A comparative study of conventional risk models and CT coronary angiography

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A dissertation submitted in partial fulfillment of MD Radiodiagnosis (Branch VIII) examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in April 2017

DECLARATION

I declare that the dissertation entitled **"A comparative study of conventional risk models and CT coronary angiography"** is my original work done in partial fulfillment of the requirement for MD Radiodiagnosis (Branch VIII) Degree Examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in April 2017

Dr. Geethu Elizabeth Punnen

Post graduate student (MD Radiodiagnosis)

Department of Radiodiagnosis

Christian Medical College

Vellore -632004

CERTIFICATE

This is to certify that the dissertation entitled **"A comparative study of conventional risk models and CT coronary angiography**" is the bonafide original work of Dr. Geethu Elizabeth Punnen submitted in partial fulfillment of the requirement for MD Radiodiagnosis (Branch VIII) Degree Examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in April 2017

Guide:

Dr. Elizabeth Joseph

Professor

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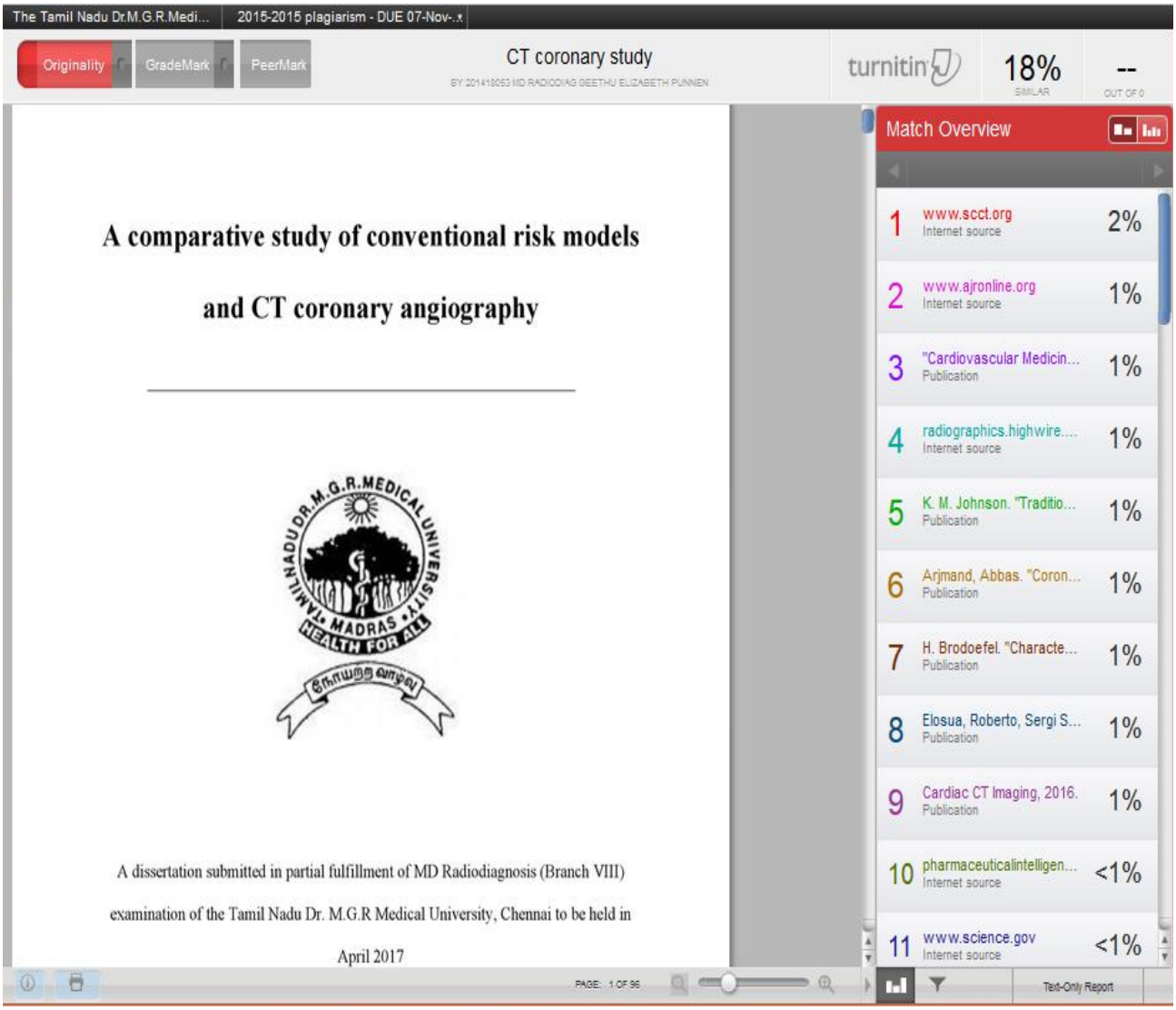

Institution review board clearance

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March 12, 2015

Dr. Geethu Elizabeth Punnen
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Sub: **Fluid Research Grant Project:**
A comparative study of conventional risk models and CT coronary angiography.
Dr. Geethu Elizabeth Punnen, PG Registrar, Dr. Elizabeth Joseph, Dr. Aparna Irodi, Dr. Binita Riya Chacko, Dr. Leena R. V, Radiology, Dr. Paul V. George,Cardiology, CMC, Vellore.

Ref: IRB Min No: 9197 [OBSERVE] dated 08.12.2014

DearDr. Geethu Elizabeth Punnen,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Alfred Job Daniel
Chairperson, Research Committee & Principal
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Cc: Dr. Elizabeth Joseph, Radiodiagnosis, CMC, Vellore.

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Ref: IRB Min No: 9197 [OBSERVE] dated 08.12.2014

Dear Dr. Geethu Elizabeth Punnen,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "A comparative study of conventional risk models and CT coronary angiography." on December 08th 2014.

The Committees reviewed the following documents:

1. IRB Application format
2. Curriculum Vitae' of Drs. Geethu Elizabeth Punnen, Elizabeth Joseph, Aparna Irodi, Binita Riya Chacko, Leena R. V, Paul V. George
3. Informed Consent form (English, Tamil, Hindi & Telugu)
4. Information Sheet (English, Tamil, Hindi & Telugu)
5. Data Collection Sheet
6. No of documents 1-5

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on December 08th 2014 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
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Fluid Grant Allocation:

A sum of 99,000/- INR (Rupees Ninety Nine Thousand only) will be granted for 15 months.

Yours sincerely

Dr. Alfred Job Daniel
Chairperson, Research Committee & Principal
Institutional Review Board
Christian Medical College, Vellore

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NOT TO BE MINISTERED UNTO BUT TO MINISTER
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Cc: Dr. Elizabeth Joseph, Radiodiagnosis, CMC, Vellore.

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I wish to express my deep gratitude to my guide Dr. Elizabeth Joseph, Professor, Department of Radiology, Christian Medical College and Hospital, Vellore for all her hard work, wisdom, expert guidance and encouragement throughout the work on my dissertation.

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And to the Lord Almighty for all his blessings, throughout my life

TABLE OF CONTENTS

INTRODUCTION

Coronary artery disease (CAD) is a pathologic process that affects the coronary arteries resulting in its narrowing or complete blockage, and is most commonly caused by atherosclerosis. Atherosclerosis is the process by which cholesterol and fatty deposits build up along the inner walls of arteries resulting in its narrowing, thereby restricting blood flow to the muscles of the heart.

In both developing and developed countries, coronary artery disease is one of the leading causes of mortality and morbidity. Although deaths due to coronary heart disease (CHD) have reduced over the past few decades, it is still the leading cause of death, accounting for 17.3 million deaths per year. By 2030, this number is expected to increase to more than 23.6 million(1). 80 % of global deaths due to CHD occurs in low and middle income countries(1).

Indian Scenario:

In India, the prevalence of CAD is extensive, both in rural and urban populations. The prevalence rates of CAD approaches ~ 11% in the urban population and ~7% in the rural population(2)(3). CAD has emerged as the leading cause of death in India. The mean age of presentation of CAD in our country is 5-6 years earlier than in the western population(4) and this is a cause of major concern(5). Therefore, preventive measures need to be

instituted early to delay onset of disease. It has also been noted that ischemic heart disease in India cannot be merely explained by the presence of traditional risk factors(6). There is evidence that in India and other developing countries, coronary artery disease is more prevalent among people belonging to the lower socioeconomic status(7).

Basis of prevention and treatment of coronary artery disease:

Risk stratification of patients plays a key role in the clinical management of patients as well as in preventing future disease. The concept of risk factors and its assessment was introduced by the Framingham Heart Study (FHS) several years ago. Risk factor assessment is the first step in primary prevention of CAD and also guides therapeutic management which is tailored according to the individual patients risk status(8).

Few of the conventional risk factors for coronary artery disease include hypertension, diabetes, high cholesterol and LDL levels, low HDL levels, smoking, obesity, physical inactivity, age and postmenopausal status(in women) and family history of premature CAD(8). Framingham risk scoring systems along with NCEP risk grading categories predicts the probability of developing a coronary artery event in the next 10 years. These systems thereby justify the initiation of pharmacological therapy as primary prevention in those patients in those with high risk status (>20% risk of developing CAD in 10 years)(8)

In most tertiary centers, a variety of investigations are used to diagnose CAD and plan their clinical management.

Noninvasive testing of atherosclerotic burden:

Various noninvasive tests and imaging modalities have the potential to identify early coronary artery disease. These include exercise tolerance testing (ETT), stress echocardiography, SPECT scan, calcium scoring, cardiac CT and cardiac MRI.

Non- invasive imaging modalities are efficient screening tools and help in detecting, measuring and monitoring CAD in asymptomatic individuals.

Non-invasive modalities are more suitable for low / intermediate risk patients as they help identify those patients, who despite of their lower risk have significant coronary artery disease and are likely to require coronary revascularization.

Gold standard:

The gold standard for detecting and quantifying coronary artery disease is coronary angiogram (CAG). Often, majority of high risk patients directly undergo coronary angiogram to assess the need for revascularization procedures.

Risk factor scoring systems and noninvasive imaging techniques – role in management

Risk factor scoring systems thereby act as “gatekeepers” for noninvasive imaging techniques. This makes little sense as it has been well acknowledged that conventional risk

scoring systems have multiple limitations leading to under treatment of low risk patients with subclinical atherosclerosis(9)

This illustrates the need for correlation between the conventional risk scoring systems and noninvasive modalities of testing for coronary artery disease.

Coronary CT angiography (CCTA) is now used as a routine clinical tool to not only detect coronary artery stenosis but also a tool that can measure the severity and thereby quantify disease burden by quantifying stenosis, plaque volume and also further characterizing coronary artery plaque. Risk stratification processes primarily use traditional risk factors to guide management regarding prevention and treatment. A correlation between conventional risk scoring systems and findings on Coronary CT angiography would add significant value to the existing risk factor scoring systems in accurate prediction of coronary artery disease. Also it will validate these risk scoring systems as gate keeper’s for noninvasive imaging based on the individual’s risk estimate

AIMS AND OBJECTIVES

Aim:

To study the degree of correlation between conventional risk models as assessed by the Framingham Risk Estimates with National Cholesterol Education Program (NCEP) -Adult Treatment Panel (ATP) III guidelines, and coronary atherosclerotic disease burden as estimated on coronary CT angiography in a tertiary care hospital in South India

Objectives:

1. To determine the Framingham risk estimate and NCEP Core risk category among patients referred for a coronary CT angiography
2. To assess the calcium score (CACS), segment involvement score (SIS), segment plaque score (SPS), segment stenosis score (SSS) and Modified dukes prognostic index (MDPI), which indicates disease burden, based on coronary CT angiography in the same group of patients
3. To correlate burden of coronary artery disease as determined by the CT scores with the conventional risk scoring systems
4. To describe plaque characteristics as non-calcified, mixed or calcified plaques based on their lipid, fibrous and calcium content.

REVIEW OF LITERATURE

Coronary artery disease (CAD), a complex chronic inflammatory disease, is typically characterized by remodeling and narrowing of the coronary arteries which supply oxygen to the heart. Atherosclerosis is the main etio-pathogenic process that causes CAD. Atherosclerosis is a silent chronic and progressive process characteristically resulting in accumulation of lipids, fibrous elements and inflammatory molecules along and within the walls of arteries. The onset and progression of disease is multifactorial and an interplay between environmental and genetic factors (Figure 1)(10).

