Sudan University of Sciences and Technology
College of Graduate Studies

Characterization of Heart and Pulmonary Vessels in Patients with Pulmonary Hypertension and Embolism using Computed Tomography

توصيف القلب والأوعية الدموية الرئوية لدى المصابين بارتفاع ضغط الدم الرئوي الانسدادت الرئوية بأستخدام التصوير بالأشعة المقطعية

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الآية الكريمة

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العلق (1-5)

صدق الله العظيم

DIDECATION

TO SOULS OF MY PARENTS

MY BROTHERS – SISTERS

MY WIFE – CHILDREN

AND MY FRIENDS

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Abstract

The study aimed to characterize the heart and pulmonary vessels in patients with PH, PE, and CTEPH using Computed Tomography.

Pulmonary embolism PE is a potentially life threatening condition which requires adequate diagnosis. And pulmonary hypertension PH is a complex disorder and may be related to a variety of diseases. It may arise in association with chronic pulmonary thromboembolism CTEPH or pulmonary embolism PE. It is a serious illness that becomes progressively worse and is sometimes fatal.

This study was conducted at Royal Care International Hospital and Doctor’s Clinic radiographic departments during the period spanned from 2013-2016 A sample of 55 patients with clinically diagnosed as PE was enrolled, their mean ages were 54.20±14.21years and a sample of 20 patients with PH mean ages were 60.4±13.96 and 25 patients with CTEPH their mean ages were 61.24±9.5 and 50 normal subjects were considered as control group, their mean ages were 50.7±14.5. The sample included both genders.

In order to evaluate PE sample the study was directed to investigate whether the presence of plural parenchymal findings correlates with the PE and to know the plural parenchymal abnormalities associated with PE, also to know the correlation of PE with the presence of heart changes and pulmonary vessels measurements. CTPA scans were

acquired and there for the clinical signs, pluroparenchymal abnormalities, pulmonary artery tree measurements, right ventricle and atrium diameters, Inter ventricular septum width as well as the myocardium thickening were characterized .The results showed that the PE patients group had dilated measurements than the normal control subjects. The right ventricle diameter changes were found to be significantly related to the presence of PE at $p \leq 0.001$. Significant changes at $p \leq 0.005$ were also noticed in the pulmonary trunk diameter as well as the right and left main pulmonary arteries with no significant changes detected in the distal portion of both pulmonary arteries diameters. The common complaints from PE patients were chest pain, shortness of breathing, lower limb swelling, tachycardia and syncope. Consolidation, ground glass opacifications, mosaic, right ventricle morphological changes and pleural effusion were present in the majority of patients. For the evaluation of PH and the association with CTEPH and pulmonary embolism PE, this study evaluated the clinical characteristics and the CTA findings. The results showed that in all patients groups, the pulmonary vascular, cardiac segments and lung parenchyma changes were detected and were significantly different from the normal control subjects at $p \leq 0.000$.

CTPA is considered as the diagnostic modality of choice in characterization of pulmonary vessels, quantifying heart segments and parenchyma changes. CT Imaging was

acceptably used in diagnosis, and in defining the cause, in order to assess the feasibility of surgery, monitoring and therapeutic planning.

المستخلص

هدفت الدراسة إلى توصيف القلب والأوعية الدموية للرئتين عند المرضى المصابين بأمراض ارتفاع ضغط الدم والانسداد الرئوي والانسداد الرئوي التجلطي، باستخدام التصوير الإشعاعي الطبقي.

يعتبر مرض الانسداد الرئوي من الحالات المهددة للحياة التي تتطلب تشخيصاً كافياً ودقيقاً. أما ارتفاع ضغط الدم الرئوي فهو معقد وقد تصاحبه عدة أمراض أخرى، ويمكن أن ينشأ جنباً إلى جنب مع الانسداد الرئوي التجلطي أو الانسداد الرئوي العادي و يعتبر ايضا من الامراض الخطيرة و القاتلة.تم إجراء هذه الدراسة في مستشفي رويال كير العالمي ومستشفي الأطباء بالخرطوم في قسم الأشعة بكل من المستشفيين، خلال الفترة بين 2013 - 2016 م.

اشتملت الدراسة على عينة من 55 مريضاً تم تشخيصهم سريرياً على أنهم مصابون بالانسداد الرئوي، وتراوح متوسط أعمارهم بين 14.21 ± 54.20 عاماً. وشملت الدراسة أيضاً عينة من 20 مريضاً بارتفاع ضغط الدم الرئوي تراوح متوسط أعمارهم بين 13.96±60.4 عاماً وعينة أخرى من 25 مريضاً بالانسداد الرئوي التجلطي تراوح متوسط أعمارهم بين 9.5 + 61.24 عاماً، بالإضافة إلى عينة من 50 من الأصحاء أخذت كمجموعة ضبط، وتراوح متوسط أعمارهم بين 14.5±50.7 عاماً. وقد شملت الدراسة كلا الجنسين.

ولتقييم الانسداد الرئوي تمت الدراسة للاستقصاء والبحث عما إذا كان وجود النتائج الخاصة بالنسيج اللبى الخاص بغشاء البلورا له علاقة ارتباط بالانسداد الرئوي، وكذلك لمعرفة أمراض النسيج اللبى للبلورا ذات الصلة بالانسداد الرئوي وايضا علاقة الانسداد الرئوي بوجود تغييرات في القلب وقياسات الأوعية الدموية الرئوية. تم إجراء صور التصوير المقطعي للأوعية الدموية للرئتين وتم من خلالها توصيف العلامات السريرية وأمراض النسيج اللبى وقياسات تفرعات الشريان الرئوي وقياس أقطار البطين الأيمن والأذين الأيمن بالإضافة إلى قياس عرض الحاجز بين البطينين وسماكة عضلة القلب الرئيسية. أظهرت الدراسة أن القياسات كانت أكبر في مجموعة الانسداد الرئوي من

مجموعة الضبط، وأن التغييرات في قطر البطين الأيمن كانت لها علاقة قوية بوجود الانسداد الرئوي (علاقة ارتباط $P \leq 0.001$). وتمت ملاحظة تغييرات كبيرة بعلاقة ارتباط تساوى $P \leq 0.005$ في قطر الجذع الرئوي، بالإضافة إلى الشرايين الرئوية الأساسية اليمنى واليسرى. لم تتم ملاحظة أي تغييرات في الجزء الأسفل من أقطار الشرايين الرئوية. كانت شكوى مرضى الانسداد الرئوي تتمثل في ألم في الصدر، ضيق في التنفس، تورم في الأطراف السفلى، زيادة خفقان القلب والاغماء أما التصلب الرئوي والتعتيمات، والأشكال الفسيفسائية، والتغييرات الشكلية في البطين الأيمن وكذلك الإنسكاب البلوري فقد كانت موجودة عند معظم المرضى. أما بخصوص تقييم ارتفاع ضغط الدم الرئوي وارتباطه بمرض الانسداد الرئوي التجلطي والانسداد الرئوي فقد قامت الدراسة بتقييم الخصائص السريرية ونتائج التصوير المقطعي للأوعية الدموية.وأوضحت الدراسة أن هناك تغييرات – لدى جميع المرضى – في الاوعية الدموية للرئتين والأجزاء القلبية والنسيج الرئوي، وكانت تختلف بصورة كبيرة عن الأجزاء المقابلة في مجموعة الضبط بعلاقة تساوى $P \leq 0.000$.

ويعتبر التصوير المقطعي للأوعية الدموية للرئتين هو الفحص المثالي الذي يجب اختياره لتوصيف الأوعية الدموية الرئوية وقياسات أجزاء القلب وملاحظة التغييرات النسيجية. وتستخدم الأشعة المقطعية في التشخيص وتحديد سبب المرض حتى يمكن اتخاذ القرار بخصوص إجراء عمليات جراحية أو وضع الخطط الخاصة بالعلاجات الأخرى، ورصد الحالات المرضية.

List of Abbreviations

Abbreviation	Phrase
BMI	Body Mass Index
CHD	Congenital heart disease
CM	Contrast Media (Material)
CO	Cardiac out put
COPD	Chronic Obstructive Pulmonary Disease
CT	Computed Tomography
CTA	Computed Tomography Angiography
CTPA	Computed Tomographyof the Pulmonary Arteries (Angiography)
CVD	Cardiovascular disease
CXR	Chest X-Ray
DAS	Data Acquisition system
DVT	Deep Venous Thrombosis
ECG	Electrocardiography
EPH	Chronic Thromboembolic pulmonary hypertension
FOV	Field Of View
HIV	Human immunodeficiency virus
HU	Hounsfield Unit
IPAH	Idiopathic pulmonary arterial hypertension
IV	Intravenous
IVC	Inferior vena cava
IVS	Interventricular septum
KPa	Kilopascals
KV	Kilovolts
KVP	Kilo-Voltage Peak
LA	Left atrium
LMPA	Left Main Pulmonary Artery
LV	Left ventricle
LVEF	Left ventricular ejection fraction
Ma	Milliampere
Mas	milliampere /second
MDCT	Multi-Detector Computed Tomography
MDCT	Multi-detector row computed tomography
MDCTPA	Multi-Detector Computed Tomography Pulmonary

	Angiography
MHU	million heat units
MI	Myocardial Infarction
mm Hg	Millimeters of mercury
MPAD	Main pulmonary artery diameter
mPAP	Mean pulmonary artery pressure
MPR	Multi-Planar Reconstruction
MRA	Magnetic Resonance Angiography
MRI	Magnetic Resonance Imaging
MSCT	multiple slice computed tomography
PA	Pulmonary Arteriography
PAH	Pulmonary Arterial Hypertension
PAOP	Pulmonary artery occlusion pressure
PAP	Pulmonary Artery pressure
PCWP	Pulmonary capillary wedge pressure
PE	Pulmonary Embolism
PH	Pulmonary Hypertension
PVOD	Pulmonary veno-occlusive disease
PVOD	Pulmonary veno-occlusive disease
PVR	Pulmonary vascular resistance
RA	Right atrium
RHC	Right – sided heart catheterization
RMPA	Right Main Pulmonary Artery
ROI	Region of interest
RV	Right Ventricle
RV	Right Ventricle
RVH	Right ventricular hypertension
SD	Standard deviation
TTE	Transthoracic echocardiography
V/Q-scan	Ventilation-Perfusion Lung Scintigraphy
VEDV	Ventricular end-diastolic volume
VSD	Ventricular septal defect
VTE	Venous Thrombo-Embolism
VTE	Venous thromboembolism
WHO	World Health Organization
WSPH	World Symposium on Pulmonary hypertension
2D	Two dimension
3D	Three dimension

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Chapter one

Introduction

Chapter One

1.1 Introduction:

The heart can be visualized in gross form on any standard chest computed tomography CT, but for detailed evaluation of cardiac anatomy exacting specifications of scanner hardware and software must be in place because : The heart is continually in motion, the structures of interest requires multiplaner reformatting for analysis. For these specifications to be met, the scanner hardware must be robust, the scanner must be fitted with ECG-monitoring equipment, and cardiac–specific software and image reconstruction servers must be installed (Budoff and Shinbane, 2016).

Due to explosion in technological development of cardiac CT systems, with concomitant gain in reliability and accuracy, especially of coronary imaging. The theme has been one of progressively improved spatial and temporal resolution, reduced scan time, and recently, a focus on driving down radiation exposure. It is easily achievable to perform a standard chest CT or an invasive coronary angiogram. The goal of future systems will be to make this more widely achievable in a layer group of patients without requiring patient selection or stringent patient preparation. Given the history of rapid technological advancement, we can expect to see this goal achieved in the near future.
(Budoff and Shinbane, 2016).

Pulmonary vascular disease span a variety of disease entities including pulmonary arterial hypertension PAH, pulmonary venous hypertension, pulmonary embolism, pulmonary arteriovenous malformation, pulmonary arterial stenosis, pulmonary artial aneurysm, pulmonary veno-occlusive disease PVOD, and pulmonary capillary hemangiomatosis. (Budoff and Shinbane. 2016).

In this study using Computed Tomography CTfor characterization the heart and pulmonaryblood vessels in patients with pulmonary hypertension PH and pulmonary embolism PE and chronic thromboembolic pulmonary hypertension CTEPH.

1.1.1 Pulmonary hypertension (PH)

PH is characterized by an elevation in resting pulmonary arterial pressure with accompanying right ventricular failure. PAH refers to a disease of the precapillary pulmonary circulation which is the result of the complex process intrinsic to the pulmonary vasculature. This process leads to a progressive increase in pulmonary vascular resistance at right ventricular RV after load, and usually results in right- sided cardiac failure. PAH is hemodynamically defined as a mean pulmonary artery pressure greater than 25 mm Hg at rest, with a normal pulmonary artery wedge pressure measured at right heart catheterization. (Mclaughlin VV., et al 2009) PAH is a progressive and life threatening condition with a poor prognosis if untreated. Most patients with PAH present with exertional dyspnea that progresses over

months to years. Exertional angina, syncope, and peripheral edema appear in more severe PH with impaired right heart function. The diagnosis of PAH is often delayed due to the nonspecific symptoms and subtle findings on physical examination. Pulmonary hypertension PH is a complex disorder. (McLaughlin VV, 2006) Definition of PH is based on shared pathophysiology that categorizes many classes of PH: pulmonary arterial hypertension PAH, which may be idiopathic IPAH or associated with left heart disease; or lung disease or in association with chronic thromboembolic pulmonary hypertension. CTEPH (Mehta S, et al 2010) In patients with PAH, progressive narrowing of the small pulmonary arteries and arterioles results in increased pulmonary vascular resistance, which may ultimately lead to right ventricular failure .Vasoconstriction and thrombosis in situ are factors rising vascular resistance. (Galie N, et al 2009).

According to the diagnostic approach to PH that was proposed in 1997 by Reaside and Peacock. (Reaside D and Peacock A 1997) the ability to differentiate between CTEPH and primary PH relies on computed tomography CT, which enables recognition of chronically obstructed vessels. (Kereiakes DJ, et al 1983,Tardivon AA, et al 1993,Falaschi F, et al 1992,Schwickert HC, et al 1994, Bergin CJ, et al 1997,Remy-Jarden M, et al 1997,Bergin CJ, et al 1999) The occurrence of CTEPH in the general population may have been significantly underestimated. Recent epidemiologic records specify an incidence of 4%

after acute symptomatic pulmonary embolism PE. (Pengo V, et al 2004, Tapson VF,2006). Given the growing number of patients undergoing chest CT who might have PE, are an increasingly common finding on chest CT images. (Eva Castaner, et al 2009) Symptoms are non specific and are related to the progress of PH. The vascular obstruction is a most important character of PH. In the majority of symptomatic patients, more than 40% of the pulmonary vascular bed is obstructed. (Fedullo PF et al 2001, Moser KM, et al 1992) Patients with CTEPH are asymptomatic before their presentation with symptoms. (Fedullo PF et al 2001,Moser KM, et al 1992,Rich S, t al1988,Frazier AA, et al 2000) The clinical worsening correspond the loss of right ventricular functional capability. In these patients, pulmonary arterial pressure is elevated and right atria pressures are high. (Moser KM, et al 1992).

Therefore early and appropriate diagnosis and treatment are required, in this study; we evaluated the clinical characteristics, the CT findings in PH, PE and CTEPH patients. We have expressed the technique for CT angiography and the CT diagnostic criteria for all cases and correlate the findings with normal control. Knowledge of the radiological signs is required to detect and accurately diagnose the condition and may improve the outcome .In the current study the pulmonary artery tree, heart segments and associated lung parenchema findings have been evaluated and the added value of CT in

prediction of estimating PH comparing with the normal control group were analyzed.

1.1.2 Pulmonary embolism (PE).

Is an obstruction of a pulmonary artery caused by a blood clot, air, fat, or tumor tissue? The most common cause of the obstruction is a blood clot (thrombus) usually from a peripheral vein; most patients with deep vein thrombosis DVT develop PE. The classic triad of signs and symptoms of PE (hemoptysis, dyspnea, and chest pain) are neither sensitive nor specific, and many patients with PE are initially asymptomatic, most patients who have symptoms often have a typical and / or nonspecific symptom, such as dyspnea, tachypnea, and chest pain.

Pulmonary embolism PE is the most common cardiovascular condition. (Giuntini C, et al 1995) Death rate after a diagnosis of PE is still 8%–15%. (Carson JL, et al 1992, Stein et al 2004) Due to lack of precise symptoms that predict or exclude the diagnosis of PE, it is frequently misdiagnosed. (Halil et al 2015) Despite technical progress, imaging the pulmonary arteries has remained costly and harmful, even with noninvasive approaches. (U. Joseph et al 2004) PE can be diagnosed accurately with pulmonary angiography, which is recognized as the gold standard, but it is invasive. (Stein PD, et al 1992).

Imaging modalities have improved over the time from plain film, scintigraphy and angiography to computed-tomography CT scan and magnetic resonance imaging MRI, which have been used for diagnosing PE.

(Waseem et al 2010) Contrast-enhanced MRA has lack sufficient spatial resolution for evaluation of peripheral pulmonary arteries. (Oudkerk M, et al 2002) Echocardiography is not recommended as a routine imaging test to diagnose suspected acute PE. (Goldhaber SZ, 2002) Several studies have shown that contrast enhanced CT has sensitivities and specificities of approximately 90% in the diagnosis of PE. (Usman MU, et al 2003,Pineda LA, et al 2001,Wittram C, 2007,Subramaniam RM, et al 2008) Spiral computed-tomographic pulmonary angiography CTPA has gained a leading role in PE diagnosis because of being less invasive than conventional pulmonary angiography. (Waseem et al 2010) The main CT limitations is the detection of small peripheral emboli. (Perrier A, et al 2001) Early studies comparing spiral CT with selective pulmonary angiography demonstrated the high accuracy of spiral CT for detecting PE (Remy-Jardin, 1996) but suggested that subsegmental pulmonary emboli may be unnoticed by CT scanning. Recent studies have shown that CT can assess the acute right-sided heart failure and can predict adverse clinical outcome. (Quiroz R, et al2004, Reid, 1998) CT angiography and high resolution CT are commonly used for the diagnosis of PE and underlying lung parenchyma disease. (Moraes D,1997,Runo J,2002,Budev mm, et al 2003,Bugnone A, et al 2002,HEY JC,2003) Asymmetric dilation of the pulmonary arteries, calcified thrombi and bronchial collaterals are considered signs of embolic

disease. (Tans RT, et al 1998, Bergeen, 1997) Deviation of the interventricular septum was reported on CT as a subjective sign of raised right heart pressure. High resolution CT of the chest can show the underlying pulmonary disease. (Sherrick A, et al1997) The literature shows variable results for the analytical role of CTPA to characterize the pluralparenchymal abnormality, pulmonary vessels and heart in order to diagnose PE. This variability may be explained by the subjective changes on CTPA because formal criteria for establishing these signs are not available. CT can diagnose the presence of a clot subjectively; since an objective and quantification method to characterize pleuralparenchymal abnormality, pulmonary vessels and heart is needed (in order to diagnose PE).To the best of our knowledge; no study has investigated whether the presence of plural parenchymal findings correlates with the PE in our Sudanese Radiology Departments. This study was directed to investigate whether the presence of plural parenchymal findings correlates with the PE and as well, it was designed to answer two basic questions based on CTPA findings that done for clinical suspicion of PE: firstly, what are the plural parenchymal abnormalities associated with PE, secondly, correlation of PE with the presence of heart changes and pulmonary vessels measurements.

1.2 Problem of the study:

The heart and pulmonary vessels can be diagnosed by different radiological methods; some diseases can

affected the heart and pulmonary vessels, but cannot be diagnosed on the conventional chest x-ray which can lead to delay in diagnosis of such cases, cardiac catheterization is an excellent method for evaluation of heart and blood vessels but its invasiveness leads to many complications, Non invasive methods is needed for study and evaluate patients with PE & PH such as CTPA.

1.3 Objectives of the study:

1.3.1 General objectives:

To characterize the heart and pulmonary vessels in patients with pulmonary embolism PE and pulmonary arterial hypertension PAH using Computed Tomography scan CT.

1.3.2 Specific Objectives:

- To evaluate and measure the right atrium RA, Right Ventricle RV and septum thickness.
- To evaluate the pulmonary trunk diameter.
- To evaluate the main right and left pulmonary arteries diameter.
- To evaluate proximal and distal pulmonary artery diameter.
- To evaluate and measure the myocardium.
- To correlate between the patients history, clinical finding, age and gender.

1.4 Overviews of the study:

This study was fall into five chapters, chapter one is an introduction, problem of the study, objectives and overview. Chapter two include literature review while chapter three include material used and the method of data collection and analysis. Chapter four presents the result of the study in a line graphs and tables and finally chapter five which include the discussion, conclusion and recommendations.

CHAPTER TWO
Literature Review

Chapter Two

2. Literature Review

2.1 Anatomy and physiology of cardiovascular system

The cardiovascular system is divided for descriptive purposes into two main parts. The circulatory system, consisting of the heart, which acts as a pump, and the blood vessels through which the blood circulates. The lymphatic system, consisting of lymph nodes and lymph vessels, through which colorless lymph flows. The two systems communicate with one another and are intimately associated. (Waugh and Grant, 2014)

The heart pumps blood into two anatomically separate systems of blood vessels. The pulmonary circulation and the systemic circulation. The right side of the heart pumps blood to the lungs (the pulmonary circulation) where gas exchange occurs; i.e. CO 2 leaves the blood and enters the lungs, and O 2 leaves the lungs and enters the blood. The left side of the heart pumps blood into the systemic circulation, which supplies the rest of the body. Here, tissue wastes are passed into the blood for excretion, and body cells extract nutrients and O 2. (Waugh and Grant, 2014).

The circulatory system ensures a continuous flow of blood to all body cells, and its function is subject to continual physiological adjustments in order to maintain an adequate blood supply. Should the supply of oxygen and nutrients to body cells become inadequate, tissue

damage occurs and cell death may follow. (Waugh and Grant, 2014).

The heart pumps blood into vessels that vary in structure, size and function, and there are several types: arteries, arterioles, capillaries, venules and veins (Waugh and Grant, 2014).

2.1.1 Arteries and arterioles

These are the blood vessels that transport blood away from the heart. They vary considerably in size and their walls consist of three layers of tissue. Outer layer of fibrous tissue, middle layer of smooth muscle and elastic tissue, inner lining of squamous epithelium called endothelium. (Waugh and Grant, 2014)

2.1.2 Veins and venules

The veins are the blood vessels that return blood at low pressure to the heart. The walls of the veins are thinner than those of arteries but have the same three layers of tissue. They are thinner because there is less muscle and elastic tissue in the middle layer. When cut, the veins collapse while the thicker-walled arteries remain open. Some veins possess valves, which prevent backflow of blood, ensuring that it flows towards the heart. Valves are abundant in the veins of the limbs, especially the lower limbs where blood must travel a considerable distance against gravity when the individual is standing. Valves are absent in very small and very large veins in the thorax and abdomen. They are formed by a fold of tunica intima strengthened by connective tissue. The cusps are

semilunar in shape with the concavity towards the heart. The smallest veins are called venules. (Waugh and Grant, 2014)

2.1.3 The Heart

The heart is a roughly cone-shaped hollow muscular organ. It is about 10 cm long and is about the size of the owner's fist. It weighs about 225 g in women and is heavier in men (about 310 g). The heart lies in the thoracic cavity in the mediastinum between the lungs. It lies obliquely, a little more to the left than the right, and presents a base above, and an apex below. The apex is about 9 cm to the left of the midline at the level of the 5th intercostal space, i.e. a little below the nipple and slightly nearer the midline. The base extends to the level of the 2nd rib. (Waugh and Grant, 2014).

2.1.3.1 Organs associated with the heart.

Inferiorly, the apex rests on the central tendon of the diaphragm

Superiorly, the great blood vessels, i.e. the aorta, superior vena cava, pulmonary artery and pulmonary veins

Posteriorly, the oesophagus, trachea, left and right bronchus, descending aorta, inferior vena cava and thoracic vertebrae

Laterally, the lungs, the left lung overlaps the left side of the heart

Anteriorly, the sternum, ribs and intercostal muscles. (Waugh and Grant, 2014)

2.1.3.2 Layers of the Heart

The heart is composed of three layers of tissue. Pericardium, myocardium and endocardium.

The Pericardium is made up of two sacs. The outer sac consists of fibrous tissue and the inner of a continuous double layer of serous membrane.The myocardium is composed of specialized cardiac muscle found only in the heart. It is not under voluntary control but, like skeletal muscle, cross-stripes are seen on microscopic examination.

(Waugh and Grant, 2014)

The myocardium is thickest at the apex and thins out towards the base. This reflects the amount of work each chamber contributes to the pumping of blood. It is thickest in the left ventricle.

(Waugh and Grant, 2014)

The endocardium this forms the lining of the myocardium and the heart valves. It is a thin, smooth, glistening membrane which permits smooth flow of blood inside the heart. It consists of flattened epithelial cells, continuous with the endothelium that lines the blood vessels. (Waugh and Grant, 2014).

2.1.3.3 Interior of the heart

The heart is divided into a right and left side by the septum, a partition consisting of myocardium covered by endocardium. After birth blood cannot cross the septum from one side to the other. Each side is divided by an atrioventricular valve into an upper chamber, the atrium, and a lower chamber, the ventricle. (Waugh and Grant, 2014).

The atrioventricular valves are formed by double folds of endocardium strengthened by a little fibrous tissue. The right atrioventricular valve (tricuspid valve) has three flaps or cusps and the left atrioventricular valve (mitral valve) has two cusps. The valves between the atria and ventricles open and close passively according to changes in pressure in the chambers. They open when the pressure in the atria is greater than that in the ventricles. During ventricular systole (contraction) the pressure in the ventricles rises above that in the atria and the valves snap shut preventing backward flow of blood. The valves are prevented from opening upwards into the atria by tendinous cords, called chordae tendineae, which extend from the inferior surface of the cusps to little projections of myocardium covered with endothelium, called papillary muscles. (Waugh and Grant, 2014).

2.1.3.4 Flow of blood through the heart.

The two largest veins of the body, the superior and inferior venae cavae, empty their contents into the right atrium. This blood passes via the right atrioventricular valve into the right ventricle, and from there it is pumped

into the pulmonary artery or trunk (the only artery in the body which carries deoxygenated blood). The opening of the pulmonary artery is guarded by the pulmonary valve, formed by three semilunar cusps. This valve prevents the back flow of blood into the right ventricle when the ventricular muscle relaxes. After leaving the heart the pulmonary artery divides into left and right pulmonary arteries, which carry the venous blood to the lungs where exchange of gases takes place: carbon dioxide is excreted and oxygen is absorbed. Two pulmonary veins from each lung carry oxygenated blood back to the left atrium. Blood then passes through the left atrioventricular valve into the left ventricle, and from there it is pumped into the aorta, the first artery of the general circulation. The opening of the aorta is guarded by the aortic valve, formed by three semilunar cusps. From this sequence of events it can be seen that the blood passes from the right to the left side of the heart via the lungs, or pulmonary circulation. However, it should be noted that both atria contract at the same time and this is followed by the simultaneous contraction of both ventricles. The muscle layer of the walls of the atria is very thin in comparison with that of the ventricles. This is consistent with the amount of work it does. The atria, usually assisted by gravity, only propel the blood through the atrioventricular valves into the ventricles, whereas the ventricles actively pump the blood to the lungs and round the whole body. The muscle layer is thickest in the wall of the left ventricle. The pulmonary

trunk leaves the heart from the upper part of the right ventricle, and the aorta leaves from the upper part of the left ventricle. (Waugh and Grant, 2014).

