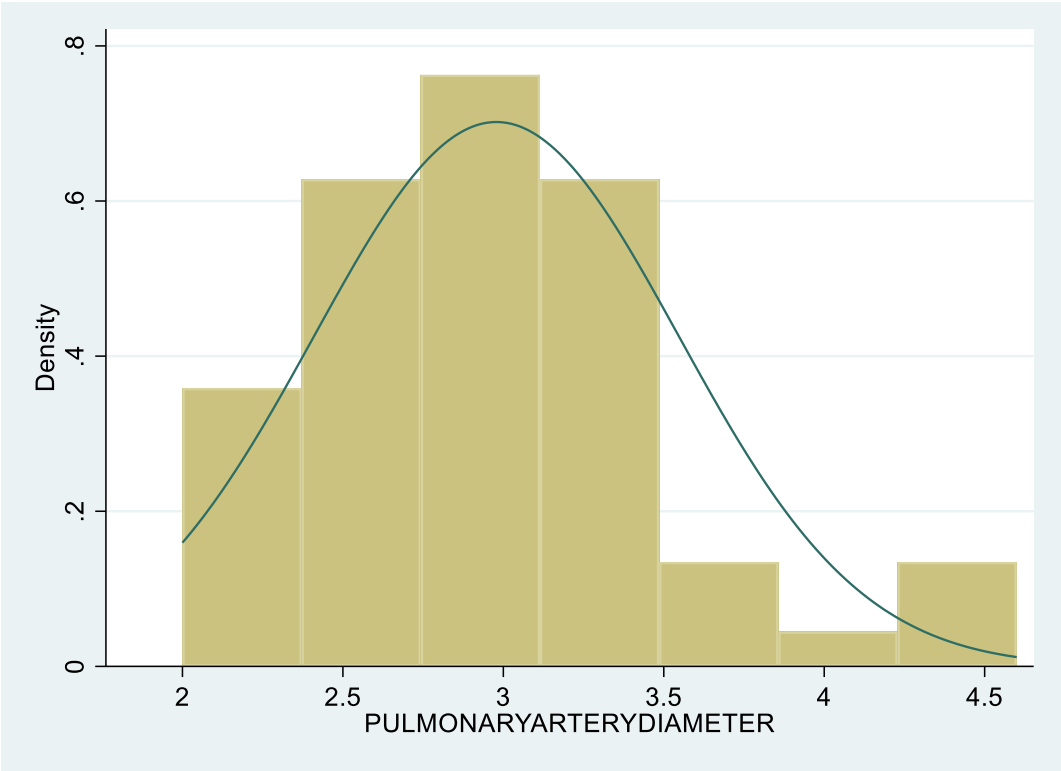


Figure 4. 15: Distribution of Normality of Pulmonary Artery Diameter

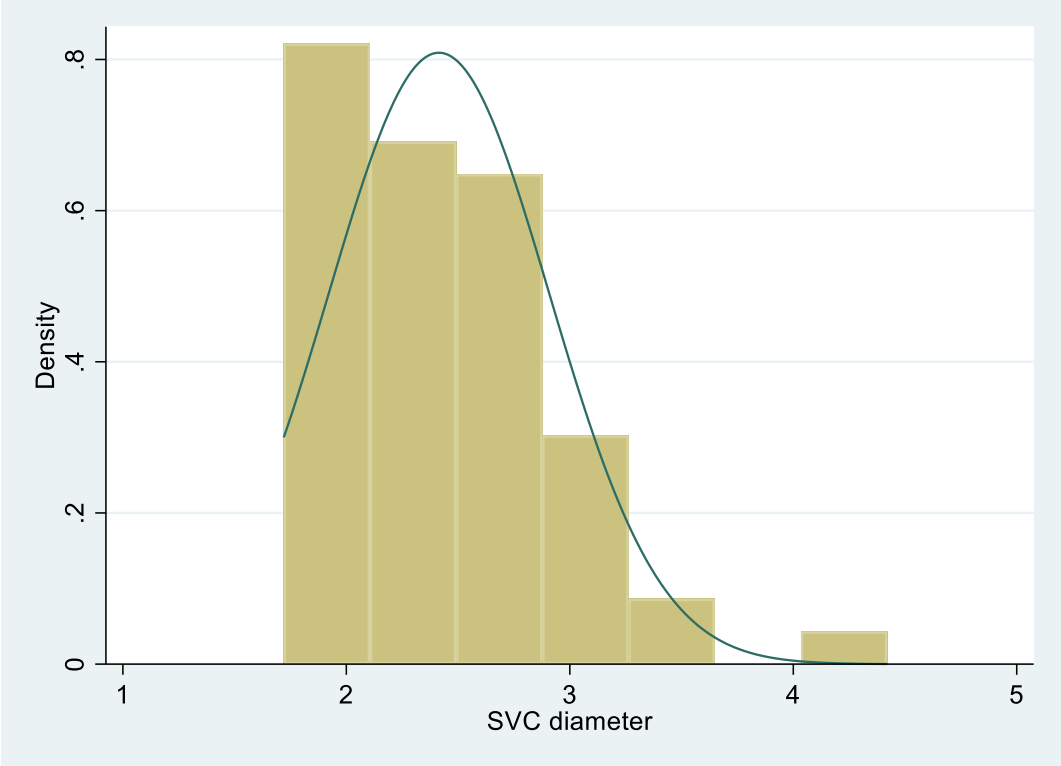


Figure 4. 16: Distribution of Normality of SVC Diameter

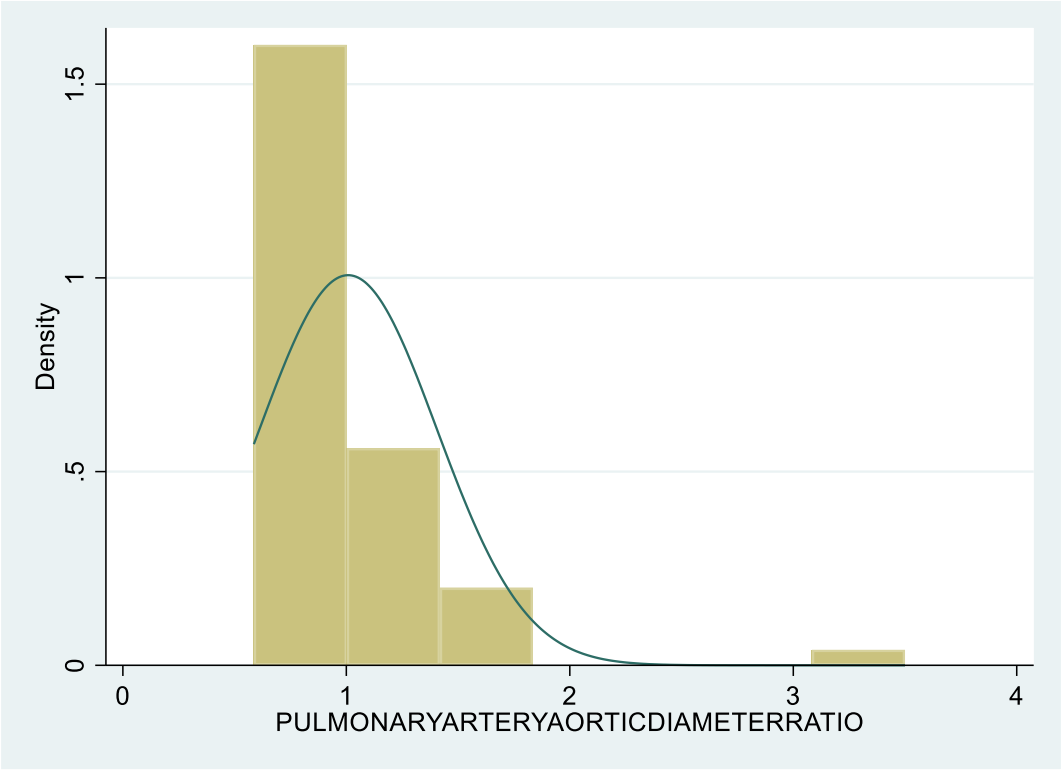


Figure 4.10: Distribution of Normality of Pulmonary Artery/Aortic diameter ratio

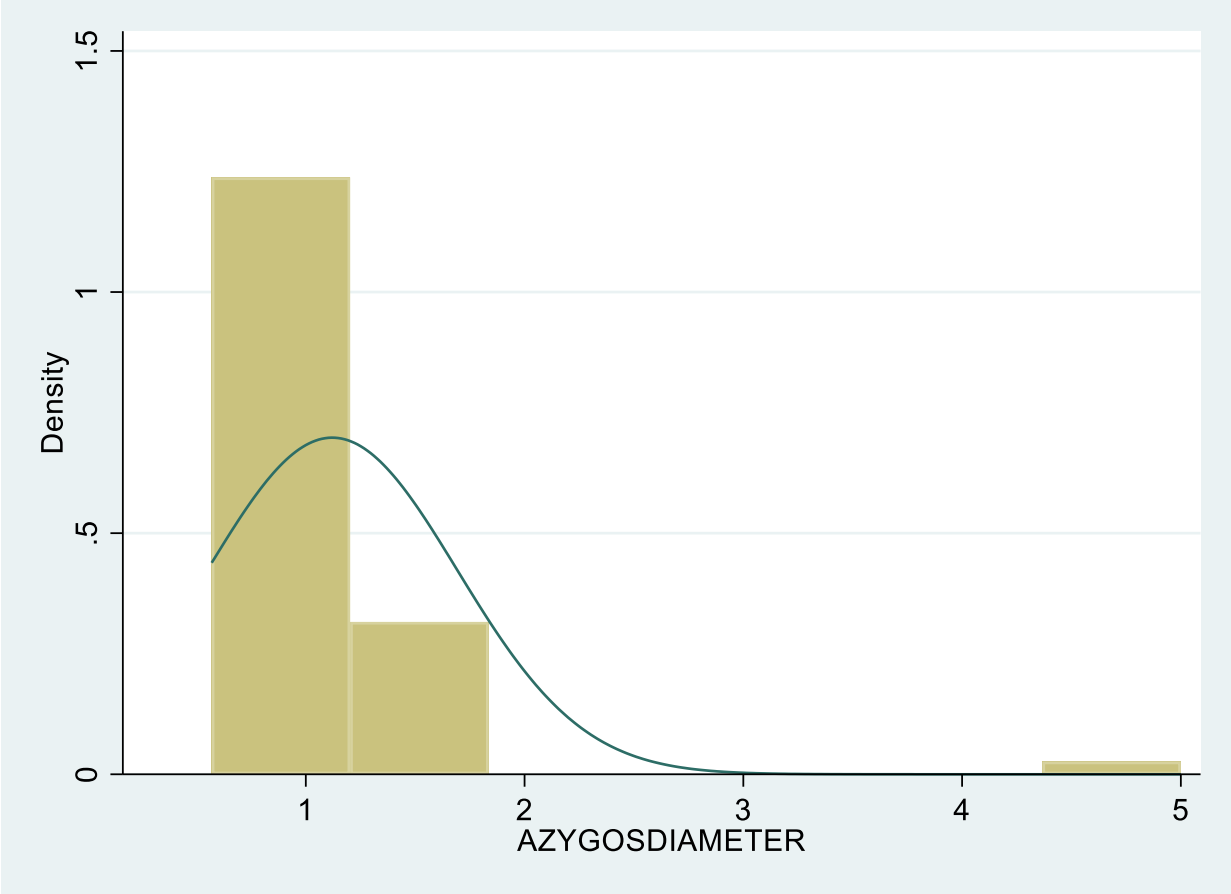


Figure 4. 11: Distribution of Normality of Azygos Diameter

Figure 4.12: Distribution of Normality of Total Clot Score

Figures 4.5, 4.6, 4.7, 4.8, 4.9, 4.10, 4.11, 4.12 represent normality graphs for the various radiological parameters evaluated. The normality curves for these parameters were skewed and did not show a normal distribution implying that the median values could be used in discussions, hence the use of means/averages in discussions.

CHAPTER FIVE

DISCUSSION

5.0 Introduction

5.1 Demographic characteristic of patients with Acute PE.

Pulmonary embolism is the presence of blood clots within the pulmonary arterial vasculature, which partially or completely occlude the lumen of the main pulmonary artery or its branches. Consequently, the occlusion of the pulmonary artery; results in the obstruction of blood flow to the lungs and pressure changes with in the heart, which if not promptly identified and managed can result in mortality. Acute PE a can be fatal if left untreated but proper risk stratification which include the use of CTPA alongside other biomarker and clinical tools, prompt diagnosis as stratification can be implemented to save lives

5.1.1 Gender and age

The majority, 56.67% of the participants in this study were females with the majority, 65% of deaths also occurring among the female population. The male participants constituted the minority, 43.3%, in terms of number of participants and in terms of negative outcomes, 35%. The age range for the participants spanned from 29 – 89 years with the mean age of the participants being 58 years. The majority of patients were between the ages of 51 – 70 years, 43.4%. The age range of male patients that presented with acute PE was 32 – 89 years (mean of 60). The age range of female patients that presented with acute PE was between 29 – 82 years (mean of 56), suggesting that generally, women presented with acute PE at a younger age compared to men.

The age and gender distribution in this study was similar to that of a study done by Furlan et al, in which the majority of the participants were female 52% with the males being in the minority, 48%. The mean age of the participants was also similar to what we found in the current study. Their overall mean age of their participants was 59 years. (mean age for men 58, mean age for women 61)[63].