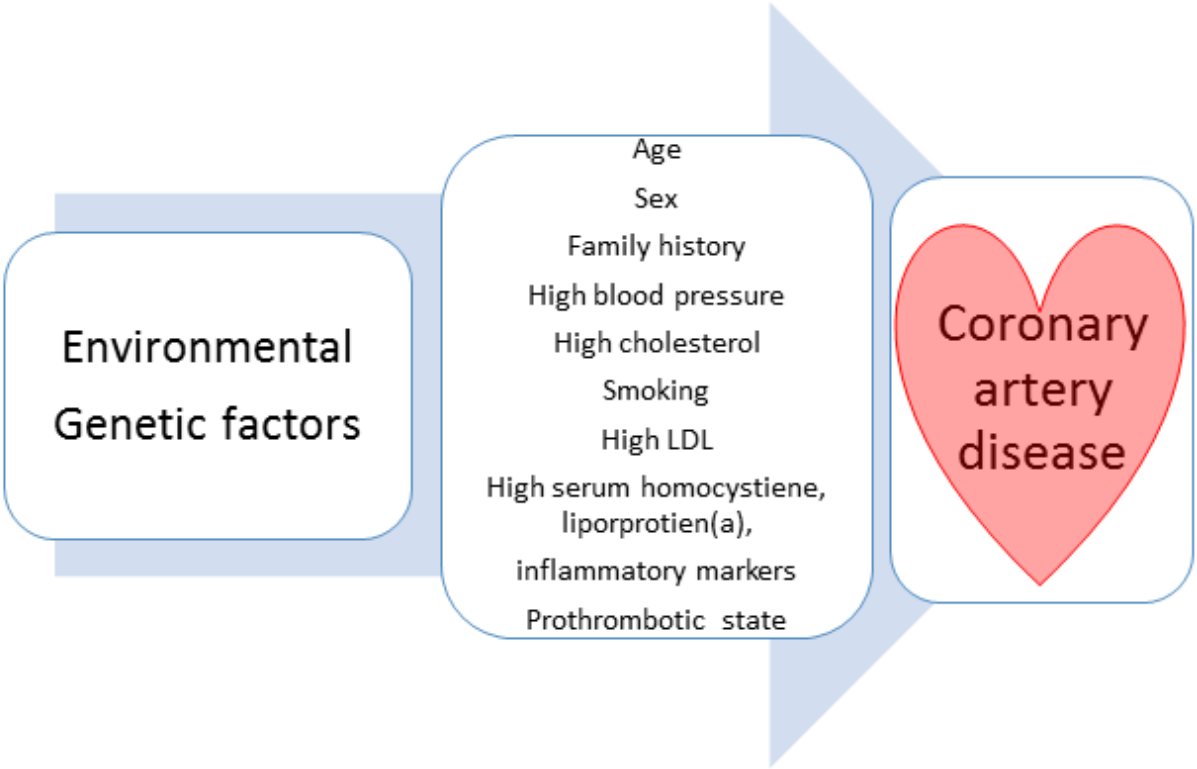


Figure 1:Multifactorial interplay between environmental and genetic factors in the onset and progression of coronary artery disease

Pathophysiology of plaque formation:

Atherosclerosis is a progressive process involving a vessel wall which ranges from early inflammatory changes in the vessel wall, lipid accumulation, minimal to severe plaque with calcification or rupture resulting in narrowing of the vessel lumen (Figure 2).

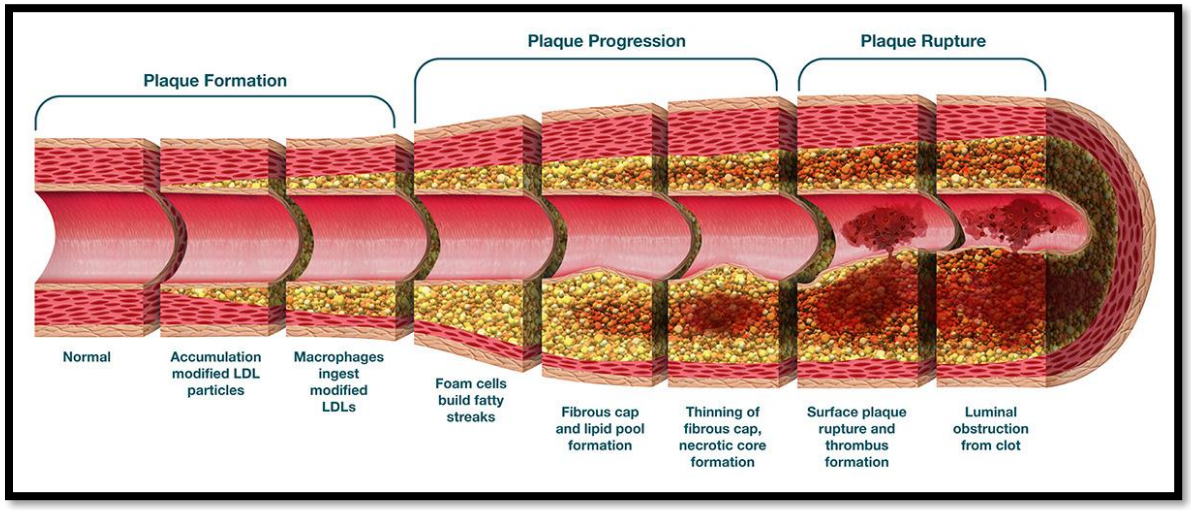


Figure 2: Pathophysiology of plaque formation
Image courtesy: essential interventional care.pdf – www.multimedicsllc.com

The first step in plaque formation is the efflux of LDL into the subendothelial space. The LDL molecules then get modified and oxidized by various agents to cause monocyte adhesion, followed by their migration into the subendothelial space. These monocytes, on reaching the intima differentiate into macrophages. Macrophages act as scavengers of LDL and become foam cells. Foam cells cause surrounding inflammation by the release of various cytokines and inflammatory markers resulting in the formation of a fatty streak. Further progression results in migration of smooth cells from the media into the intima. These smooth muscles cells produce a fibrous cap. This fibrous cap covers the initial fatty

streak. The foam cells within the fibrous cap become necrotic and release lipids which forms a necrotic core within the fibrous cap forming a fibrotic plaque.

The thickness of the fibrous cap differentiates the plaque into a stable plaque and unstable plaque. A stable plaque has a thick fibrous cap and it protrudes into vessel lumen, producing flow limiting stenosis. Vulnerable plaques have a thin fibrous cap. They are hence prone to erosion and rupture. This exposes the core of the plaque to circulating proteins which cause thrombosis and sudden occlusion of the artery lumen. This usually causes an acute coronary syndrome.

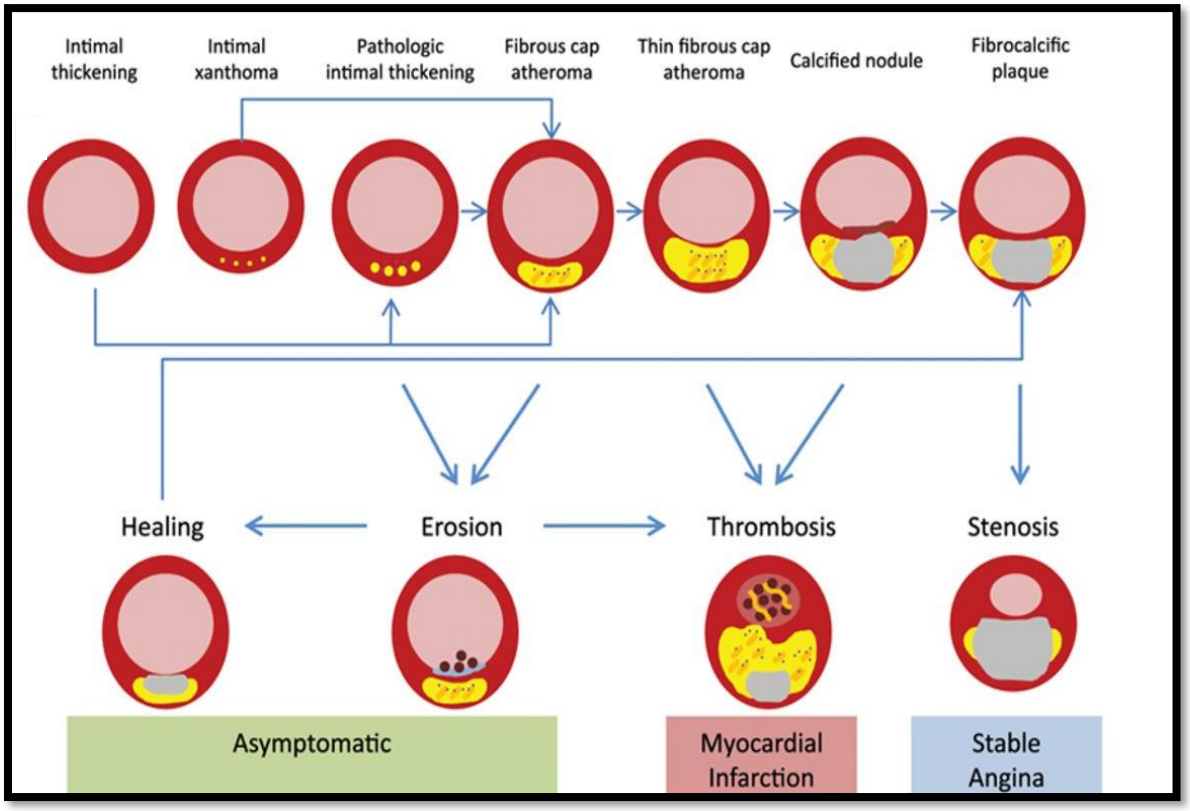


Figure 3: Depicts nonlinear atherosclerotic progression. Early plaque can lead to asymptomatic healing or erosion and lumen thrombosis and myocardial infarction. Repeated cycles of rupture and healing might lead to the more stable lesion with luminal narrowing and stable angina. Image courtesy: Veit Sandfort et al. Circ Cardiovasc Imaging. 2015;8: e003316

Epidemiology of coronary artery disease:

Coronary artery disease as described earlier is the leading cause of mortality in the world(11). It is also the leading cause of death in India with its contribution to mortality rising with the rapid urbanization, change in lifestyle, physical inactivity and presence of other risk factors(3). India currently is in a state of epidemiological transition where the burden of communicable diseases have decreased and are replaced by an increasing prevalence of non-communicable diseases(12). The prevalence of CAD is extensive, both in rural and urban populations. The prevalence rates of CAD approaches ~ 11% in the urban population and ~7% in the rural population(2)(3). Indians are also shown to have a higher risk factor burden at much younger ages as compared to Western populations. Though earlier studies on migrant Indians suggested that conventional risk factors did not account for the high burden and premature onset of coronary artery disease, the large cross sectional INTERHEART study which recruited inhabitants from all continents and 52 countries with a significant number of Indian subjects concluded that conventional risk factors did account for the significant CAD burden(13). However, for all practical purposes, all conventional risk prediction models used are developed in Western countries. There are currently no specific risk models that are based on Indian data. Western risk scoring systems may not be suitable for the Indian population and may actually underestimate CHD risk in Indians. Due to lack in evidence regarding risk based coronary artery disease prediction models in the Indian population, physicians do not have a choice but to adopt risk scoring systems used for western population.

Risk factors of coronary artery disease:

Conventional risk factors for coronary artery disease were established by the Framingham heart study several years back. They can be divided into modifiable and non-modifiable risk factors. Modifiable risk factors include hypertension, diabetes, obesity, dyslipidemia, physical inactivity and smoking. Non modifiable risk factors are age, sex and family history of CAD.

Risk stratifying algorithms and scoring systems:

Risk stratifying algorithms are for use in healthy individuals to help guide prevention strategies. Risk factors for atherosclerosis and coronary artery disease(CAD), including age, sex, lipid levels, smoking, blood pressure and diabetes are incorporated in risk algorithms to predict an individual's absolute risk for CVD in the general population.

Various risk stratifying algorithms have been developed to suit various population groups in the world such as the Framingham Risk scoring system (USA), SCORE (Europe), PROCAM (Germany), ASSIGN (UK) etc.

Widely used risk assessment tools like the Framingham risk score (FRS) or the National Cholesterol Education Program guidelines guide initial management of patients at risk for coronary artery disease. Based on the Framingham Risk Score (FRS) and the NCEP guidelines, a person with a <10% likelihood of developing a cardiac event in the next 10

years is considered to be low risk, while a person with a >20% risk of developing a cardiac event in the next 10 years is considered to be high risk. Although these risk factors are useful to predict risk in populations, their accuracy in predicting cardiovascular risk in individuals varies considerably across populations(14). This can potentially lead to patients in high risk CHD group with limited or no plaque to be treated to life-long drug therapy, and those with low risk CHD but with significant plaque might be undertreated or not treated at all.