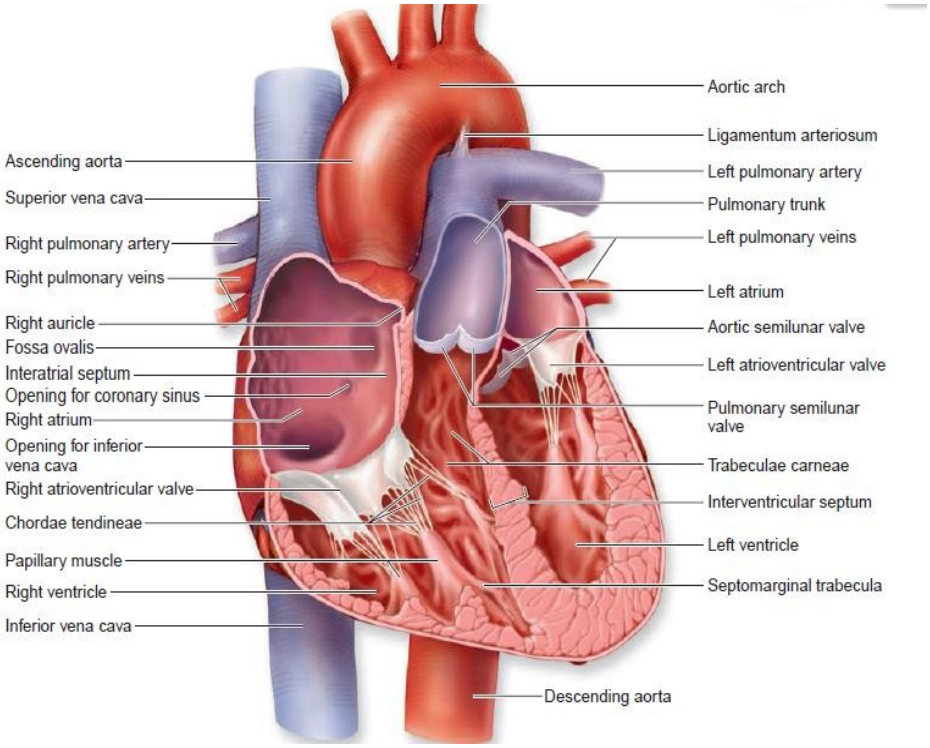


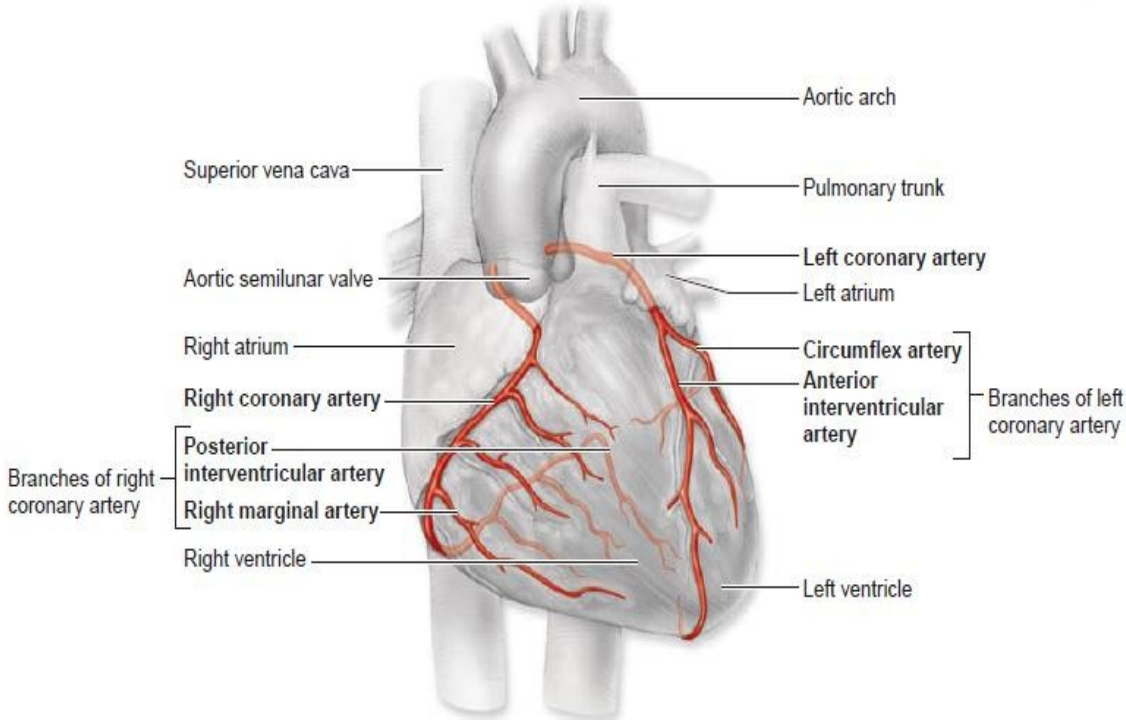
Figure 2.1 Internal Anatomy of the Heart. An illustration reveals the internal structure of the heart, including the valves and the musculature of the heart wall. (wikipedia.org, 2016).

2.1.3.5 Blood supply to the heart

Arterial supply: The heart is supplied with arterial blood by the right and left coronary arteries which branch from the aorta immediately distal to the aortic valve. The coronary arteries receive about 5% of the blood pumped from the heart, although the heart comprises a small proportion of

body weight. This large blood supply, especially to the left ventricle, highlights the importance of the heart to body function.The coronary arteries traverse the heart, eventually forming a vast network of capillaries. (Waugh and Grant, 2014)

Venous drainage: Most of the venous blood is collected into several small veins that join to form the coronary sinus which opens into the right atrium. The remainder passes directly into the heart chambers through little venous channels. (Waugh and Grant, 2014).



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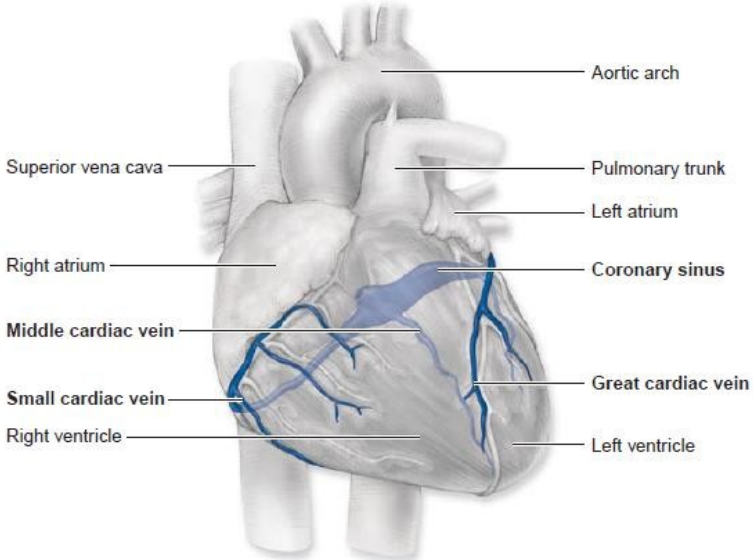

Figure 2.3 Coronary Circulation. Anterior view of (a) coronary veins. (Tortora and Derrickson, 2012)

2.1.3.6 The cardiac cycle

The function of the heart is to maintain a constant circulation of blood throughout the body. The heart acts as a pump and its action consists of a series of events known as the *cardiac cycle*.

During each heartbeat, or cardiac cycle, the heart contracts and then relaxes. The period of contraction is called *systole* and that of relaxation, *diastole*. (Waugh and Grant, 2014).

2.1.3.7 Cardiac output

The cardiac output is the amount of blood ejected from the heart. The amount expelled by each contraction of the ventricles is the stroke volume. Cardiac output is expressed in liters per minute (1/min) and is calculated by multiplying the stroke volume by the heart rate (measured in beats per minute).Cardiac output = Stroke volume x Heart rate. In a healthy adult at rest, the stroke volume is approximately 70 ml and if the heart rate is 72 per minute, the cardiac output is 51/minute. This can be greatly

increased to meet the demands of exercise to around 251/minute, and in athletes up to 351/minute. This increase during exercise is called the cardiac reserve. When increased blood supply is needed to meet increased tissue requirements of oxygen and nutrients, heart rate and/or stroke volume can be increased. (Waugh and Grant, 2014).

2.1.3.8 Stroke volume

The stroke volume is determined by the volume of blood in the ventricles immediately before they contract, i.e. the ventricular end-diastolic volume (VEDV), sometimes called preload. This depends on the amount of blood returning to the heart through the superior and inferior venae cavae (the venous return). Increased VEDV leads to stronger myocardial contraction, and more blood is expelled. In turn the stroke volume and cardiac output rise. This capacity to increase the stroke volume with increasing VEDV is finite, and when the limit is reached, i.e. the cardiac output cannot match the venous return, the cardiac output decreases and the heart begins to fail. Other factors that increase myocardial contraction include, increased stimulation of the sympathetic nerves innervating the heart and hormones, e.g. adrenaline, noradrenaline, thyroxine. (Waugh and Grant, 2014).

2.1.4 Circulation of The blood

The cardiovascular system is composed of two circulatory paths: pulmonary circulation, the circuit through the lungs where blood is oxygenated; and

systemic circulation, the circuit through the rest of the body to provide oxygenated blood (wikipedia.org, 2016).

2.1.4.1 Systemic Circulation

Systemic circulation is the movement of blood from the heart through the body to provide oxygen and nutrients, and bringing deoxygenated blood back to the heart. Oxygen-rich blood from the lungs leaves the pulmonary circulation when it enters the left atrium through the pulmonary veins. The blood is then pumped through the mitral valve into the left ventricle. From the left ventricle, blood is pumped through the aortic valve and into the aorta, the body's largest artery. The aorta arches and branches into major arteries to the upper body before passing through the diaphragm, where it branches further into arteries which supply the lower parts of the body. The arteries branch into smaller arteries, arterioles, and finally capillaries. Waste and carbon dioxide diffuse out of the cell into the blood, while oxygen in the blood diffuses out of the blood and into the cell. The deoxygenated blood continues through the capillaries which merge into venules, then veins, and finally the venae cavae, which drain into the right atrium of the heart. From the right atrium, the blood will travel through the pulmonary circulation to be oxygenated before (wikipedia.org, 2016).

2.1.4.2 Pulmonary Circulation

At birth we are primed to take our first breath. Instantly there is a dramatic reduction in pulmonary

vascular resistance (PVR) accompanied by closure of the ductus arteriosus, which is used in foetal life to bypass the pulmonary circulation. Subsequently the pulmonary arterial pressures (PAPs) rise and the lungs assume their prime function of gaseous exchange. (wikipedia.org, 2016)

Pulmonary circulation is the movement of blood from the heart to the lungs for oxygenation, then back to the heart again. Oxygen-depleted blood from the body leaves the systemic circulation when it enters the right atrium through the superior and inferior venae cavae. The blood is then pumped through the tricuspid valve into the right ventricle. From the right ventricle, blood is pumped through the pulmonary valve and into the pulmonary artery. The pulmonary artery splits into the right and left pulmonary arteries and travel to each lung. At the lungs, the blood travels through capillary beds on the alveoli where respiration occurs, removing carbon dioxide and adding oxygen to the blood. The alveoli are air sacs in the lungs that provide the surface for gas exchange during respiration. The oxygenated blood then leaves the lungs through pulmonary veins, which returns it to the left atrium, completing the pulmonary circuit. Once entering the left heart, the blood flows through the bicuspid valve into the left ventricle. From the left ventricle, the blood is pumped through the aortic valve into the aorta to travel through systemic circulation, delivering oxygenated blood to the body before returning again to the pulmonary circulation. (wikipedia.org, 2016).

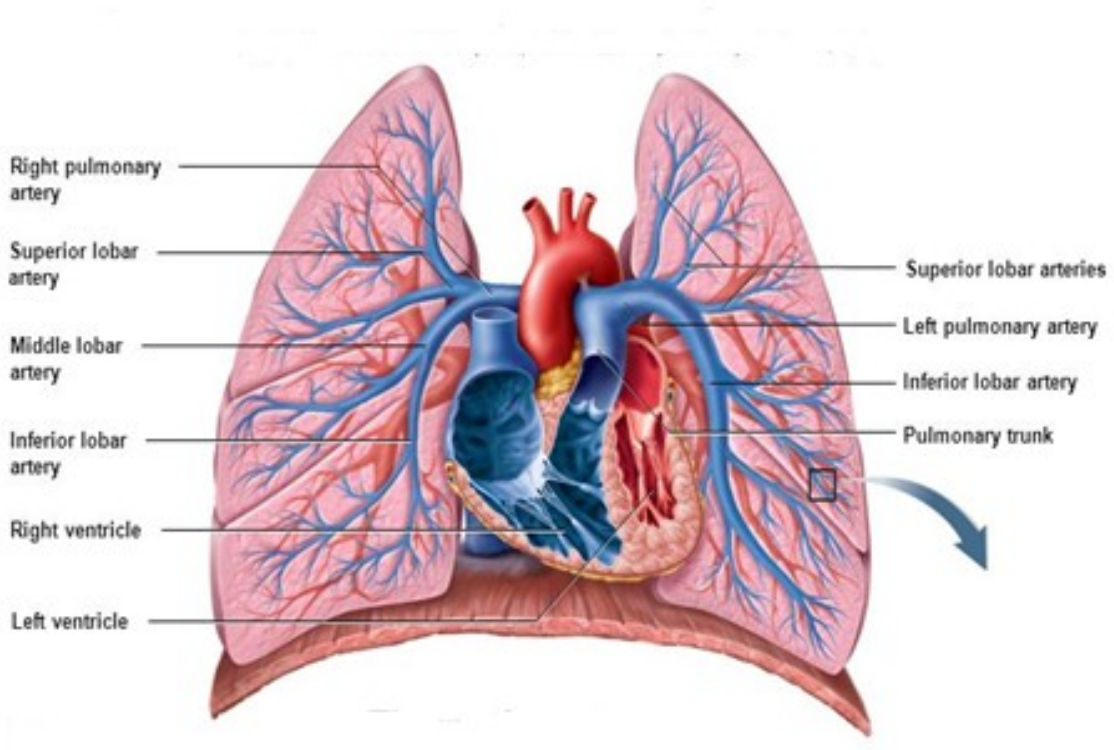

Figure 2.4 Pulmonary trunk to pulmonary arteries to lungs Lobar branches for each lobe (3 right, 2 left) Pulmonary veins to left atrium Increased O2 and reduced CO2 levels. (wikipedia.org, 2016).

2.1.4.3 Pulmonary vascular structure and function

Deoxygenated blood drains into the right atrium of the heart from the superior and inferior vena cava returning blood from the upper and lower extremities. During the diastolic contraction of the heart, the tricuspid valves open allowing blood to flow into the right ventricle. During systole of the heart, the tricuspid valves close and blood is pushed through the semi-lunar valves into the

main pulmonary artery which bifurcates into the left and the right pulmonary arteries. Each artery then enters its respective lung at the hilum through the parenchyma and is there after referred to as the intra-lobar pulmonary artery. This runs parallel to the respiratory tree alongside the bronchus to the alveoli where it becomes a mesh-like network of millions of capillaries from which gas exchange can occur. Only a very thin barrier exists between the pulmonary capillaries and alveoli allowing for passive diffusion of carbon dioxide and oxygen. There are approximately 480 million alveoli in the lungs with the prime purpose of increasing the surface area for gas exchange (Ochs et al., 2004). The pulmonary arteries and veins each have 15 orders of branching between the main pulmonary artery and the capillaries and between the capillaries and left atrium, respectively (Huang et al., 1996).The lungs are unique in that they are the only organ that receives the entire cardiac output (Collins and Stern) resulting in a high flow system of about 5 litres of blood per minute, which increases to about 25 litres during exercise. The primary function of the pulmonary circulation is gas exchange. Hence the pulmonary arteries have thin walls with a minimal smooth muscle cell layer resulting in a low-pressure, low-resistance system. The pulmonary artery is the only artery in the entire body that carries deoxygenated blood and similarly, the pulmonary vein is the only vein that carries oxygenated blood. The normal mean PAP is between 14mmHg and 20mmHg,

which allows for adequate oxygen replenishment and unloading of carbon dioxide. In contrast, in the systemic circulation, mean pressures are of the order of 100mmHg. PAP is a result of CO and PVR and thus PAP = CO X PVR. PVR is related to the intraluminal vessel wall diameter - the smaller the diameter, the greater the PVR. For this reason, arteries in the pulmonary circulation are normally fully dilated. Distension and recruitment of closed arteries are important mechanisms that are employed to reduce PVR when the cardiac output is increased, for example during exercise.The lungs also contain a functionally distinct second circulation known as the bronchial circulation. The bronchial circulation arises from the systemic circulation and serves as the supplier of oxygen and nutrients to the conducting portions within the lung. (Badesch et al., 2009).

2.1.4.4 Pulmonary Trunk

The pulmonary trunk carries deoxygenated blood from the right ventricle of the heart to the lung circulation. It is about 5 cm in length and 3 cm in diameter, and arises from the right ventricle base It is a short vessel, arising from the pulmonary conus of the right ventricle at the pulmonary semilunar valves. The pulmonary trunk lies totally within the pericardium. It divides into the left and right pulmonary arteries The diameter of the right pulmonary artery ranges between 17 and 30 mm (mean, 23.4 mm). The caliber of the main pulmonary artery is between 20 and 30 mm (mean, 26.4 mm). The sum of the

diameters of the left and right main branches is greater than the diameter of the main pulmonary artery (Kaufman, 1997).

2.1.4.5 Right Pulmonary Artery

The right pulmonary artery is only slightly smaller in caliber than the main artery, as seen in angiograms. It runs a horizontal, sometimes slightly downward. Where it divides into superior and inferior branches. It lies behind the ascending aorta and the superior vena cava and in front of the tracheal bifurcation and esophagus. The right pulmonary artery divides at the right hilum into two main branches: the ascending branch, to the right upper lobe, and the descending branch, to the right middle lobe and the right lower lobe. The ascending branch of the right pulmonary artery supplies the right upper lobe. The descending branch of the right pulmonary artery supplies the right middle and lower lobes.(Kaufman, 1997).

2.1.4.6 Left Pulmonary Artery

The left pulmonary artery is a short continuation of the main pulmonary artery. It lies in front of the descending aorta, beneath the curve of the aortic arch the left pulmonary artery is short and bifurcates in the left hilum into ascending and descending branches, which supply the left upper and lower lobes, respectively. (Kaufman, 1997).

2.1.4.7 Pulmonary arteries, veins and capillaries

The pulmonary arteries and veins have three distinct vascular layers. The tunica intima is the innermost layer of the vessel and is composed of a homogenous population of endothelial cells. The medial layer, the tunica media, is comprised of smooth muscle cells. The tunica externa is the outermost layer that consists primarily of collagen and fibroblasts. Each respective layer is separated by an extracellular matrix known as the basement membrane. Within the distal component of the lung, an extensive capillary network separates arteries from veins. The structural composition of pulmonary arteries is functionally altered as it extends down the length of the vessel towards the base of the lung. Pulmonary arteries can be defined according to their structural composition as elastic, muscular or partially muscular pulmonary arteries. Elastic vessels contain numerous elastic laminae bound by external and internal elastic laminae and extend peripherally into transitional vessels which contain fewer elastic laminae. Once only an internal and external elastic lamina exists around the smooth muscle cell layer, these vessels are termed muscular. As the artery extends into the more distal portions of the lungs, the smooth muscle cell layer becomes sparse (partially-muscular) or absent (non-muscular) prior to extension into the capillary bed. (DeMello &Reid, 1991; Jones & Capen, 2011). Pre-acinar arteries (including the main pulmonary artery) are associated with bronchi, bronchioles or terminal

bronchioles and contain numerous elastic laminae between smooth muscle layers and are more than 3200µm in diameter. As it extends beyond the ninth airway generation, the vessels become muscular and are generally more than 150µm in diameter. (Elliot & Reid, 1964; Jones & Capen, 2011). Partially muscular pulmonary arteries are typically 75µm to 90µm in diameter. (Jones & Capen, 2011). Pulmonary arteries are much less muscular than systemic arteries as the pressure and resistance is much lower within these arteries.Pulmonary arteries follow a branching pattern closely associated with the branchingpattern of the bronchial tree, although there are many more pulmonary arterial branches than there are bronchial branches and these increase within the periphery. (Elliot & Reid, 1964). The pulmonary artery will eventually extend into the alveolar capillaries, which form a dense anastomosing hexagonal network for which gas exchange can occur. (Weibel, 1963) Oxygenated blood is then drained into the pulmonary vein, which carries the blood to the left atria where it is retained until diastole, allowing it to enter the left ventricle for subsequent pumping around the body.

2.1.4.8 The function of the pulmonary circulation

The primary function of the pulmonary circulation is to facilitate gas exchange unloading of carbon dioxide and loading of oxygen. Oxygen is obtained from inspired air and binds with haemoglobin within red blood cells and is

essential to sustain metabolic processes throughout the entire body. Re-oxygenation is exquisitely facilitated by the gas-blood interface between the alveoli and the extensive alveolar capillary network. In addition to facilitating gas exchange, the pulmonary circulation functions as a filtration system to remove fine particles and potentially lethal thromboemboli from the mixed venous blood before it returns to the systemic circulation. (Comroe, 1966) This process is chiefly regulated by the pulmonary endothelium which releases mediators that promotes fibrinolysis. The location of the lungs together with the vast surface area of the pulmonary vasculature allows for this unique filtration function. Additionally the pulmonary circulation also serves as a blood reservoir for the left ventricle. (Comroe, 1966).

2.1.4.9 Regulation of blood flow in the pulmonary circulation

Pulmonary blood flow is most profoundly regulated by gravity and increases about 9 fold from the apex to the base of the lung. (West et al., 1964) Arterial, venous and alveolar pressures affect the distribution of blood flow within the lungs (West et al., 1964). Blood flow and ventilation is regulated by ventilation-perfusion matching (West & Dollery, 1960). In 1946, Von Euler and Liljestrand characterised a vital difference in response to hypoxia between the systemic and pulmonary circulations (Euler & Liljestrand, 1946). In the systemic circulation hypoxia caused vasodilatation. In contrast, they observed that the

pulmonary arteries uniquely constricted in response to hypoxia. This is perhaps not surprising considering the functional role of the two separate systems. In the pulmonary circulation the vasoconstrictor response to hypoxia aids in moving the passage of blood to well aerated areas mediating ventilation-perfusion matching. In the systemic circulation, hypoxia results in vasodilation in order to increase perfusion to meet the energy requirements of tissues and organs. In the lungs, ventilation-perfusion matching is also achieved by airway constriction in response to pulmonary arterial occlusion. This serves to direct inspired air towards alveoli with a denser blood flow. The matching of blood to a sufficient oxygen supply is therefore a critical regulator of blood flow in the lungs. (Zilmer Johansen, 2014).

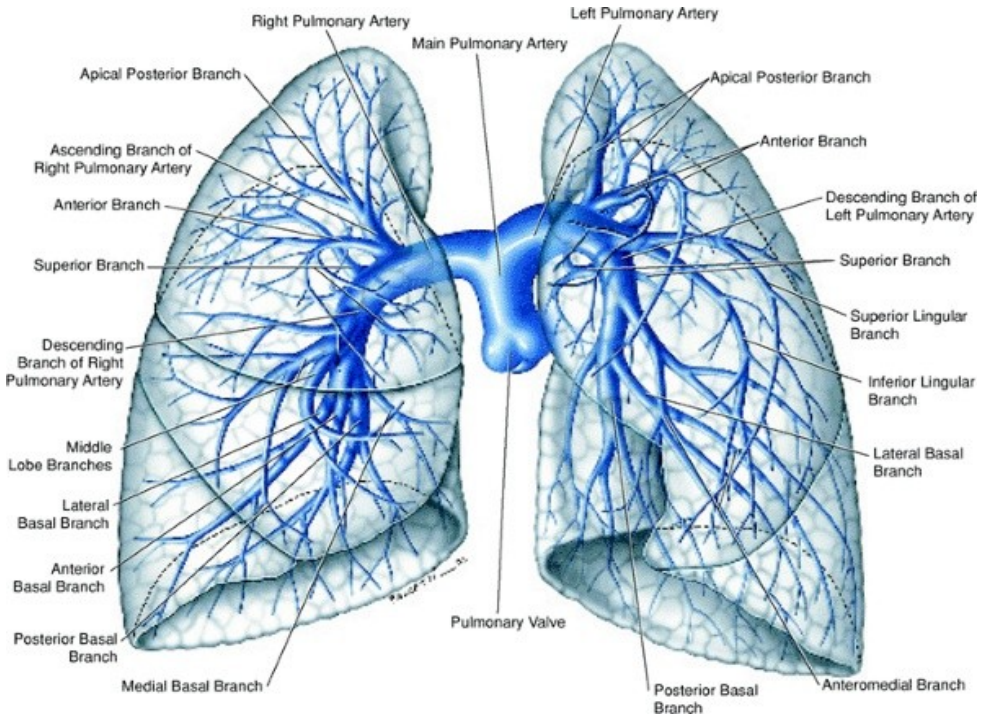

Figure 2.5 Distribution of the pulmonary artery in both lungs. (Lippincott Williams & Wilkins 2007)

2.2 The respiratory System

Throughout this study, the reader will discover that the respiratory tract is delicate and complicated system that can be involved in number of disease processes. And understanding of the anatomy and physiology of the respiratory tract is critical to understanding this elaborate system to maintain respiratory health and treat respiratory diseases. (Snell, 2011)

2.2.1 The Thoracic cavity

The cavity of the thorax can be divided into a median partition, called the mediastinum, and the laterally placed pleurae and lungs. The lungs are covered by a thin membrane called the visceral pleura, which passes from each lung at its root to the inner surface of the chest wall, where it is called the parietal pleura. In this manner, two membranous sacs called the pleural cavities are formed, one on each side of the thorax, between the lungs and the thoracic walls. (Snell, 2011)

2.2.2 Mediastinum

The mediastinum, though thick, is a movable partition that extends superiorly to the thoracic outlet and the root of the neck and inferiorly to the diaphragm. It extends anteriorly to the sternum and posteriorly to the vertebral column. It contains the remains of the thymus, the heart and large blood vessels, the trachea and esophagus, the thoracic duct and lymph nodes, the vagus and phrenic nerves, and the sympathetic trunks.

For purposes of description, the mediastinum is divided into superior and inferior mediastina. The inferior is further subdivided into the middle mediastinum which consist of the pericardium and heart. The anterior mediastinum which is space between the pericardium and the sternum. The posterior mediastinum which lies between the pericardium and the vertebral column. (Snell, 2011).