According to Meer et al, the mean age for the participants of his study was also 59 years[48] which was also not significantly different from the mean age in the current study.

In a study done by Ghaye et al, slightly higher means were found for the ages of the study participants. In his studies his mean age was 61 years, this may be due to the fact that his study was assessing severe cases of pulmonary embolism which may have occurred more commonly in the elderly. However, Ghaye et's study also demonstrated similar demographic findings for gender, with a higher female distribution, constituting the majority, 51.2%, and the males constituting the minority,48.8% for his patient population[50].
In Turkey, Bulbul et al's research also suggested increased occurrence of acute PE among women, 62.7%, but his overall percentages were higher than those seen in the other researches.
Generally the higher incidence of acute PE seen in women may be due to the fact that cardiovascular diseases (such as hypertension), which are also known and well documented risk factors for acute PE, increase with menopause[64]. The data obtained for this research found mean age of the female participants to be 56 years suggesting that many of them were menopausal and peri-menopausal. So based on the above argument, one can presuppose that their peri-menopausal/premenopausal state was a predisposing factor for cardiovascular disease which in this study was noted to be one of the most significant co-morbidities associated with acute PE.
The fact that women make up the majority, 57% of patients in this study, could also be due to the fact that in addition to all the risk factors that the men and women have in common, the women have additional risk factors such as pregnancy, contraceptive use, surgery; by way of caesarean section for child birth and the need for hormone replacement therapies in some peri-menopausal/postmenopausal women. All of which are known risk factors for acute PE[26].
Also, it is worth noting that in this study the youngest participant to present with acute PE was a 29-year-old female, in her reproductive age who had had caesarean section for child birth. This buttresses the point that pregnancy, contraceptive use and child birth by Caesarean section may also be the reason why acute PE was commoner in females compared to males and also explain why the occurrence of the disease was also seen in in women at a younger age compared to men.