Each of these risk scoring algorithms have their own limitations, leading to inappropriate treatment especially in the setting of subclinical atherosclerosis. Thereby, as compared to risk estimation charts, imaging is probably superior in predicting the risk of a coronary event since:

- Imaging allows direct visualization of coronary artery plaque as an evidence of atherosclerosis. This is better than identifying just risk factor exposure.
- Re-classification of low-risk subjects based on risk algorithms into a strata of higher risk if coronary artery disease is identified on imaging, will help guide therapy.
- The identification of patients with higher plaque will encourage and might improve adherence of patients to risk-modifying therapy(15).

Noninvasive imaging assessment of coronary artery disease:

Figure 4 illustrates the capabilities of various imaging techniques (Fig 4A) to delineate each pathological correlate of CAD (Fig 4B). Optical coherence tomography (OCT) and intravascular ultrasound (IVUS) are modalities that are capable of detecting earliest phases of plaque formation such as the intimal xanthoma or pathological intimal thickening. These are however invasive methods. In contrast, computed tomographic (CT) calcium score imaging (non–contrast imaging) detects a later stage plaque with calcification. Coronary CT angiography (CCTA) can detect earlier lesions such as fibrous cap atheroma without calcification.

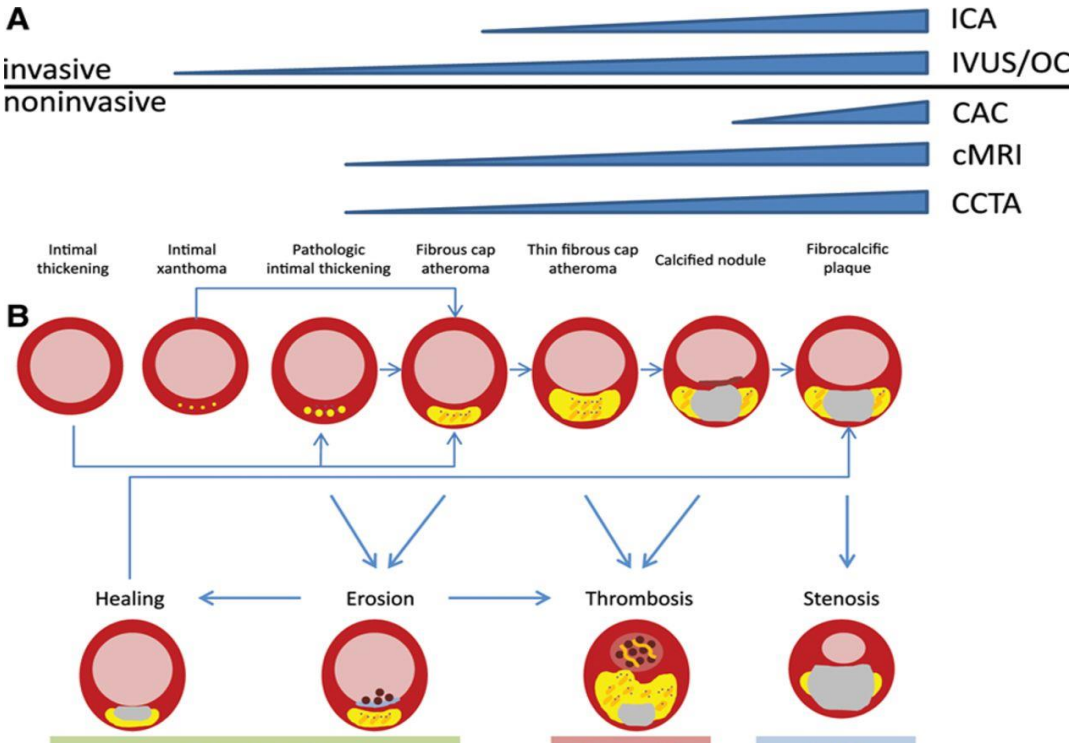


Figure 4 A,B: Depicts nonlinear atherosclerotic progression as seen previously (B) with the imaging modality likely to pick up each of these stages of atherosclerosis. Image courtesy: Veit Sandfort et al. Circ Cardiovasc Imaging. 2015;8: e003316

Coronary CT angiography

Coronary CT angiography (CCTA) has found its way into clinical practice as it is an accurate noninvasive method for the evaluation of coronary artery disease (CAD), stenosis severity, extent, and distribution of disease. Its greatest advantage is that is allows direct visualization of plaques, enabling its characterization, an advantage over conventional catheter coronary angiography which is the established gold standard.

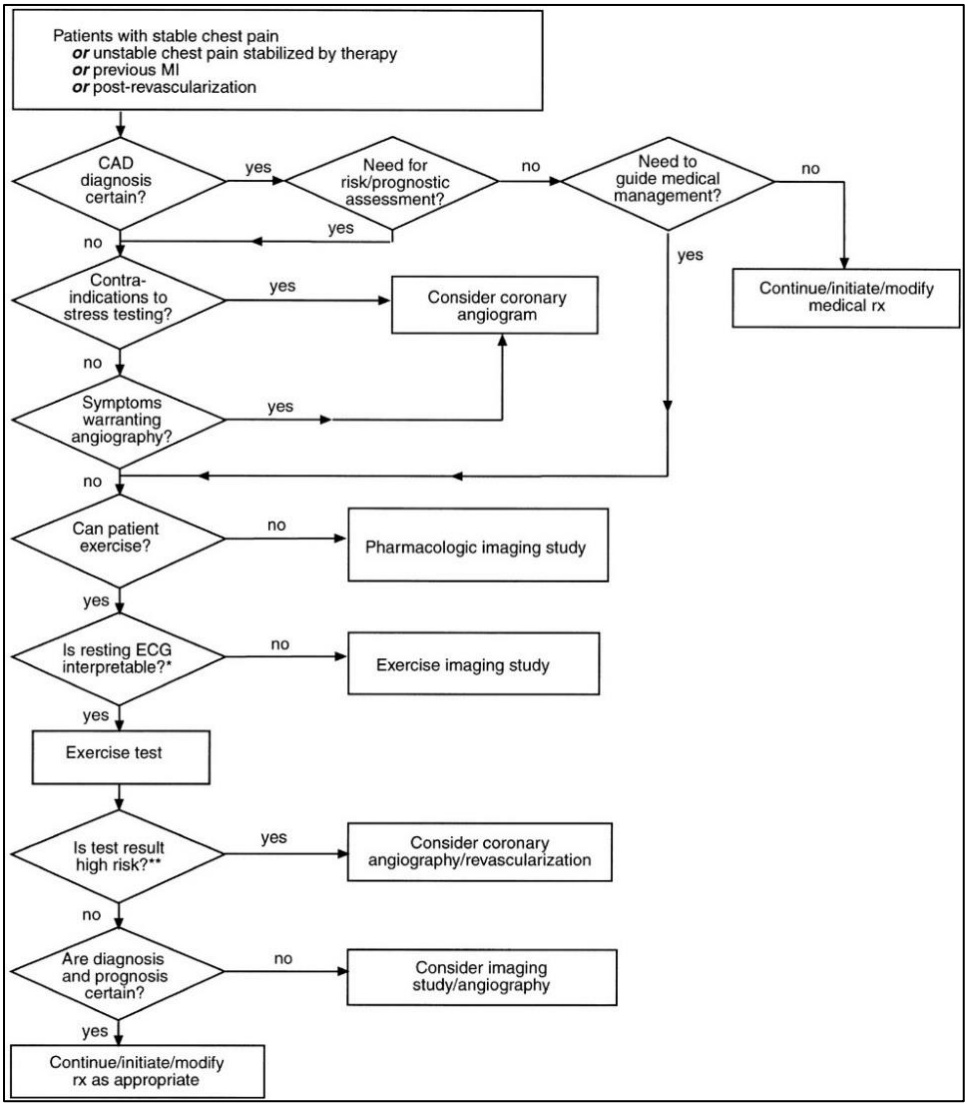


Figure 5:Clinical context for non-invasive and invasive diagnostic testing of patients with known or suspected ischemic heart disease, AHA 1999Patrick J. Scanlon et al. Circulation. 1999; 99:2345-2357

Coronary CT angiography has therefore replaced invasive cardiac catheterization in a selected group of patients (Figure5).

What is CT coronary angiogram?

It is a noninvasive test that uses computed tomography (CT) to image the beating heart. Good visualization of the coronary arteries and diseases affecting it enables accurate detection and grading of the stenosis. Also, it plays an important role in assessing other anomalies in individuals with suspected coronary artery disease.

Rationale for imaging

Imaging plays a role in screening of asymptomatic patients for subclinical or occult atherosclerotic disease which may not be detectable on conventional noninvasive testing. This is especially true in low and intermediate risk patients (16). Small group of asymptomatic patients with high risk factors may also benefit from this noninvasive imaging modalities. Preoperative screening for clearance in patients with suspected coronary artery disease undergoing non cardiac surgery is an established indication.

CT coronary angiography has a high negative predictive value, and this is of significant clinical value in evaluation of patients with low or intermediate Framingham risk estimates

with atypical chest pain since there is considerable concern regarding the possibility of an underlying cardiac etiology for the chest pain. The need for an invasive coronary angiogram is obviated if the CT coronary angiogram is normal and calcium score is zero.

In patients who present with atypical chest pain to the emergency department and identified to have acute coronary syndrome with low to intermediate risk features, CT coronary angiography is a quick, noninvasive test to "rule out" coronary artery disease. Also other causes of chest pain like acute pulmonary embolism and aortic dissection can also be excluded, by what is thereby popularly called the "triple rule out" study. This avoids unnecessary and expensive admissions for patients whose symptoms do not have a cardiac etiology(16).

Patient preparation:

Patient preparation prior to study is essential to obtain good quality images as well as reduce risk of possible adverse effects related to contrast and radiation dose.

Heart rate control:

Heart rate control is a significant part of patient preparation. Slow heart rates enable acquiring of images free of motion artefacts at points of minimal motion of the heart. Also

ECG gating is possible at slow and regular heart rates and thereby allows ECG gated dose modulation and subsequent reduction of radiation doses. Heart rate of 55-65 beats per min is highly desirable.

Drugs used for heart rate control:

Oral β-blockers and Ivabradine, which is funny channel blocker are drugs that are commonly used to control heart rate(17). It is important to ensure that there are no contraindications to heart rate controlling drugs such as heart block, severe aortic stenosis or asthma. When β-blockers are contraindicated, nondihydropyridine calcium channel blockers may be used.

Vasodilatation and anxiolytic methods:

Sublingual nitroglycerine or nitroglycerine spray is used just prior to scanning will cause coronary vasodilatation and thereby increase visualization of all branches including the septal branches and relieve any non-fixed abnormality like coronary spasm. This increases the overall diagnostic quality of the study. Patients should be well hydrated prior to study to avoid sudden hypotension or arrhythmias during the study due to the effect of above mentioned drugs. Heart rate as well as blood pressures need to be monitored prior to the study.

An anxiolytic drug such as midazolam or lorazepam will calm the patient and prevent sudden rise or irregularity in heart rates at the time of scan. Rehearsal of breathing instructions prior to the scan is advantageous as it improves patient compliance, reduces anxiety and as a result reduces motion artefacts. It also helps in identifying any heart rate irregularities that may develop on breath holding(17).

Safety aspects of patient medication:

All medications are administered by trained nursing staff under the supervision of a doctor. According to protocol for any imaging study requiring medication, blood pressure and heart rate prior to first dose of drug is measured, followed by after the study and at the time of discharge. Since this is an outpatient procedure, patients are observed for 30 min after the study to ensure that there are no adverse effects related to the medication or contrast administered.

Contrast related preparation:

Documentation of any allergies, asthma or hypersensitivity reaction and premedication with anti-allergic medication and prednisolone or IV hydrocortisone decreases the risk of allergies with contrast injection. Serum creatinine values need to be checked to ensure normal renal function. If renal function is borderline or compromised in patients planned

for a CCTA, caution with regard to use of contrast agents is necessary. Informed consent is obtained prior to contrast administration. Intravenous access with a large bore IV cannula in the right cubital vein is preferred since contrast is injected at high flow rates of about 5ml/second.

Patient positioning and ECG lead placement:

Patient is positioned supine and usually feet first position in the scanner gantry. ECG leads (3 or 12 lead ECG) is connected ensuring good electrical contact. Using additional conductive gel and shaving the chest if very hairy are recommended to prevent lead detachment during scan acquisition.

ECG gating:

ECG gating during cardiac imaging is a method that uses information from electrocardiographic signal to time the cardiac cycle and hence enable selective acquisition of images at specific points in the cardiac cycle. Gating techniques help in improving temporal resolution and minimizing motion related imaging artifacts. Also, gating allows for reduction of radiation doses.