2.2.3 Pleurae

The pleurae and lungs lie on either side of the mediastinum within the chest cavity. Each pleura has two parts: a parietal layer, which lines the thoracic wall, covers the thoracic surface of the diaphragm and the lateral aspect of the mediastinum, and a visceral layer, which completely covers the outer surfaces of the lungs. The parietal and visceral layers of pleura are separated from one another by a slitlike space, the (pleural cavity). The pleural cavity normally contains a small amount of tissue fluid, the pleural fluid, which covers the surfaces of the pleura as a thin film and permits the two layers to move on each other with the minimum of friction. (Snell, 2011)

2.2.4 Lungs

The lungs are situated so that one lies on each side of the mediastinum. There are soft and spongy and very elastic. They are therefore separated from each other by the heart and great vessels and other structures in the mediastinum. Each lung is conical, covered with visceral

pleura, and suspended free in its own pleural cavity, being attached to the mediastinum only by its root. Each lung has a blunt apex, which projects upward into the neck for about 1 in. (2.5 cm) above the clavicle; a concave base that sits on the diaphragm; a convex costal surface, which corresponds to the concave chest wall; and a concave mediastinal surface, which is molded to the pericardium and other mediastinal structures. At about the middle of this surface is the hilum, a depression in which the bronchi, vessels, and nerves that form the root enter and leave the lung. The anterior border is thin and overlaps the heart; it is here on the left lung that the cardiac notch is found. The posterior border is thick and lies beside the vertebral column. The right lung is slightly larger than the left and is divided by the oblique and horizontal fissures into three lobes: the upper, middle, and lower lobes. The left lung is divided by a similar oblique fissure into two lobes: the upper and lower lobes. There is no horizontal fissure in the left lung. (Snell, 2011).

2.3 Pathology of cardiovascular system

Pulmonary vascular disease span a variety of disease entities including pulmonary arterial hypertension (PAH), pulmonary venous hypertension, pulmonary embolism, pulmonary arteriovenous malformation, pulmonary arterial stenosis, pulmonary artial aneurysm, pulmonary veno-occlusive disease (PVOD), and pulmonary capillary hemangiomatosis.(Budoff and Shinbane, 2016) Pulmonary vascular disease is a relatively common cause of chest

pain and dyspnea. It can be acute, as in pulmonary embolism, or chronic, as in most cases of pulmonary arterial hypertension (PAH). (Collins and Stern, 2012).

In this study using CT for characterization of heart and pulmonary vessels in patients with pulmonary hypertension and pulmonary embolism. (Swanson et al. 2008)

2.3.1 Blood pressure (BP)

Blood pressure is the force or pressure which the blood exerts on the walls of the blood vessels. The systemic arterial blood pressure, usually called simply arterial blood pressure, is the result of the discharge of blood from the left ventricle into the already full aorta. When the left ventricle contracts and pushes blood into the aorta the pressure produced within the arterial system is called the systolic blood pressure. In adults it is about 120 mmHg (millimeters of mercury) or 16 kPa (kilopascals).When complete cardiac diastole occurs and the heart is resting following the ejection of blood, the pressure within the arteries is called diastolic blood pressure. In an adult this is about 80 mmHg or 11 kPa. The difference between systolic and diastolic blood pressures is the pulse pressure. These figures vary according to the time of day, the posture, gender and age of the individual. During bed rest at night the blood pressure tends to be lower. It increases with age and is usually higher in women than in men. Arterial blood pressure is measured with a

sphygmomanometer and is usually expressed in the following manner:

BP = 120/80 mm Hg or BP = 16/11 kPa. (Waugh and Grant, 2014)

2.3.2 Pulmonary hypertension

Pulmonary hypertension is a type of high blood pressure that affects the arteries in the lungs and the right side of the heart. Pulmonary hypertension begins when tiny arteries in the lungs, called pulmonary arteries, and capillaries become narrowed, blocked or destroyed. This makes it harder for blood to flow through the lungs, and raises pressure within the lungs' arteries. As the pressure builds, the heart's lower right chamber (right ventricle) must work harder to pump blood through the lungs, eventually causing the heart muscle to weaken and ventually fail. Pulmonary hypertension is the hemodynamic consequence of vascular changes within the precapillary (arterial) or post capillary (venous) pulmonary circulation. These changes may be idiopathic, as in primary pulmonary hypertension or pulmonary veno-occlusive disease, but more commonly they represent a secondary response to alterations in pulmonary blood flow (Frazier et al., 2000).

Pulmonary hypertension is hemodynamically defined as a mean pulmonary artery pressure greater than 25 mm Hg at rest or greater than 30 mm Hg during exercise, with increased pulmonary vascular resistance (Burke Ap, et al.1991). The diagnosis is made with clinical assessment

of hemodynamic parameters, medical history, and histologic findings. Both precapillary (arterial) and postcapillary (venous) pulmonary hypertension are regarded as secondary when a cause is established. (Burke A, et al. 1996).

Pulmonary hypertension is a serious illness that becomes progressively worse and is sometimes fatal. Although pulmonary hypertension isn't curable, treatments are available that can help lessen symptoms and improve your quality of life. Pulmonary hypertension is defined as a resting mean pulmonary arterial pressure of 25 mmHg or more at catheterization of the right side of the heart, a resting mean pulmonary arterial pressure of 20 mmHg or less is considered normal, and mean pulmonary arterial pressure of 21–24 mmHg is considered abnormal.(Badesch DB, et al.2009) Use of the term pulmonary arterial hypertension is restricted to those with a hemodynamic profile in which high pulmonary pressure is a result of elevated precapillary pulmonary resistance and normal pulmonary venous pressure and is measured as a pulmonary wedge pressure of 15 mmHg or less. (Badesch, 2009 & Simonneau G 2009) A diagnosis of pulmonary arterial hypertension is made only in the absence of other causes of precapillary pulmonary hypertension such as that resulting from lung disease, Pulmonary hypertension resulting from heart disease implies an increase in pulmonary arterial pressure due to backward transmission of pressure elevation (postcapillary

pulmonary hypertension) and is defined as a mean pulmonary arterial pressure of 20 mmHg or more and a pulmonary wedge pressure greater than 15 mmHg. (Elena Pena, MD. et al 2012) Pulmonary hypertension is a progressive disease of the pulmonary arteries and is characterized by abnormally elevated pressure in the pulmonary circulation, a result of extensive vascular proliferation and remodeling. Without treatment, pulmonary hypertension progresses rapidly to right ventricular failure and death, typically within 3 years of the diagnosis. (Rubin LJ 1997&Runo JR 2003).

2.3.2.1 Idiopathic pulmonary hypertension

When an underlying cause for high blood pressure in the lungs can't be found, the condition is called idiopathic pulmonary hypertension (IPH).Some people with IPH may have a gene that's a risk factor for developing pulmonary hypertension. But in most people with idiopathic pulmonary hypertension, there is no recognized cause of their pulmonary hypertension. (Swanson et al., 2008).

2.3.2.2 Secondary pulmonary hypertension

Pulmonary hypertension that's caused by another medical problem is called secondary pulmonary hypertension. This type of pulmonary hypertension is more common than is idiopathic pulmonary hypertension. Causes of secondary pulmonary hypertension include: Blood clots in the lungs (pulmonary emboli), chronic obstructive pulmonary diseases, such as emphysema, connective tissue disorders, such as scleroderma or lupus,

sleep apnea and other sleep disorders, heart abnormalities at birth (congenital heart defects), sickle cell anemia, chronic liver disease (cirrhosis), AIDS, lung diseases such as pulmonary fibrosis, a condition that causes scarring in the tissue between the lungs' air sacs (interstitium), left-sided heart failure, living at altitudes higher than 8,000 feet , climbing or hiking to altitudes higher than 8,000 feet , Use of certain stimulant drugs, such as cocaine. Eisenmenger syndrome, a type of congenital heart defect, causes pulmonary hypertension. It is most commonly caused by a large hole in the heart between the two lower heart chambers (ventricles), called a ventricular septal defect (VSD). This hole in the heart causes blood to circulate abnormally in the heart. Oxygen-carrying blood (red blood) mixes with oxygen-poor blood (blue blood). The blood then returns to the lungs instead of going to the rest of the body, increasing the pressure in the pulmonary arteries and causing pulmonary hypertension. (Swanson et al., 2008).

2.3.2.3 Classification of pulmonary hypertension

Since 1973 the World Symposium on Pulmonary Hypertension (WSPH) has brought together experts within pulmonary vascular diseases together to discuss and collate the latest scientific contributions within the field. From this, the World Health Organization (WHO) classification of PH is derived, which is categorised according to shared histologies and vascular pathologies. Identification of PH WHO category is essential to direct the

correct treatment regimen and to predict the potential outcome. The most recent WSPH was held in Nice in February 2013 from which the table below is derived (Table 1-1) (Simonneau et al., 2013). The WHO classification is subcategorised into five groups of disorders that are known to cause PH: PAH (group 1); PH owing to left heart disease (group 2); PH owing to lung diseases and/or hypoxia (Group 3); chronic thromboembolic PH (Group 4); and PH with unclear multifactorial mechanisms (Group 5).

Table 2.1 WHO classification of pulmonary hypertension (2013)

Group 1 Pulmonary arterial hypertension (PAH)

1.1 Idiopathic (IPAH)
1.2 Heritable (HPAH)
1.2.1 BMPR-2
1.2.2 ALK1, ENG, SMAD9, CAV1, KCNK3
1.2.3 Unknown
1.3 Drug- and toxin-induced
1.4 Associated PAH
1.4.1 Connective tissue diseases
1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart diseases
1.4.5 Schistosomiasis
1.4.6 Chronic haemolytic anemia
1' Pulmonary veno-occlusive disease and/or pulmonary hemangiomatosis
1'' Persistent pulmonary hypertension of the newborn

Group 2 Pulmonary hypertension owing to left heart disease

2.1 Systolic dysfunction
2.2 Diastolic dysfunction

2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

Group 3 Pulmonary hypertension owing to lung diseases and/or hypoxia

3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

Group 4 Chronic thromboembolic pulmonary hypertension (CTEPH)

Group 5 Pulmonary hypertension with unclear multifactorial mechanisms

5.1 Hematologic disorders: chronic haemolytic anemia, myoproliferative disorders, splenectomy
5.2 Systemic disorders:sarcoidosis, pulmonary Langerhans cell histiocytosis:

lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders:glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

BMPR-2 = bone morphogenic protein receptor 2; ALK1 = activin receptor-like kinase; CAV1 = caveolin 1; KCNK3 = potassium channel subfamily K member 3.

2.3.3 Pulmonary arterial hypertension

PH is characterised as PAPs exceeding 25mmHg at rest (Badesch et al., 2009). The diagnosis of group 1 PH, PAH, requires the additional diagnosis of pulmonary wedge

pressures equal or greater than 15mmHg (Badesch et al., 2009). PAH is the most fatal subtype of PH and is a progressive and devastating vasculopathy of the pulmonary arteries characterised by dysregulated endothelial cell proliferation and apoptosis paired with exuberant proliferation of apoptotic-resistant smooth muscle cells (Schermuly et al., 2011).

Previously non-muscular pulmonary arteries develop a smooth muscle layer eventually leading to obliteration and loss of the small distal arteries and the formation of complex vascular lesions there is currently no cure for the treatment of PAH and newer, more effective therapies are urgently required. The WHO have subcategorized PAH as is shown in Table 1-1: idiopathic PAH (IPAH), heritable PAH (HPAH), and drug and toxin-induced and PAH secondary to other diseases. (Cool et al., 1999).

2.3.3.1 Idiopathic and heritable pulmonary arterial hypertension

In IPAH, the cause is neither inherited nor does it carry any identified risk factor. Germline mutations in the bone morphogenic receptor 2 gene (BMPR-2), a member of the transforming growth factor-β signaling (TGF-β) family, are accountable for at least 70% of HPAH and 10% to 40% of apparently sporadic cases of IPAH (Lane et al., 2000;Machado et al., 2001;Thomson et al., 2000). In a few cases, mutations in other genes belonging to the TGF-β super family have been reported: activin receptor-like kinase type 1 (ALK1), endoglin (ENG) and Sam and Mad

(mothers against decapetaplegic)-related proteins (SMAD) Additionally novel gene mutations in caveolin-1 (CAV1) (Austin et al., 2012) and the gene encoding the potassium channel super family K member-3 (KCNK3) have been identified (Ma et al., 2013).

2.3.3.2 Drug and toxin-induced pulmonary arterial hypertension

Anorectic drugs have been associated with the development of PAH. In the 1960s there was an epidemic of PAH amongst obese patients taking the anorectic drug aminorex. These findings were later confirmed by the observation that patients taking the pharmacologically related drug dexfenfluramine for more than 3 months were at a high risk of developing PAH (Abenhaim et al., 1996; Kramer & Lane, 1998).

To date, there are now several drugs and toxins that have been associated with the development of PAH and these have been classified on the strength of evidence for their association with PAH into definite, possible, likely and unlikely (Simonneau et al., 2013). Definite associations according to the updated clinical classification of PAH (Simonneau et al., 2013) include aminorex, fenfluramines, dexfenfluramines, toxic rapeseed oil, benfluorex and selective serotonin reuptake inhibitors. Possible associations include cocaine, phenylpropanolamine, St. John’s wort, chemotherapeutic agents, interferon α and β and amphetamine-like drugs. Likely risk factors include amphetamines, tryptophan, methamphetamines and

dasatinib. Unlikely risk factors include estrogen, oral contraceptives and cigarette smoke (Simonneau et al., 2013).

2.3.3.3 Associated pulmonary arterial hypertension

The development of PAH is also recognised to occur secondary to other diseases. These include connective tissue diseases, such as scleroderma, human immunodeficiency virus (HIV), portal hypertension, and congenital heart disease in adults, schistosomiasis and chronic haemolytic anaemia (Simonneau et al., 2013).

2.3.3.4 The diagnosis, prognosis and epidemiology of pulmonary arterial hypertension

Primary pulmonary hypertension is a rare disease of unknown etiology, whereas secondary pulmonary hypertension is a complication of many pulmonary, cardiac and extra thoracic conditions. Chronic obstructive pulmonary disease, left ventricular dysfunction and disorders associated with hypoxemia frequently result in pulmonary hypertension. Regardless of the etiology, unrelieved pulmonary hypertension can lead to right-sided heart failure. Signs and symptoms of pulmonary hypertension are often subtle and nonspecific. The diagnosis should be suspected in patients with increasing dyspnea on exertion and a known cause of pulmonary hypertension. Two-dimensional echocardiography with Doppler flow studies is the most useful imaging modality in patients with suspected pulmonary hypertension. If

pulmonary hypertension is present, further evaluation may include assessment of oxygenation, pulmonary function testing, high-resolution computed tomography of the chest, ventilation-perfusion lung scanning and cardiac catheterization. (Nauser and Stites, 2001).

The symptoms of PAH are non-specific and include breathlessness, fatigue and syncope (Rich et al., 1987) making a prompt diagnosis challenging. Electrocardiograms provide valuable information on right ventricular function by measuring RVH. Chest radiographs, pulmonary functional tests and echocardiography amongst other tests are all useful indicators of lung and heart functions. However, right heart catheterisation is essential for the diagnosis of PAH and to test the vasoreactivity of the pulmonary circulation (Galie et al., 2004). The epidemiology of PAH has been outlined by three major registries (Badesch et al., 2010; Humbert et al., 2006; Ling et al., 2012). In the UK/Ireland (Ling et al., 2012) and France (Humbert et al., 2006) the estimated incidence of PAH is 6.6 cases per million and 15 cases per million, respectively. In all three registries, the median age at diagnosis was 50 years old and IPAH was the most common form of PAH diagnosed. A higher proportion of patients were female with a reported 70% in the UK and Ireland (Ling et al., 2012), 65.3% in France (Humbert et al., 2006) and 80% in the USA (Badesch et al., 2010). In addition, there appeared to be an association with obesity

and an increased body mass index and the development of PAH.

2.3.3.5 Pulmonary arterial hypertension arteriopathy

Along the media of the pulmonary artery there is a heterogeneous population of phenotypically distinct vascular cells. The main pulmonary artery is composed of three distinct layers of cells as mentioned previously; endothelial cells in the tunica intima, heterogeneous smooth muscle cells within the tunica media and both muscular and non-muscular cells in the tunica adventitia (Frid et al., 1994; Stiebellehner et al., 2003). As the artery extends from the extra-lobar pulmonary artery and into the intra-pulmonary artery the lumen and the arterial wall narrow with fewer vascular cell types. In the distal pulmonary artery only a homogeneous population of smooth muscle cells exists (Stiebellehner et al., 2003). The smooth muscle cell layer eventually ceases and only a thin layer of endothelial cells remains (occasionally with a single smooth muscle cell or pericytes: smooth muscle cell precursors). In utero, the initial development of larger blood vessels involves the recruitment of pre-cursor smooth muscle cells by endothelial cells in the mesoderm. Smooth muscle cells will proliferate and undergo differentiation and maturation into the quiescent adult smooth muscle cell (Stenmark & Mecham, 1997). Pulmonary vascular remodeling is a key feature of PAH and is defined as any structural changes that occur within the

vascular wall and can occur within all three vascular layers. In particular, a key feature of restructured pulmonary arteries includes an increase in smooth muscle cells and endothelial cells. It appears that in the vasculature normally quiescent cells resistant to mitogenic stimulation exhibit cellular responses similar to developmental processes when injured (Stenmark & Mecham, 1997). Non-muscular pulmonary arteries are typically compromised of endothelial cells and in some cases, pericytes. In response to injury, pericytes can differentiate into vascular smooth muscle cells, which contributes to muscularisation of previously non-muscular arteries. Injurious insults include inflammation, hemodynamic stress (increased shear stress), mechanical injury and hypoxia. There is a general acceptance that the distal pulmonary arteries are the most crucial mediators of increased vascular resistance that precede the development of RVH. However, recent indications have challenged this notion, suggesting that stiffening of the proximal pulmonary artery by deposition of collagen may impact PAPs and RVH in the absence of any structural changes in the distal pulmonary circulation (Vanderpool et al., 2013). Interestingly, distal smooth muscle cells have a very low proliferative capacity compared to proximal smooth muscle cells. Furthermore, hypoxia actually reduces their proliferative capacity (Stiebellehner et al., 2003). Thus, a phenotypic switch in the homogeneous population of smooth muscle cells in the distal pulmonary

arteries is presumed to occur to permit vascular proliferation and remodeling. Phenotypic switching is defined as a change in the gene expression of a cell that alters its behavioural response to various stimuli. For example, a previously non-proliferative cell may undergo phenotypic-switching into a highly proliferative cell. In addition, mature vascular endothelial cells can also transdifferentiate into smooth muscle cells through a mesenchymal transition (Frid et al., 2002). Alternatively, proliferative smooth muscle cells of the proximal artery may migrate and extend into previously non-muscular pulmonary arteries contributing to distal pulmonary vascular remodeling. The lung is composed of more than 40 different cell types that are essential to facilitate gas exchange and metabolic and endocrine functions. The lung has a remarkable regenerative capacity after injurious insults, yet the cell types that contribute to this effect remain obscure. There is now evidence for resident stem cells within the lung (Kajstura et al., 2011) implicating that the phenotypically distinct smooth muscle cells that appear in the distal artery could also be differentiated stem cells. Alternatively, the origin of these cells could be from distinct regions, such as blood-borne progenitor cells or bone marrow-derived progenitor cells (Toshner et al., 2009). However, there is currently much speculation of the role of progenitor cells in PAH as to whether they play a role in repairing damage that has occurred or whether they are indeed intricate to the

pathogenesis of PAH (Toshner & Morrell, 2010). The pathological features observed in PAH are primarily within the pulmonary arteries with the veins unaffected. PAH pathology includes pulmonary arterial vascular lesions within the distal pulmonary arteries (<500µm in diameter), characterised by medial hypertrophy, adventitial thickening, inflammation, complex vascular lesion (plexiform) formation and thrombotic lesions (Galie et al., 2009).

Medial hypertrophy of both muscular and elastic arteries is a common pathological feature of all categories of PH (Pietra et al., 1989; Pietra et al., 2004). Alongside, dilatation of elastic pulmonary arteries and intimal atheromas and RVH are all manifestations of PH. Medial hypertrophy is an increase in the size of the vessel wall by hyperplasia and hypertrophy of both pre- and intra-acinar arteries eventually extending into previously non-muscularised acinar arteries (Pietra et al., 2004). The pulmonary artery runs parallel to the respiratory tree and the pulmonary acinus is the region beyond the terminal bronchus. The pulmonary acinus consists of the most delicate arterial structure with a discontinuous smooth muscle cell layer, which eventually ceases to exist (Pietra et al., 2004). Plexiform, dilatation and arteritis have been classified as complex vascular lesions that occur as part of the arteriopathy associated with PH (Pietra et al., 2004).

Plexiform lesions are formed by extensive hyperplasic and hypertrophic responses of cells that constitute the

arterial wall. Within their structures, vascular channels, lined with numerous proliferating endothelial cells are a typical feature (Jonigk et al., 2011). Plexiform lesions consist of numerous cell types, including smooth muscle and inflammatory cells but predominantly consist of endothelial cells (Tuder et al., 1994; Jonigk et al., 2011). Plexiform lesions can occur in both pre- and intra-acinar regions of the pulmonary arterial tree, but typically occur at arterial branching points (Pietra et al., 2004) and are present in 90% of patients with PAH It is, however, difficult to determine the stage at which plexiform lesions start to occur as we are unable to assess the presence of lesions prior to lung transplantation. Thus, plexiform lesions may only be present at end-stage disease. (Stacher et al., 2012).

2.3.3.6 Signs and symptoms of pulmonary hypertension

The signs and symptoms of pulmonary hypertension in its early stages may not be noticeable for months or even years. As the disease progresses, symptoms become worse. Pulmonary hypertension symptoms include:Shortness of breath (dyspnea), initially while exercising and ventually while at rest, Fatigue, Dizziness or fainting spells (syncope), Chest pressure or pain, Swelling (edema) in the ankles, legs, and eventually in the abdomen (ascites), Bluish color on lips and skin (cyanosis), Racing pulse or heart palpitations. (Swanson et al., 2008)

2.3.3.7 Causes of pulmonary hypertension

The heart has two upper and two lower chambers. Each time blood passes through the heart, the lower right chamber (right ventricle) pumps blood to the lungs through a large blood vessel (pulmonary artery). In the lungs, the blood releases carbon dioxide and picks up oxygen. The oxygen-rich blood then flows through blood vessels in the lungs (pulmonary arteries, capillaries and veins) to the left side of the heart. Ordinarily, the blood flows easily through the vessels in the lungs, so blood pressure is usually much lower in the lungs. With pulmonary hypertension, the rise in blood pressure is caused by changes in the cells that line the pulmonary arteries. These changes cause extra tissue to form, eventually narrowing or completely blocking the blood vessels, making the arteries stiff and narrow. This makes it harder for blood to flow, raising the blood pressure in the pulmonary arteries. (Swanson et al., 2008).

Causes of precapillary pulmonary hypertension include congenital cardiac left-to-right shunt; thromboembolic disease; tumor embolism; embolization of parasites, talc crystals, and other foreign materials; chronic alveolar hypoxia; and chronic interstitial lung disease (Burke A, 1996; Edwards WD.1988; Rubin LJ.1993). Primary pulmonary hypertension (PPH) is an idiopathic condition at the precapillary level that occurs in the absence of an embolic source or any other identifiable cause such as cardiac shunt, toxic insult, or interstitial lung disease (Burke AP, &Farb A, 1991).

Postcapillary lesions producing pulmonary venous hypertension include mediastinal fibrosis (which may also affect the precapillary vessels); an obstructive left atrial mass; mitral valve stenosis; left ventricular failure; and, rarely, invasive neoplasm, congenital venous stenosis, or anomalous pulmonary venous connections (Burke A,1996; Rubin LJ.1993). The postcapillary counterpart to PPH is pulmonary veno-occlusive disease (PVOD), a rare idiopathic condition that diffusely affects the postcapillary pulmonary circulation (Burke AP, & Farb A, 1991).

2.3.3.8 Risk factors of pulmonary hypertension

Although anyone can develop either type of pulmonary hypertension, older adults are more likely to have secondary pulmonary hypertension, and young people are more likely to have idiopathic pulmonary hypertension. Idiopathic pulmonary hypertension is also more common in women than it is in men. Another risk factor for pulmonary hypertension is a family history of the disease. Some genes could be linked to idiopathic pulmonary hypertension. These genes might cause an overgrowth of cells in the small arteries of the lungs, making them narrower. (Swanson et al., 2008)

2.3.3.9 Complications of pulmonary hypertension

Pulmonary hypertension can lead to a number of complications, including: Right-sided heart failure (cor pulmonale): In cor pulmonale, the heart's right ventricle becomes enlarged and has to pump harder than usual to move blood through narrowed or blocked pulmonary

arteries. At first, the heart tries to compensate by thickening its walls and expanding the chamber of the right ventricle to increase the amount of blood it can hold. But this thickening and enlarging works only temporarily, and eventually the right ventricle fails from the extra strain.

(Swanson et al., 2008).

Blood clots: Clots help stop bleeding after been injuring. But sometimes clots form where don't needed. A number of small clots or just a few large ones dislodge from these veins and travel to the lungs, leading to a form of pulmonary hypertension that is reversible with time and treatment. Having pulmonary hypertension makes it more likely develop clots in the small arteries in the lungs, which is dangerous if already have narrowed or blocked blood vessels. Arrhythmia: Irregular heartbeats (arrhythmias) from the upper or lower chambers of the heart are complications of pulmonary hypertension. These can lead to palpitations, dizziness or fainting and can be fatal. (Swanson et al., 2008)

Bleeding: Pulmonary hypertension can lead to bleeding into the lungs and coughing up blood (hemoptysis). This is another potentially fatal complication. The complications of sustained pulmonary hypertension include central arterial thrombosis, premature atherosclerosis of central elastic and muscular pulmonary arteries, aneurysmal dissection of pulmonary arteries, and hypertrophy and dilatation of the right side of the heart (Wagenvoort CA,

1977; Edwards WD.1988; Masuda S, 1996; Moser KM, 1995; Moore GW, 1982).

2.3.4 Pulmonary embolism

Pulmonary embolism is a blockage in one or more pulmonary arteries in the lungs. In most cases, pulmonary embolism is caused by blood clots that travel to the lungs from the legs or, rarely, other parts of the body (deep vein thrombosis). Because pulmonary embolism almost always occurs in conjunction with deep vein thrombosis, most doctors refer to the two conditions together as venous thromboembolism. Although anyone can develop deep vein thrombosis (DVT) and pulmonary embolism, factors such as immobility, cancer and surgery increase the risk. Pulmonary embolism can be life-threatening, but prompt treatment can greatly reduce the risk of death. Taking measures to prevent blood clots in the legs will help protect against pulmonary embolism. (Swanson et al., 2008).

Acute pulmonary embolism is an under-diagnosed but potentially fatal condition. This condition presents with a wide clinical spectrum, from asymptomatic small PE to life-threatening one causing cardiogenic shock. (Çobanoğlu, 2012).

Deep venous thrombosis (DVT) and pulmonary embolism constitute clinical presentations of the same vascular disease, known as venous thromboembolism (VTE). VTE It is associated with high morbidity and mortality and represents a primary cause of preventable

death. There is strong evidence that obesity is an independent risk factor for DVT and PE. (Çobanoğlu, 2012).

PE is an obstruction of a pulmonary artery caused by a blood clot, air, fat, or tumor tissue. The most common cause of the obstruction is a blood clot (thrombus) usually from a peripheral vein. Most patients with deep vein thrombosis (DVT) develop PE. Left untreated, PE has a high mortality rate and accounts for 5–10% of all in-hospital deaths. The classic triad of signs and symptoms of PE (hemoptysis, dyspnea, and chest pain) are neither sensitive nor specific, and many patients with PE are initially asymptomatic; most patients who have symptoms often have atypical and/or nonspecific symptoms, such as dyspnea, tachypnea, and chest pain. (Budoff and Shinbane, 2016).