5.1.2 Occupation:

In this research, majority, 58.33%, of the participants were employed whiles a smaller number of participants at the time of the study were unemployed constituting 41.7%. Among the unemployed category of participants, majority were unemployed because they

had reached their retirement age. Out of the working population of participants to develop acute PE, 18 were traders constituting 30% of the participants

The category with the lowest occurrence of acute PE were the category of professionals; with no professional recorded to have died within the 30 - day period.

This may be as a result of professionals having higher levels of education and having a better financial standing. So, they can afford and have access to better healthcare at their every whim. And it may also be due to the fact that because of their higher levels of education they adopt healthier life style choices and avoiding/reducing the incidence acquired PE-related risk factors among this category. Also, for professional, as part of some company policies, the staff of the company are required to do regular check-ups at the expanse of the company, so disease processes such as hypertension and diabetes are identified and managed early to avoid the occurrence acute PE or its related complications that can arise in the presence of these risk factors.

The majority of the unemployed category of participants were retirees. A study done by Igbokew et al in Nigeria indicated that depression was high among patients on retirement[65]. Many people go through depression during the period of retirement, and because of this depression they might not take proper care of their own healthcare needs and some go through a period of financial difficulty since they are not earning regular income. At the age of a retirement, a lot of people also have age-related co-morbidities; So if they do not have a firm financial support system, they might not able to maintain a regular supply of their medications or afford proper healthcare or regular routine check-ups, hence, resulting in their co-morbidities being poorly managed and consequently resulting in worsening of preexisting comorbidities or the predisposition to risk factors such as cardiovascular disease, diabetes mellitus putting them at a higher risk of acute PE from a poorly controlled or managed co-morbidity.

A study done by Bulbul et al, which sought to assess the correlation between socio-demographics characteristic of patient with acute PE and diagnostic delay indicated that the majority, 58.4% of patients recruited with acute PE were housewives [66]. Comparing the two researches it was realised that the majority PE occurring among the unemployed category of participants occurred among people who were mainly confined to the home environment. In this study the unemployed who were mainly retirees and in Bulbal's study majority were housewives both of which had similar environmental factors, such as they both probably spend majority of their time at home, they may have reduced social functioning, reduced satisfaction and perceived loneliness.

During retirement and also among some housewives, poor health habits are acquired such as lack of exercise and a sedentary life style which are all predisposing factors to acute PE.

The occurrence of acute PE in farmers in this study 13.3%, was consistent with that identified in the study by Bulbul et al, 13.6%[66]. This may also be as a result of the poor economic social standing of farmers which prevents them from being able to achieve respectable levels of health care.

Under occupation, the evaluation of the individual categories suggested that the majority, 45% of patients that died within the 30 - day period were traders. This may be due to the fact most of these traders are self-employed and live a sedentary life style. Because they are self-employed taking time off to seek their own health care needs at the expense of leaving their business unattended may be a challenge because they would not want to have to close their businesses or for long periods at the risk of losing customers, unless they are critically ill.

5.1.3 Educational Level

The majority, 80% of the participants in this study population have received some form of education (Table 4.1). The lowest PE-related mortality was identified among patients with a higher (tertiary) education (Table 4.2) with 30% dying from acute PE. The population of participants that did not have any education, 20%, had a significantly high PE-related mortality rate of 71.42% (Table 4.2). These discrepancies between participants of higher educational levels and those with no educational level could be due to the fact that educated are more knowledgeable of healthier life style options which they might employ and also, that the educated have better job opportunities, which can afford them better financial standing and access to better health care compared to the uneducated.

5.2 Clinical considerations in patients presenting with acute PE

5.2.1 Presenting Complaints

At imaging patients presented with varying complaints (Table 4.4). In this study, of the entire patient population. The commonest presenting symptom was breathlessness (dyspnea), with more than half of the patient population, 60% presenting with this. This was followed by chest pain or discomfort which was seen in 30% of the participants. This was consistent with

Bulbal et al's study. In Bulbul et al's study, the majority, 73.1% of his participants which consisted of more than half of his study population, had dyspnea as their commonest presenting complaint [67]. Chest pain and discomfort as the second commonest presentation of acute PE in this study was also in agreement with Bulbal's study, in that in Bulbul's study, chest pain was the second commonest presenting complaint among patients; 51.3%. However, lower limb swelling due to DVT was the third commonest presenting complaint occurring in 18.35% of participants in this study while according Bulbal et al, detected signs of DVT occurred in 15.5% of his patient population and it was the fourth most common presenting symptom in his study[66]. According to a study done by Dalen et al and Kearon et al , about 70% of patients with acute PE, will have a lower limb DVT, which can be found if searched for using sensitive diagnostic methods [20] [18].

Other identified presenting complaints in patients with acute PE were malaise which occurred in 16.7%, shock which occurred in 1.7%, cough which occurred in 8.3%, dizziness which occurred in 5.0%, hemoptysis which occurred in 3.3% and easy fatiguability which occurred in 5.0%, These symptom are similar to symptoms found in other patients with acute PE done in other studies[66] [38].

5.2.3 Risk factors

A lot of risk factors are associated with PE. For the sake of simplicity, they were grouped under various heading; namely Cardiovascular, Systemic, Malignancy, Lung disease, Immobilisation, and Clotting abnormalities as risk factors.

The cardiovascular factors consisted of hypertension, and heart failure. The systemic factors consisted of diabetes mellitus, renal failure and obesity. Clotting abnormalities consisted of patients with a history of DVT or recurrent PE. The Immobilization category constituted patient who had had recent surgery, tibial fractures and history of recent long travel. Lung diseases included Asthma and COVID 19 pneumonia.

Out of the patient population in this study, 25% had no identifiable risk factor (Idiopathic/unprovoked PE) for acute PE (Figure 4.2). This was slightly higher to the findings of the ICOPER (International cooperative pulmonary embolism study) studies which indicated that 20% of patients with acute PE had no identifiable risk factor for the acute PE[25]. 40% had one (1) PE associated risk factor and 40% had two (2) or more identifiable risk factors. Majority of the patient had at least 2 risk factors (average 1 - 4).

In Bulbul's study, out of the entire population, 84.6% had at least one risk factor[66]. This was similar to the findings of this study, in that approximately 80% of our participants had at least one risk factor.

The commonest risk factor identified was hypertension, occurring in 45% of participants. Diabetes mellitus was the second commonest risk factor, occurring in 25%, followed by recent surgery,11.7%, and clotting abnormalities, 10%. Hypertension combined with heart failure, 33.3%, to form the cardiovascular category of risk factors, made cardiovascular causes the most dominant risk factor in acute PE. This was similar to finding of research done in Turkey where cardiovascular diseases formed the majority of the risk factors associated with acute PE. Malignancy as a risk factor had the lowest ranking in this study, occurring in only in 1.7% of the patient population. This was different from what was seen in Turkey where 8.3% of the patients with acute PE had malignancy as a risk factor. In Ghana, this may be due to the fact that there is an oncology hospital within the teaching hospital where oncology cases are seen and managed wholistically hence not many oncological cases or their related complications are seen or managed outside the Teaching hospital setting. During the duration of this study, COVID – 19 pneumonia was hovering around in the system, an increase in cases every now and then.

Some of the patients in this study had had an episode or two of COVID – 19 pneumonia and were presenting currently with acute PE as a complication of prior infection. Chest symptoms like asthma, 5%, and Covid-19 pneumonia, 8.3%, were combined and categorised as lung disease, was also a relevant risk factor. Other risk factors such as obesity, malignancy, fractures standing on their own as individual entities were not major risk factors.