Two approaches are commonly used for cardiac gating – Prospective and retrospective ECG gating. Cardiac motion is the least during diastole, when passive filling of the

ventricles takes place. So in prospective ECG gating, ECG signal is used to acquire data only during cardiac diastole, by generating X-rays and receiving projection data only during cardiac diastole. This reduces the total radiation dose to the patient. However, prospective ECG gating and triggering have its limitations. It is effective only for slower heart rate as it is sensitive to heart rate changes and arrhythmias. In order to overcome these limitations, retrospective gating is used. Retrospective gating allows faster coverage of the cardiac volume with improved z axis resolution. Imaging happens throughout the entire cardiac cycle. But this is at the expense of high radiation dose. Also, since the entire cardiac cycle is imaged, functional analysis can also be performed(18) (19).

Scanning techniques and parameters:

Collimation and gantry rotation:

Since the anatomy to be imaged is minute and in continuous rapid motion, at CT coronary angiography, the universal rule is that regardless of the scanner used, the collimation chosen should be the thinnest possible and the gantry rotation time chosen should be the fastest possible.

Tube current and voltage:

Tube current and voltage adjustment is patient specific so that the lowest possible tube current setting is used in keeping with the ALARA (as low as reasonably achievable) principle(16). Adjustments are made based on patient's body habitus such that a diagnostic study is obtained. For example, when scanning a normal sized adult for suspected CAD, using a 64 slice CT scanner with 0.625mm collimation and 330msec gantry rotation a tube current of 400Mas, with pitch ranging from 0.20 to 0.43 depending on the heart rate is adequate. In thinner adults a lower kV can be used(16).

Contrast:

High vascular enhancement is required to visualize the coronary arteries and their branches. Therefore, a high concentration of intravenous iodine containing nonionic contrast media with a fast injection rate (5ml/sec) is used. A saline chaser is used to prolong the plateau phase of contrast enhancement and also reduce streak artefacts as when present they can simulate stenosis of the RCA and result in its improper evaluation.(16) Individual scan delay time is determined by using a test bolus or by automated attenuation based triggering at a predetermined attenuation within the ascending aorta. The total amount of contrast including the test bolus used for a CT coronary angiography study ranges from 80 -115ml

Radiation dose optimization:

Applying the ALARA principle is crucial in radiation safety and dose optimization. Prospective ECG gating should be used where possible. In cases were retrospective gating is required, ECG gated dose modulation technique should be used to reduce radiation. Scan range and scan protocols should be tailored to each patient. Scan range should be set inferior to shoulders. This prevents the automated prescribed mAs being set for the width of the shoulders instead of the thorax. Scan protocols are planned based on the patient's weight or BMI. For smaller patients, as discussed earlier, tube voltage should be reduced to 100 kVp with corresponding increase in tube current to account for the increase in image noise. For each patient, displayed predicted computed tomography dosage indicator vol (CTDIvol) and the displayed dose length product should be documented and reviewed at time of reporting(17).

Image reconstruction and post processing:

CT coronary angiogram studies are acquired as sub millimeter ECG gated data sets which can be reconstructed and displayed in various imaging formats for diagnostic purposes. Dedicated workstations that allow 2D and 3D reconstructions and reformation such as multiplanar reformation(MPR), maximum intensity projection(MIP), curved multiplanar reformation(cMPR) and volume rendering techniques(VRT) should be available for use.

Various workstation have been developed by providers such as GE, Terarecon, Toshiba to name a few.

Raw data:

Raw data consists of 2 dimensional images which are stacked in the cranio-caudal direction or the z axis as they were acquired. Scrolling through the slices displays the coronary and cardiac anatomy with minimum distortion or errors related to post processing. The main disadvantage of reading from a raw data set is that the reader has to mentally reconstruct in 3 dimensions the arteries and its anatomical relation with other structures in the thorax(20).

Optimal window choosing:

Window level and window width needs to be adjusted for accurate interpretation. This is crucial to differentiate calcified plaque from normal contrast containing lumen and to distinguish intramural non calcified plaque from interstitium. Ideal window level should be at the mean of HU values within the region of interest, and 2.5 times the window level should be the corresponding window width(20). The reader often will have to make readjustments of window width and level, though a useful starting point for initial use is a window width of 800 and a window level of 300.

In order to assess cardiac morphology, the phase with minimum cardiac motion is selected. Relative percentage based approach of determining the point in the cardiac cycle is widely practiced. This means that the cardiac cycle is divided into 20 image sets reconstructed at different R -R positions in 5% increments or as 10 image sets in 10% increments (0% - 95% RR interval). The 60% R-R position yields good diagnostic quality images of the coronary in most patients. However, different R-R positions can be chosen for RCA and LCA based on their least motion(16).

Image reconstruction parameters

Field of view:

In order to maximize spatial resolution, it is essential that the smallest possible field of view that covers the entire anatomy of the heart is chosen. In addition, often full field of view of the chest is acquired along the z plane in lung algorithm to look for concurrent lung abnormalities. When the indication for scanning is triple rule out, specifically tailored protocols are used to include vascular phase of aorta and the pulmonary arteries.

Reconstruction kernel:

Kernels are dedicated reconstruction filters used for CT angiography. They help in providing a degree of edge enhancement to enable better visualization of smaller vascular detail by improving spatial resolution. They suppress image noise and thereby improve visual impression and contrast resolution between vessel wall and myocardium(16).

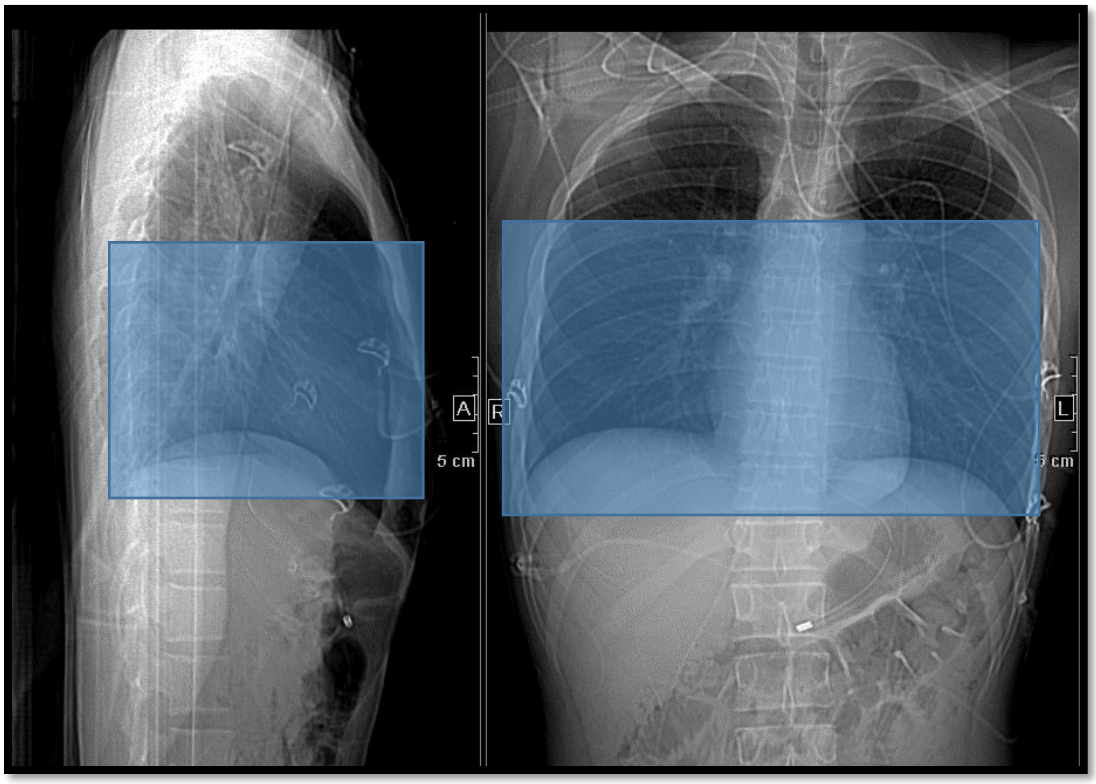


Figure 6: Planning scanogram prior to CTCA, with ECG leads connected for ECG gating. Blue box indicates the area to be scanned

Interpretation formats:

Calcium scoring:

Calcium scoring involves a preliminary non contrast examination to look for calcification of the coronary arteries as well as the valves and pericardial surfaces. Dedicated computer software programs are supplied by vendors which recognize pixels above 130 HU in a non-contrast study, as levels corresponding to calcium. The reader identifies each discrete calcific focus in the respective vessel distribution. A summed score for each vessel and for the total study (sum of all vessels) is calculated based on an area-density scoring system (Agatston) or volumetric measurement of each calcific focus(20). Calcium score in aorta, aortic valve, mitral valve and annulus, myocardium and pericardium is separately mentioned.

Multiplanar reconstruction(MPR):

MPR is the most commonly used alternative reconstruction format. It reconstructs planar images at any angular section through the acquisition plane. This allows visualization of the coronaries in the axial, orthogonal and oblique planes that are along the course of the arteries in the thorax. The result of these reconstructions are images that are similar to the familiar invasive angiography views. Usually, for MPR reconstruction, the thinnest available slice width is used. Workstations allow rotation of vessel on its longitudinal axis for 360 degrees or also scroll through transverse cuts through the length of the vessel

(Figure 7). These techniques help in identifying plaque, assessing its morphology and effect on the lumen and the adjacent vessel wall. Curved MPR format produces the entire course of the vessel in one image (Figure 9). For accurate interpretation, the centerline of the vessel needs to be tracked correctly, else can cause artefactual lesions. Advantage is that longer course of vessels, especially if they are tortuous with change in direction can be followed and visualized