PE is a sudden occurence of a blood clot in a pulmonary artery with obstruction of the blood supply to the lung circulation. Embolization occurs when a venous thrombus is dislodged from the endothelial wall of a vein and passes through to the lung circulation. Depending on its size and length, the embolus may occlude different parts of the arterial branch, from the main pulmonary artery, through the bifurcation (saddle embolus), to the left or right pulmonary artery along to the smaller branching pulmonary arteries. The clots arise to a large extent from thrombi within the large deep veins in the legs, mainly the iliac, femoral, and popliteal veins, and

less commonly from more distal veins or veins from other locations, such as the heart. (Marten soderberg, 2008).

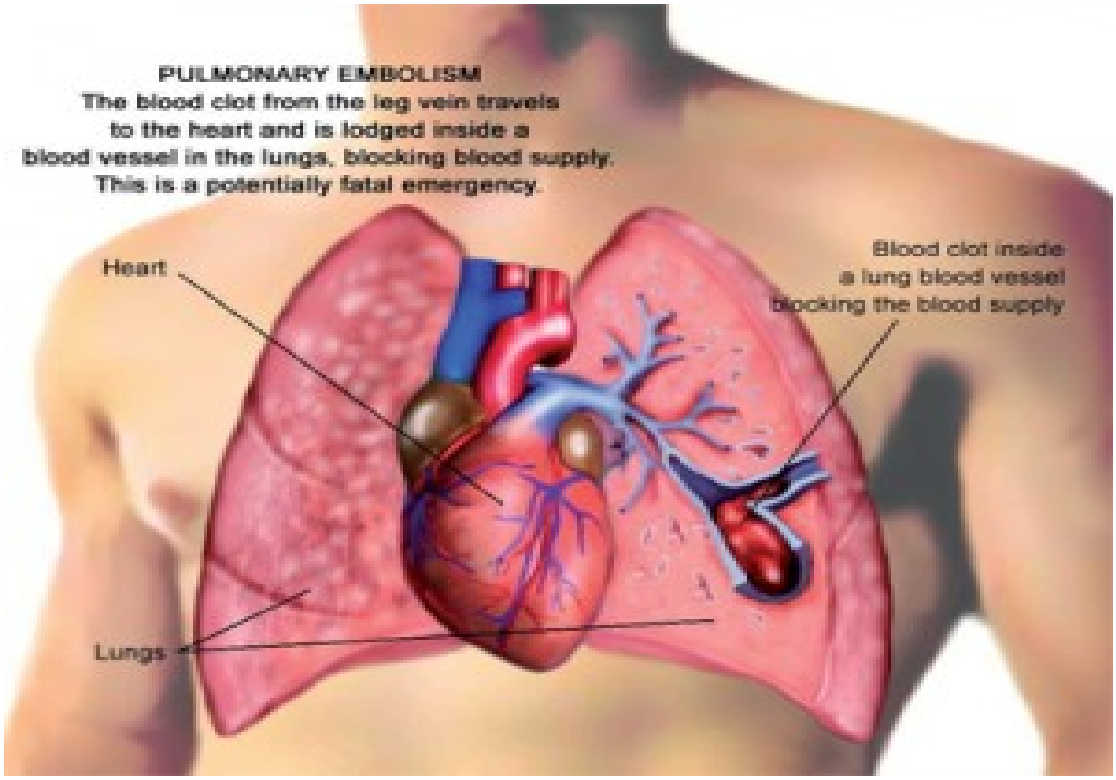

Figure 2.6 Pulmonary Embolism: Blood clot from the leg vein travels to the heart and lodged inside a blood vessel in the lungs, blocking blood supply. This is a potentially fatal emergency. (wikipedia.org, 2016).

2.3.4.1 Classifications of pulmonary embolism

Acute PE: PE developed over a short period of time and Chronic PE: PE with recurring embolization despite treatment. The disease develops over several years. Clinical classification of PE: Idiopathic PE: No known risk factor, Primary PE: Thrombophilia as risk factor, Secondary PE: Identifiable risk factor(s) such as pregnancy, cancer, surgery or trauma. Anatomically massive PE: More than 50% obstruction of the vascular bed or two or more of the lobar arteries. Clinically massive PE: PE with signs of shock or hypotension (blood pressure <90 mmHg or a

pressure drop >40 mmHg for >15 min) Non massive PE: all other PE. Sub massive PE: Nonmassive PE with signs of right ventricular dysfunction on echocardiography but without hemodynamic instability. Massive and Submassive PE can be divided into Type A: PE with highly mobile emboli, arising from peripheral veins (poorer prognosis). And Type B: PE with immobile emboli, originating in the RV (better prognosis (Palla, A and Perrser, A. 2000,Wood, K.E. 2002)

2.3.4.2 Signs and symptoms of pulmonary embolism

Many pulmonary emboli occur silently, but there are three typical clinical presentations. A clinical deep venous thrombosis not commonly observed, although detailed investigation of the lower limb and pelvic veins will reveal thrombosis in more of the cases. (A.V. Hoffbrand et al, 2001).

2.3.4.2.1 Small/ medium pulmonary embolism:

In this situation an embolus has impacted in a terminal pulmonary vessel. Symptoms are pleuritic chest pain and breathlessness. Haemoptysis occurs in 30% often three or more days after the initial event. (A.V. Hoffbrand et al, 2001).

2.3.4.2.2 Massive pulmonary embolism:

This is a much rare condition where sudden collapse occur due to an acute obstruction of the right ventricular outflow tract. The patient has sever central chest pain (cardiac ischaemia due to lack of coronary blood flow) and becomes shocked, pale and sweaty. Syncope may result if

the cardiac output is transiently but dramatically reduced, and death may occur. (A.V. Hoffbrand et al, 2001)

2.3.4.2.3 Multiple recurrent pulmonary emboli:

This leads to increased breathlessness often over weeks or months. It is accompanied by weakness, syncope on exertion and occasionally angina. The physical signs are due to pulmonary hypertension that has developed from multiple occlusions of the pulmonary vasculature. (A.V. Hoffbrand et al, 2001)

Pulmonary embolism symptoms can vary greatly, depending on how much of the lung is involved, the size of the clots and the overall health especially the presence or absence of underlying lung disease or heart disease. (Swanson et al., 2008).

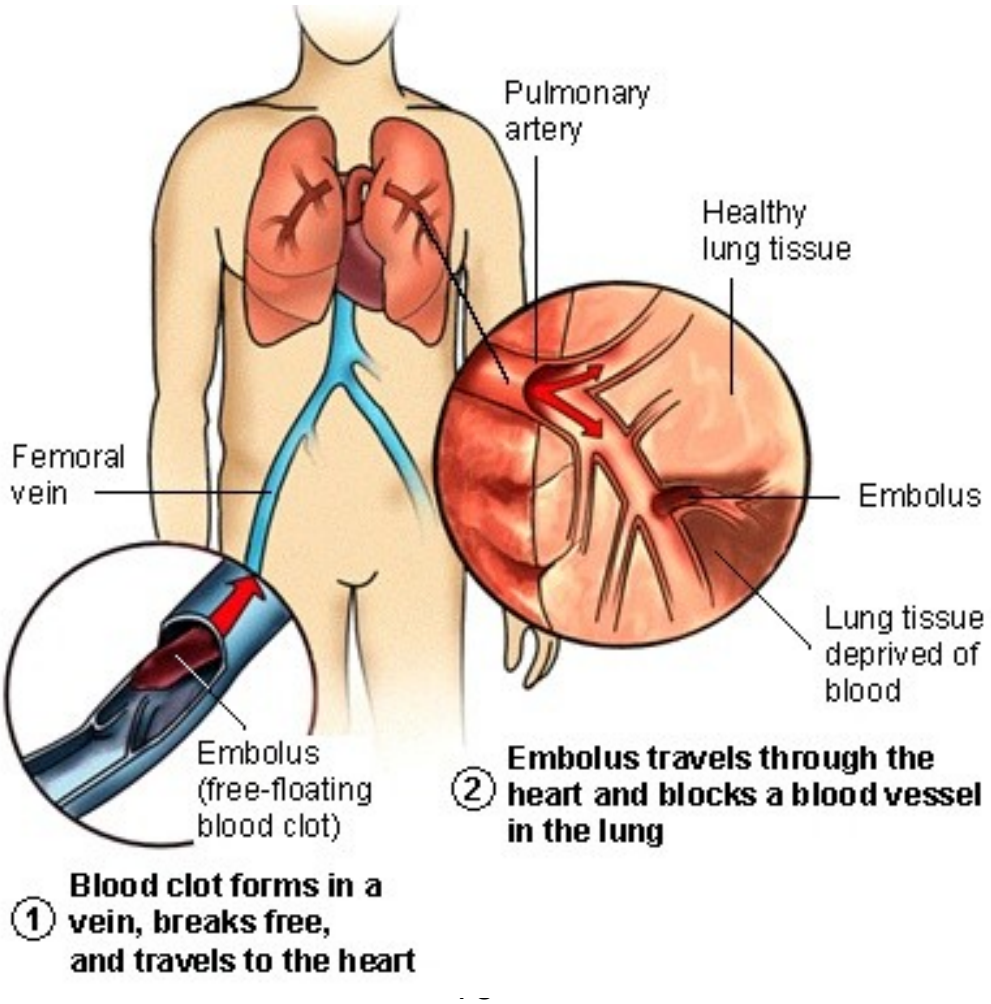

Figure 2.7 Pulmonary Embolism: Blood clot forms in a vain, and travels to the heart and through the heart to blocks a blood vessel in the lung.

2.3.4.3 Common signs and symptoms of pulmonary embolism:

Shortness of breath: This symptom typically appears suddenly and always gets worse with exertion.

Chest pain: The patient feel like he having a heart attack. The pain may become worse when breathe deeply (pleurisy), cough, eat, bend or stoop. The pain will get worse with exertion but won't go away during the rest.

Cough: The cough may produce bloody or blood-streaked sputum.

Other signs and symptoms that can occur with pulmonary embolism include: Leg pain or swelling, or both, usually in the calf, Clammy or discolored skin (cyanosis), Fever, Excessive sweating, Rapid or irregular heartbeat, Lightheadedness or dizziness. (Swanson et al., 2008).

PE is a disease with different clinical expressions in different patients. The presentation can vary from a clinically silent disease to an acute life-threatening condition requiring intensive care treatment with thrombolysis. PE is potentially fatal. The clinical accuracy and recognition of signs of PE are often inaccurate, and objective diagnostic tests are mandatory in patients with clinical suspicion of PE. Concomitant medical conditions,

especially cardiovascular and pulmonary disease, as well as malignancy, along with findings of ongoing medication, hereditary anamnesis, body constitution, and time from onset of the first symptom (patient's delay), can significantly affect the attending physician's ability to diagnose PE. The degree and extent of the vessel occlusion also influences the presentation. Both symptoms and signs of suspected PE can be found in patients with other diseases when PE is excluded (Miniati, M., & Monti, S 2003; Stein, P.D. & Henry, J.W. 1997).

Overt and easily recognizable symptoms of PE occur when the compensatory mechanisms in the body are unable to maintain hemodynamic stability; hence, the symptoms can arise from several different organ systems. Prodromal symptoms in PE are most often respiratory or cardiovascular, but can also present as neuro-logical (fainting, seizures, confusion), psychological (apprehension, anxiety), or gastrointestinal (nausea, vomiting) symptoms. (Marten soderberg, 2008).

The most common clinical findings in PE are acute onset of dyspnoea at rest or on exertion, and tachypnoea (respiratory rate ≥ 20 min-1). In a study by (Stein, P.D, &Saltzman, H.A. (1991), 90% of patients with PE presented with these symptoms. Other common findings are pleuritic chest pain, shortness of breath, and tachycardia. Less frequent are fainting, anxiety, hemoptysis, nonspecific chest pain, swollen legs (concomitant DVT), cough, or unexplained fatigue or worsening of known chronic

disease such as chronic heart failure COPD (Stein, P.D et al. 2007) . PE can present as supra-ventricular arrhythmia such as atrial fibrillation or can mimic pneumonia with productive cough, fever, and dyspnoea. Stein et al also showed that 98% of patients with PE have one or more of the following findings: dyspnoea, tachypnoea, pleuritic chest pain, atelectasis on chest X-ray (CXR), or parenchymal abnormality on CXR. The most common symptoms and signs of PE are listed in (Table 2.2).

Table 2.2 Common symptoms and signs in patients with PE. Frequencies in % (Henry, J.W. 1997; Stein, P.D, &Saltzman, H.A. (1991; Stein, P.D et al. 2007)

Symptoms	%	Signs	%
Dyspnoea	73-80	CXR abnormalities	84
dyspnoea at rest	60	Tachypnoea, ≥ 20 min-1	51-70
dyspnoea at exertion	13-18	Lung examination (any)	32-45
Orthopnoea	31-39	rates (crackles)	26-51
Cough	37-44	Wheezes	3-4
Wheezing	25-33	Rhonchi	4-6
Pleuritic chest pain	33-66	decreased sounds	29
Swollen leg	28-46	Tachycardia, >100 min-1	21-30
Unspecific chest pain	13-26	Signs of DVT	11
Hemoptysis	13	Hypotension, <100mmHg	8
Syncope	10	Fever, >38.5°C	0-7
Palpitations	10	Cyanosis	1

2.3.4.4 Causes of pulmonary embolism:

Pulmonary embolism occurs when a clump of material, most often a blood clot, gets wedged into an artery in the lungs. These blood clots most commonly

originate in the deep veins of the legs, but they can also come from other parts of the body. This condition is known as deep vein thrombosis (DVT). Not all DVT blood clots result in pulmonary embolism. Occasionally, substances other than blood clots can form blockages within the blood vessels inside the lungs. Examples include: Fat from within the marrow of a broken long bone,Part of a tumor, Air bubbles. It's rare to have a single pulmonary embolism. In most cases, multiple clots are involved but not necessarily all at once. The portions of lung tissue served by each blocked artery are robbed of blood and may die. This is known as pulmonary infarction. This makes it more difficult for the lungs to provide oxygen to the rest of the body. (Swanson et al., 2008).

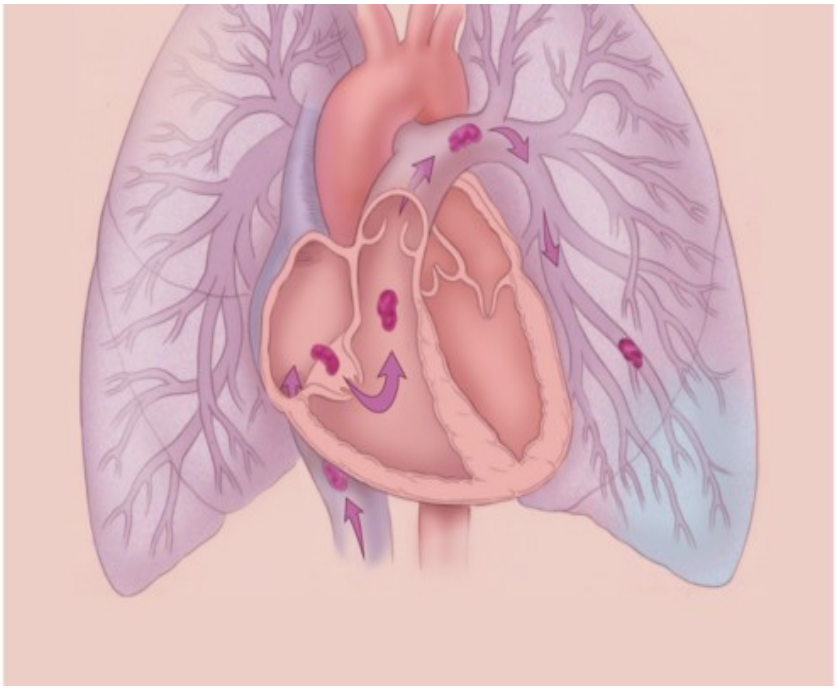

Figure 2.8: An embolus most frequently travels from peripheral vein through the inferior vena cava and right

heart before becoming lodged in the heart. (wikipedia.org, 2016).

2.3.4.5 Risk factors of pulmonary embolism:

Although anyone can develop blood clots and subsequent pulmonary embolism, certain factors can increase your risk.

2.3.4.5.1 Medical history

The patient at higher risk if he had venous blood clots or pulmonary embolism in the past. This may be due to inherited disorders that affect blood, making it more prone to clot. In addition, certain medical conditions can put the patient at risk, such as:

Heart disease: Cardiovascular disease, specifically heart failure, makes clot formation more likely. (Swanson et al., 2008)

Cancer: Certain cancers especially pancreatic, ovarian and lung cancers, and many cancers with metastasis can increase levels of substances that help blood clot, and chemotherapy further increases the risk. Women with a personal or family history of breast cancer who are taking tamoxifen or raloxifene also are at higher risk of blood clots. (Swanson et al., 2008)

2.3.4.5.2 Prolonged immobility

Blood clots are more likely to form in the legs during periods of inactivity, such as:

Bed rest: Being confined to bed for an extended period after surgery, a heart attack, leg fracture, trauma or any serious illness makes far more vulnerable to blood clots.

When the lower extremities are horizontal for long periods of time, the flow of venous blood slows and blood pools in the legs. (Swanson et al., 2008)

Long journeys: Sitting in a cramped position during lengthy plane or car trips slows blood flow, which contributes to the formation of clots in legs. (Swanson et al., 2008)

2.3.4.5.3 Surgery

Surgery is one of the leading causes of problem blood clots, especially seen after joint replacements of the hip and knee. During the preparation of the bones for the artificial joints, tissue debris may enter the bloodstream and contribute to causing a clot. Simply being immobile during any type of surgery can lead to the formation of clots. The risk increases with the length of time under general anesthesia. For this reason, most people undergoing a type of surgery predisposing them to DVT will receive medication before and after surgery to prevent clot formation. (Swanson et al., 2008)

2.3.4.5.4 Other risk factors of pulmonary embolism

Smoking: For reasons that aren't well-understood, tobacco use predisposes some people to blood clot formation, especially when combined with other risk factors. (Swanson et al., 2008)

Being overweight: Excess weight increases the risk of blood clots particularly in women who smoke or have high blood pressure. (Swanson et al., 2008)

Supplemental estrogen: The estrogen in birth control pills and in hormone replacement therapy can increase clotting factors in the blood, especially in smoking or overweight. (Swanson et al., 2008)

Pregnancy: The weight of the baby pressing on veins in the pelvis can slow blood return from the legs. Clots are more likely to form when blood slows or pools. (Swanson et al., 2008)

Age: Older people are at higher risk of developing clots. Factors include:

Valve malformation: Tiny valves located every few inches within the larger vein keep the blood moving in the right direction. However, these valves tend to degrade with age. When there don't work properly' blood pools and sometimes form clots. (Swanson et al., 2008)

Dehydration: Older people are at higher risk of dehydration, which may thicken the blood and make clots more likely. (Swanson et al., 2008)

Medical problems**:** Older people are also more likely to have medical problems that expose them to independent risk factors for clot-such as joint replacement surgery, cancer or heart disease. It is rare for children to develop DVT or VTE. (Swanson et al., 2008).

2.3.4.6 Complications of Pulmonary embolism

Pulmonary embolism can be life-threatening. About one-third of people with undiagnosed and untreated pulmonary embolism don't survive. When the condition is diagnosed and treated promptly, however, that number drops dramatically. Pulmonary embolism can also lead to pulmonary hypertension, a condition in which the blood pressure in the lungs and in the right side of the heart is too high. When obstructions in the arteries inside the lungs, the heart must work harder to push blood through those vessels. This increases the blood pressure within these vessels and the right side of the heart, which can weaken the heart. In rare cases, small emboli occur

frequently and develop over time, resulting in chronic pulmonary hypertension, also known as chronic thromboembolic pulmonary hypertension (CTEPH). (Swanson et al., 2008).

2.3.4.7 Tests and diagnosis of pulmonary embolism

Pulmonary embolism can be difficult to diagnose, especially in people who have underlying heart or lung disease. For that reason, ordering a series of tests to help find the cause of the symptoms.
(Marten soderberg, 2008).

The clinical presentation combined with a history and physical examination can help in the diagnostic work-up in patients with suspected PE. Arterial blood gases, ECG, and CXR can help identify attemative diagnoses, and echocardiography can help assess the severity of PE. These investigations are nonspecific and patients "with PE can have pathological findings, although normal findings do not exclude PE (Goldhaber, A. Z. & Elliott, C.G. (2003).

2.3.4.7.1 Arterial blood gases

The most classical findings on arterial blood gases in patients with PE are hypoxemia and hypocapnia. However, the blood gases are normal in >50% of patients with suspected PE (Cvitanic, O. & Marino, P.L. 1989), and in 15% of patients with proven PE (Stein, P.D., et al 1996).

2.3.4.7.2 Blood tests

The blood test is order for the clot-dissolving substance D dimer in the blood. High levels may suggest an increased likelihood of blood clots, although D dimer

levels may be elevated by many other factors, including recent surgery. In addition, blood tests may be done to determine an inherited clotting disorder. (Swanson et al., 2008)

2.3.4.7.3 Echocardiography (ECG)

The ECG can show sinus tachycardia, atrial fibrillation and signs of right ventricular strain with S1Q3T3-syndrome, right bundle-branch block, and T-wave inversion in lead V1-3. These signs are nonspecific and the most common finding in PE is normal ECG, although patients with massive PE often show dramatic changes in ECG.

(Grifoni, S. et al. 2000).

This is performed to determine whether there is right heart strain which occurs only in relatively sever cases. In small/medium pulmonary emboli is usually normal, in multiple recurrent pulmonary emboli can be normal or show signs of pulmonary hypertension.

(Kumar and Clark, 1998)

The echocardiography is well studied in PE, (Goldhaber, S.Z. 2002; Riberio, A., 1997) Echocardiography is of value at the time of diagnosis and in the follow-up of patients with PE.Signs of right –sided systolic dysfunction are associated with increased mortality and echocardiography is mandatory in the work-up of patients with signs of massive PE requiring thrombolytic therapy, More than 50% of patients with PE have a normal echocardiography pattern.(Kearon C et al 2008, Toosi, M. S. et al 2008).

2.3.4.7.4 Chest X-ray

This noninvasive test shows images of the heart and lungs on film. Although X-rays can't diagnose pulmonary embolism and may even appear normal when pulmonary embolism exists, they can rule out conditions that mimic the disease.

The chest x-ray is often abnormal in PE (Investigators, 1990,Stein, P.D. & henary 1997) and a variety of findings has been described, such as atelectasis, parenhymal consolidations (infiltrates), pulmonary oedema elevated hemidiaphragm, focal oligemia (an area with diminished blood supply; westermark's sign), enlarged right pulmonary artery (palla's sign), pleuric fluid, and a wedged- shaped density indicating an early lung infarction (Hampton's hump) etc. The main value of CXR is to find an alternative diagnosis. A current chest X-ray is required at the time lung scintigraphy is performed, mainly as an aid in categorizing in the lung scintigram, and to exclude other abnormalities, such as cardiac failure, chest infection or pulmonary hypertension, which may a ccount for the patient's symptoms. (Sharp et al; 1989)

2.3.4.7.5 Ultrasound

A noninvasive "sonar" test known as duplex ultrasonography (sometimes called duplex scan, or compression ultrasonography) uses high-frequency sound waves to check for blood clots in the thigh veins. In this test, we use a wand-shaped device called a transducer to

direct the sound waves to the veins being tested. These waves are then reflected back to the transducer and translated into a moving image by a computer. The absence of the presence of clots reduces the likelihood of DVT. If the upper thigh vessels are clear, the ultrasonography will also scan the veins behind the knee looking for residual clots. If clots are present, treatment likely started immediately. (Swanson et al., 2008)

2.3.4.7.6 Pulmonary angiogram

This test provides a clear picture of the blood flow in the arteries of the lungs. It's the most accurate way to diagnose pulmonary embolism, but because it requires a high degree of skill to administer and has potentially serious risks, it's usually performed when other tests fail to provide a definitive diagnosis. In a pulmonary angiogram, a flexible tube (catheter) is inserted into a large vein usually in the groin and threaded through into the heart and on into the pulmonary arteries. A special dye is then injected into the catheter, and X-rays are taken as the dye travels along the arteries in the lungs. One risk of this procedure is a temporary change in the heart rhythm. In addition, the dye may cause kidney damage in people with decreased kidney function. (Swanson et al., 2008).

PA is considered the most specific test for PE and is used as the reference method in many studies. Although the performances cannot be calculated, studies have shown that it is safe to withhold anticoagulants in patients with a normal PA (Nilsson, T. et al 1998). PA is an invasive

investigation- contrast medium is injected IV directly into the pulmonary arteries through a catheter introduced in the femoral vein. PA has several advantages because it can be used to visualize the emboli, directly and because it provides hemodynamic data and opportunities for direct treatment through the insertion of thrombotytic agents and vena caval filters. PA also has several disadvantages: for example, the high cost, limited availability. Invasive technique with risk for bleeding and arrhythmias. and complications related to the contrast media, the use of PA has diminished during the past decade. in favor of CTPA, mainly because of the disadvantages, but there are still clinical conditions when PA should be used for example in patients with contraindications for or, inconclusive CTPA. (Stein, P. D. et al, 1992).

2.3.4.7.7 Ventilation-perfusion lung scintigraphy (V/Q-scan)

Radionuclide imaging is used to distinguish pulmonary embolism from other acute lung disease to demonstrate chronic obstructive airways disease and fibrosis. (Pulmonary embolism, unlike other acute lung disease, shows defects in regional perfusion without comparable changes in regional ventilation. Lung scintigraphy comprises two components, ventilation (V) and perfusion- (Q) Imaging of the lung circulation. The investigation is noninvasive, and the perfusion part is performed by IV injection of radioactive particles, mainly 99mTechnetium labeled micro aggregates of albumin

.These particles block the pulmonary capillaries, if there is an embolus present .The ventilation part is performed by inhaling of a radioactive isotope. The difference in the distribution of particles in the artenal pulmonary circulation, called mismatch, is then analysed. The perfusion scan is matched against ventilation scan. A normal V/Q scan is considered to exclude PE safely (Torbicki, A et al 2014) . Acombined ventilation/perfusion (V/Q) lung scintigram is a non-invasive investigation, which can be used for screening with sufficiently high diagnostic specificity to be use in the clinical situation. (Sharp et al, 1989).

2.3.4.7.8 Computed tomography (CT scan)

Regular CT scans take X-rays from many different angles and then combine them to form images showing 2-D "slices" of the internal structures. In a spiral (helical) CT scan, the scanner rotates around the body in a spiral like the stripe on a candy cane to create 3-D images. This type of CT can detect abnormalities within the arteries in the lungs with much greater precision, and it's also much faster than are conventional CT scans. In some cases, contrast material is given intravenously during the CT scan to outline the pulmonary arteries. (Swanson et al., 2008).

Computed tomography is now able to enhance radiology in general. It is helpful in the investigation of non-malignant diseases, abnormalities of lung parenchyma for example.Pulmonary angiography fine

slices of the lung are scanned by spiral CT so that filling defects in the pulmonary arteries is visualized. (A.V Hoff brand et al, 2001) It can show good sensitivity and specificity for medium-sized pulmonary emboli. They do not exclude pulmonary emboli in small arteries.
(Kumar and Clark, 1998).