Among patients who died within the 30-day period, majority of the patients had Hypertension, occurring in 25% of participants or Diabetes mellitus occurring in 25% of participants or both. Clotting abnormalities, 15%, was the third most significant risk factor that occurred in patients that died with the 30 – day period. Even though this is the occurrence of risk factors in patients with short term mortality, it is interesting to know that the 50% of the patient who had clotting abnormalities died within the 30-day period, 33.3% of patients with diabetes mellitus died and 18.5% of patients with hypertension died suggesting that when it comes to mortality, even though majority of the patients had Hypertension, the most significant proportion of the deaths occurred among those with clotting abnormalities,50%). This may be due the fact that hypertension is commonly and easily identified, diagnosed and managed compared to clotting abnormalities.

5.2.4 Duration between diagnosis and death

Data collected within the study period shows that out of 60 patients, the minority, 33% patients died within 30 days and 40 survived beyond the 30-day period, with the point reference being the date acute PE was diagnosed using CTPA. Out of these deaths, 35% died within less than a day. 45% died between days 1 – 7, and 20% died between the 8 -30 days. The majority, 36% of deaths occurred between days 1-7 with the age range of these patients spanning from 51 – 60 years. And the minority, 16% on deaths occurred after 8 days. The deaths that occurred in patient that died in less than a day was among patients aged 41 – 50 years

Significantly, there was no evidence to prove any association between age group and duration from diagnosis to death (P- Value = 0.453) or association between age group and death (P-Value = 0.112)

Considering all the patients that survived this illness, it is interesting to know that patients that presented with the most symptoms were between the age of 51 – 80. Even though this age group reported with the most symptoms, the majority of the survivors, constituting 25% were also found in this category with the majority of the people who survived being between ages of 61 - 70 years (Table 4.6). Conversely, in as much as a greater number survived within this age group, the majority of patient who died are from this category.

Even though the majority, 36% of deaths in this study occurred between days 1 – 7 (Figure 4.4). The range of duration was narrower than what was seen in the research done by Ghyusen et al, where the average number of deaths occurred between days 1 – 14[52]. But their mean days to mortality within our 1 – 7day range with the mean of their death being 5.61 days. Wu et al also had an even wider duration between diagnosis and death with the average days to death in his study ranging between 0 – 20 days, with average of 6 days[61]. Comparing these studies to the current study, it could be due to the fact these other researches were conducted in countries that had more sophisticated pre-hospital (e.g., functional ambulance services) and in-healthcare systems that are better equipped to handle such emergencies and sustain patients for longer, thus affording patients a longer chance of survival from time of diagnosis.

5.3 Accuracy of the various radiological parameters for prediction of short-term mortality in acute PE on CTPA

In this discussion the various right dysfunction parameters (Rv short -axis diameter, Lv short axis diameter, Pulmonary artery/Aortic diameter ratio, (PA/Ao ratio) RV enlargement, Diameters of the Superior Vena Cava, and Azygos vein, interventricular septal bowing and reflux into the Inferior vena cava) and Clot load scores were assessed for their value in with short term mortality in comparison to findings in other studies.

5.3.1 Right Heart dysfunction parameters in predicting short term mortality

5.3.1.1 RV short axis and LV short axis Parameter

In this study, using bivariate analysis, the short axis Rv diameter of the heart acquired in the 4-chamber view and its diameter measured from the inner wall to the inner wall of the right ventricle at the level of its respective valve was identified as a good predictor of 30 - day mortality (P-value of 0.003, OR = 2.85, 95% CI = 11.4 – 5.6), the Lv short axis diameter as a parameter under bivariate analysis carried a poor predictive ability (P-value of 0.15). in predicting adverse outcomes within 30 days.

5.3.1.2 RV enlargement (Rv/Lv diameter ratio)

The Rv/Lv ratio as a predictor of short-term mortality, using a bivariate analysis, was found, to be a good predictor of short - term mortality (P -value = 0.001). This was in keeping with other studies done by Quiroz et al[57], Schoepf et al[49] and Van der Meer et al [59] who all indicated that and increased Rv/Lv ratio of more than 0.9 or 1.0 or more were good predictors of short term mortality. In this study Rv/Lv ratio of greater than 1.0 was considered as right ventricular enlargement. The average Rv/Lv ratio seen among the entire patient population with acute PE in this study was 1.42 with the range of Rv/Lv ratios of 0.7 – 2.63 (± 0.05, 95% CI =1.31 – 1.53) (Table 4.10).

The Rv/Lv associated with short term mortality in this study was 1.73 with a range between 1.10 - 2.63. (Table 4.10)

The majority of the participants in this study, 93.3% had increased Rv/Lv ratio of greater than 1.0 with only 6.67% having an Rv/Lv ratio of less than 1.0 (Table 4.1). its worth noting that all the patients with an Rv/Lv ratio of less than 1.0 survived beyond the 30 – mortality mark.

Interestingly, all of the participants that died had an Rv/Lv ratio of more than 1.0 (Table 4.11). That is to say that there is not participant that died within the 30 – day mortality period that had and Rv/Lv ratio of less than 1.0.

Overall, cumulative mortality rate within the thirty-day period, was higher in participants with increased (>1.0) Rv/Lv ratios, being 35.7%, compared to those who did not have increased ratios. The median Rv/Lv ratio for participants who died in this study was found to be 1.76 and 1.2 (range, 0.7 to 1.91) for those who survived within the 30-day period.

Schoepf et al defined right ventricular enlargement as an Rv/Lv ratio of > 0.9 (which in effect is approximately equal to 1.0) because he found that participants with ratios above this were more likely to be at risk of in-hospital complications[49]. In his study, he found that an increase in Rv/Lv ratios (RV enlargement) was a good predictor of mortality which was consistent with this study (P-value of 0.001), (Table 4.8). According to his study, RV enlargement was present in the majority, 64.0% of his patient population which was consistent with our finding in that a majority of our patient population, 93.9% also had RV enlargement. Schoepf's mortality rates at thirty days were 15.6% in patients who had RV enlargement and 7.7% in patient who did not have RV enlargement.

The mortality rate of this study at thirty days was 35.7% for those who had RV enlargement and 0% for those who did not have and RV enlargement.

Both studies showed an increase in mortality among the population of patient with RV enlargement and a reduction in mortality among those with no RV enlargement but mortality among those with no RV enlargement was higher in the study done by Schoepf et al, possibly due to the fact that they might have increase mortality from other causes such as malignancy, since a large number of their participants had cancers, 53.8%[49] contributing to their patient population, while factors like malignancy, 1.67% was close to negligible among our patient population (Table 4.3).

According to Schoepf, the median Rv/Lv ratio was 1.01 (range, 0.69 - 2.55) in participants who died and 0.95 (range, 0.62 to 1.97) in participants who survived 30 days. In this study, the median Rv/Lv ratio was 1.76 (range, 1.1 to 2.63) for those who died and 1.2 (range, 0.7 to 1.91) for those that survived. In both studies the median Rv/Lv ratios were high among the people who died, however in this study it was significantly higher. This might be due to the fact that this study was conducted in the peri-COVID 19 era and COVID 19 was major risk factor for Acute pulmonary embolism. So even though lung disease was not a major risk factor in could be possible that some of these participants had previously suffered some indolent form of the disease and their cardiovascular systems had compensated for it without

their knowledge resulting in an underlying silent/mild right ventricular hypertrophy that they were unaware of and which became worse after an embolic episode.

In the study by Schoepf, RV enlargement was seen among the majority, 78.2% of the participants that died. Among those that survived, the majority, 62% had RV enlargement[49]. In this present study, RV enlargement was identified in all the participants that died. According to a study done by Van der Meer et al[48] the baseline parameters of RV enlargement, was useful in predicting mortality during follow-up. Their follow up period, was however after 3 months. In their study, their mean Rv/Lv ratio was 1.17 which was lower than that found in this current study, which stood at 1.42 for the general patient population with acute PE. Similar to this study in which, a statistically significant association was found between Rv/Lv ratio and mortality (P- value of 0.001, 95% CI 4.92 – 309.9), they also identified a strong association between the Rv/Lv ratio (P- value < 0.001) and PE related mortality.