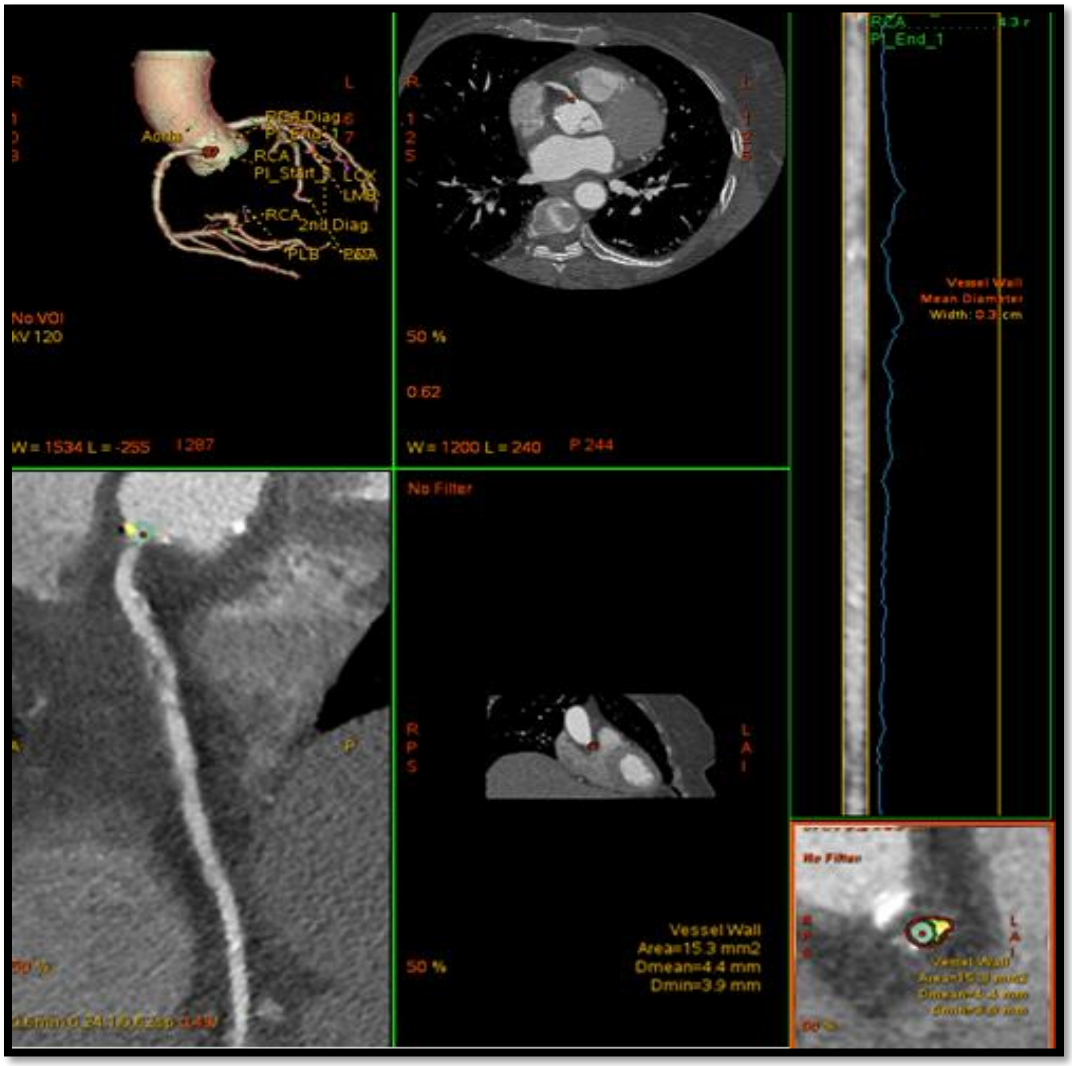


Figure 7:Example of workstation interface which allows multiplanar imaging

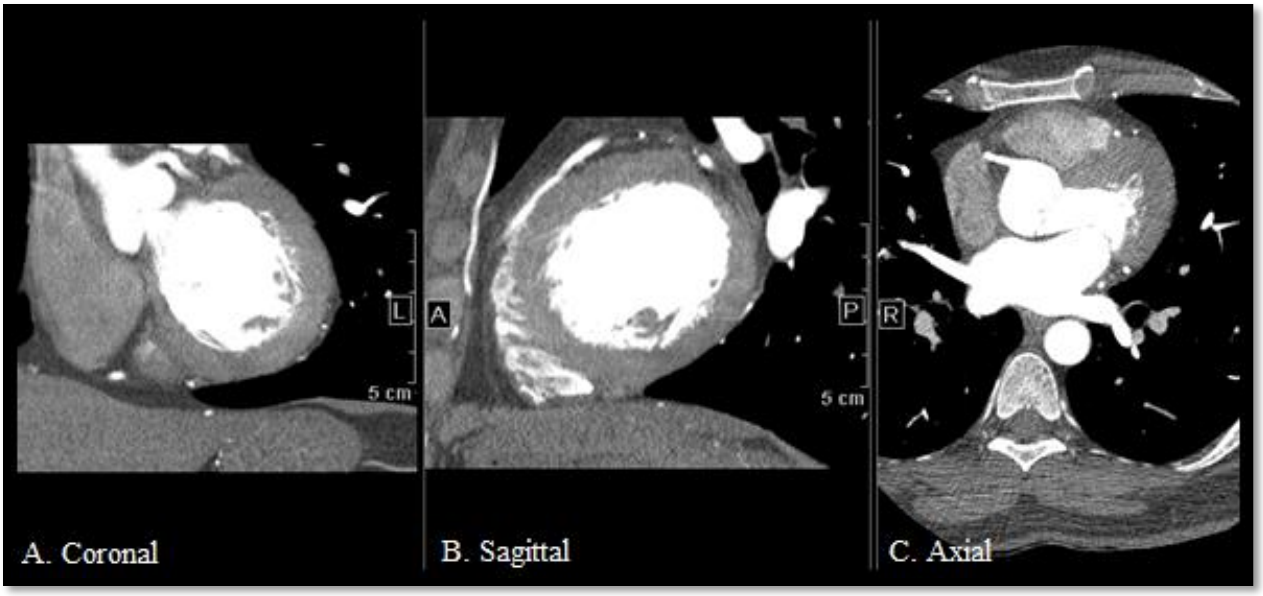


Figure 8: Basic reconstruction in the 3 standard imaging planes

Maximum intensity projection (MIP):

MIP and MPR though similar in the fact that various orthogonal and oblique views can be assessed, MIP is reconstructed in thicker sections to include the entire volume of the vessel and wall diameter (commonly used thickness for interpretation is 5mm) (Figure 10B). Longer segment of vessel is viewed with reduction in noise. But there is lack of detail regarding lesion or its attenuation characteristics. Therefore, MIP is never used as the sole technique for interpretation.

Volume rendering technique (VRT):

Commonly used technique that creates volumetric 3 dimensional representations of the cardia or coronary vasculature with an illusion of spatial integrity and color (Figure 10A). Spatial relationships are well demonstrated but this technique has limited use in the evaluation of coronary artery disease. Window settings and computer algorithms can affect apparent thickness of vessels. It is of better use in visualizing coronary anomalies, presence and position of bypass grafts and for patient illustration, education and counselling(20).

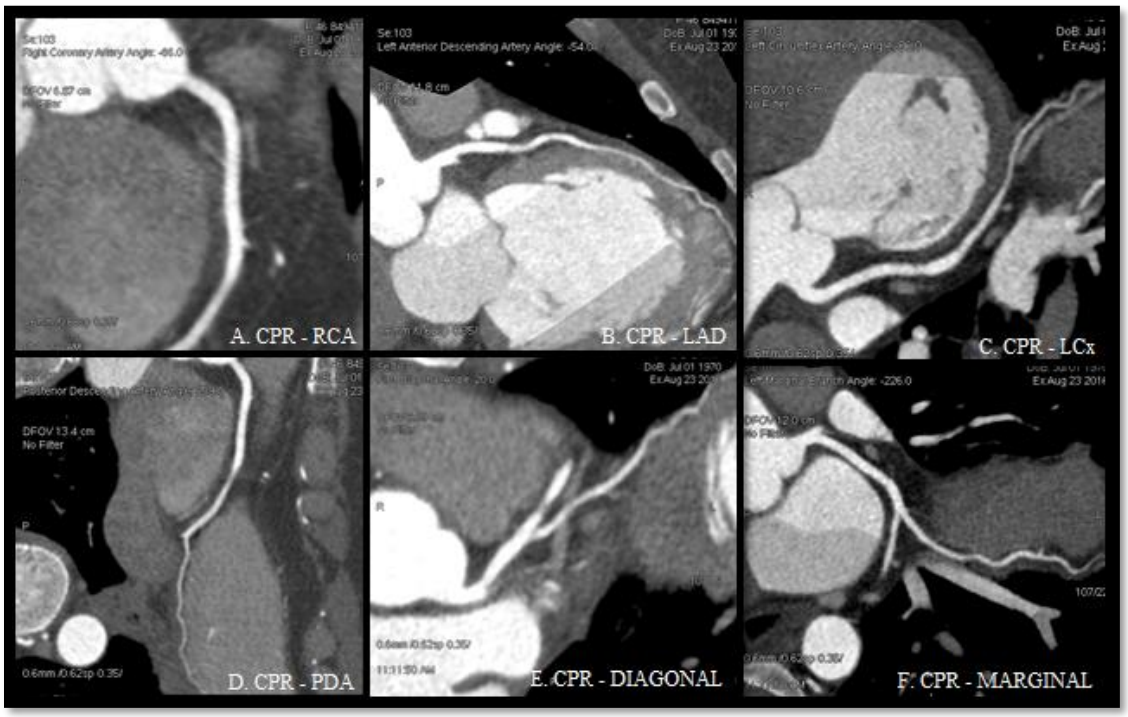


Figure 9, A- F: Curved MPR images of the coronaries allow visualization of the entire tortuous course of the arteries in one image

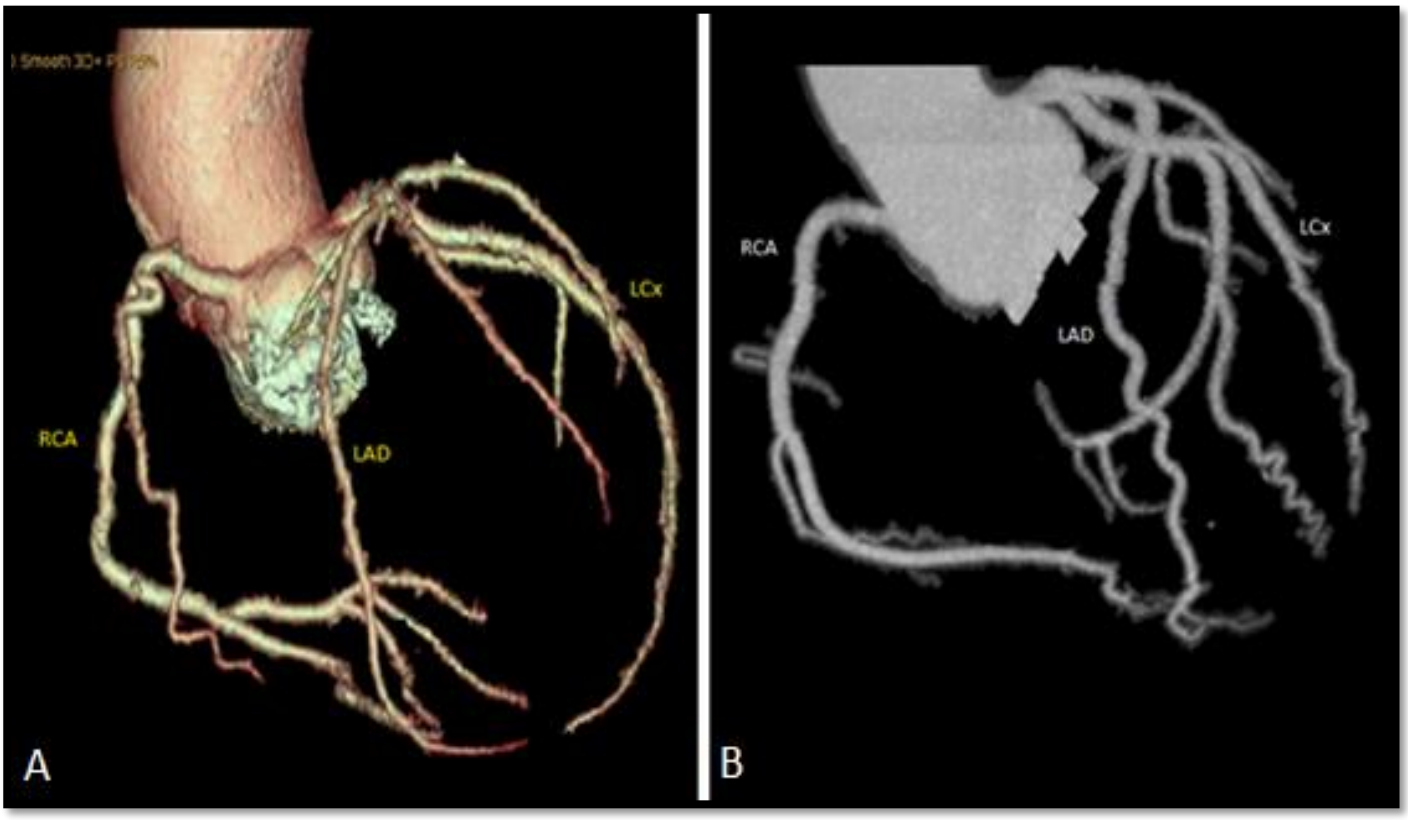


Figure 10: A- volume rendered reformation of the aortic root and the coronaries; B – Maximum intensity projection (MIP) images of the aortic root and the coronary arteries

Coronary artery anatomy:

The heart is supplied by two main coronary arteries namely the right coronary artery and the left main coronary artery. These arteries arise from the aorta and it receives 5% of the total cardiac output.