Pulmonary embolism is a potentially life threatening condition requiring adequate diagnosis and treatment. Computed tomography pulmonary angiography (CTPA) is excellent for including and excluding PE, therefore CT is the first choice diagnostic imaging technique in patients suspected of having acute PE. Due to its wide availability and low invasiveness, CTPA tends to be overused. Correct implementation of clinical decision rules in diagnostic workup for PE improves adequate use of CT. Also, CT adds prognostic value by evaluating right ventricular (RV) function. CT-assessed RV dysfunction and to lesser extent central emboli location predicts PE-related mortality in normotensive and hypotensive patients, while PE embolic obstruction index has limited prognostic value. Simple RV/left ventricular (Frazier et al.) diameter ratio measures >1.0 already predict risk for adverse outcome, whereas ratios <1.0 can safely exclude adverse outcome. Consequently, assessing the RV/LV diameter ratio may help identify patients who are potential candidates for treatment at home instead of treatment in the hospital. A minority of patients develop chronic thromboembolic pulmonary hypertension (CTEPH) following acute PE,

which is a life-threatening condition that can be diagnosed by CT. In proximal CTEPH, involving the more central pulmonary arteries, thrombectomy usually results in good outcome in terms of both functional status and long-term survival rate. CT is becoming the imaging method of choice for diagnosing CTEPH as it can identify patients who may benefit from thrombectomy. New CT developments such as distensibility measurements and dual-energy or subtraction techniques may further refine diagnosis and prognosis for improved patient care.(Doğan et al., 2015).

2.3.4.7.9 Computed tomography of the pulmonary arteries (CTPA)

CTPA has become more widely used as a diagnostic tool in PE because of the disadvantages of PA and V/Q scans, and the development of the computed tomography CT technique. A CTPA can be used both to exclude and to diagnose PE (Musset, D. et al 2002) and it can confirm alternative diagnoses with high sensitivity and specificity (Rathbun, S. W. et al 2000). Indirect signs of PE, such as atelectasis, (i.e. pleural-based densities), dilatations of pulmonary arteries and pleural effusions can also be visualized on CTPA. (Coche, E E. et al 1998).

CTPA is available at almost all hospitals and is considered as the firstline investigation in many recommendations. (Torbicki, A et al 2014) CTPA is fast, and relatively inexpensive, and requires less contrast media than PA. Newer CT techniques with multi-detector row CT

(MDCT) and multiple slices CT (MSCT) are thought to increase the diagnostic safety of subsegmental PE. CTPA can safely diagnose PE down to the subsegmental part of the pulmonary arteries, although the investigation is less specific more distally. Recent studies show that MDCT and conventional single-detector row CT have similar accuracy in detecting subsegmental PE (Nijkeuter, et al 2008).

2.3.4.7.10 Magnetic Resonance Imaging (MRI scan)

MRI scans use radio waves and a powerful magnetic field to produce detailed images of internal structures. Because MRI is expensive, it's usually reserved for pregnant women (to avoid radiation to the fetus) and people whose kidneys may be harmed by dyes used in other tests. This study can be performed with or without respiratory and ECG-gated studies. The mediastinum and hilar structure are well shown, more peripheral lesion is less clearly identified. Gadolinium-enhanced MRI is a relatively new expensive but accurate technique. (Glenda J. Bryan, 1987)

2.3.4.8 Treatments and drugs of pulmonary embolism

2.3.4.8.1 Medications

Blood thinners (anticoagulants): These drugs prevent new clots from forming while the body works to break up the clots. Heparin is a frequently used anticoagulant that can be given through the vein or injected under the skin. It acts quickly and is often overlapped for several days with an oral anticoagulant, such as warfarin, until it becomes

effective, which can take days. A newer class of anticoagulants has been tested and approved for treatment of venous thromboembolism, including pulmonary embolism. These medications have the advantage of being given by mouth, without the need for overlap with heparin. Also, they work quickly and have fewer interactions with other medications. All blood thinners have side effects, with bleeding being the most common. (Swanson et al., 2008).

Clot dissolvers (thrombolytics): While clots usually dissolve on their own, there are medications given through the vein that can dissolve clots quickly. Because these clot-busting drugs can cause sudden and severe bleeding, they usually are reserved for life-threatening situations. (Swanson et al., 2008).

2.3.4.8.2 Surgical and other procedures

Clot removal: can be removing large, life-threatening clot in the lung, via a thin, flexible tube (catheter) threaded through the blood vessels. (Swanson et al., 2008).

Vein filter: A catheter can also be used to position a filter into the body's main vein called the inferior vena cava that leads from the legs to the right side of the heart. This filter can help keep clots from being carried into the lungs. This procedure is typically reserved for people who can't take anticoagulant drugs or when anticoagulant drugs don't work well enough or fast enough. The catheter with the filter in the tip is usually inserted in a vein in the neck, and

then into the vena cava. Some filters can be removed when they are no longer needed. (Swanson et al., 2008)

2.4 Previous studies:

Study done by (Ahuva Grubstein et, al 2008) which include Computed Tomography Angiography in Pulmonary Hypertension They studied in 38 patients with PH who underwent CT angiography and HRCT as part of their routine evaluation.They found that the Mean main pulmonary artery diameter in the study group was 3.55 ± 0.66 cm, pulmonary artery/ascending aorta ratio 1.2 ± 0.29, right pulmonary artery 2.63 ± 0.49 cm, left pulmonary artery 2.57 ± 0.5 cm. All diameters were significantly different from the control group ($P < 0.0001$). Main and right pulmonary artery diameters correlated with the pressure measurement by echocardiography ($P = 0.001$). Bronchial collaterals were found in 11 patients (30%). The position of the interventricular septum correlated well with the echocardiography study.They concluded that the size of the main pulmonary artery on CT angiography has a good predictive value regarding the severity of PH.

Study done by (Martine Remy-Jardin et, al 2005) which include Systemic Collateral Supply in Patients with Chronic Thromboembolic and Primary Pulmonary Hypertension: by using multi–detector row helical computed tomographic CTangiography. They studied thirty-six consecutive patients, including 22 patients (four men, 18 women;

mean age, 46.0 years) with chronic thromboembolic pulmonary hypertension (group 1) and 14 patients (five men, nine women; mean age, 63.0 years) with primary pulmonary hypertension (group 2), underwent multisection spiral CT angiography of the pulmonary and systemic circulations. They found that the degree of pulmonary hypertension was comparable in groups 1 and 2. Abnormally enlarged systemic arteries were identified in 16 (73%) of 22 patients from group 1 and in two (14%) of 14 patients from group 2 (P .002). The systemic collateral supply in group 1 comprised enlargement of both bronchial and nonbronchial systemic arteries in nine (56%) of the 16 patients; the remaining seven patients had an exclusive enlargement of bronchial systemic arteries (n 6, 38%) or nonbronchial (n 1, 6%) systemic arteries. A total of 31 enlarged nonbronchial systemic arteries were depicted, including 13 inferior phrenic arteries, 10 intercostal arteries, seven internal mammary arteries, and one lateral thoracic artery. The mean standard deviation of abnormal nonbronchial systemic arteries per patient was 1.4 1.9. No relationship was found between the mean number of abnormally enlarged nonbronchial systemic arteries and the CT angiographic features of chronic pulmonary embolism. They concluded that these results demonstrate the higher frequency of abnormally enlarged bronchial and nonbronchial systemic arteries in patients who have chronic thromboembolic pulmonary hypertension compared with patients who have primary

pulmonary hypertension; this finding could help distinguish these two entities on CT angiograms.

Doğan et al 2015 reported that pulmonary embolism PE is a potentially life threatening condition requiring adequate diagnosis and treatment. Computed tomography pulmonary angiography CTPA is excellent for including and excluding PE, therefore CT is the first-choice diagnostic imaging technique in patients suspected of having acute PE. Due to its wide availability and low invasiveness. Also, CT adds prognostic value by evaluating right ventricular (RV) function. CT-assessed RV dysfunction and to lesser extent central emboli location predicts PE-related mortality in normotensive and hypotensive patients, while PE embolic obstruction index has limited prognostic value. Simple RV/left ventricular LV diameter ratio measures >1.0 already predict risk for adverse outcome, whereas ratios <1.0 can safely exclude adverse outcome. Consequently, assessing the RV/LV diameter ratio may help identify patients who are potential candidates for treatment at home instead of treatment in the hospital. A minority of patients develop chronic thromboembolic pulmonary hypertension CTEPH following acute PE, which is a life-threatening condition that can be diagnosed by CT. In proximal CTEPH, involving the more central pulmonary arteries, thrombectomy usually results in good outcome in terms of both functional status and long-term survival rate. CT is becoming the imaging method of choice for

diagnosing CTEPH as it can identify patients who may benefit from thrombectomy. New CT developments such as distensibility measurements and dual-energy or subtraction techniques may further refine diagnosis and prognosis for improved patient care.

Study done by (Karazincir, et al 2008) which include (CT assessment of main pulmonary artery diameter). Right cardiac catheterization is considered to be a gold standard for measuring pulmonary artery pressure (PAP). However, this is an invasive procedure and carries a risk of mortality and morbidity. Therefore, researchers have carried out several studies seeking a reliable and reproducible diagnostic imaging method for the assessment of the pulmonary artery diameter in order to predict the PAP. Some investigators have found reasonable correlations with pulmonary arterial size and PAP in studies with chest radiography. In addition, it has been reported that measurement of the pulmonary artery size by chest radiography is poorly reliable as a method for the examination of pulmonary artery diameter. Several factors contribute to the problem: superposition of the mediastinal and hilar structures; concurrent parenchymal diseases; architectural distortion; and magnification differences. After the introduction of helical CT, several studies have been performed to measure the pulmonary artery diameter, and have shown that the increase in the main pulmonary artery diameter (MPAD) is a reliable

indicator of pulmonary hypertension (PH). However, there are only a few studies with small series that measure the MPAD in normal individuals by CT to determine the normal range of the pulmonary artery diameter. To the best of our knowledge, only Edwards et al. measured the MPAD by CT in a large series of patients .The purpose of this study was to determine the normal range of the pulmonary artery diameter by CT in persons with normal PAP, and then to evaluate the relationship of the diameter with age, gender, and body surface area (BSA). Between October 2005 and June 2007, among patients who had previously undergone a contrast-enhanced thorax CT scan, 112 persons (47 females, 65 males) without pulmonary pathology were selected for the study. All patients had normal mean pulmonary artery pressure PAP ≤ 25 mm Hg. The widest diameter perpendicular to the long axis of the main pulmonary artery was measured at the pulmonary artery bifurcation level. The outer limits of the contrast were used to determine vessel diameter. The purpose of this study was to determine the normal range of the main pulmonary artery diameter (MPAD) by computed tomography (CT) in persons with normal pulmonary artery pressure, and then to evaluate the relationship of the diameter with age, gender, and body surface area (BSA).They found that Pulmonary artery diameters showed a homogeneous distribution; the CT determined mean pulmonary artery diameter was 26.6 ± 2.9 mm. The mean MPAD in males was 27 ± 2.8 mm, and 25.9 ± 3.0 mm in

females. This difference was considered to be statistically significant (P = 0.048). There was a significant relationship between the MAPD and age and BSA (P= 0.043, P < 0.001).And they concluded that the present study demonstrated that in individuals with normal pulmonary artery pressure, the upper limit of the MPAD is 32.6 mm and that MPAD is well correlated with BSA.

Study done by (Truong et al, 2012) which include (Reference Values for Normal Pulmonary Artery Dimensions by Non contrast Cardiac Computed Tomography) Main pulmonary artery diameter (mPA) and ratio of mPA to ascending aorta diameter (ratio PA) derived from chest CT are commonly reported in clinical practice. We determined the age- and sex-specific distribution and normal reference values for mPA and ratio PA by CT in an asymptomatic community-based population.They studied 3171 men and women (mean age, 51±10 years; 51% men) from the Framingham Heart Study, a noncontrast, ECG-gated,8-slice cardiac multidetector CT was performed. We measured the mPA and transverse axial diameter of the ascending aorta at the level of the bifurcation of the right pulmonary artery and calculated the ratio PA. We defined the healthy referent cohort (n=706) as those without obesity, hypertension, current and past smokers, chronic obstructive pulmonary disease, history of pulmonary embolism, diabetics, cardiovascular disease, and heart

valve surgery. The mean mPA diameter in the overall cohort was 25.1±2.8 mm and mean ratio PA was 0.77±0.09. The sex specific 90th percentile cutoff value for mPA diameter was 28.9 mm in men and 26.9 mm in women and was associated with increase risk for self-reported dyspnea (adjusted odds ratio, 1.31; P=0.02). The 90th percentile cutoff value for ratio PA of the healthy referent group was 0.91, similar between sexes but decreased with increasing age (range, 0.82–0.94), though not associated with dyspnea. They concluded that for simplicity, established 29 mm in men and 27 mm in women as sex-specific normative reference values for mPA and 0.9 for ratio PA. (Circ Cardiovasc Imaging. 2012; 5:147-154.)

Grubstein, et al 2008; which include (Computed Tomography Angiography in Pulmonary Hypertension). Diseases causing increased pulmonary pressure will subsequently cause a dilation of the pulmonary arteries and right heart chambers. To assess the capability of computed tomography angiography and high resolution CT to diagnose and stimate the severity of pulmonary arterial hypertension as compared with standard means of right heart catheterization, echocardiography and pulmonary function tests. Methods: The study included 38 patients with PHT who underwent CT angiography and HRCT as part of their routine evaluation. Diagnoses included: primary PHT (n=20), Eisenmenger syndrome

(n=6), cleroderma (n=3), thromboembolic disease (n=3), and others (n=6). Mean pulmonary artery pressure was 58 mmHg (range 39–92 mmHg) by catheterization and peak systolic pressure 79 mmHg (range 40–135) by chocardiography. Findings for the diameters of the main pulmonary artery and its main branches, the ascending aorta, the right atria and ventricle as well as the position of the interventricular septum were compared with 22 chest CT scans of patients with no known clinical history of pulmonary hypertension, performed for other reasons (trauma, oncology follow-up) during the study period. Correlations were also calculated with recent right heart catheterization, echocardiography and pulmonary function tests of the study group. Results: Mean main pulmonary artery diameter in the study group was 3.55 ± 0.66 cm, pulmonary artery/ascending aorta ratio1.2 ± 0.29, right pulmonary artery 2.63 ± 0.49 cm, left pulmonary artery 2.57 ± 0.5 cm. All diameters were significantly different from the control group ($P < 0.0001$). Main and right pulmonary artery diameters correlated with the pressure measurement by echocardiography ($P = 0.001$). Bronchial collaterals were found in 11 patients (30%). The position of the interventricular septum correlated well with the echocardiography study. Conclusions: The size of the main pulmonary artery on CT angiography has a good predictive value regarding the severity of PHT.

Study done by (Chaouat, et al 2005) which inlciude (Severe Pulmonary Hypertension and Chronic Obstructive Pulmonary Disease) severe pulmonary hypertension occurs occasionally in patients with chronic obstructive pulmonary disease (COPD), but no detailed description of these patients is available. Objectives: To identify and characterize patients with COPD and severe pulmonary hypertension. They studied 27 patients with COPD with severe pulmonary hypertension (pulmonary artery mean pressure [Ppa], ≥40 mm Hg) among 998 patients who underwent right heart catheterization between 1990 and 2002 as part of a workup for chronic respiratory failure during a period of disease stability.

They found that Of the 27 patients, 16 had another disease capable of causing pulmonary hypertension. The remaining 11 (11 of 998, 1.1%) patients had COPD as the only cause of pulmonary hypertension, with a median Ppa of 48 mm Hg (inter quartile range, 46–50). They had an unusual pattern of cardiopulmonary abnormalities with mild to moderate airway obstruction, severe hypoxemia, hypocapnia, and a very low diffusing capacity for carbon monoxide ($p < 0.01$ compared with a control group of patients with COPD). Exertional dyspnea was more severe ($p < .01$) and survival was shorter ($p=0.0026$) than in the control subjects.They concluded that Severe pulmonary hypertension is uncommon in patients with COPD. When it occurs, another cause must be sought. COPD with severe pulmonary hypertension and no other possible cause

shares features with pulmonary vascular diseases, such as idiopathic pulmonary hypertension.

Study done by (Bešlić, et al 2005), which include (Multislice computed tomography of pulmonary embolism).The purpose of this study is to analyze the contribution of multislice computed tomography (MSCT) as a diagnostic method in the diagnosis of pulmonary embolism (PE) and spectrum of findings in our material.

During the period of one and a half year, they found PE in 25 patients (15 males and 10 females). The average age of the patients was 54.4 years (25 - 74). The examination was performed by »Somatom Volume Zoom« Siemens CT machine with four row detectors, with retrospective ECG gating, collimation 4 x 2.5 mm and reconstructed section with 0.8 mm. Contrast medium (130 ml) and 10 ml of saline was applied, administered with a flow rate of 3.5 ml/s and with time delay of 22 seconds.

During the examination, they found embolism of the main branches of pulmonary artery in 14(56%) patients, at the right branch in 10 (40%), at the left one in 4 (16%), and bilateral pulmonary embolism in 11 (44%) patients. Subsegmental pulmonary emboli were noticed in 8 (32%) patients. Pulmonary infarct was found in 12 (48%) patients, and was followed up with ipsilateral pulmonary artery dilatation in 11(44%) cases, redistribution of the circulation and pulmonary artery branches dilatation in infarct zone in 9(36%) cases, contrast enhanced

consolidation of pulmonary parenchyma in 10 (40%), rag zones of ground glass attenuation in 15 (60%), haemorrhage in 21 (84%), striped and reticular pulmonary drawing in 11(44%), and mosaic olighemy in 3 (12%)cases. Thrombi were rare, found only in the R/L atrium in 2(8%)cases, pericardial haemorrhage in 1 (4%), mediastinal lymph nodes in 1(4%) case, sudden cut off of peripheral branch leading to infarct apex in 1 (4%), and haemoptysis in 1 (4%) case. In addition to deep vein thrombosis, heart failure was found as aetiology factor in 7 (28%) and malignancy in 3 (12%) cases.They concluded that MSCT is an excellent non-invasive method for visualization of thrombus in the pulmonary artery. In their study, they have more often found embolism of the right branch of pulmonary artery, and pleural effusion, infarct contrast enhanced consolidation of pulmonary parenchyma, ground glass attenuation zone, ipsilateral pulmonary artery dilatation, circulation redistribution with pulmonary artery branches dilatation nearby infarct zone. This diversity of findings cannot be noticed by any other method, with the possibility of making alternative diagnosis, which has led MSCT in the foreground when pulmonary embolism diagnostics is at stake.

The study done by Singanayagam, et al 2010(Right ventricular dilation on CT pulmonary angiogram independently predicts mortality in pulmonary embolism) The aim of this study was to determine the prognostic

significance of right ventricular dilation on CT pulmonary angiogram in acute pulmonary embolism and to distinguish if this feature predicts mortality independently of the Pulmonary Embolism Severity Index, an established admission severity score.They studied a retrospective patients admitted with pulmonary embolism confirmed by CT pulmonary angiogram to three teaching hospitals in East Scotland between January 2005 and July 2007. Two radiologists judged presence of right ventricular dilation on CT pulmonary angiogram independently. The outcome of interest was 30 day mortality. Multivariable logistic regression was used to compare this outcome in patients with right ventricular dilation compared to those without right ventricular dilation, adjusting for Pulmonary Embolism Severity Index score. They found that there were 585 patients included and 30.4% had right ventricular dilation on CTpulmonary angiogram. Patients with right ventricular dilation had increased 30 day mortality rates compared to patients without right ventricular dilation (12.4% vs. 5.4%; p Z 0.006). Survival analysis showed that a significantly greater proportion of deaths in the right ventricular dilation group occurred within the first 48 h after admission compared to the groupwithout right ventricular dilation (45.5% deaths vs. 9.1%; p Z0.016). On multivariable analysis, adjusting for Pulmonary Embolism Severity Index score, right ventricular dilation was independently associated with

increased 30 day mortality (OR 2.98; 95% CI 1.54e5.75; p Z0.001).

Study done by (Storto et al 2005), studied the Incidental Detection of Pulmonary Emboli on Routine MDCT of the Chest his aim to assess the prevalence of pulmonary embolism incidentally detected on routine MDCT of the chest and to determine whether the use of wide window settings can improve detection of unsuspected pulmonary embolism, they studied 589 patients with CT angiograms obtained for suspected pulmonary embolism or thoracic aorta disease were not considered. Image evaluation was performed' on a. dedicated workstation during two separate review sessions using different window settings: standard, with a width of 400 H and level of 40 H; and wide, with a width of 600 H and level of 100-150 H. The quality of vascular enhancement was recorded. Eight examinations were excluded because of poor quality. Unsuspected pulmonary embolism was present hi 20 (3.4%) of 581 patients with an inpatient prevalence of 4.0% (19/474) and outpatient prevalence of 0.9% (1/107). Fourteen patients (70.0%) with unsuspected pulmonary embolism had cancer. The proximal extent of pulmonary embolism involved the main pulmonary artery in five patients, a lobar artery in five, and a segmental artery in 10; isolated subsegmental thrombi were never found. The use of wide window settings allowed detection of

pulmonary embolism in two more patients than did the standard settings.

Study done by Kim et al 2010 in detection of Pulmonary Embolism in the Postoperative Orthopedic Patient Using Spiral CT Scans to compare the clinical presentations of a suspected versus a documented PE/DVT and to determine the actual incidence of PE/DVT in the post-operative orthopedic patient in whom CT was ordered. All 695 patients at our institution who had a postoperative spiral CT to rule out PE/DVT from March 2004 to February 2006 were evaluated and information regarding their surgical procedure, risk factors, presenting symptoms, location of PE/DVT, and anticoagulation were assessed. Statistical analysis was performed using ^an independent samples t test with a two-tailed p value to examine significant associations between the patient variables and CT scans positive for PE. Logistic regression models were used to determine which variables appeared to be significant predictors of a positive chest CT. Of 32,854 patients admitted for same day surgery across all services, 695 (2.1%) had a postoperative spiral CT based on specific clinical guidelines. The incidence of a positive scan was 27.8% (193/695). Of these, 155 (22.3%) scans were positive for PE only, 24 (3.5%) for PE and DVT, and 14 (2.0%) for DVT only. The most common presenting symptoms were tachycardia (56%, 393/695), low oxygen saturation (48%, 336/695), and shortness of breath

(19.6%, 136/695). Symptoms significantly associated with DVT were syncope and chest pain. A past medical history of PE/ DVT was the only significant predictor of a positive scan. Patients who have a history of thromboembolic disease should be carefully monitored in the postoperative setting.

CHAPTER THREE

Materials and Methods

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3.1 Place and time of the study

This study was done in Royal Care International Hospital and Doctor's Clinic radiographic departments; in the period between

(2013-2016)

3.2 Patient's Population

Prospective study of 150 Sudanese patients with clinically suspected PE, PAH, and CTEPH were enrolled. All patients were examined by using multislice CT scanner. This study is a practical study, included random samples of 150 patients in different genders and ages.

Those were referred to CT examination, (92) patient were female while the (58) were males and their ages are ranged from (21-95) years old. The study design was approved by the Research Council Ethical Committee College of Medical Radiological Sciences.

3.3 Instrumentation

All patients were examined on multislice CT scanner Toshiba: (64 multi-slice detector) in Royal Care International Hospital and Neusoft: (64 multi-slice detector) in Doctor's Clinic. Spiral / helical CT scanners are not different in external appearance from conventional CT scanner. However, there are significant differences in several major equipment components.

Figure 3.1 CT Toshiba Aquilion CX 64 Slice

Figure 3.2 CT Neusoft 64 Slice

3.4 Equipment Components

The rotating part of the system consists of the X-ray tube, High voltage generator, Detectors and Data acquisition system (DAS). The stationary part consists of the front-end memory and computer and the first stage high voltage component.

The X-ray tube and detectors rotate continuously during data collection because the cable wraparound problem has been eliminated by slip ring technology. Because large amounts of projection data are collected very quickly, increased storage is needed. This accommodated by the front-end memory fast solid state, and magnetic disk storage. In spiral CT scanners, the X-ray tube is energized for longer periods of time compared with conventional CT tubes. This character requires X- ray tubes that are physically larger than conventional X-ray tubes and have heat unit's capacities greater than 3 million heat units (MHU) and anode cooling rates of 1 MHU per minute.

X-ray detectors for single slice spiral CT scanning are one dimensional (ID) array and should be solid state because their overall efficiency is greater than gas ionization detectors.

The high voltage generator for spiral CT scanner is a high frequency generator with high power output. The high voltage generator is mounted on the rotating frame of the CT gantry and positioned close to the X-ray tube. X-ray tubes operate are high voltages (about 80 to 140 kVp)

to produce X- rays with the intensity needed for CT scanning. At such high voltages, arcing between the brushes and rings of the gantry may occur during scanning. To solve this problem, one approach (high voltage SR) is to divide the power supply into a first stage on the stationary part of the scanner, where the voltage is increased to an intermediate level and a second stage on the rotating part of the scanner, where the voltage is increased to the requirement high voltages needed for X-ray production and finally rectified to direct current potential. Another approach passes a low voltage across the brushes to the slip rings, the high voltage generator and then the X-ray tube. In both designs, only a low to intermediate voltage is applied to the brush / slip ring interface, thus decreasing the chances of arcing.

3.5 Slip Ring Technology

One of major technical factors that contribute to the success of spiral CT scanning is slip ring technology. The purpose of the slip ring is to allow the X-ray tube and detectors (in third generation CT systems), to rotate continuously so that a volume of slices, rather than one slice, can be scanned very quickly in a single breath hold. The slip rings also eliminate the long, high tension cables to the X-ray tube used in conventional start stop CT scanners. As the X-ray tube rotates continuously, the patient also moves continuously through the aperture of the gantry so that data can be acquired from a volume of tissue.

3.6 Basic scan parameters

Several scan parameters for spiral CT' are the same as for conventional CT, however, there are a few parameters as well as a set of terms associated only with spiral pitch is of particular significance because it affects image quality and patient dose and also plays role in the overall outcome of the clinical examination. Other parameters that affect the performance of spiral CT and demand effective communication between the radiologist and technologist are collimation, table speed, duration of the scan, and the reconstruction increment.

3.7 Technique

A significant advantage of spiral CT data acquisition is its application to 3D imaging of vascular structures with an intravenous injection of contrast medium. This application CT angiography (CTA) is defined as "any CT image of a blood vessel that has been opacified by a contrast medium".

During spiral data acquisition, the entire area of interest can be scanned during the injection of contrast. Images can be captured when vessels are fully opacified to demonstrate either arterial or venous phase enhancement through the acquisition of both data sets (arterial and venous).

CTA was been applied successfully to number of examinations investigating vascular anatomy, problems and disease. In particular, CTA techniques have proved

useful in imaging the abdominal and thoracic aorta (renal and pulmonary arteries).

1- Volume of contrast medium 100-150 ml or when dual phase injector availability 80-100ml of contrast medium flowed by saline chase 30-50ml

2- Delay: Preset delay of approximately 15sec for single slice, 22sec for 16 slice scanner, and 26sec for 64 slice scanner. OR bolus tracking using soft ware supplied with most multi detector scanner. A ROI (region of interest) is positioned over the pulmonary artery at the level of the carina. After commencing the injection a (trecker scan) monitors the Hounsfield level at the ROI and the scan is the triggered when the density at the ROI reaches a preset value.

3- Rate of injection 2-4 mls.

4- Detector width- reconstruction (mm)-0.625-1.25.

5- Scan direction and extension-caudocranial direction helps reduce respiratory motion artifact at the lung bases, less important with faster multislice scanner, scan from hemi diaphragm to the lung apex. Imaging review and post-prossing, imaging should be reviewed at three setting:

- (Mediastinal window (window width-window level (400-40 HU
- (Pulmonary embolism -specific window (700-1OO HU
- (Lung window (l500-600 HU

Multiplanar reformatted images through the longitudinal axis of a vessel can be helpful to overcome difficulties

encountered on axial section of obliquely oriented arteries, adding confidence in diagnosis or" exclusion of thrombus.