The study by Van der Meer et al et al, further categorized participants into Rv/Lv ratio of 1.0 or less, RV/LV ratio greater than 1.0 but less than or equal to 1.5 and RV/LV ratio greater than 1.5. Among these categories, they found that RV/LV ratio of 1.0 or less had no PE related mortalities, Rv/Lv ratios of more than 1.0 but less than or equal to 1.5 had a PE - related mortality in 8% of participants and the category with Rv/Lv of more than 1.5 had, 15% of participants dying and of those with an Rv/Lv ratio > 1.5, 15% patients died.

In this current study,6.67% participants had an Rv/Lv ratio of less than 1.0. 56.67% of patients had an Rv/Lv ratio greater that 1.0 but less than 1.5 and 36.67% had an Rv/Lv ratio of 1.5 and above. However, with respect to mortality, the majority, 65% had an Rv/Lv ratio of 1.5 and above and a few, 35% of more than 1.0 but less than 1.5 There was no patient with and Rv/Lv ratio of less than 1.0 died, but, participants with and Rv/Lv ratio of 1.5 and above are 5 times more likely to die within a 30 - day period compared to those with an Rv/Lv ratio of 1.0 or more and but less than 1.5 [(OR: 5.57), (P-value: 0.005), (CI:1.69 -18.29)]

Van der Meer et al in their study identified that 42% of their participants had an Rv/Lv ratio of 1.0 or less and of this number, none died before follow up[48]. In this current study only 5% of the total study population had an Rv/Lv ratio of less than 1.0, however the similarities of these two studies show forth in that, in both of these studies, none of the patients with Rv/Lv ratio of 1.0 died.

Aroaz et al on the contrary the indicated that Rv/Lv ratios had no correlation with predicting short term mortality. But rather Araoz, indicated Rv/Lv ratio though is not a significant predictor of PE related mortality, was rather useful in predicting less severe morbidity such as

ICU admissions[60]. But this may be due to the fact the images were reviewed by 2 independent reader and interobserver differences may have influence his results and contributed to his contrary findings.

5.3.1.3 Diameters of the Superior Vena Cava and Azygos vein.

Pressure increments on the right side of the heart directly are likely to result in pressure build up in the more proximal venous structures such as the superior vena cava and Azygos vein which are direct extension of the right atrium, which in turn is a direct extension of the right ventricle. In this study, the mean SVC diameter among the entire participant population was 2.4 [(range1.7 – 4.4cm) (SD=0.49)] (Table 4.7). The mean SVC diameter of those who died and survived within 30 days period were 2.59 (range; 1.74 – 3.1) and 2.3 (range: 1.72 – 4.42) respectively. The results showed that there was a fairly significant difference [(P-value: 0.005,) (CI: 2.41)] in the SVC diameters between those who died and the survivors. However, a logistic regression shows no statistically significant between short tern mortality and the SVC diameter. [(OR: 3.08), P-value: 0.06), (CI:0.93 – 10.23)]. Ghaye et al also showed a statistically significant difference in the diameters SVC of patient who survived acute PE episodes and those that did not[14].

In this current study, the Azygos diameter among the entire participant population ranged between 0.57 and 5.0 cm (Mean=1.12, SD=0.57) (Table 4.7). The mean diameter of those who died within and survived within the 30 days was 1.11 (0.76 – 1.72 range) and 1.12 (0.57 – 5.0) respectively. Statistically there is no difference [(P-value) (0.95, CI: 0.98 – 1.24)] between the diameters of those who died those who survived. This was contrary to what Ghaye et al found in their studies. Their findings indicated that there was a statistical difference between survivors and non-survivors[50]. In this study logistic regression shows no statistically significant relation between short term mortality and the Azygos diameter [(OR: 0.96) (P-value: 0.94) (CI: 0.36 -2.53)].

5.3.1.4 Pulmonary artery/Aortic diameter ratio (PA/Ao ratio)

The mean PA/Ao diameter in this study was 2.63 (range: 0.56 to 2.63) (Table 4.7). In this study, there was no relationship between the PA/Ao ratio and short-term mortality (P-value 0.94). Out of the participants that died, the mean PA/Ao ratio was 1.0 (range: 0.58 -1.44) and of those whose survived the PA/Ao ratio was 1.01 (range: 0.59 – 3.5).

Statistically there is no relationship between survival and mortality with respect to the PA/Ao diameter (P-value 0.96)

Van der Meer et al, in agreement with this current study also found no correlation between the PA/Ao ratio (P=0.66). A relationship between this parameter and mortality in PE could not be established.[59]

Furlan et al, also using a univariate analysis to asses short-term mortality along with measures of clot volume and right dysfunction parameters realized increased PA/Ao ratio (P= 0.52) was not significantly associated with short term mortality[63].

5.3.1.5 Interventricular septal bowing

In this study, it was noted that 56.67% of the patient population had interventricular septal bowing, while 26 patients did not have interventricular septal bowing. Out of the 20 patients that died within the follow up period, 75% had interventricular septal bowing. Among the survivors less than half ,47.50% had interventricular septal bowing. Interventricular septal bowing was identified as a good predictor of short-term mortality (P = 0.04) (Table 4.9).

This was consistent with our findings, Aroaz et al in his study also indicated interventricular septal bowing as a good predictor of mortality in a univariate analysis (P = 0.04). But he acknowledged that it had low sensitivity and a high variability among interpreters. Van der Meer et al, found that interventricular septum bowing had no predictive value as far as the outcome of PE was concerned[54]

5.3.1.6 Contrast reflux into IVC

Majority, 51.67% of the participants of the total study population had reflux of contrast into the IVC, while 48.33% had no reflux into the IVC. Suggesting that the majority of the patient in the total patient population had reflux into the IVC. Out of the patients with short term mortality, 55% had reflux into the IVC and 45% of the survivors had reflux into the IVC (Table 4.9). In this study there was no statistical association between contrast reflux into the IVC and short-term mortality, however, patients having reflux of contrast in the IVC have increasing odds of 88% as compared to not having reflux. [(OR:1.22), (P- value of 0.7) (CI: 0.4 – 3.58)]. The finding of this current study were in contradiction to that of the study done by Furlan et al where, reflux of contrast into the IVC was one of the right heart dysfunction parameters that had a strong association with short term mortality [51]. It was also in

contradiction to a study done by Collomb which also indicated that reflux of contrast into the IVC a predictor of short term mortality[53].

5.4 Clot load scores in predicting short term mortality

The mean clot load score in percentages for the entire participant population in this study was 45.58 (range 5 – 75) (Table 4.7). In relation to those who died, the mean clot score for who died and those who survived was 60.62 (range 12.5 - 75) (Table 4.13) and 38.06 (5 – 75) respectively Statistically, there was a strong relationship between and whether a patient died or survived and total clot score [(OR: 1.07) (P-value: 0.001), (CI: 1.03 – 1.11)]. More than half; 61.67% of the participants had a clot score of 40% and above, while a few, 38.33% had a clot score of less than 40.

Out of those who had a clot score of less than 40%, only 8.70% died with more than 75% surviving. Of these two participants who died, one was 35 years and had an underlying renal malignancy and the other was 81 years. It stands to suggest that the two participants that died with a clot load score of less than 40% probably died from complications of the underlying condition or their age respectively

However, 61.67% participants had clot scores of more than 40%. Out of this, almost half, 48.65% died while 51.35% survived.

Van der Meer et al[48], in their study had the mean clot load score be 31.8% which was lower than that found in this current study. They also found a statistically significant association between the vascular obstruction index and PE-related mortality which was similar to this current study which also found a significant association (P- value 0.001) between the clot scores and short-term mortality. Van der Meer et al determined that the patients who had died during follow up had significantly higher clot load scores than those who survived, with a P-value of these figures being 0.001. The finding in the study by Van der Meer et al are consistent with mine in that we both identified a statistically significant relationship between the clot load score of non-survivors and survivors, indicating a consistency in finding between studies.