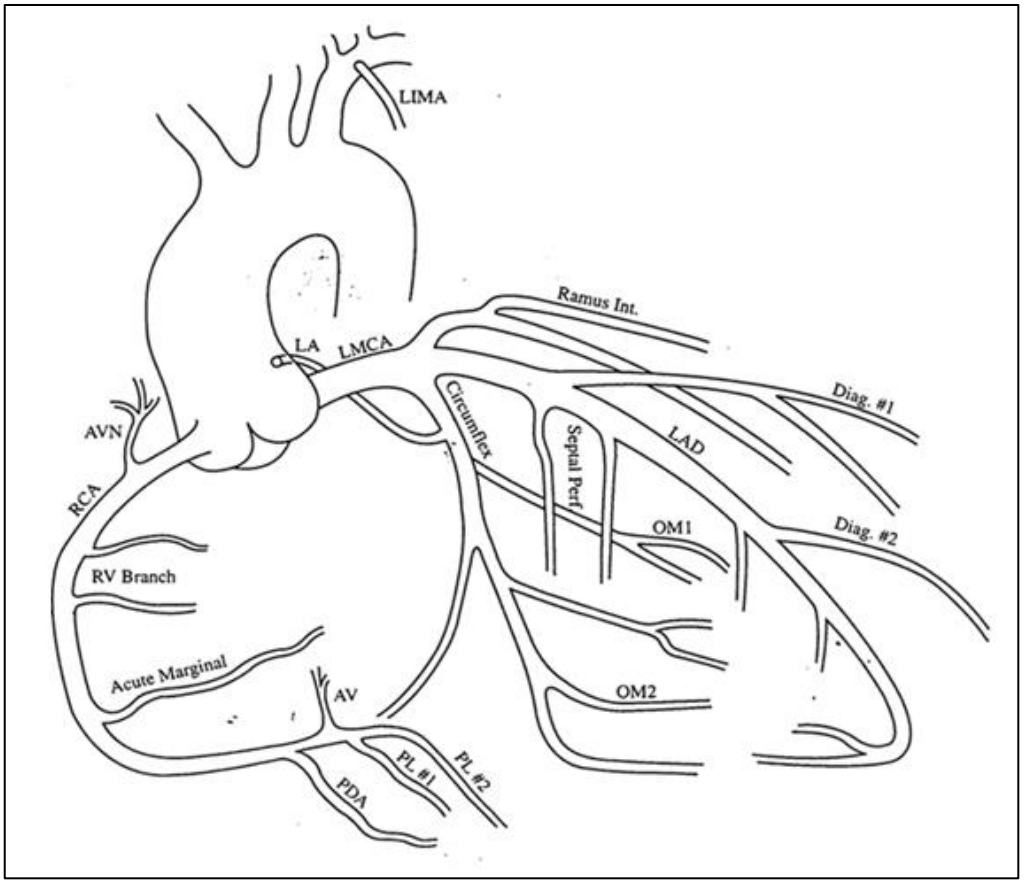


Figure 11: Diagrammatic representation of the coronaries arteries and their branches. Image courtesy: www.meddean.luc.edu

Left main coronary artery (LMCA):

The LMCA arises from the left sinus of Valsalva, near the sinotubular ridge in the region of the left coronary cusp. Its length is variable, ranging from 10-15mm and it divides into the left circumflex artery (LCx) and the left anterior descending artery (LAD). Sometimes the left main coronary artery trifurcates into three branches, the third branch called the ramus intermedius (RI) arising between the LAD and LCx. This variation can be seen in 15% of the normal population. The RI branch course laterally along the free wall of the left ventricle, similar to the course of diagonal branch of the LAD artery.

Left anterior descending artery (LAD):

The LAD courses through the anterior interventricular groove up to the apex of the left ventricle. It lies in the epicardial fat and gives off multiple septal perforating branches which course medially and supply the anterior part of the interventricular septum, atrioventricular bundle as well as proximal bundle branch and diagonal branches which course laterally and supply the anterior free wall of the left ventricle.

The first diagonal branch (D1) denotes the distinction between proximal and mid portion of LAD. More than one diagonal branch may be seen.

Left circumflex artery (LCx):

The LCx is located in the left atrio-ventricular groove and supplies the lateral wall of left ventricle through vessels which branch off with an obtuse angle. They are hence known as obtuse marginals or also referred to as lateral marginals. They supply the lateral margin of the left ventricle and a variable portion of the anterolateral papillary muscle. In about 10 to 20% of the population, left dominant circulation is seen in which case the left circumflex artery supplies the posterior descending coronary artery.

Right coronary artery(RCA):

The RCA arises from the right coronary sinus of Valsalva and traverses the right atrio-ventricular groove towards the crux of the heart. The first branch in 50-60% cases is a small conus branch which supplies the RV outflow tract. In few cases (30- 35%) the conus artery arises from the aorta. In 60% cases, a sinus node artery arises as the second branch of RCA which runs posteriorly to the sino-atrial node (in the rest of the 40%, it originates from the circumflex artery).

The next branches are marginal branches which supply the anterior wall of right ventricle. The largest of these branches is called the acute marginal branch (AM). It comes off at an acute angle and supplies the anterior wall of right ventricle. The RCA continues down to give off a branch to the AV node. 70 to 80 % of the population has right dominant circulation in which the right coronary artery gives off the posterior descending artery which supplies the inferior wall of the left ventricle and inferior part of the septum.

Dominance:

The artery which is referred to as dominant is the artery which gives rise to the posterior descending artery (PDA) and the posterolateral branch (PLB). In 70% of cases, RCA is dominant. In 10% of cases, LCA is dominant with the LCx giving rise to the PDA and PLB. The remaining cases have a co dominant system with portions of the diaphragmatic LV wall being supplied by both RCA and LCx.

Segmental coronary artery anatomy:

Conventional coronary angiography uses a classification system that divided coronary arteries into 18 segments(21). In 1975, the segmentation model was proposed by 'The American Heart Association' (AHA). This segmentation is based on anatomic structures which act as standard landmarks.

A similar system is used in CTCA as well in order to maintain uniformity of nomenclature to aid better communication among physicians and reproducibility.

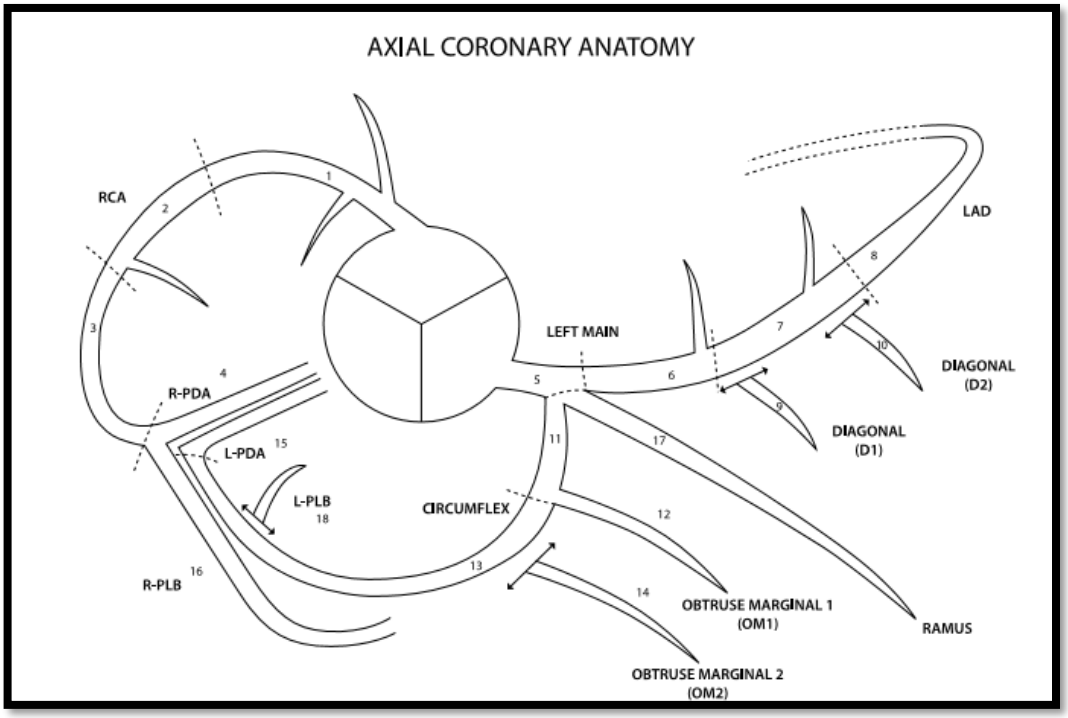


Figure 12: SCCT Coronary Segmentation Diagram

Axial coronary anatomy definitions derived, adopted, and adjusted from WG Austen, JE Edwards, RL Frye, GG Gensini, VL Gott, LS Griffith, DC McGoon, ML Murphy, BB Roe: A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. Circulation. 1975;51:5–40.

Schematic representation (figure 12) of the same have been released for use and reference by the society of cardiovascular computed tomography (SCCT)(21). The segmentation is described in detail in Table 1.

Table 1: Segmentation model of coronary arteries

Segment	Segment number	Description
Proximal RCA	Segment 1	Ostium of the RCA (right coronary artery) to one-half the distance to the acute margin of heart
Mid RCA	Segment 2	End of proximal RCA to acute margin of the heart
Distal RCA	Segment 3	End of mid RCA to origin of PDA
PDA - RCA	Segment 4	PDA from RCA
PLB – RCA	Segment 16	PLB from RCA
Left main	Segment 5	Ostium of left main to bifurcation of LAD and LCX
Proximal LAD	Segment 6	End of LM to first large septal branch or D1, whichever more proximal
Mid LAD	Segment 7	End of proximal LAD to one half of the distance to the apex
Distal LAD	Segment 8	End of mid LAD to end of LAD
Diagonal 1	Segment 9	First diagonal branch (D1)
Diagonal 2	Segment 10	Second diagonal branch (D2)
Proximal LCx	Segment 11	End of LM to origin of OM1(first obtuse marginal)
OM1	Segment 12	First obtuse marginal traversing the lateral wall
Mid and distal LCx	Segment 13	Traveling in the AV groove, distal to OM1 to the end of the vessel or origin of the L-PDA
OM2	Segment 14	Second obtuse marginal
PDA - LCx	Segment 15	PDA from LCx
Ramus intermedius	Segment 17	Vessel originating from the left main between the LAD and LCx in case of a trifurcation
PLB - LCx	Segment 18	PLB from LCx

Adapted from Society of Cardiovascular Computed Tomography published guidelines for interpretation and reporting of coronary CT angiography, 2010

Normal coronary artery diameter:

Normal coronary artery diameter has not been established with MDCT.

Focal aneurysms are defined by focal abnormal dilatation of more than 1.5 times the diameter of the adjacent coronary artery. When the coronary artery is diffusely dilated it is called as ectatic.

Analysis of coronary artery pathology:

Coronary arteries are initially studied for anomalies in the course of branching of the main coronary vessels. Any variations in their relationship to the major cardiac structures also need to be noted.

Coronary artery lumen and wall imaging:

Pathologies affecting the lumen such as focal plaque or diffuse narrowing, wall irregularity, aneurysm or ectasia need to be looked for. Overall caliber and contour of the lumen with variations in density within the vessel wall and intraluminal portion of the coronary artery need to be noted. Intraluminal plaque when present, is localized based on its segmental position as per the AHA segmentation model. Plaque characteristics are described as non-calcific with lipid or fibrous component or calcified based on its CT attenuation values (discussed later).

Assessment of burden of coronary artery disease:

Calcium score (CACS):

Arthur Agatston and his colleagues introduced the quantitative CACS protocol in 1990(22). This remains the standard method in calcium scoring. Any structure with densities of 130 Hounsfield units (HU) or more and of an area of 1mm^2 or more is segmented as a calcified focus (Figure 13). The calcified foci that overly the anatomic sites of coronary arteries are considered to represent calcified plaques. They are given stratified density scores 1, 2, 3 and 4 which represent the densities 130-199 HU, 200-299 HU, 300-399 HU and ≥ 400 HU, respectively.

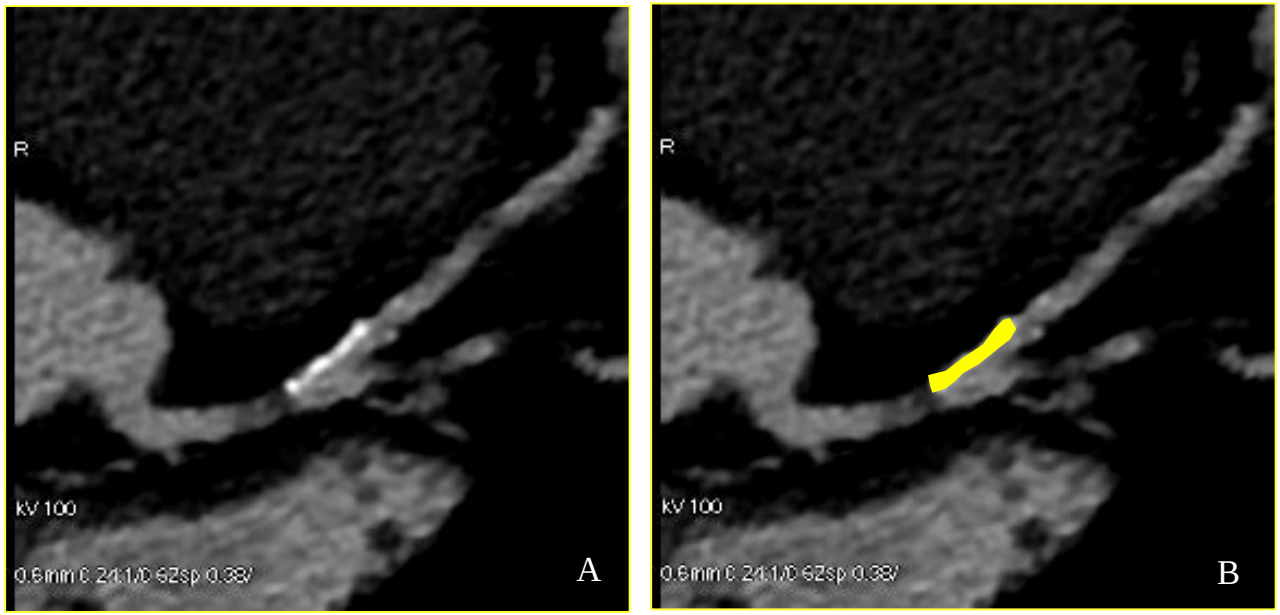


Figure 13: (A, B): Segmentation of calcium on non-contrast CT by identification of any structure with densities of 130 Hounsfield units (HU) or more and of an area of 1mm^2

The total Agatston score (AS) of each individual is calculated by summing the scores of every calcified focus through all of the coronary arteries(21). Coronary artery calcium scoring has been established as a strong tool for prediction of coronary events, reflecting the burden of coronary artery disease. Calcium scoring is considered the "gatekeeper" for CCTA.