3-8 Requirements

At least four major steps are crucial to caring out a CT pulmonary angiography (CTPA) examination. Careful execution of these steps will serve to optimize the examination and produce high-quality images that will aid the radiologist in making an accurate diagnosis. These steps include Patient preparation, Acquisition parameters, Contrast medium administration and Post-processing technique.

3.8.1 Patient preparation

A successful CTPA examination depends on careful preparation of the patient before the examination. Such preparation requires that both the technologist and radiologist work together to obtain the appropriate and correct information from the patient and to ensure that the patient understands the procedure, particularly breath-holding techniques.

Preceding the CTPA, a patient history was obtained to identify patients with histories of iodine allergy, renal dysfunction, cardiac disease and asthma. Steroid Pre-medication was administrated to those patients with a history of iodine allergy or previous reaction to iodinated contrast agents. Patients with a history of renal dysfunction were further evaluated with creatinine level and blood urea nitrogen level assessed before the

procedure.

Patients were instructed on breath-holding techniques and practicing with the patient, before the examination, helped in providing a successful motion- free examination. Hyperventilation was performed immediately before the examination facilitates patient breath-holding ability.

3.8.2 Acquisition Parameters

The CTPA was been determined; a number of parameters were carefully chosen to optimize both the quality of the images and the accuracy of the CTPA examination. These parameters include the total spiral scan time, T (Sec); the slice thickness, S (mm); and the speed of the patient through the gantry, which is the table speed D (mm I Sec).

Also influencing the quality of the CTPA examination was upon careful selection of KVP and MA values and the images reconstruction intervals. 120 kVp was commonly used; the MA values selected were based on the size of the patient's body section to be examined. The image reconstruction interval referred to the spacing between the centers of the slices. Reconstruction intervals were important because they play a role in the quality of the 3D - CTPA images.

3.8.3 Contrast Medium Administration

Imaging the contrast while it was in vascular area of interest during the CTPA examination was a critical step in the acquisition of images. Contrast injection techniques

took into consideration the volume of contrast needed to opacity vascular regions; the contrast injection rate, and the timing between the start of contrast medium injection and the start of the spiral scan. Measuring the contrast circulation times for different patients was important in CTPA to ensure that images were recorded when flow-in of contrast was optimum in the pulmonary arteries. To help with this task, various automated systems such as smart prep (Neusoft medical system), and Toshiba's assured its availability commercially. These products ensured optimized contrast monitoring in CTPA. Consideration was given to the size of the needle and the site of the injection. Various size intravenous angio-catheters such as 18 or 20 gauge, using volumes of about 100 ml of non-ionic contrast injected at rates that vary from 3 to 4 ml/Sec to 5 ml/ Sec. parameters for pulmonary arteries applications of CTPA were given in following tables.

Table 3.1 CT Angiography parameters for pulmonary artery:

Collimation (mm)	1-2 mm
Table speed (mm)	2-4 mm/sec
Gantry rotation time (ms)	330-420 mm/sec
Tube voltage (KV)	120 kv
Tube current time product (mAs)	125 mAs
Normal pitch (mm)	0.9
Reconstruction slice	0.6

thickness (mm)	
Scan range	Upper aperture to diaphragm
Scan direction	craniocaudal

Table 3.2 CT Angiography contrast parameters for pulmonary artery:

Concentration (mg iodine/ml)	350-400
Injection Rate (ml/s)	3ml / sec
Volume (mL)	60-120 ml
Delay (s)	12 sec
Saline chaser (ml , ml/s)	30,3.0

3.8.4 Post Processing Technique

3.8.4.1 Visualization Tool

The algorithm used to display 3D images from the axial data set was post processing technique or visualization tool which were used quite extensively in CTPA currently, the following technique was common-place in CTPA.

3.8.4.2 Multiplanar reconstruction (MPR)

MPR was the first visualization tool used in CTPA. It was simple and faster to reconstruct than any other 3D technique and enabled visualization of the volume data set in any plane including curved planes.

3.8.4.3 Statistical analysis

The data obtained were analyzed statistically by computing descriptive statistics like mean ± SD values and percentages, with an independent T-test, ANOVA test, and by correlation analysis using an IBM SPSS Statistics software package (Inc., Chicago, Illinois version 16). Comparisons between groups showed results which were significant at

P ≤0.05. Detailed results are shown in the table and figures.

3.8.4.4 Interpretation

All the images were diagnosed by two professional radiologists and the measurements of the variables were done by one technologist.

All measurements were taken according to the following images:

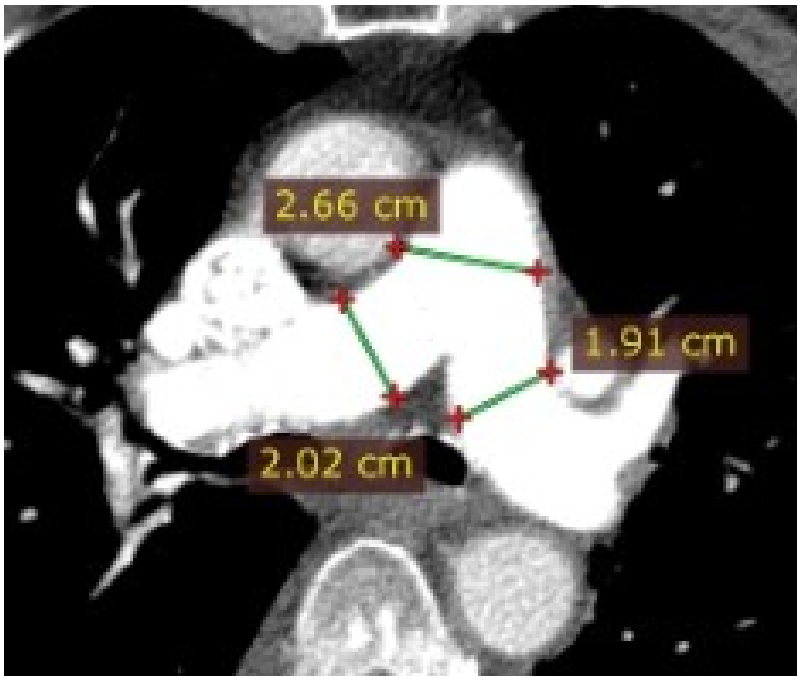

Figure 3.4. Showed the method of measurement of main pulmonary diameters

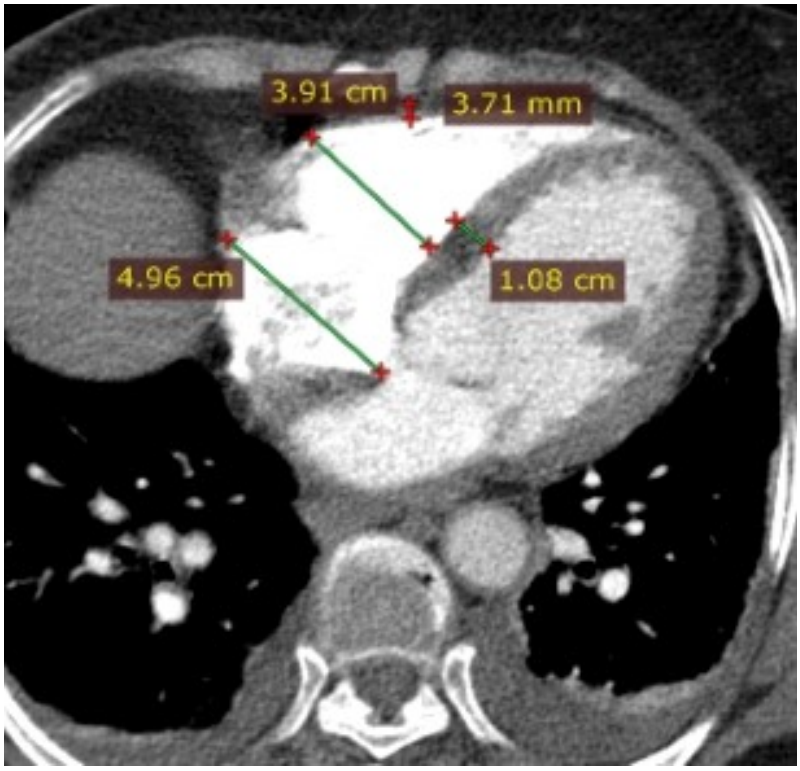

Figure 3.5. Showed the method of measurement of cardiac champers diameters including ventricular septal and myocardial diameters.

CHAPTER FOUR

Results

Chapter Four

Results

Table 4.1. Classification of the sample (patients with PE, PH, CTEPH) according to age class, frequency and percentages, age intervals of 10years.

		Type of Disease				Total
		Patients with PE* N=55	**Patients with PH** N=20**	**Patients with CTEPH** * N=25**	**Normal Subjects N=50**	
Age	21-30	3(5.5%)	1(5.0%)	0(0.0%)	5(10.0%)	9(6.0%)
	31-40	7(12.7%)	3(15.0%)	0(0.0%)	12(24.0%)	22(14.7%)
	41-50	11(20.0%)	0(0.0%)	4(16.0%)	10(20.0%)	25(16.7%)
	51-60	18(32.7%)	4(20.0%)	11(44.0%)	8(16.0%)	41(27.3%)
	61-70	11(20.0%)	7(35.0%)	6(24.0%)	12(24.0%)	36(24.0%)
	˃71	5(9.1%)	5(25.0%)	4(16.0%)	3(6.0%)	17(11.3%)

* Pulmonary embolism (PE), ** pulmonary hypertension (PH), *** chronic thromboembolic pulmonary hypertension (CTEPH).

Table 4.2. Frequency (expressed in percentage) of patients complains in patients PE, PH, and CTEPH

Patient Complain	Type of Disease		
	Patients with PE N=55	Patients with PH N=20	Patients with CTEPH N=25
Chest pain	38(69.1%)	19(95.0%)	18(75.0%)
Short of Breathing	33(60.0%)	16(80.0%)	22(88.0%)
Leg swelling	2(3.6%)	0(0.0%)	0(0.0%)
Tachycardia	1(1.8%)	0(0.0%)	2(8.0%)
Syncope	1(1.8%)	0(0.0%)	0(0.0%)

* pulmonary embolism (PE), ** pulmonary hypertension (PH), *** chronic thromboembolic pulmonary hypertension (CTEPH).

Table 4.3. Frequency (expressed in percentage) of the CT findging in patients with PE, PH, CTEPH

CT Findings	**Type of Disease**		
	Patients with PE (N=55)	**Patients with PH(N=20)**	**Patients wit CTEPH (N=25)**
Pleural Effusion	21(38.2%)	2(10.0%)	3(12.0%)
Consolidation	25(45.5%)	6(30.0%)	14(56.0%)
Ground Glass Opacity	3(5.5%)	3(15.0%)	3(12.0%)
Mosaic Appearance	5(9.1%)	2(10.0%)	7(28.0%)
Abnormal Right ventricle amorphology	11(20.0%)	6(30.0%)	9(36.0%)
Cardiomegally	0(0.0%)	1(5.0%)	6(24.0%)

Table 4.4. Mean and standard deviation of the measured variables (heart segments and pulmonary tree) in all the patients and normal.

Variables	Cases	N	Mean(mm)± Std. Deviation	Minimum (mm)	Maximum (mm)
Right Atrium diameter (mm)	PE	55	49.51±8.54	33.20	87.30
	PH	20	60.31±11.49	37.50	90.70
	CTEPH	25	57.42±9.19	41.70	84.70
	Normal	50	46.43±6.44	36.70	77.00
Right Ventricle diameter (mm)	PE	55	46.03±6.23	32.90	68.30
	PH	20	51.41±6.34	41.30	64.60
	CTEPH	25	51.31±5.94	36.50	58.70
	Normal	50	42.25±3.85	35.60	53.70
Inter-ventricular Septum Width(mm)	PE	55	11.38±1.82	8.30	20.80
	PH	20	10.81±2.14	6.00	12.90
	CTEPH	25	12.16±1.98	5.70	15.30
	Normal	50	11.00±1.13	8.30	13.00
Myocardium Thickening	PE	55	7.1636±0.97	5.50	10.50
	PH	20	6.95±0.66	6.20	9.20
	CTEPH	25	7.37±0.88	6.10	9.10
	Normal	50	6.95±0.77	5.30	9.60
Pulmonary Trunk diameter (mm)	PE	55	28.00±3.70	19.50	37.10
	PH	20	34.54±6.97	26.00	55.00
	CTEPH	25	33.86±3.63	27.20	42.30
	Normal	50	25.17±3.33	19.00	34.30

Right Main Pulmonary Artery diameter(mm)	PE	55	20.70±3.33	15.40	29.70
	PH	20	23.02±3.63	19.20	31.50
	CTEPH	25	24.09±2.05	19.20	27.50
	Normal	50	18.89±2.81	12.90	25.10
Left Main Pulmonary Artery diameter(mm)	PE	55	21.05±3.37	15.20	30.00
	PH	20	23.82±3.54	18.90	33.70
	CTEPH	25	24.122.19	20.00	29.10
	Normal	50	19.56±3.02	14.10	26.70
Right Distal Pulmonary Artery diameter(mm)	PE	55	3.21±0.40	2.50	4.50
	PH	20	3.34±0.30	2.70	3.70
	CTEPH	25	3.43±0.39	2.50	4.10
	Normal	50	3.22±0.32	2.50	4.10
Left Distal Pulmonary Artery diameter(mm)	PE	55	3.23±0.38	2.60	4.80
	PH	20	3.31±0.35	2.50	3.90
	CTEPH	25	3.42±0.38	2.40	4.20
	Normal	50	3.15±0.29	2.40	3.80

Table 4.5. Independent Samples Test for equality of means between the measured variables in patients with and without PE.

Independent Samples Test*

Patients with and without PE	t-test for Equality of Means	
	t	Sig. (2-tailed)
Right atrium diameter(mm)	2.071	.041
Right Ventricle diameter (mm)	3.692	.000
Inter-ventricular Septum Width(mm)	1.281	.203
Myocardium thickening(mm)	1.233	.220
Pulmonary Trunk diameter(mm)	4.100	.000
Right Main Pulmonary Artery diameter(mm)	2.982	.004
Left Main Pulmonary Artery diameter(mm)	2.370	.020
Right Distal Pulmonary Artery diameter(mm)	-.101	.920

Left Distal Pulmonary Artery diameter(mm)	1.170	.245

*Correlation is significant at p≤0.05

Table 4.6. Independent Samples Test for Equality of Means between the measured variables in patients with and without PH.

Independent Samples Test*

Patients with and without PH	t-test for Equality of Means	
	t	Sig. (2-tailed)
Right atrium diameter(mm)	6.418	.000
Right Ventricle diameter (mm)	7.389	.000
Inter-ventricular Septum Width(mm)	-.480	.633
Myocardium thickening(mm)	.025	.980
Pulmonary Trunk diameter(mm)	7.624	.000
Right Main Pulmonary Artery diameter(mm)	5.092	.000
Left Main Pulmonary Artery diameter(mm)	5.059	.000
Right Distal Pulmonary Artery diameter(mm)	1.482	.143
Left Distal Pulmonary Artery diameter(mm)	1.934	.057

*Correlation is significant at p≤0.05

Table 4.7. Independent Samples Test for Equality of Means between the measured pulmonary tree in patients with and without CTEPH.

Independent Samples Test*

Patients with and without CTEPH	**t-test for Equality of Means**	
	t	**Sig. (2-tailed)**
Right atrium diameter(mm)	6.013	.000
Right Ventricle diameter (mm)	7.956	.000
Inter-ventricular Septum Width(mm)	3.208	.002
Myocardium thickening(mm)	2.120	.037
Pulmonary Trunk diameter(mm)	10.323	.000
Right Main Pulmonary Artery diameter(mm)	8.198	.000

Left Main Pulmonary Artery diameter(mm)	6.694	.000
Right Distal Pulmonary Artery diameter(mm)	2.529	.014
Left Distal Pulmonary Artery diameter(mm)	3.453	.001

*Correlation is significant at p≤0.05

Table 4.8. Descriptive statistics (mean and standered diviation) of the studied variables in patients with and without pulmonary embolism.

Variables	Sample	N	Mean (mm)	Std. Deviation	Minimum (mm)	Maximum (mm)
Right Atrium Diameter	With PE	55	49.51	8.54	33.20	87.30
	Without PE	50	46.43	6.44	36.70	77.00
Right Ventricle Diameter	With PE	55	46.03	6.23	32.90	68.30
	Without PE	50	42.25	3.85	35.60	53.70
Interventricular Septum Width	With PE	55	11.38	1.82	8.30	20.80
	Without PE	50	11.00	1.13	8.30	13.00
Myocardium Thickening	With PE	55	7.16	0.97	5.50	10.50
	Without PE	50	6.95	0.77	5.30	9.60
Pulmonary Trunk Diameter	With PE	55	28.00	3.70	19.50	37.10
	Without PE	50	25.17	3.33	19.00	34.30
Right Main Pulmonary Artery Diameter	With PE	55	20.70	3.33	15.40	29.70
	Without PE	50	18.89	2.81	12.90	25.10
Left Main Pulmonary Artery Diameter	With PE	55	21.05	3.37	15.20	30.00
	Without PE	50	19.56	3.02	14.10	26.70
Right Distal Pulmonary Artery Diameter	With PE	55	3.21	0.40	2.50	4.50
	Without PE	50	3.22	0.32	2.50	4.10
Left Distal Pulmonary Artery Diameter	With PE	55	3.23	0.38	2.60	4.80
	Without PE	50	3.15	0.29	2.40	3.80

Table 4.9. Independent samples test for equality of means shows the difference between patients with and without pulmonary embolism.

Independent Samples Test Patients with and without Pulmonary Embolism	t-test for Equality of Means	
	t	Sig. (2-tailed)
Right Atrium Diameter	2.071	.041*
Right Ventricle Diameter	3.692	.000*
Inter Ventricular Septum Width	1.281	.203
Myocardium Thickening	1.233	.220
Pulmonary Trunk Diameter	4.100	.000*
Right Main Pulmonary Artery Diameter	3.006	.003*
Left Main Pulmonary Artery Diameter	2.370	.020*
Right Distal Pulmonary Artery Diameter	-.102	.919
Left Distal Pulmonary Artery Diameter	1.170	.245

* The mean difference is significant at the .05 level.

Table 4.10. The frequency of the complains findings in patients with and without pulmonary embolism.

Complain	Posative/Negative	Patients with (PE) N=55	Patients without (PE) N=50
Chest pain	+Ve	38 69.1%	23 46.9%
	−Ve	17 30.9%	26 53.1%
Shortness of breathing	+Ve	33 60.0%	39 78.0%
	−Ve	22 40.0%	11 22.0%
Leg swelling	+Ve	2 3.6%	3 6.0%
	−Ve	53 96.4%	47 94.0%
Tachycardia	+Ve	1 1.8%	0 .0%
	−Ve	54 98.2%	50 100.0%
Syncope	+Ve	1 1.8%	0 .0%
	−Ve	54 98.2%	50 100.0%

Table 4.11 the frequency of parenchymal findings in patients with and without pulmonary embolism.

Parenchyma Findings	Condition	Patients with (PE)N=55	Patients without (PE)N=50

Associated effusion	Pleural	+Ve	21 38.2%	34 68.0%
		−Ve	34 61.8%	16 32.0%
Consolidation		+Ve	25 45.5%	13 26.0%
		−Ve	30 54.5%	37 74.0%
Ground Glass Opacity		+Ve	3 5.5%	3 6.0%
		−Ve	52 94.5%	47 94.0%
Mosaic appearance		+Ve	5 9.1%	1 2.0%
		−Ve	50 90.9%	49 98.0%
Right ventricle morphology		Normal	44 80.0%	49 98.0%
		Abnormal	11 20.0%	1 2.0%

*PE was found unilaterally in 34(61.8%) cases and bilaterally in 21(38.2%)

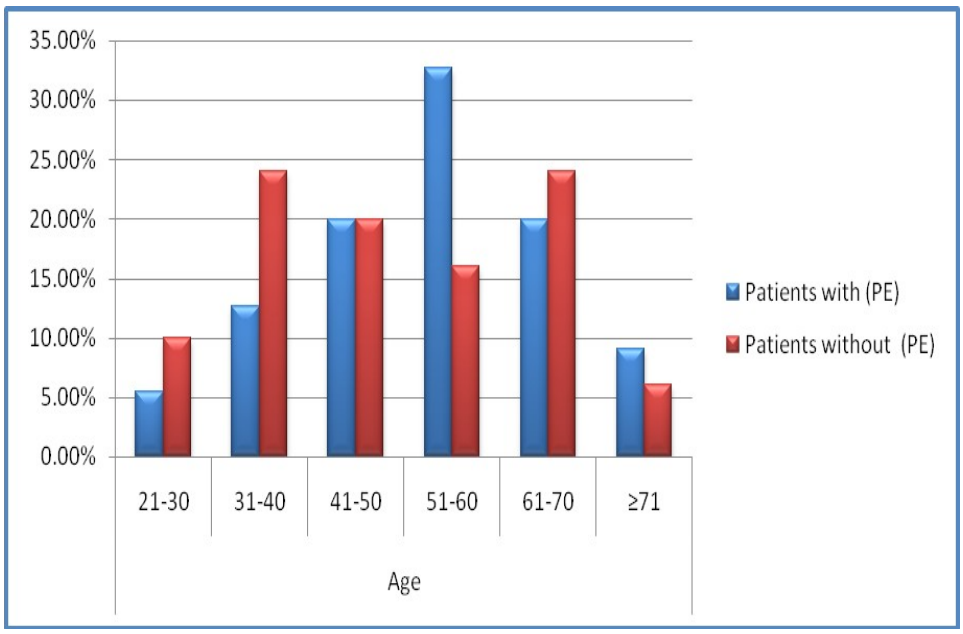

Figure 4.1 Distribution of patients with PE (N=55) and without PE (N=50) according to age classes presented in percentage.

CHAPTER FIVE
Discussion, Conclusion and Recommendations

Chapter Five
Discussion, Conclusion and Recommendations

5.1 Discussion

Evaluation of patients with suspected pulmonary hypertension requires proper investigations to confirm the diagnosis, clarify and determine the specific cause. Thus, evaluating patients with pulmonary hypertension involves four steps: suspicion, detection, classification and functional evaluation. (Barst RJ, 2004) Suspicion including symptoms and conditions which are associated with a risk for developing pulmonary hypertension. Early detection of pulmonary hypertension is vital for appropriate treatment. (Trow TK, 2007, Benza R, et al 2008, Biederman RW, 2009) Classification with a systematic approach to determine its cause to rule out the more common clinical groups of pulmonary hypertension such as left-sided heart disease, lung disease, and chronic thromboembolic pulmonary hypertension CTEPH. CTEPH is often has been misdiagnosed because patients present with nonspecific symptoms. Knowledge of the radiologic imaging signs is required to detect and accurately diagnose the condition. Because CTEPH is potentially curable with pulmonary thromboendarterectomy, early recognition may improve the outcome (Elena Pena, et al 2009) therefore this study was obtained to characterize patients with PE, PH and its complications. Thus the following tables presented the results of the characterization of the cardiac segments,

pulmonary changes in PH, PE and CTEPH. Our sample demonstrate that the patients affected with PH after affected with PE were 25 patient with the most affected ages were between 51-60 years constituting 11(44.0%), where those who were affected with PE only were 18(32.7%) for the same age group however the PH percentage were distributed in all group of ages between 21years and ages ˃71years old. This was presented in table (4.1).

Classification of patients according to their complains has been studied as seen in table (4.2). Studies have mentioned that patients with CTEPH may be asymptomatic for several years before their presentation with symptoms such as dyspnea, atypical chest pain, tachycardia and syncope .The clinical deterioration parallels the loss of right ventricular functional capacity (Fedullo PF et al 2001, Moser KM, et al 1992, Rich S, t al1988, Frazier AA, et al 2000) .Our study evaluated all of the clinical and radiological findings in patients with PH, PE and CTEPH.

The main clinical finding was chest pain. In PE patients; leg swelling was found in only 2(3.6%) of the cases, it is important to acknowledge a history of deep vein thrombosis (sign: as lower limb swelling) as an element that can guide the diagnosis, but it lacks sensitivity. Previous studies had mentioned that many patients with CTEPH haven’t had a documented DVT. (Bonderman D, et al, 2012, Dartevelle P, et al 2004)

Patients monitored for pulmonary hypertension of another cause may exhibit symptoms similar to those of CTEPH (McLaughlin VV, et al 2004) this was similar to the findings of our study. Tachycardia and Syncope were also present with least frequencies.

The classic multidetector computed tomography pulmonary angiography CTPA findings of pulmonary hypertension were divided into three categories: vascular, cardiac, and parenchymal. (Tan RT, et al, 1998) Table (4.3) presented classification of the sample according to the associated findings in the pluroparenchema and heart, and were presented in frequency and percentages and were cross tabulated with the type of disease. The current study mentioned that several pulmonary parenchymal findings are associated with PH, these findings include mosaic attenuation which is commonly seen in chronic pulmonary thromboembolic disease constituting 7(28.0%), but also seen in cases with PH, 2(10.0%). Similar findings were mentioned by another similar study done by Eduardo Jose et al, 2012 (Eduardo et al, 2012).

In order to diagnose the CTEPH, CTPA features should be identified. We classify the features of chronic pulmonary thromboembolism as vascular signs or parenchymal signs. The vascular signs include direct pulmonary artery signs and signs due to pulmonary hypertension. The parenchymal signs include mosaic perfusion pattern, focal groundglass opacities. This method and findings was similar to the study done by Eva

Castañer, et al 2009. (Eva Castaner, et al 2009) Pleural Effusion was seen with the highest score of percentage constituting 21 (38.2%) in (PE) cases. Ground Glass Opacity was also been detected as a complication of PH in CTEPH. Similar previous studies have mentioned that the parenchymal signs as centrilobular ground-glass nodules are common in patients with pulmonary hypertension (Horton MR,2004) however nodules are also seen in patients with other pulmonary capillary diseases (Resten A, et al,2002,Hansell DM,2002). The occurrence of that appearance in our cases; is that the systemic perfusion of the peripheral pulmonary arterial bed accounts for the presence of isolated focal areas, this area was described in previous studies as ground-glass attenuation (Tardivon AA, et al, 1993, Chitwood WR Jr, et al, 1985) .Arakawa et al (Arakawa H, et al, 2003) found direct evidence of airway obstruction air trapping in patients with chronic pulmonary thromboembolism. Air trapping is commonly seen in areas of hypo perfusion due to chronic embolism. This is what our study perceived is that the most of the patients came with shortness in breathing in both PE and CTEPH as seen in table (4.2).

Consolidation scored the high frequency in both CTEPH and PE.Cardiomegally constituting 6/25 (24.0%) of the CTEPH cases. The current study showed that 30% of patients with PH and 36% with CTEPH have abnormal right ventricle morphology and supposed that the hypertrophied right ventricle made it spherical shape and

greater than the left ventricle .The justification of this fact is that the demand of the right ventricle for oxygen exceeds the available supply, causing chamber dilation that leads to tricuspid regurgitation, a result of tricuspid annular dilatation and incomplete valve closure, these processes eventually result in right-sided heart morphology changes ,this process is described well in other related studies. (Elena Pena, et al 2009, Nauser TD, 2001, Bristow MR, et al, 1998) This was presented in table (4.3).