Van der Meer et al on the other hand had 16.2% out of his participants with an obstruction index of 40% or greater died of PE as against 1.2% of 83 participants with an obstruction index of less than 40%. In their study, the positive predictive value of a clot load score of 40% or more in PE-related mortality was 16.2% (95% CI: 4.1%, 28.3%). The negative predictive value for a non-eventful outcome with an obstruction index of less than 40% was 98.8% (95% CI: 96.4%, 100%).

Finding in a study done by Wu et al agreed with the findings in this current research and also with the research by Van der Meer et al. Wu et al, demonstrated that the clot load scores was a notable predictor of outcome of patients with PE[61]. The consistency in the findings of clot load score being a good predictor in participants with short term mortality, in the research done by Wu et al and this current study may be due to the fact that the sample size (59 patients) and age distribution (age range, 22 – 89 years, mean age, 61 years;) bore a great similarity to the sample size (60 participants) and age distribution (29 – 89 years, mean age of 58 years) that of this current study. However, the limit for the clot load score in his study was 60%.

Collomb et al, indicated that the clot load scores were useful in providing information on how severe a recent episode of PE may be, but had limitations in its ability to predict the possible of the outcome in affected participants [47]. On the contrary the findings of the study done by Wu et al, which showed the clot load scores to be a notable predictor of outcome of patients with PE[15]. Van der Meer et al's finding[54] concur with Wu et al in that, they both agreed that clot load scores are a relevant predictor of patient outcome. Araoz et al, stated that PA clot scores as a poor parameter in predicting outcome in patients with acute PE[55]. In a study done by Apfaltrer et al, it was stated that the clot load scores were of value in the identification of the presence right ventricular dysfunction from a PE, but was limited in its ability to predict adverse clinical outcome, of which included mortality[68].

5.7 Most significant radiological parameter to predict short-term mortality in patient with Acute PE

In this current study, the clot load score on multivariate analysis (with RV short axis diameter, Rv/Lv ratio and Total clot score) the, was identified as the most significant radiological parameter (P-value: 0.03) associated with short term mortality. The other parameters, consisting of Rv short axis diameter, RV enlargement and SVC diameter had low predictive powers when inputted for multivariate analysis. (P-values of 0.381, 0.118, 0.504). The findings of the current study do not agree with studies done by Furlan et al and Schoepf et al. Furlan proposed that among the various pulmonary angiographic signs, only the RV enlargement (Rv/Lv ratio) with a cut off of 1.0 was independently associated with short term mortality in a multivariate analysis. Furlan's study was consistent with a study done by Schpoef et al, who suggested that on multivariable analysis, RV enlargement best predicted 30-day death (hazard ratio, 5.17; 95% CI, 1.63 to 16.35; P-0.005). The differences between these two researches and the findings of this study, may be due to the fact that the patient population under studied in this current research are of a completely black race. Common

knowledge has it that Hypertension and its related cardiovascular complications are predominant among people of the black race when compared to Caucasians. In this study majority of the participants, 70% had Hypertension or diabetes as risk factors, both of which predispose to cardiovascular disease which is strongly associated with increased risk of PE even in this study. Thus, it could be inferred that there is a possibility that the majority of participants in this study already had some under lying base line cardiovascular disease due to the majority of them had hypertension or diabetes, so the determining factor in this study most likely would not be the cardiovascular disease which affects right heart dysfunction parameters such as Rv/Lv ratio, septal bowing or Rv short axis diameter, but rather the clot burden would be the predictor of patient outcome.

In addition to this, some studies done, for example by Scheopf et al, showed that the majority, 53.8% of his sample population had cancer, and not cardiovascular disease. Thus, cancers were the commonest risk factor associated with mortality. Cancers have been known to carry an increased risk of clotting abnormalities and hence it may be the inferred that the majority of his participants had some underlying clotting abnormalities by virtue of the fact they had underlying malignancies and hence the determining factor in this case could be the right heart dysfunction parameters such as the Rv/Lv ratio.

The two studies were conducted in setting where the Caucasian population is higher. Hence inferring that hypertension and its related complication might also be lower and as such cardiovascular disease may be lower. In our previous discussions we discussed the fact that the outcome of acute PE does not only depend on the clot burden, but the presence of an underlying cardiovascular or pulmonary disease significantly affects outcome. In this current study, the greatest risk factor among those who died within the 30-day period were those with hypertension and diabetes mellitus suggesting that majority of the patients already had hypertension as a baseline risk factor, the making the clot burden a significant underlying determinant of risk of short- term mortality.

This study was conducted in the peri-post COVID 19 era. Patients with associated co-morbidities have a higher risk of being affected negatively by COVID-19 pneumonia. the risk factors for COVID-19 pneumonia were similar to those of PE (Hypertension Diabetes, Asthma etc), and COVID- 19 pneumonia itself was associated with an increased risk of acute PE. So it is possible that majority of the patients in this study had had some exposure to and indolent form COVID-19 pneumonia and this had possibly left behind some unidentified

cardiovascular or pulmonary complication, so the clot load thus became the determining factor of mortality.

5.8 Limitations of the study

1. This current study consisted of data that was collected from a single site which may have had a specific kind of clientele therefore creating an element of bias.
2. A lot of the other studies that this current study was compared to were multicenter studies, which afforded them a larger sample size thereby eliminating bias collected, however in comparison to other studies from around the world, there are incidents where similar results were found.
3. Assessment of management of Acute PE by way of anticoagulation, thrombolysis could not be ascertained as majority of the patients and their accompanying relatives were not knowledgeable of what treatment they had received or medications that they were on.

CHAPTER SIX

CONCLUSION AND RECOMMENDATION

6.0 Introduction

In view of the fact that proper risk stratification and prompt diagnosis can be implemented to save lives, this study has sought to identify various parameter that are indicative of predictive of short-term mortality. In Ghana where the number of CT scan to patient ratio is gradually increasing, studies to inform doctors on the use of CTPA in the stratification of Acute PE episodes for prompt treatment and possible reduction in fatal outcome is limited. This present study has assessed the various parameters of right ventricular dysfunction and clot load score on CTPA and their ability to predict short term mortality. This Chapter brings to light the conclusions derived from the findings of this study.

6.1 Conclusion

This current study revealed that acute PE occurs more commonly among women, and among the employed. The commonest presenting symptom is dyspnea. Majority of the patients that died within the 30-day period were between the ages of 51 – 80 years. The commonest risk factors associated with acute PE were diabetes and hypertension. Univariate analysis the most significant predictors of short-term mortality were, Right ventricular short axis diameter (Rv), Rv/Lv ratio (RV enlargement), clot load score, and interventricular septal bowing. They were significantly associated with short term mortality. Rv/Lv ratio of greater than 1.0 have a 39.0 chance of dying compared to patients with Rv/Lv ratio of 1.0 and below of mortality within a 30 day-period. Patients with a clot score of 40% or more have a 93% increased risk of dying; compared to patients with clot load score of below 40% with in 30 days. In this current study, the clot load score on multivariate analysis, was identified as the most significant radiological predictor of short-term mortality. This study supports the alternative hypothesis that some CTPA parameters of acute PE are significant parameters of short-term mortality.