Contrast enhanced CT in determining atherosclerotic burden:

Contrast enhanced CT of the coronary arteries provide further information with regards to presence of calcified and non-calcified plaques and the degree of stenosis, thereby arriving at an accurate estimation of the burden of atherosclerotic disease.

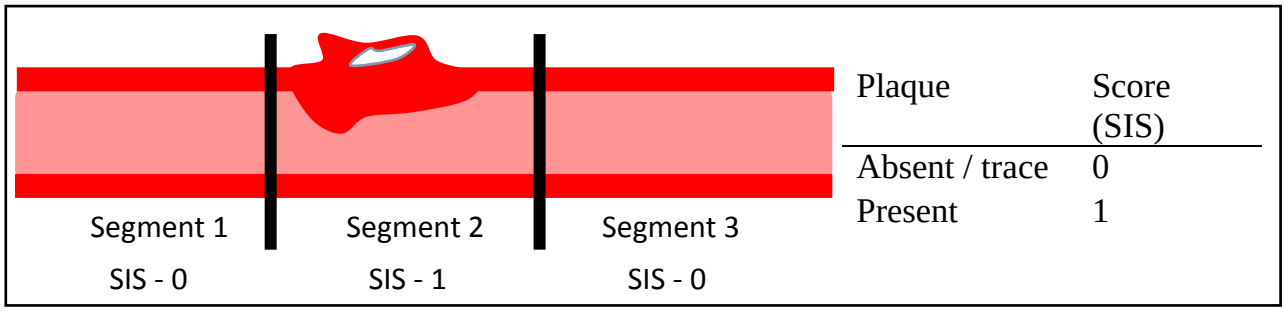
Apart from calcium scoring, various other scores have been developed to grade the amount of plaque and resultant stenosis. Johnson et al used a scoring system which utilizes 4 parameters to grade the burden of coronary artery disease(23). These are:

1. Segment involvement score
2. Segment plaque score
3. Segment stenosis score
4. Modified Duke's prognostic index

Each of the coronary artery segments are scored based on the presence of plaque and degree of stenosis. Sum of the scores of each segment gives the final scores for that particular patient(23).

Segment involvement score (SIS):

A segment of the coronary artery is scored as involved if there is plaque. Each segment is scored according to the its involvement as absent or trace or as present (Figure 14). Absent / trace plaque is scored as 0 and presence of plaque is scored as 1.

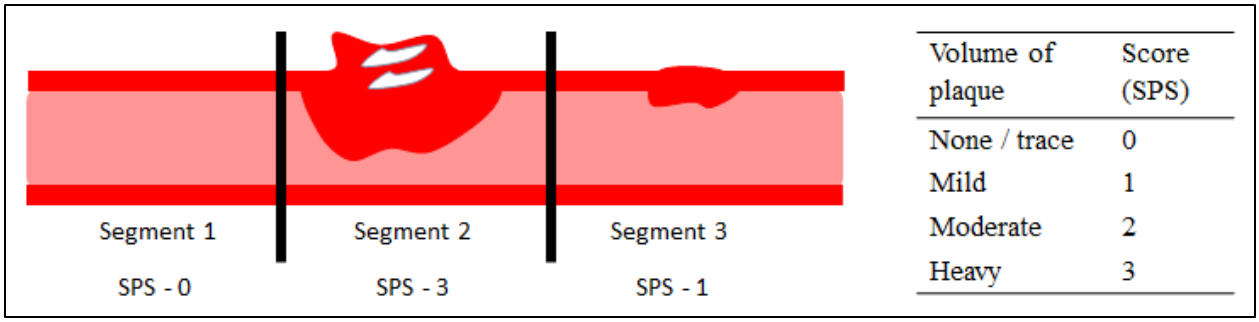


Plaque	Score (SIS)
Absent / trace	0
Present	1

Figure 14: Diagrammatic representation of estimation of segment involvement score

Segment plaque score (SPS):

The segment plaque score is an indicator of plaque burden. For each segment, the amount (volume) of plaque, whether calcified or not is scored as none or trace (0), mild (1), moderate (2), or heavy (3). When there are multiple lesions in a given segment, the segment is scored as a whole. The SPS for each patient is calculated as the sum of individual segments' burdens(23).

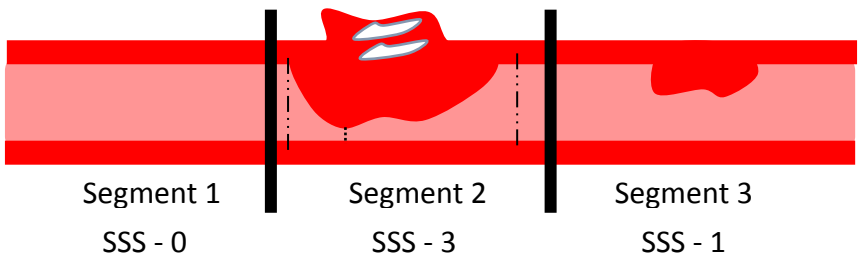


Volume of plaque	Score (SPS)
None / trace	0
Mild	1
Moderate	2
Heavy	3

Figure 15: Diagrammatic representation of estimation of segment plaque score

Segment stenosis score (SSS):

Segment stenosis score estimates the diameter of stenosis caused by the plaque. It is scored as very mild < 30%, mild 30-50%, moderate 50-69%, or severe >=70%, scored as 0, 1, 2, and 3 respectively. The sum of the individual segments is calculated as the segment stenosis score(23)



Percentage stenosis	Score
Very mild (<30%)	0
Mild (30 -50%)	1
Moderate (50-69%)	2
Severe (>=70%)	3

Figure 16: Diagrammatic representation of estimation of segment stenosis score

Modified Duke's prognostic index:

This score is derived from conventional angiography and modified to suit computed tomography coronary angiography. The Duke's prognostic index is shown to correlate with cardiac mortality. With a higher Duke's score, the risk of cardiac mortality increases(23). The modified Duke's prognostic index criteria has been described in Table 2.

Table 2: Modified Duke's prognostic criteria

Modified Duke's prognostic criteria	Description
Duke 0	No stenosis
Duke 1	Very mild/ Mild stenosis
Duke 2	Two or more mild stenoses with one proximal or one moderate stenosis
Duke 3	Two moderate stenoses or one severe stenosis
Duke 4	Three moderate stenoses, two severe stenoses, or one severe stenosis of the proximal left anterior descending (LAD) coronary artery
Duke 5	Three severe stenoses or two severe stenoses with the proximal LAD involved
Duke 6	Moderate or severe left main artery stenosis.

Plaque characteristics

Plaques in the coronary arteries due to atherosclerosis are primarily asymmetrical focal areas of intimal thickening. The result from accumulation of various components such as foamy macrophages, smooth muscle, necrotic debris and calcium.

Pathological studies have shown that components of plaque have an important role to play in the pathophysiology of coronary artery disease. Acute coronary syndromes which present with acute chest pain are often result of plaque rupture(24). Plaque rupture is related to high percentage of intra-plaque lipid core within non-calcified plaques.

Therefore, the imaging not only identifies and delineates the plaque boundaries but also helps to identify the various components within the plaque such as lipid, fibrous tissue and calcium.

Figure 17:Diagrammatic represent of different plaque characteristics within vessel lumen that help classify them as lipid, fibrous, mixed and calcified plaque.

Intravascular ultrasound and optical coherence tomography have been shown to provide most accurate information regarding plaque morphology that matches the findings on histopathology(25)(26). The use of these modalities are however limited due to the invasiveness, limited availability and high cost.

Therefore, less invasive modalities like CT and MRI play a more important role in plaque characterization, especially among patients with low or intermediate risk of coronary artery disease where imaging is more of a screening tool(27).

Researchers since the early days of CCTA identified the ability of CT to depict attenuation differences within an atherosclerotic plaque. This therefore helps to differentiate plaques as lipid rich, fibrous and calcific(28).

With rapid development in CT technology, characterization as well as quantification of plaque is now possible. Good correlation between plaque classification on CT as compared to IVUS has been observed (29) (30).

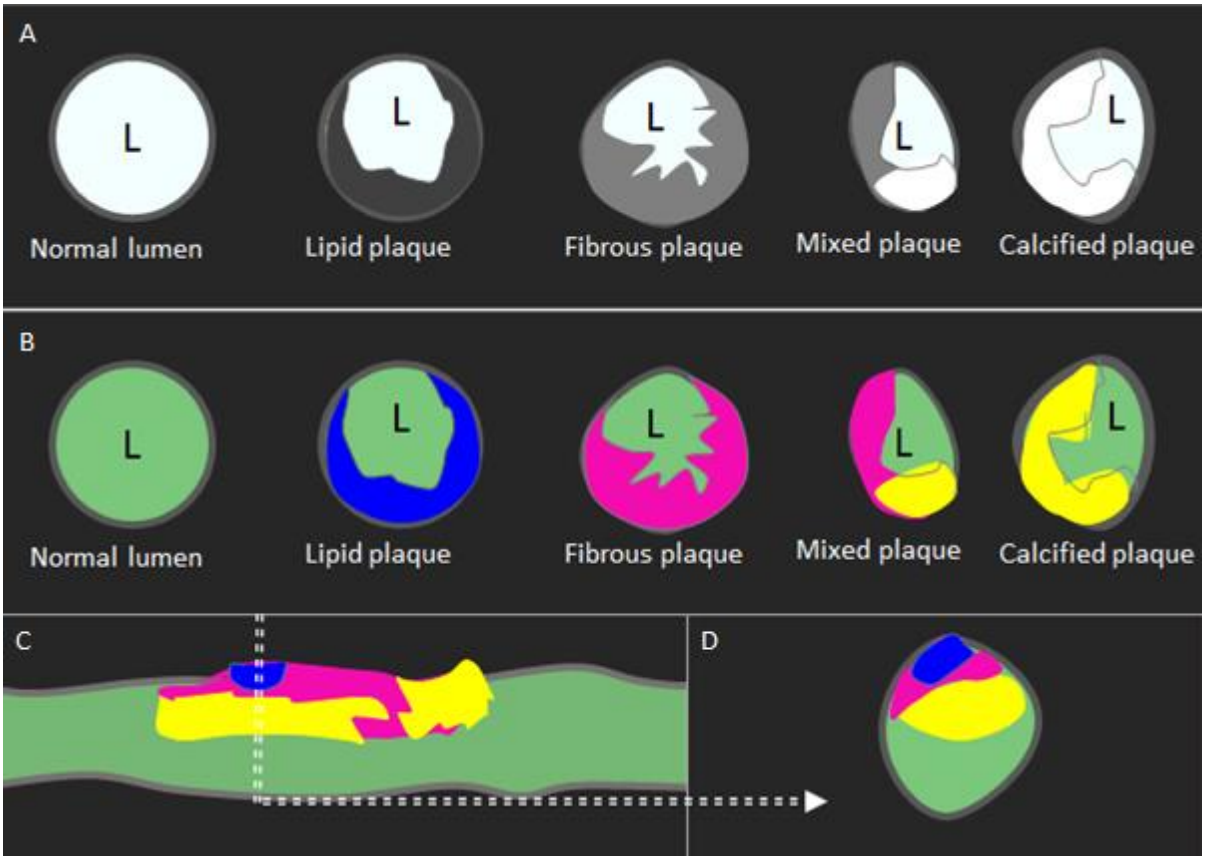


Figure 18A & B: Representation of grey scale and colour mapping of coronary artery plaque based on CT Hounsfield units

Different vendors provide software that are capable of automatic plaque segmentation, differentiation of plaque components using various attenuation thresholds and also provides color maps of plaque composition(31).

Attenuation value limits to identify various components of plaque can be customized and predefined. The ranges for different components are <30HU for lipid plaque, 30-149HU for fibrous plaque and >150HU for calcific plaque(32)

Available software provides automated, semi-automated plaque identification and manual quantification methods. Segmentation is performed on curved multiplanar reformatted images of the respective coronary artery. Completely automated software identify plaque and quantify them based on predefined HU values. This can be technically difficult and inaccurate due to variations in lumen attenuation, overlap in CT numbers of iodine and calcified plaque, and inherently low tissue contrast of CT(33).