Pulmonary trunk diameter in PH patients and CTEPH was found to be larger than patients with PE and normal control. The maximum width were found to be 55mm and 42 mm which were consistent with the diagnostic criteria of pulmonary hypertension, that was mentioned previously that the enlargement of the main pulmonary artery to a diameter of more than 29 mm occurs in the presence of pulmonary hypertension (Frazier AA, et al, 2000) regardless of the cause; such enlargement is a common finding in patients with chronic thromboembolic pulmonary hypertension. (Schmidt HC, et al, 1996) The study also presented that the least effect on the main trunk diameter was found in cases of PE table (4.4).The diameter of the main pulmonary artery is measured in the scanning plane of its bifurcation, at a right angle to its long axis, followed by measurements done for right and left main pulmonary arteries diameter. The normal value of main pulmonary trunk diameter was found to be

25.17±3.33mm measured for 50 normal Sudanese subjects .Several published studies provide different normative data. Edwards et al. reported that the mean pulmonary artery dimension was 27.2 mm (SD 0.6) in 100 Caucasian participants (Edwards, P.D, et al, 1998). Karazincir et al. reported a mean diameter of the main pulmonary artery of 26.6 mm (SD 2.9) in 112 patients (Karazincir, S. et al, 2008).Kuriyama et al. reported a somewhat smaller mean pulmonary artery size of 24.2 mm (SD 2.2) in sample of Japanese origin (Kuriyama, K, et al 1984). The possible discrepancy may be due to the differences in race or CT technique. (Kamonpum, et al 2014).It is important to emphasize that a diameter of less than 29 mm does not necessarily exclude pulmonary hypertension. In patients with mild pulmonary hypertension, the pulmonary artery may be only slightly dilated, and the findings in patients with (PH) may overlap with those in control subjects without (PH) (Edwards, P.D, et al, 1998, Devaraj A, 2009). The diameters of the segmental pulmonary arteries should also been dilated in the presence of pulmonary hypertension. (Tan RT, et al, 1998).

The maximum changes in diameter differs from the normal by 1.81mm, 4.13mm, 5.2mm for the right main pulmonary artery diameter and 1.49mm, 4.26, 4.56mm left main pulmonary artery diameter in PE, (PH) and CTEPH respectively with the maximum changes detected in the (PH) cases (table4),also changes were detected in

both right and left distal pulmonary artery diameter with greater changes detected in PH and CTEPH .Another similar study have also mentioned that pulmonary enlargement typically seen in pulmonary hypertension and chronic thromboembolic pulmonary hypertension. (King MA, 1998).

Cardiac signs in PH are the adaptation and failure of the right side of the heart that may be seen as right ventricular hypertrophy, straightening or leftward bowing of the interventricular septum; right ventricular dilatation and other findings. (Reid JH, 1998, Van RW, et al, 2005, Groves AM, et al, 2004, Baque-Juston MC, et al, 1999) Therefore the heart segments of all of the study sample were also been evaluated including right atrium diameter, right ventricle diameter, interventriculer width, and myocardium thickening in all of the studied cases, these were presented in table (4.4).Our study measured the right atrium and right ventricle diameters, they were of largest values in patients affected with PH and CTEPH; mean diameter 60.31±11.49, 57.42±9.19 and 51.41±6.34, 51.31±5.94 in respectively. The inter-ventricular septum width was also changed with the presence of the diseases; however the myocardium thickening changes does not differ with different presentations of diseases. Changes are compensatory mechanisms that allow the right ventricle to maintain cardiac output (Dell, Italia LJ, 1998, Mcgoon M, et al, 2004). These scientific facts justify our findings. Tables

(4.5, 4.6, and 4.7) presented the significant difference between the variables which have been evaluated in patients with and without PE, PH and CTEPH. Right atrium, right ventricle, pulmonary trunk, right main pulmonary artery, left main pulmonary artery diameters measurements were changed significantly in both patients with PE and PH when compared with the normals. While in CTEPH all of the anatomical structures which have been evaluated including (heart segments, pulmonary tree) were differed significantly at $p \leq 0.05$. Numerous studies have investigated the correlation between CT measurements of the pulmonary artery and the presence of PH. Overall, the measurement of the main pulmonary artery size by using CT shows a moderate to strong correlation with PH. (Kamonpum, et al 2014) However, Moore et al. reported no correlation between main pulmonary artery size in patients with PH and chronic thromboembolic pulmonary hypertension CTEPH (Moore, N.R, et al, 1998). The presence of significant parenchymal lung disease, which can distort the great vessel anatomy, also appears to affect the correlation between PH and pulmonary artery size. (Tan RT, et al, 1998) The significant difference that was noticed in the measurements done in both normal patients and patients with CTEPH give the evaluation of the pulmonary artery and its branches an important approach; because the pulmonary artery size was associated with unexpected death. (Zylkowska, J., et al 2012). The current findings were reliable with Aran

Singanayagam et al 2010 scientific findings. (Aran et al 2010).

5.2 Conclusions

Knowledge of the radiological features of (PH),(PE) and (CTEPH) is mandatory for accurate diagnoses of the cases and improving the outcome .

Awareness of the various disease entity associated with (PH) and knowledge of the entire spectrum of their (CT) imaging features showed an essential tract for diagnosis.

The pulmonary artery tree, cardiac segments and associated lung parenchyma findings have great value in prediction of (PH) comparing with the normal control group.

It was found that CTA plays an important role in the diagnostic evaluation of patients with (PH). CT Imaging is acceptably used in establishing the diagnosis, defining the cause, quantifying heart segments and parenchyma changes in order to assess the feasibility of surgery, therapeutic planning and monitoring patients with (PH).

CTPA provides concrete evidence of an embolus, and also allows the evaluation of other intrathoracic structures.

Regarding the current study results; the answers of the two raised questions based on findings of CTPA performed for clinical suspicion of PE have been answered: consolidation, ground glass opacifications, and mosaic, right ventricle morphological changes and pleural effusion were found to be present in the majority of patients undergoing CTPA for the clinical suspicion of PE. The presence of heart changes and pulmonary vessels measurements findings were found to have correlation

with the presence of PE. The clinical implication of this finding is likely to be different in patients with PE.

CT measurements of pulmonary artery dimensions have shown a correlation with the presence of PH, PE and CTEPH while the strength of the correlation is highly variable.

Our results suggest that right ventricle; right atrium dilation on CTPA may represent an additional marker of severe PE, PH and CTEPH. CTPA is considered as the diagnostic modality of choice in the characterization of pulmonary vessels, atrium and ventricle changes as well as pleuroparenchymal abnormalities in patients with or without PE.

5.3 Recommendation

- Other quantification methods must be used to diagnose PE including blood gas values and lung attenuation.
- Other investigations must be done before CTPA, as CXR, ECG, and echocardiography.
- New CT developments such as distensibility measurements and dual-energy or subtraction techniques may further refine diagnosis and prognosis for improved patient care.
- As the CT measures of pulmonary artery size are simple and can suggest a possible reason for dyspnea it should be interpreted cautiously and not be used solely in either screening or guiding management in the patients with suspected PH or patients with PE and CTEPH.

- Future research is recommended for characterizing the heart and pulmonary vessels in patients with PE and PH associating anther modalities with CT.

- Future studies could focus on specific disease and changes in the pulmonary artery size as a marker of prognosis, disease activity, and treatment response, rather than as an isolated measure.

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Appendices

Appendix (A)

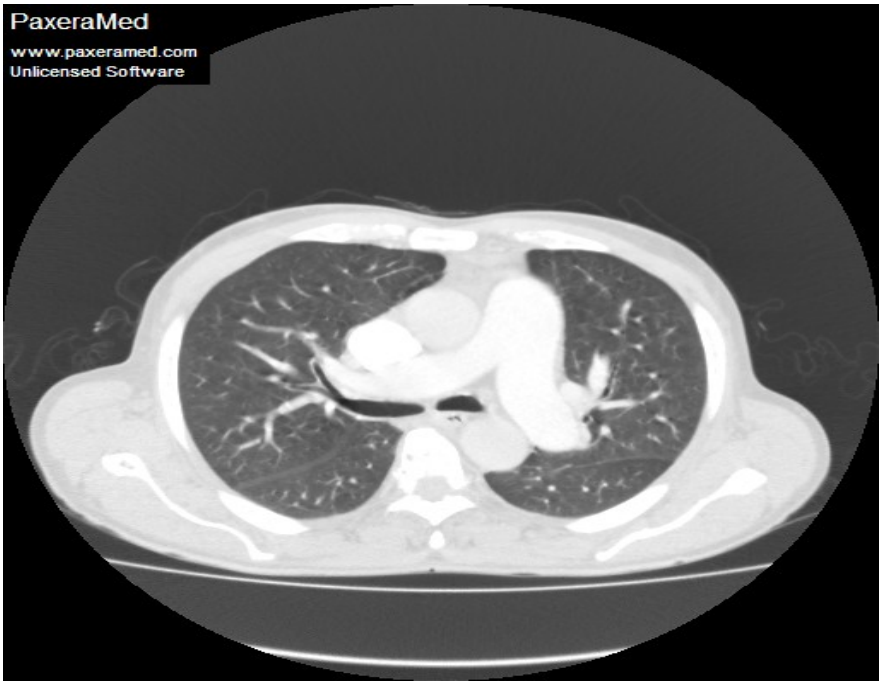


Figure: 1 Sixty-four slice MDCT in a 36-year-old man with Normal CTPA.

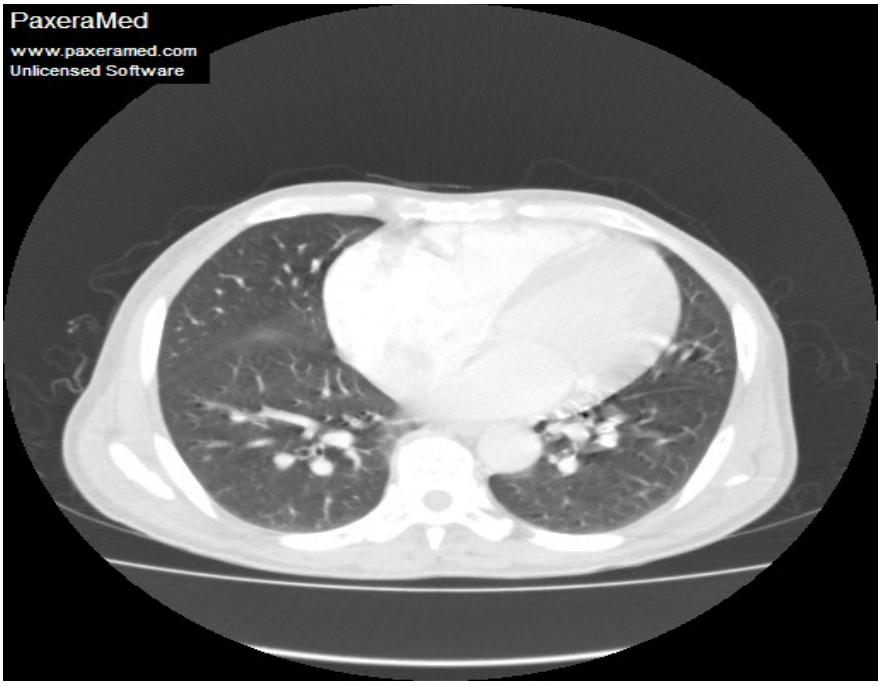


Figure: 2 Sixty-four slice MDCT in a 31-year-old man with cardiomegally + PHTN.

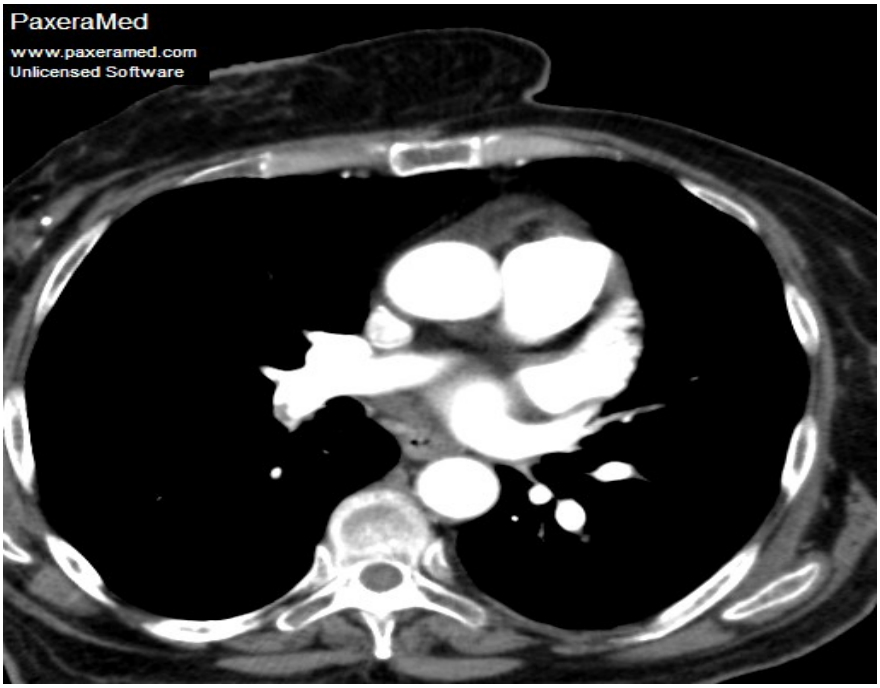


Figure: 3 Sixty-four slice MDCT in a 45-year-old woman with a filling defect in descending branch of the right pulmonary artery (RT pulmonary Embolism).

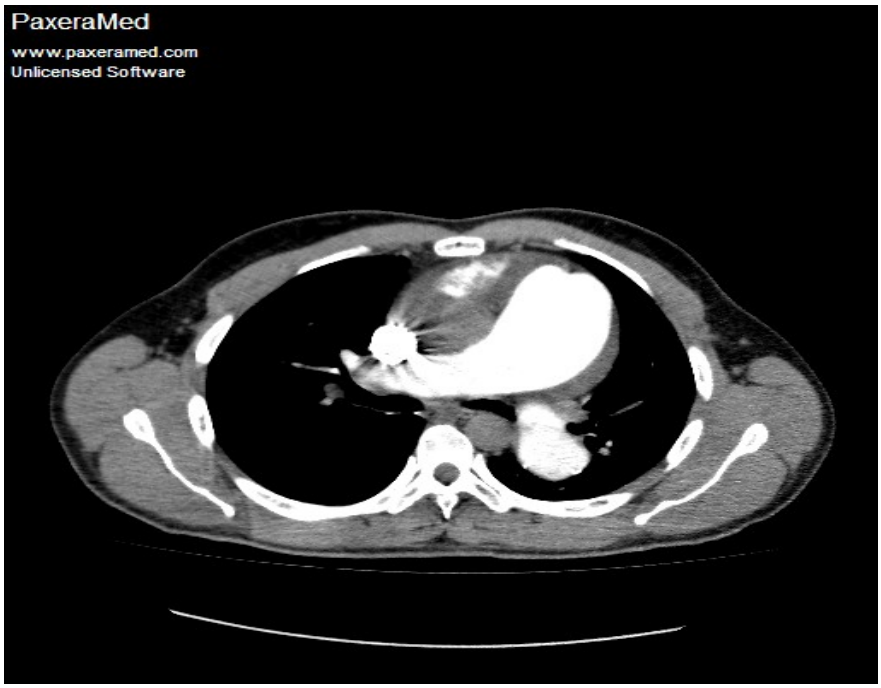


Figure: 4 Sixty-four slice MDCT in a 53-year-old man with enlarged main pulmonary signs suggestive of primary pulmonary hypertension.

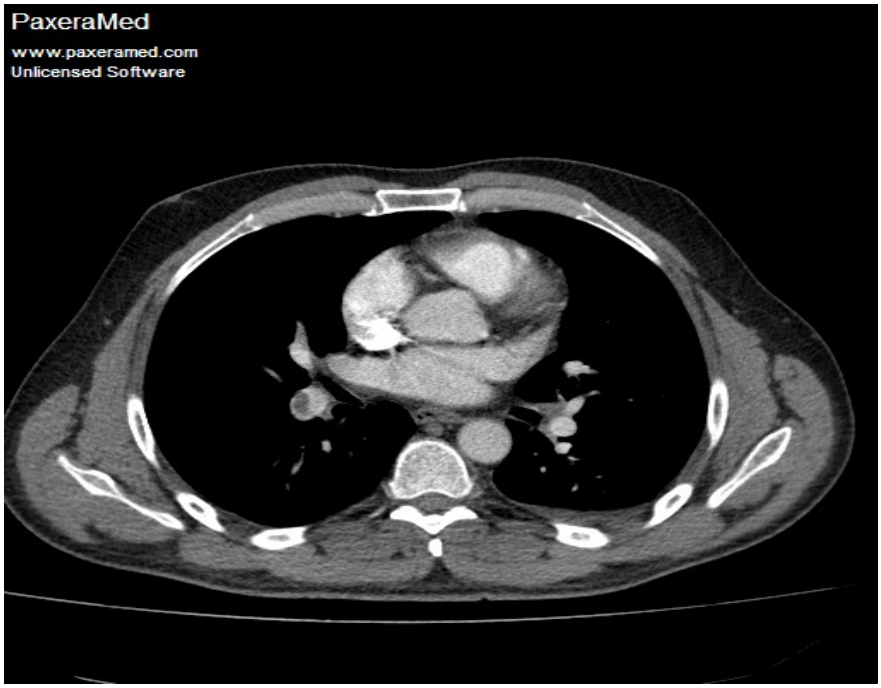


Figure: 5 Sixty-four slice MDCT in a 43-year-old man with bilateral thromboembolism.

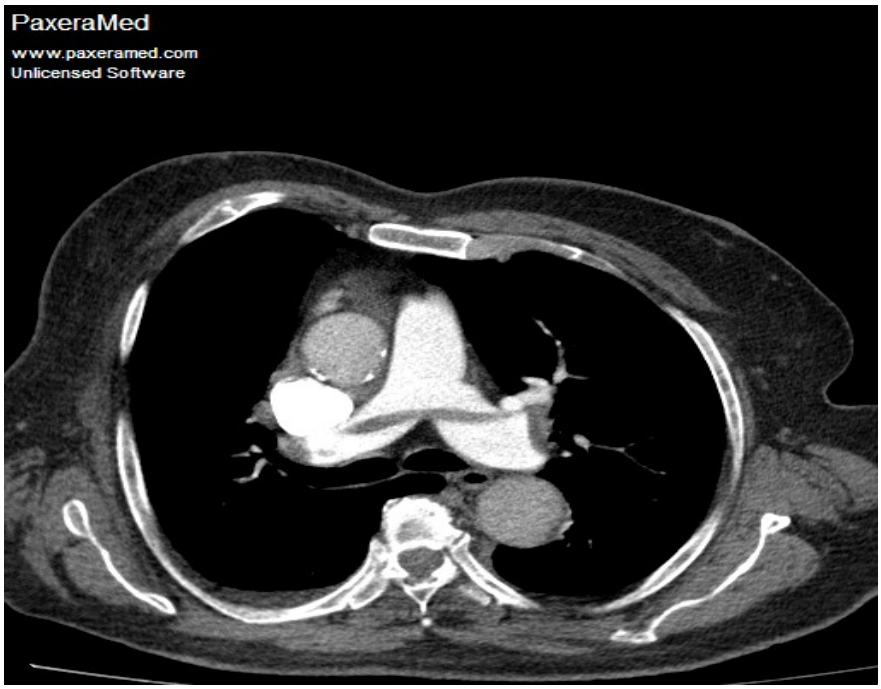


Figure: 6 Sixty-four slice MDCT in a 56-year-old man with bilateral thromboembolism and mild right pleural effusion.

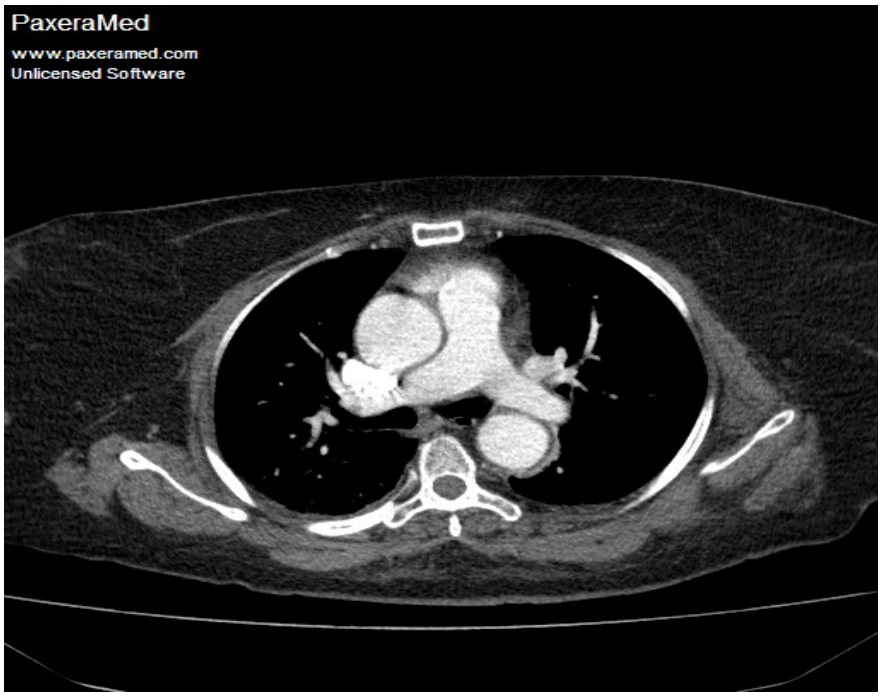


Figure: 7 Sixty-four slice MDCT in a 65-year-old woman with Normal CTPA

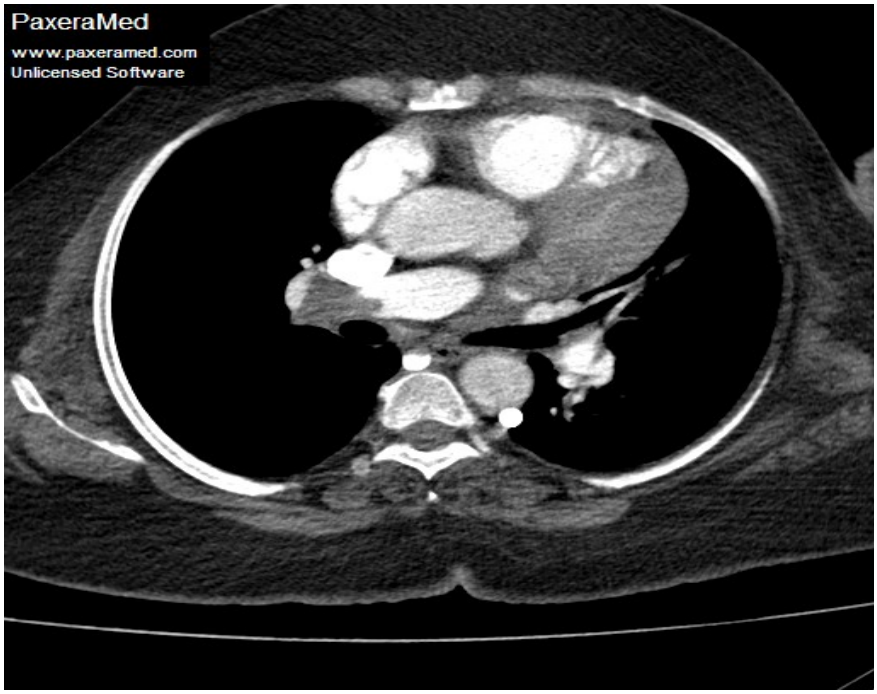


Figure: 8 Sixty-four slice MDCT in a 50-year-old woman with bilateral pulmonary thromboembolism and mild PHT

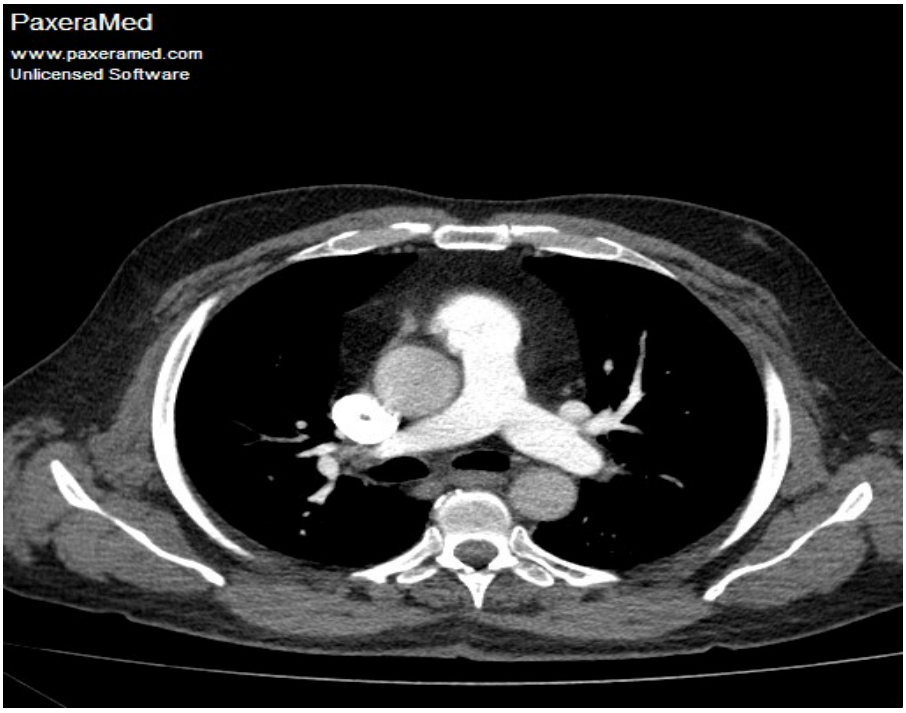


Figure: 9 Sixty-four slice MDCT in a 55-year-old man with Normal CT appearance of the pulmonary vessels.