6.2 Recommendations

A delay in identifying the predictors of short-term mortality in Acute pulmonary embolism can delay proper risk stratification for optimal care and may likely result in negative out comes. Based on the findings of this present study,

1. A shortened validated reporting template with only parameters with significant predictive values should be created and implemented in various radiological departments in an attempt to reduce reporting time as a sense of urgency in acute PE management.
2. The radiologist should be educated on the use and significance of the various parameters in CTPA risk stratification to be able to alert physician to enhance patient management.
3. The Physician should be educated to understand radiological reports that make use of the various parameters on CTPA risk stratification and their significance to enhance patient management.
4. Radiographer should be trained to accurately acquire images using CTPA in cases of acute PE.
5. A composited validated risk stratification protocol should be made available and employed in hospitals to ensure focused and standardized management of acute PE.

6.3 Future Research

This current study was a single center study so further studies should be carried out in the major Radiology centers in the country to generate a shortened validated reporting template with only parameters with significant predictive values.

6.4 Concluding remarks

Right ventricular short axis diameter (Rv), Rv/Lv ratio (RV enlargement), and clot load score are significantly associated with short term mortality. Clot score being the most significant predictor should be the single most relevant piece of information that is stated in reports instead of having physicians wait while lengthy reports which do not highlight significant parameter of short-term mortality, and also cause unnecessary delays, are generated. The results of this present study hopefully serves as a baseline upon which future studies build to improve patient outcomes in patients with acute PE

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APPENDICES

Appendix 1: Participant Information Leaflet and Consent Form

CORRELATION OF EMBOLIC BURDEN AND RIGHT HEART DYSFUNCTION PARAMETERS WITH MORTALITY IN ACUTE PULMONARY EMBOLISM USING COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAPHY

Names and affiliations of researcher:

This study is being conducted by Dr. Nana Akua Konama Asamoah in partial fulfilment of the requirements for the conferment of a Fellow of the Ghana College of Physicians.

Background:

Acute Pulmonary embolism is a condition associated with a high mortality rate if not identified and managed promptly. Acute pulmonary embolism is caused by the presence of blood clots within the pulmonary vasculature. Computed tomography has become the gold standard in diagnosing this disease process and identifying and differentiating it from mimickers such as pneumonia.

Various parameters have been identified and are being used in assessing the severity and the association and acute pulmonary embolism with short term mortality (defined as death within 3 months of disease onset.)

The purpose of this study is to evaluate the various CTPA parameters associated with short term mortality, to identify which of the parameters/parameter is most significant in predicting short term mortality. In doing this the most significant can be in co-operated into patients reports in an attempt to reduce reporting times and allowing for a timelier intervention for such patient, which hopefully will result in a reduction in Acute pulmonary embolism related short term mortality.

Procedure of the research:

The study will be carried out at an affiliate radiological facility of the Kwame Nkrumah University of Science and Technology, namely Spectra Health Ltd.

Convenient sampling technique will be used. All CT pulmonary angiograms scan images of patients 18 years and above who undergo CTPA on account of suspected acute pulmonary embolism and are diagnosed by the reporting radiologist at Spectra health as having an acute pulmonary embolism will have their images retrieved by the principal investigator and the various parameters or right dysfunction and the pulmonary clot load scores will be evaluated by a radiologist, as defined by the questionnaire. The radiologist will have at least 5 years of experience in reviewing CT pulmonary angiograms. With exception of the diagnosis of acute PE the reader will be blinded from the clinical information and the outcomes of the patients, as well as any form of prior imaging findings of the patient. The demographics of the patient will be taken on site by a research assistant. 30 days after the initial presentation, patients will be followed up on by way of telephone calls by the research assistants and their outcomes recorded. In total I hope to recruit a minimum of thirty-three (33) patients into this study.

Risks: The study poses no known risk to the study participants.

Benefits: The main of the study is to identify, out of numerous parameters, the most significant parameter on CT pulmonary angiography that predicts short-term mortality in patients with Acute pulmonary embolism, in co-operate it into radiological reports to aid physicians in making prompt, evidence-based management choices which we hope will reduce the number of people who die from Acute Pulmonary embolism and save more lives.

Confidentiality: All information collected in this study will be given code numbers. No name will be recorded. Data collected cannot be traced back to participants in anyway. No name or identifier will be used in any publication or reports from this study. However, as part of our responsibility to conduct this research properly, we may allow officials of the ethics committees to have access to your records.

Voluntariness: Taking part in this study should be out of your own free will. You are not under obligation to participate.

Alternatives to participation: If you choose not to participate or you show disinterest in participating in the study, your management in the facility will not be affected in anyway, it will have no effect on the reporting time of your images and your images will not be used for the study.

Withdrawal from the research: You may choose to withdraw images and information from the research at any time without having to explain yourself. You may also choose not to answer any question you find uncomfortable or private.

Consequences of withdrawal: There will be no consequence, loss of benefit or care to you if they choose to withdraw from the study. Please note however, that some of the information that may have been obtained from you without identifiers (name etc), before you chose to withdraw, may have been modified or used in analysis reports and publications. These cannot be removed anymore. I promise to make good faith effort to comply with your wishes as much as practicable.

Costs/Compensation: There will be no additional costs or compensation to you.

Contacts: If you have any question concerning this study, please do not hesitate to contact Dr. Nana Akua K. Asamoah on 024 501 8699.

Further, if you have any concern about the conduct of this study, your welfare or your rights as a research participant, you may contact:

The Office of the Chairman
Committee on Human Research and Publication Ethics
Kumasi
Tel: 03220 63248 or 020 5453785

Appendix 2: Consent Form

Consent Form

Statement of person obtaining informed consent:

I have fully explained this research to _____

and have given sufficient information about the study, including that on procedures, risks and benefits, to enable the prospective participant make an informed decision to or not to participate.

DATE: _____NAME: _____

Statement of person giving consent:

I have read the information on this study/research or have had it translated into a language I understand. I have also talked it over with the interviewer to my satisfaction.

I understand that my participation is voluntary (not compulsory).

I know enough about the purpose, methods, risks, and benefits of the research study to decide that I want to take part in it.

I understand that I may freely stop being part of this study at any time without having to explain myself.

I have received a copy of this information leaflet and consent form to keep for myself.

NAME:

_____

DATE: _____SIGNATURE/THUMB PRINT: _____

Statement of person witnessing consent (Process for Non-Literate Participants):

I _____ (Name of Witness) certify that information given to

_____ (Name of Participant), in the local language, is a true reflection of what l have read from the study Participant Information Leaflet, attached.

WITNESS' SIGNATURE (maintain if participant is non-literate):

_____

Appendix 3: Data Extraction sheet

DATA EXTRACTION SHEET

EMBOLIC BURDEN AND RIGHT HEART DYSFUNCTION PARAMETERS ON CT PULMONARY ANGIOGRAPHY: MORTALITY CORRELATION IN ACUTE PULMONARY EMBOLISM

Identification number…….

Study ID …….. **Date (dd/mm/yyyy) ……**

DEMOGRAPHICS

1. Age (completed years) …….

2. Sex a. Male [ ] b. Female [ ]

3. Telephone number of patient/caregiver …….

4. Patient Occupation
a. Unemployed [ ] b. Student [ ] c. Skilled worker [ ]
d. Professionals [ ] e. Famers [ ] f. Traders [ ]
g. Others [ ]

5. Educational level of patient. a. No Education [] b. Primary [ ]

c. Junior High [ ] d. Senior High [ ] e. Tertiary [ ]

f. Vocational [ ] g. Other [ ] please state……

CLINICAL FINDINGS

Symptoms of Acute Pulmonary Embolism

6. Chest Pain or Discomfort a. Yes [ ] b. No [ ]

7. Breathlessness a. Yes [ ] b. No [ ]

8. Malaise a. Yes [ ] b. No [ ]

9. Lower Limb swelling a. Yes [ ] b. No [ ]

10. Shock a. Yes [ ] b. No [ ]

11. Other symptoms a. Yes [ ] b. No [ ]

11a. If other symptoms, please state……

Risk factors

12. Hypertension/cardiac disease a. Yes [ ] b. No [ ]

13. Diabetes mellitus a. Yes [ ] b. No [ ]

14. Clotting abnormalities a. Yes [ ] b. No [ ]

15. Malignancy a. Yes [ ] b. No [ ]

16. Recent surgery a. Yes [ ] b. No [ ]

17. History of Recent Travel a. Yes [ ] b. No [ ]

18. Immobilization a. Yes [ ] b. No [ ]

19. Other a. Yes [ ] b. No [ ]

==19a. If other, please specify ……

20. Patient's state of health at time of imaging

a. Stable/ Walk-in patient [ ] b. critically ill-patient [ ]