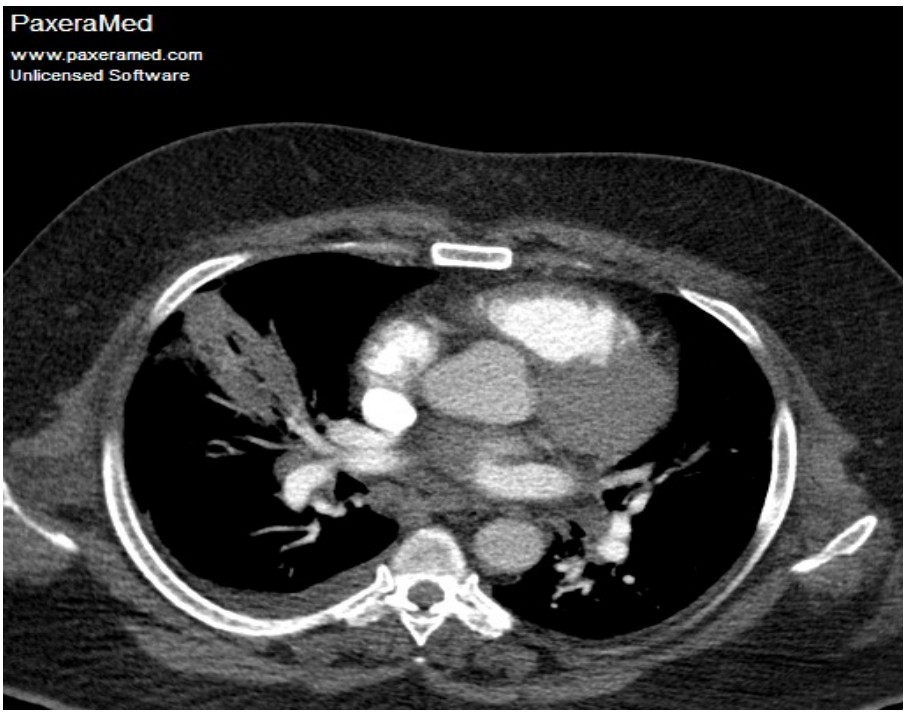


Figure: 10 Sixty-four slice MDCT in a 60-year-old man with right segmental pulmonary emboli and right middle and lower lung lobes consolidation and mild right side pleural effusion

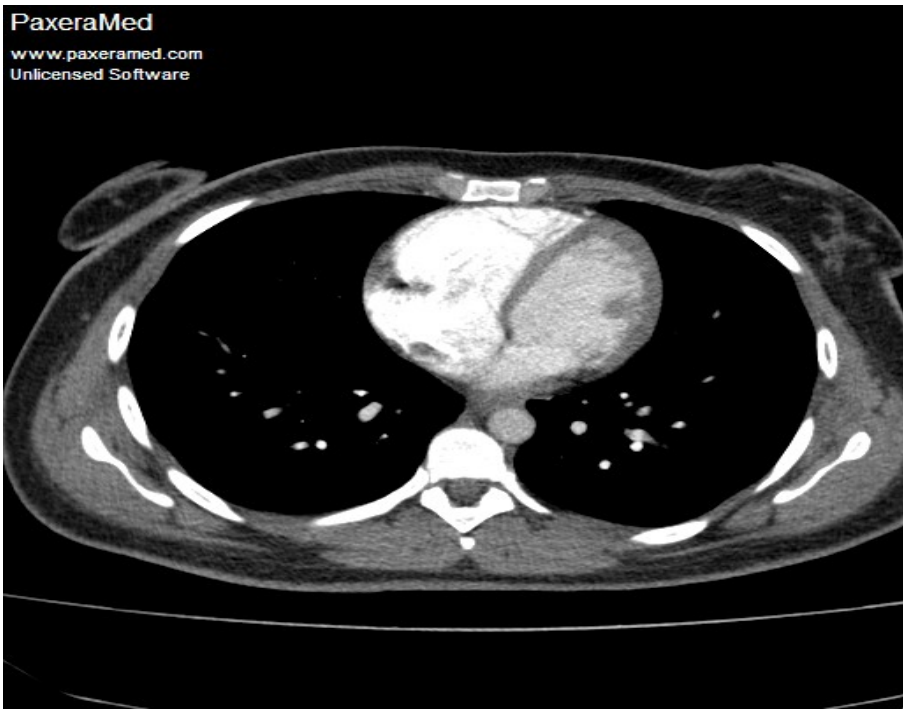


Figure: 11 Sixty-four slice MDCT in a 30-year-old woman with Normal CT appearance of the heart.

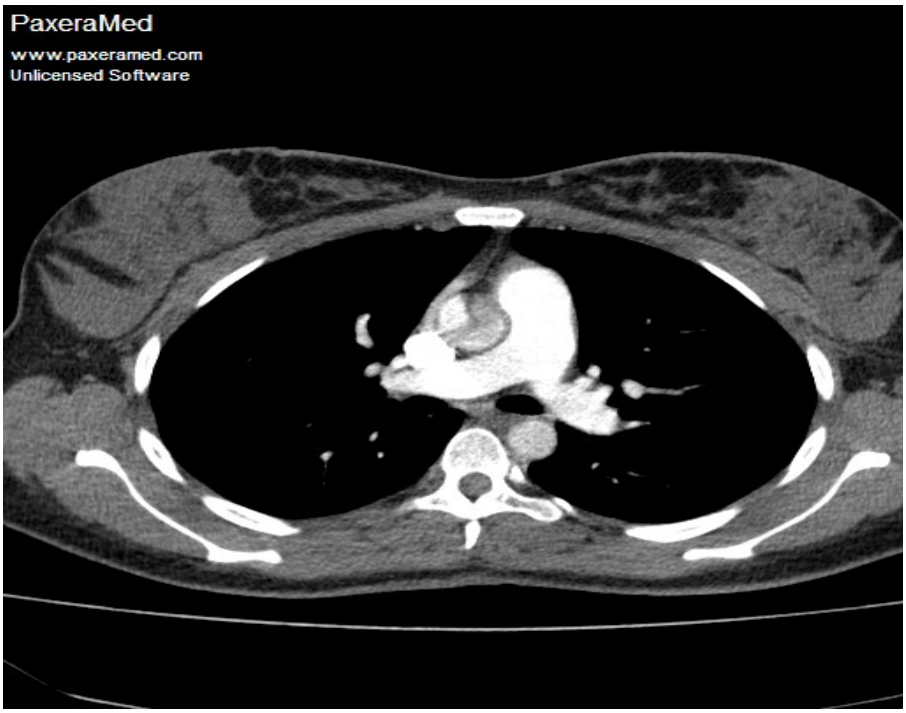


Figure: 12 Sixty-four slice MDCT in a 35-year-old woman with Normal CT appearance of the pulmonary vessels and lungs fields

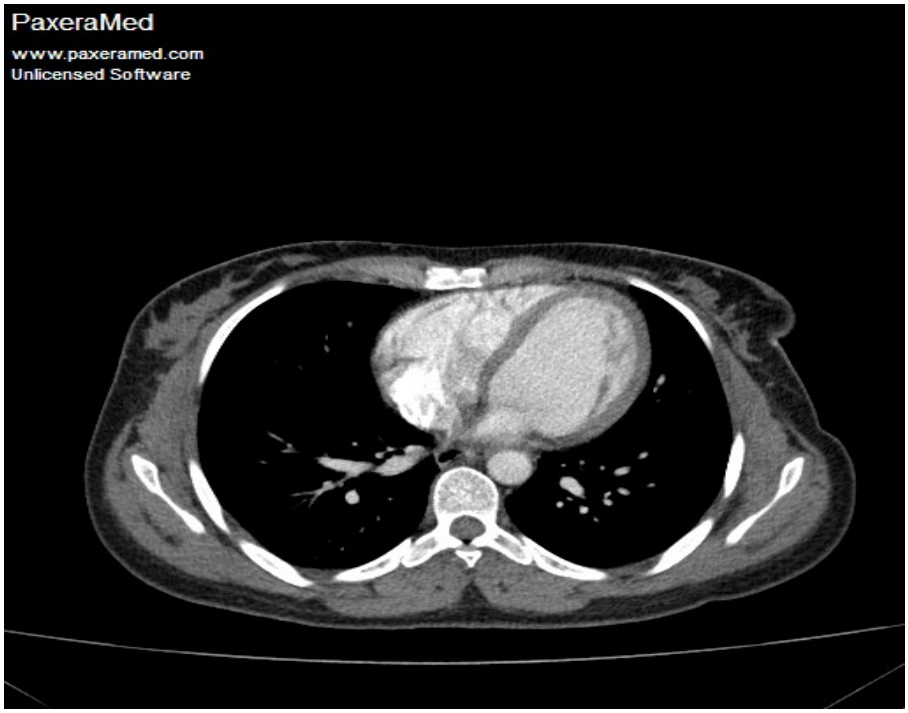


Figure: 13 Sixty-four slice MDCT in a 30-year-old woman with Normal CT appearance of the pulmonary vessels and lungs fields

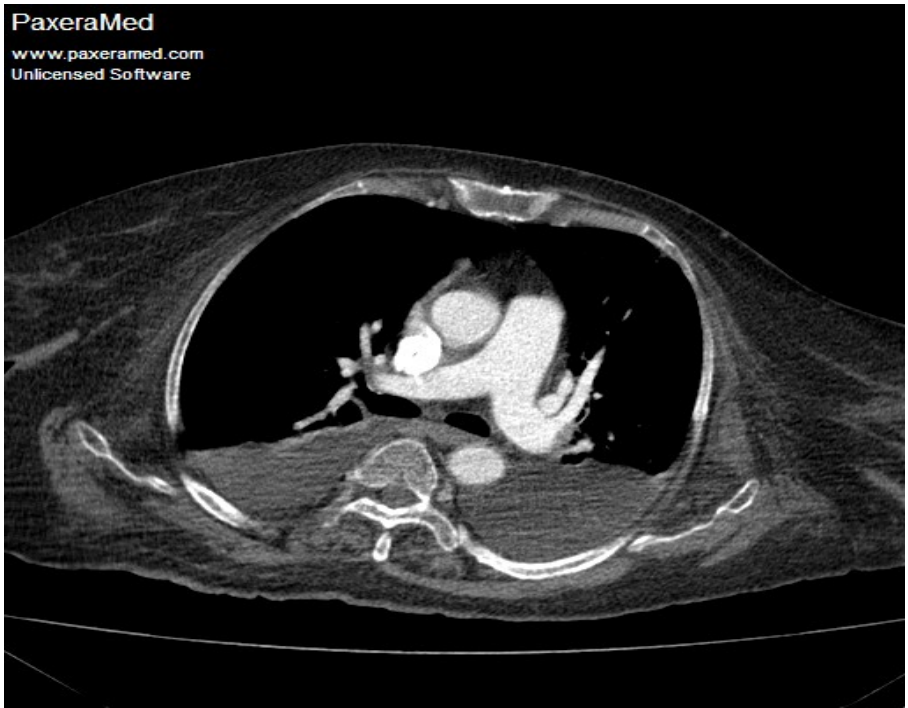


Figure: 14 Sixty-four slice MDCT in a 46-year-old woman with Normal CT appearance of the pulmonary vessels and bilateral moderate pleural effusion with underlying bilateral lower lobar relaxation collapse.

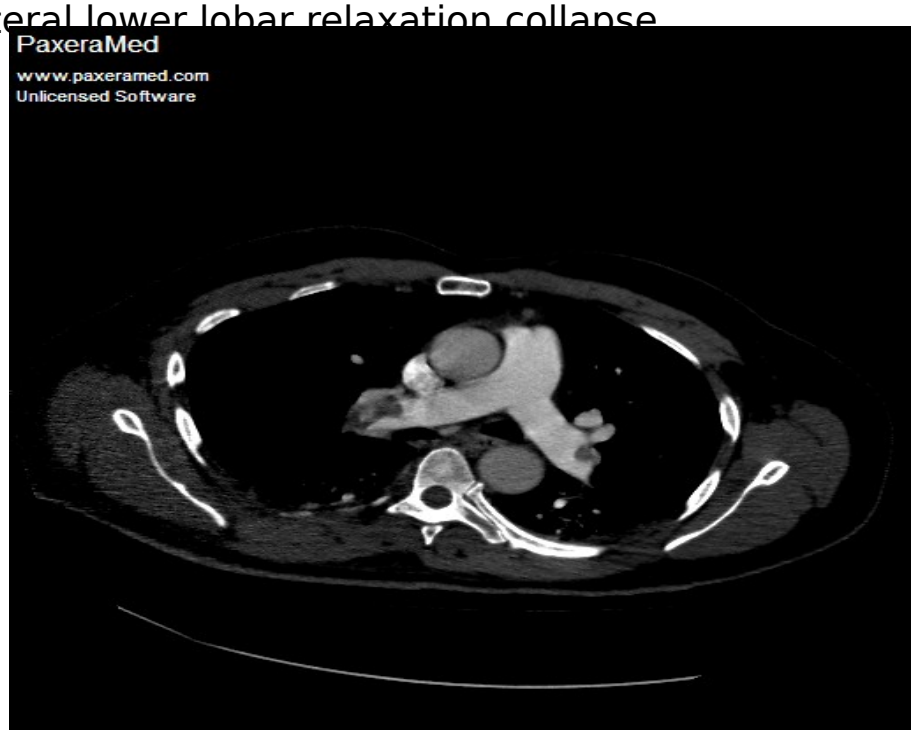


Figure: 15 Sixty-four slice MDCT in a 54-year-old man with t s.

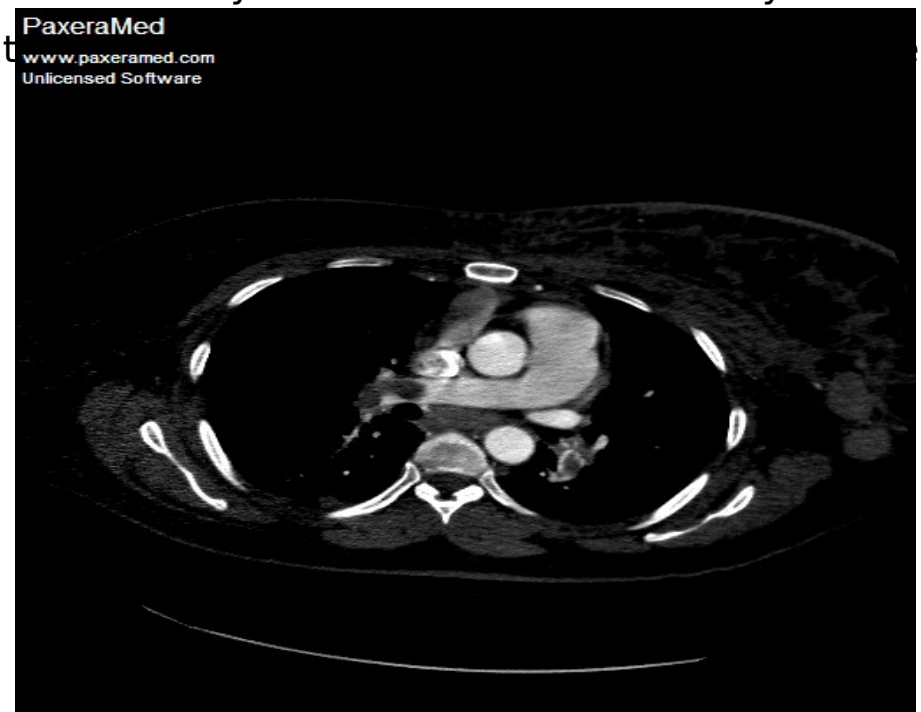
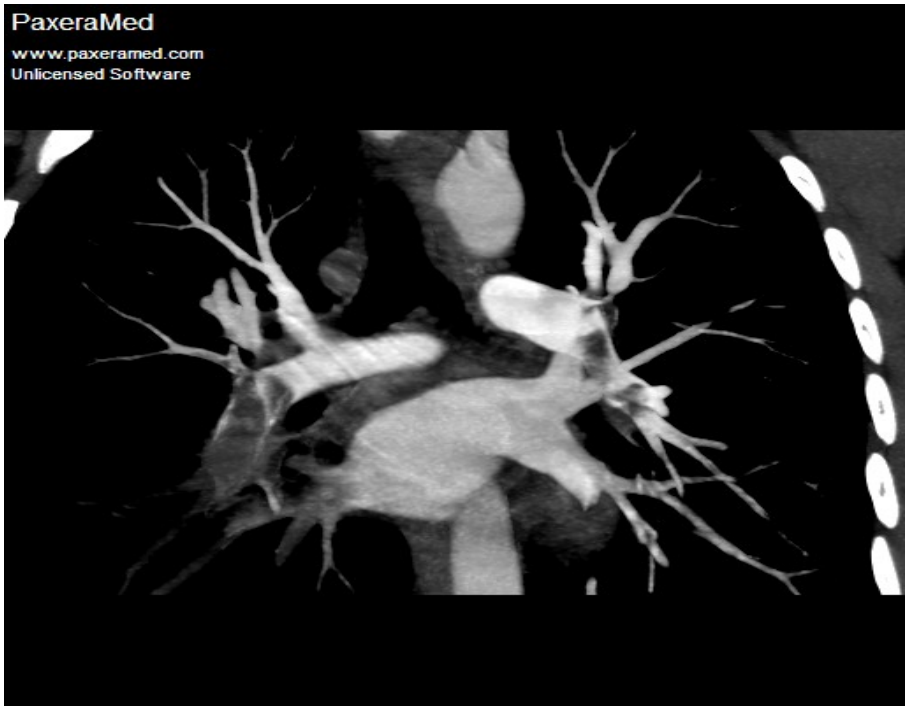


Figure: 16 Sixty-four slice MDCT in a 56-year-old woman with bilateral pulmonary embolism filling the distal aspect of both pulmonary arteries and main divisions.



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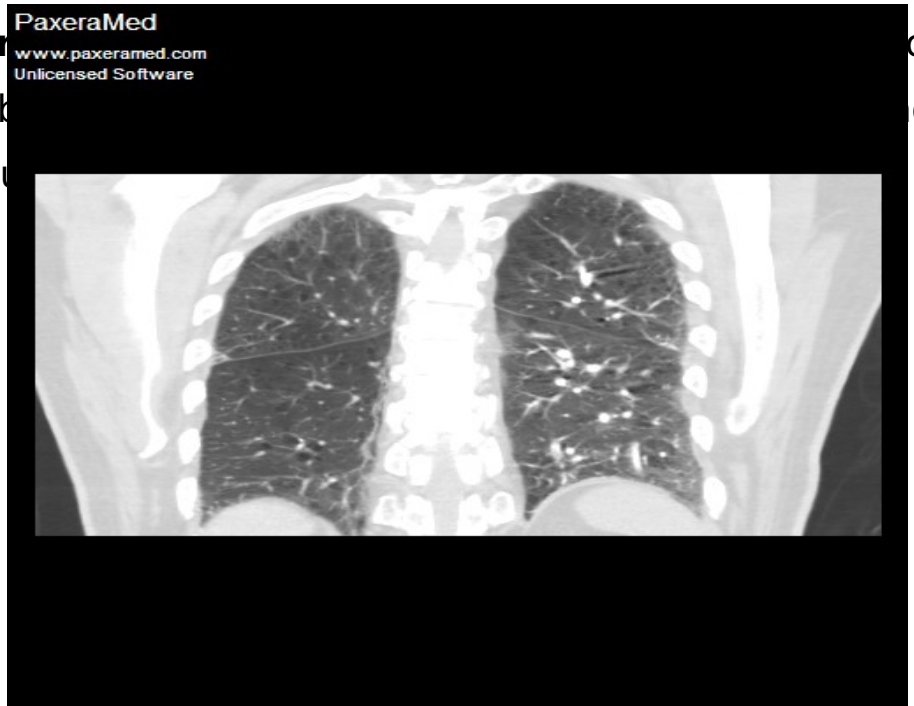

Figure: 18 Sixty-four slice MDCT in a 70-year-old man with ground glass opacification and small left nodular consolidation more on the left.

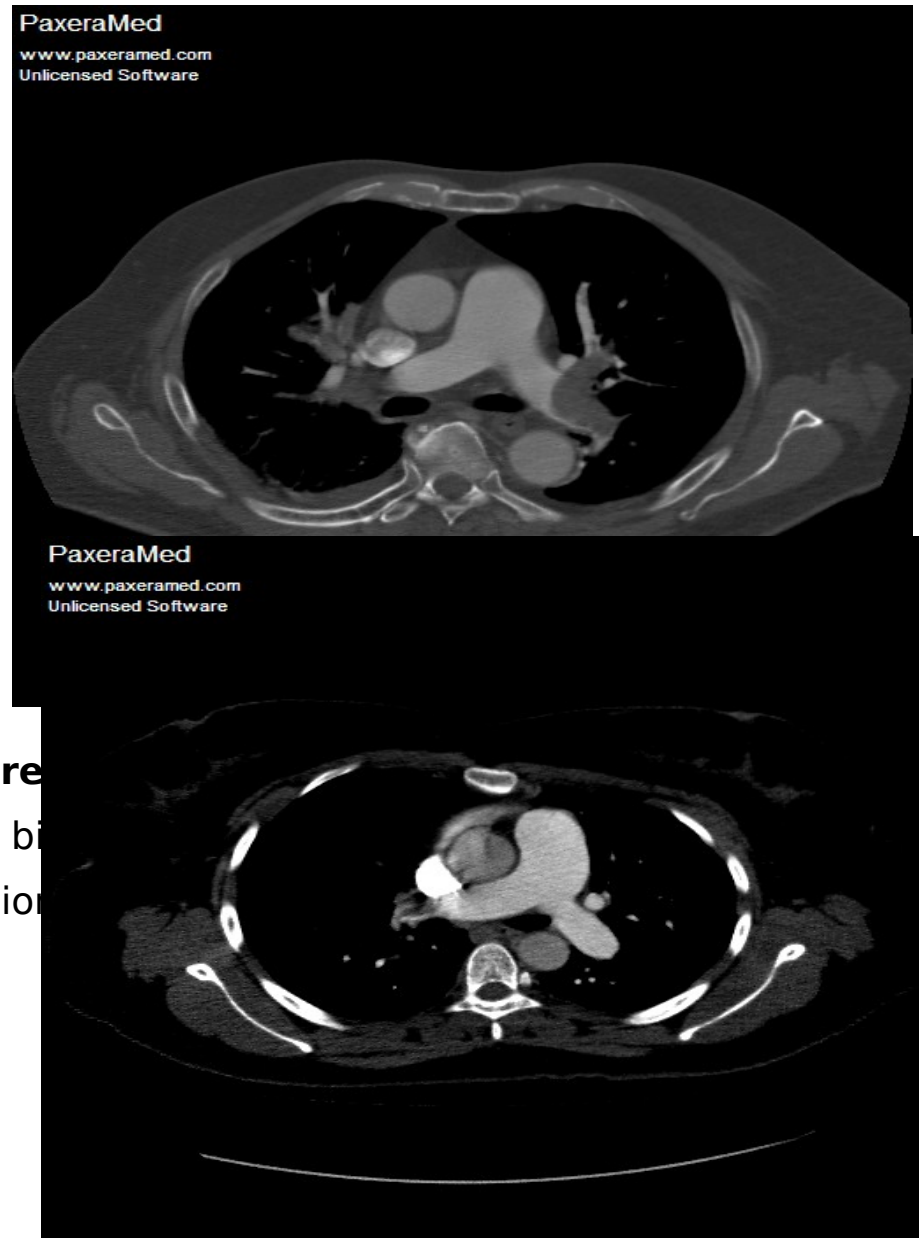

Figure man with bi ural effusio

Figure: 20 Sixty-four slice MDCT in a 45-year-old woman with pulmonary embolism in the distal right main pulmonary artery.

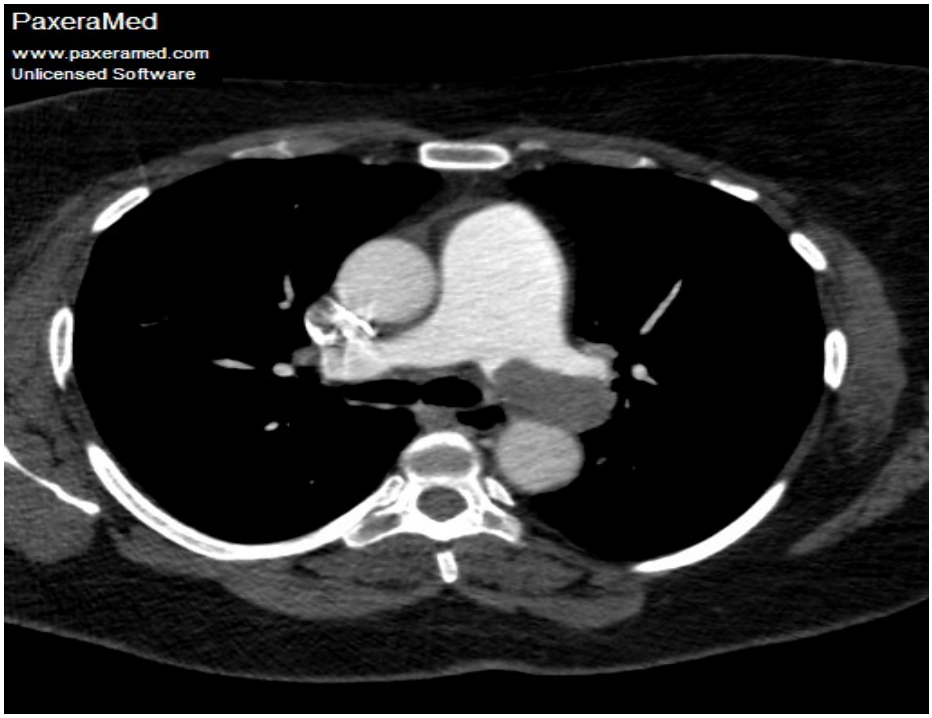

Figure: 21 Sixty-four slice MDCT in a 50-year-old woman with pulmonary embolism in the main left pulmonary arte

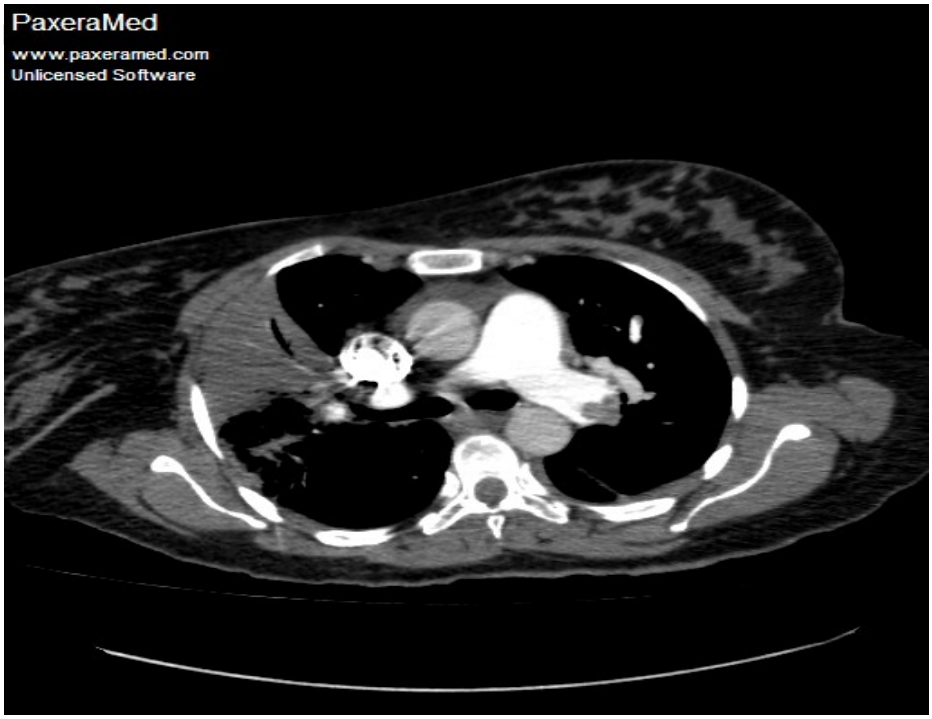

Figure: 22 Sixty-four slice MDCT in a 48-year-old woman with pulmonary embolism in the main left pulmonary artery and there is a wedge shaped pulmonary infraction in the right mid zone and left side pleural effusion.

ndix (B) Data Collection Sheet

Data Collection sheet

Patient nformation		Heart					Pulmonary Arteries				
nd	Patient history and Clinical finding	Right atrium	Right ventricle	Right ventricle shape	Interventricular septum width	Myocardium thickening	pulmonary trunk	Rt main pulmonary artery	Lt main pulmonary artery	Rt Distal pulmonary artery	Lt Distal pulmonary artery

Appendix (C) Published papers

Two papers were published:

1- Salah Eldein Hassan Aloub, Caroline Edward Ayad .Diagnostic Evaluation of Pulmonary Embolism: A Computerized Tomography Based Study , Open Journal of Radiology, 2016, 6, 157-167

2- Salah Eldein Hassan Aloub, Caroline Edward Ayad, Mohammed Elfadil Mohammed Gar Elnabi Findings Associated with Pulmonary Hypertension: CT Angiography Based Study. Open Journal of Radiology, 2016, 6, 191-201