CLINICAL MANAGEMENT

21. Anticoagulation a. Yes [ ] b. No [ ]

22. Thrombolysis a. Yes [ ] b. No [ ]

23. No management a. Yes [ ] b. No [ ]

24. Other management a. Yes [ ] b. No [ ]

24a. If other management, please state ……

IMAGING FINDINGS

CT measurements for Right Heart Strain

25. Right ventricular diameter (cm) ……..

26. Left ventricular diameter (cm) …….

27. RV/LV ratio ……

28. Pulmonary artery diameter …….

29. Aortic Diameter ……

30. Pulmonary Artery / Aortic Diameter Ratio …….

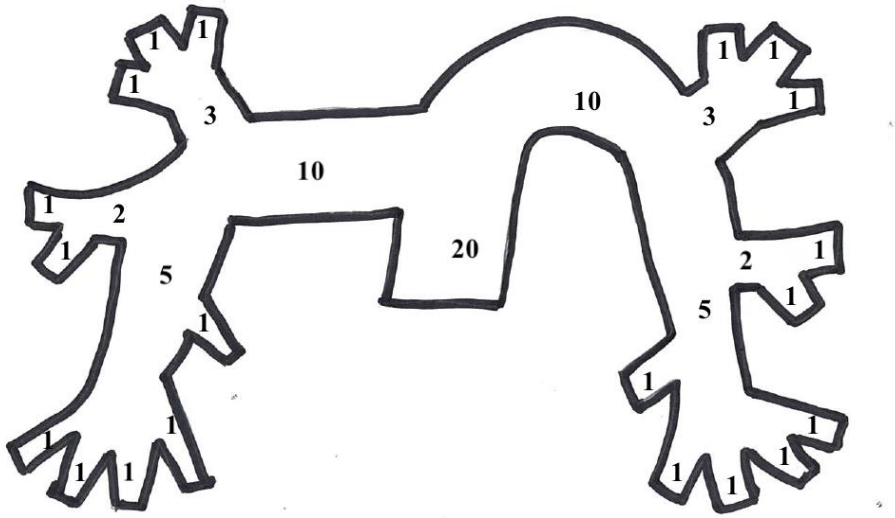
31. Azygos diameter ……..

32. Reflux into IVC a. Yes [ ] b. No [ ]

33. Left ward bowing of interventricular septum a. Yes [ ] b. No [ ]

Clot Burden Scoring

32.



Qanadli score
N =

D =

Total Clot score =

Other CTPA findings of Acute PA

33. Pleural effusion a. Yes [ ] b. No [ ]

34. Please specify other CTPA findings **……**

Follow up after 30 days

35. Patient status a. Alive [ ] b. Dead [ ]

36. Date of Death:

37. Duration between date of diagnosis and death

37. Recurrence of disease process with in the period a. Yes [ ] b. No [ ]

Appendix 4: Letter of Approval from study site (Spectra Health Ltd)

spectrahealth
Imaging & Interventional Radiology

24th January, 2022

Dr. (Mrs.) Nana Akua Konama Asamoah
K.N.U.S.T – S.M.D
Department of Radiology

Dear Dr. (Mrs.) Nana Akua Konama Asamoah,

LETTER OF APPROVAL

With reference to your letter dated 5th January, 2022, I am glad to inform you that the management of Spectra Health has ranted you the approval to use Spectra Health as a research site for your dissertation in partial fulfillment of the requirements for the award of the Fellowship of the Ghana College of Physicians and Surgeons.

We look forward to supporting you in whatever way possible to make your study a success.

Yours faithfully,

Dr. George Asafu Adjaye Frimpong C.E.O

SPECTRA HEALTH LIMITED SEAL 2016 KUMASI P.O.BOX 5431 ADUM

No. 12 Opoku Adjei Avenue Patasi, off the Friends Garden Junction, Kumasi
(T) +233 (0) 322 299 310, +233 (0)507 676 769 (E) info@spectrahealthgh.com www.spectrahealthgh.com

Appendix 5: Request for Ethical Approval

GHANA COLLEGE OF PHYSICIANS AND SURGEONS

OUR REF: BA.100.001.48
Tel: +233-(0)302-238650/238703
Cell: 0243-690073
Email: exams@gcps.edu.gh

P. O. Box MB 429
Ministries-Accra
Ghana

21st February 2022

The Head
Department of Radiology
Komfo Anokye Teaching Hospital
Kumasi

Dear Sir/Madam,

REQUEST FOR ETHICAL APPROVAL

Dr. Nana Akua Konama Asamoah, a Senior Resident in Radiology, Ghana College of Physicians and Surgeons has submitted the revised Research Proposal for her Dissertation. Comments by the College Dissertation Review Committee have been duly addressed.

Kindly arrange for this Research Proposal to be submitted to the Research and Ethics Committee of the Komfo Anokye Teaching Hospital for ethical approval to enable her start her research work which is a requirement for the award of the Fellowship of the College.

Attached is a copy of the Research Proposal.

Counting on your usual cooperation.

Yours sincerely,

Adanu

Prof. Richard Adanu
Rector

cc: Dr. Nana Akua Konama Asamoah ✓

Appendix 6: Ethical Approval from CHRPE KNUST

Spectra Health, affiliate site of KNUST

Kwame Nkrumah
University of Science
and Technology, Kumasi

College of Health Sciences
SCHOOL OF MEDICINE AND DENTISTRY

COMMITTEE ON HUMAN RESEARCH, PUBLICATION AND ETHICS

Our Ref: CHRPE/AP/095/22

17th March 2022

Dr. Nana Akua Konama Asamoah
Directorate of Radiology
Komfo Anokye Teaching Hospital
Post Office Box 1934
KUMASI

Dear Madam,

LETTER OF APPROVAL

Protocol Title: ***"Correlation of Embolic Burden and Right Heart Dysfunction Parameters with Short Term Mortality in Acute Pulmonary Embolism Using Computed Tomography Pulmonary Angiography"***

Proposed Site: ***Spectra Health Imaging and Interventional Radiology.***

Sponsor: ***Principal Investigator.***

Your submission to the Committee on Human Research, Publications, and Ethics on the above-named protocol refer.

The Committee reviewed the following documents:

- A notification letter of 24th January 2022 from the Spectra Health Imaging and Interventional Radiology (study site) indicating approval for the conduct of the study at the facility.
- A Completed CHRPE Application Form.
- Participant Information Leaflet and Consent Form.
- Research Protocol.
- Data Capturing Sheet.

The Committee has considered the ethical merit of your submission and approved the protocol. The approval is for a fixed period of one year, beginning **17th March 2022** to **16th March 2023** renewable thereafter. The Committee may, however, suspend or withdraw ethical approval at any time if your study is found to contravene the approved protocol.

Data gathered for the study should be used for the approved purposes only. Permission should be sought from the Committee if any amendment to the protocol or use, other than submitted, is made of your research data.

The Committee should be notified of the actual start date of the project and would expect a report on your study, annually or at the close of the project, whichever one comes first. It should also be informed of any publication arising from the study.

Thank you for your application.

Yours faithfully,

Rev. Prof. John Appiah-Poku.
Honorary Secretary
FOR: CHAIRMAN