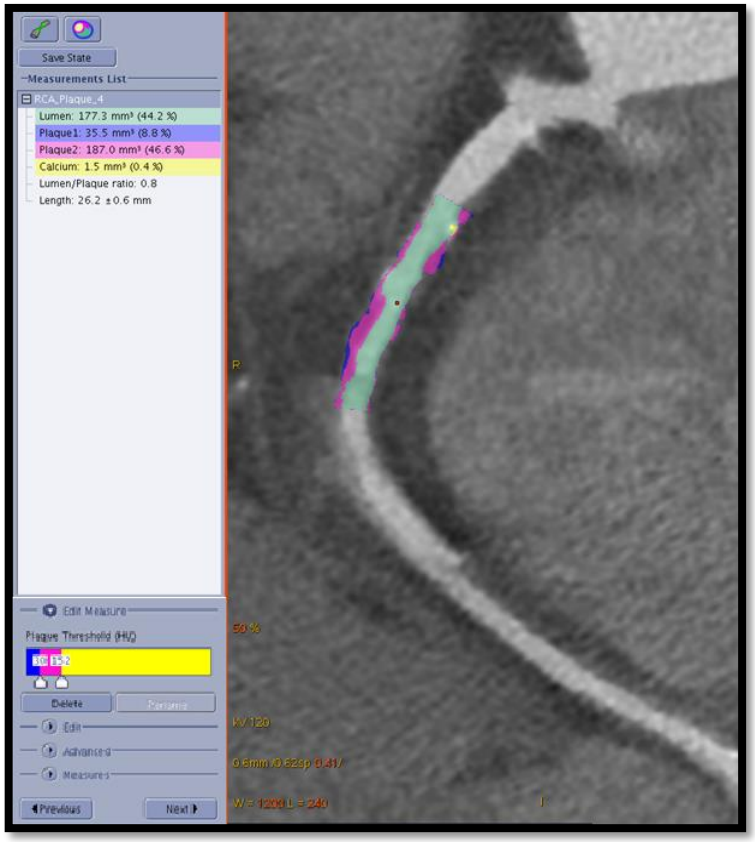


Figure 19: Colour mapping software Plaq ID segments various components of plaque and provides volume of each component

To overcome this softwares offer semi-automated and manual modes. These allow manual adjustment in case of obvious divergence from the outer limit of the vessel wall by the semi-automatic segmentation of vessel edge(31). The outer wall and the lumen can be manually defined. This process is however time consuming and observer dependent. Overall, studies have shown that manual plaque quantification and automated systems provide similar results(33). Once the plaque is identified and marked out, based on predefined HU threshold levels, the plaque is segmented. Plaque mapping software uses calibrated HU thresholds to automatically segment and measure volumes of vessel, lumen as well as low, medium and high density plaque components.

Good agreement is observed between manual plaque quantification and IVUS(34). Plaques are primarily classified as calcified and non-calcified based on the presence of calcium (calcified plaque is defined by attenuation values more than 150HU and forming >50% of plaque volume). Motoyama et al. in their study classified non-calcified plaque as lipid plaques when mean CT density was <30HU and fibrous plaques when mean CT density values were 30-150HU(35) However, it should be emphasized that differentiation of non-calcified plaque into lipid and fibrous plaques by using CT attenuation values is confounded by the significant overlap of attenuation values between the two types of plaque(35)(32)

Only 20% of the total atherosclerotic plaque burden is represented by calcified plaque. It is thought to be seen in advanced and late stages of atherosclerosis. Early atherosclerotic plaques are often non calcified.(36). The association between traditional risk factors and calcified plaque have been extensively studied. Recent study by Vergallo et al also explored the association between the Framingham Risk Score (FRS) and coronary plaque characteristics assessed by optical coherence tomography (OCT) imaging(37). Further evidence on association of cardiovascular risk factors with vulnerable plaques is required to establish additional information on risk assessment using MDCT in this population of patients (36).

The purpose of this study is to evaluate the degree of correlation between the conventionally used risk models such as the Framingham risk score, along with the NCEP core risk score and the burden of coronary artery disease as assessed by various scores on coronary CT angiography

MATERIALS AND METHODOLOGY:

Study period:

The study was conducted in the Department of Radiology in the period between Jan 2015 and May 2016 after obtaining approval from the Institutional Review Board (IRB Min No 9197 (OBSERVE) DATED 8.12. 2014)

Study design: Prospective cross sectional descriptive study

Recruitment of subjects:

Inclusion criteria:

Consecutive patients with suspected coronary artery disease, who were advised to undergo coronary CT angiography in the period between Jan 2015 and May 2016 and gave informed consent for the same, were included.

Informed consent was taken by the principal investigator after ensuring that there was no contraindication for undergoing a CT coronary angiogram.

Exclusion criteria:

1. Patients with contraindication to the administration of iodinated contrast.
2. Previous history of myocardial infarction, stenting, coronary artery bypass graft stenting.
3. Poor image quality resulting in suboptimal image analysis.
4. Pregnancy
5. If lipid profile of the patient was not readily available.

Sampling strategy

All consecutive patients with suspected coronary artery disease, who fulfilled the inclusion criteria, have none of the exclusion criteria, and have given consent to be a part of the study were included.

Sample size calculation

Using a pilot retrospective review, a sample of 144 (72 cases and 72 controls)was arrived at to detect 20% difference in high risk (i.e. above 20% of Framingham risk score) among those with coronary artery disease and those without coronary artery disease, with a power of 80% and 5% type 1 error using two tailed chi square test, assuming that 30% of patients are high risk group among those with coronary artery disease on CT angiogram

and 10% of patients are of high risk group in those with no coronary artery disease on CT angiogram

Data collection

Demographic details of the patient with history of risk factors, such as diabetes, hypertension, treatment for hypertension, dyslipidemia, smoking and positive family history was collected using a questionnaire which was part of the clinical research form (Annexure 2). Indication for referral was noted. Weight and height, systolic and diastolic blood pressure along with lipid profile values were also documented.

Risk stratification of patients

Risk stratification of each patient according the NCEP core risk score was performed as diagrammed in Figure 20. Patients with diabetes directly fell into the high risk category as per this criteria.

Using risk calculators, with the above information collected, Framingham Risk Estimates (FRE) were calculated for each patient. This estimates the percentage risk of developing coronary artery disease in the next 10 years. Based on latest NCEP/ATP III guidelines along with calculated FRE, each patient was assigned a low, intermediate, moderately high or high risk category as per the following algorithm.

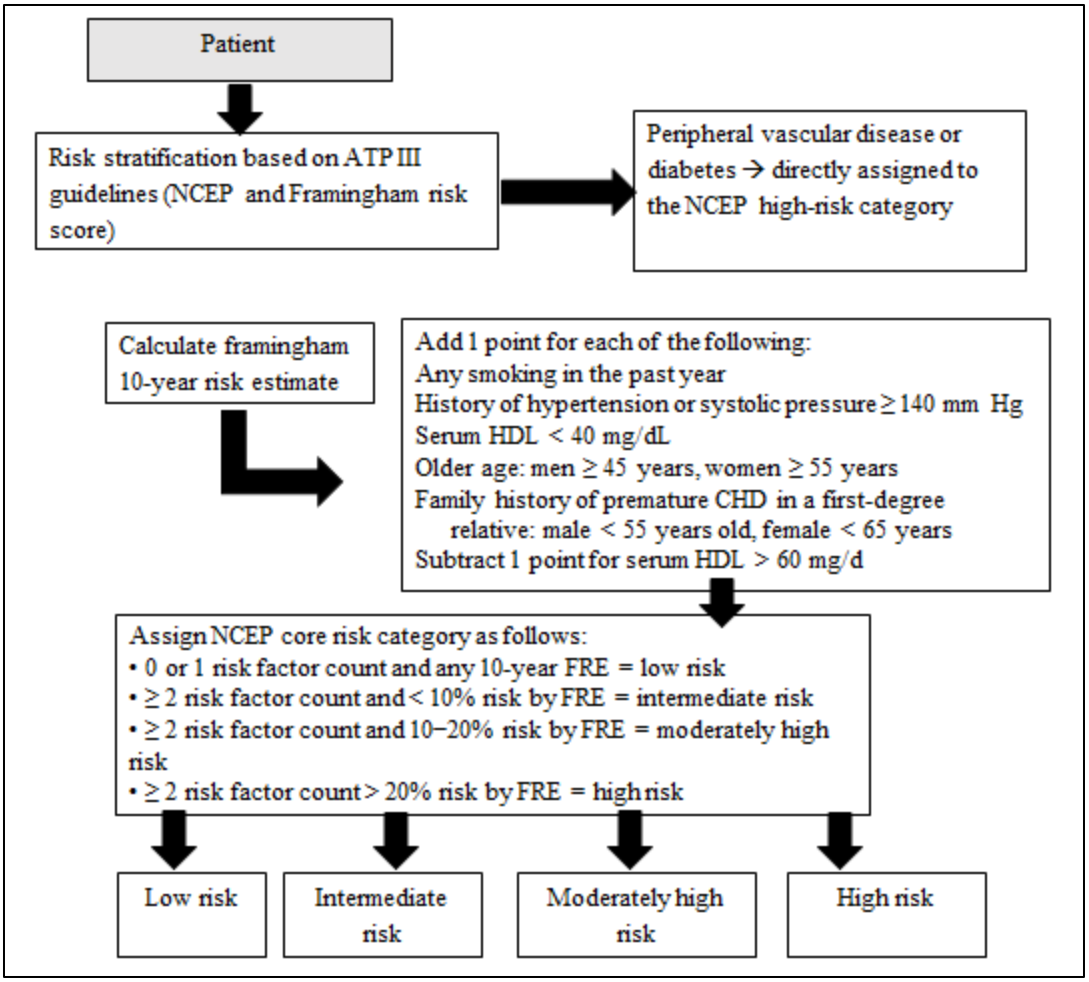


Figure 20: Risk scoring algorithm used to categorize study population

Patients were classified as low risk if they had no or only 1 risk factor with any FRE, intermediate risk if they had 2 or more risk factors with <10% risk of coronary artery disease in 10 years, moderately high risk if they had 2 or more risk factors with 10-20% risk of coronary artery disease in 10 years and high risk if patients had 2 or more risk factors with more than 20% risk of coronary artery disease in 10 years. The high risk group also included patients with diabetes and peripheral vascular disease irrespective of their FRE and risk factor count.

Coronary CT angiography

ECG gated coronary CT angiography was done in CT Room 22, using the GE Advantage 750 HD 64 slice dual energy CT machine. Retrospective or prospective approach of ECG gating was decided based on the patient's heart rate.

For heart rates less than 60, prospective gating was used. Most patients were prescribed β-blocking drugs or Ivabradine, to control heart rate. If patient's heart rate was more than 72 beats per minute (bpm) at the time of scan, injection Metaprolol was given IV on table just before the scan.

Heart rate, blood pressure and ECG were monitored. 2 puffs of nitroglycerin spray was given on table before beginning image acquisition. 1mg midazolam diluted in 1ml NS prior to commencement of calcium scoring was given intravenously in case of anxiety related to the test.

ECG gated unenhanced scan from the level of the carina to the diaphragm was acquired for calcium scoring followed by contrast enhanced angiogram of the coronary arteries. In order to time the commencement of the contrast enhanced scan, bolus tracking was done with the ROI in the ascending aorta. Nonionic iodinated contrast was injected by a pressure injector at the rate of 5ml/sec(80-100ml of contrast) followed by a saline chaser also at 5ml/sec(~40ml of saline) .

Images were acquired using collimation of 0.6 mm, slice acquisition 64 × 0.6 mm using the z-flying focal spot technique, gantry rotation time 330 ms, pitch 0.20–0.43 adapted to heart rate, tube voltage 80 - 120 kV (depending on body habitus) and maximum tube current 400 mAs per rotation

Image reconstruction and post processing:

The acquired images were reconstructed to reduce noise and improve spatial resolution in the thinnest possible slice thickness. In retrospective gating, optimal cardiac phase with minimal motion was chosen to analyze the right coronary artery and left coronary artery respectively.

Curved multiplanar reformations, maximum intensity projections, volume rendered images were generated on dedicated workstations (AW Server, TeraRecon) for reporting.

Image interpretation:

The coronary CT angiography studies were interpreted by the principal investigator and checked by a radiologist of professor grade (guide and co-guides).

Steps in image interpretation:

1. Calcium scoring was done using Smartscore, a semi-automated software provided by GE Healthcare. The total score obtained was graded as insignificant (<10AU), mild (10-100AU), moderate (101-400 AU) and severe (>400AU)

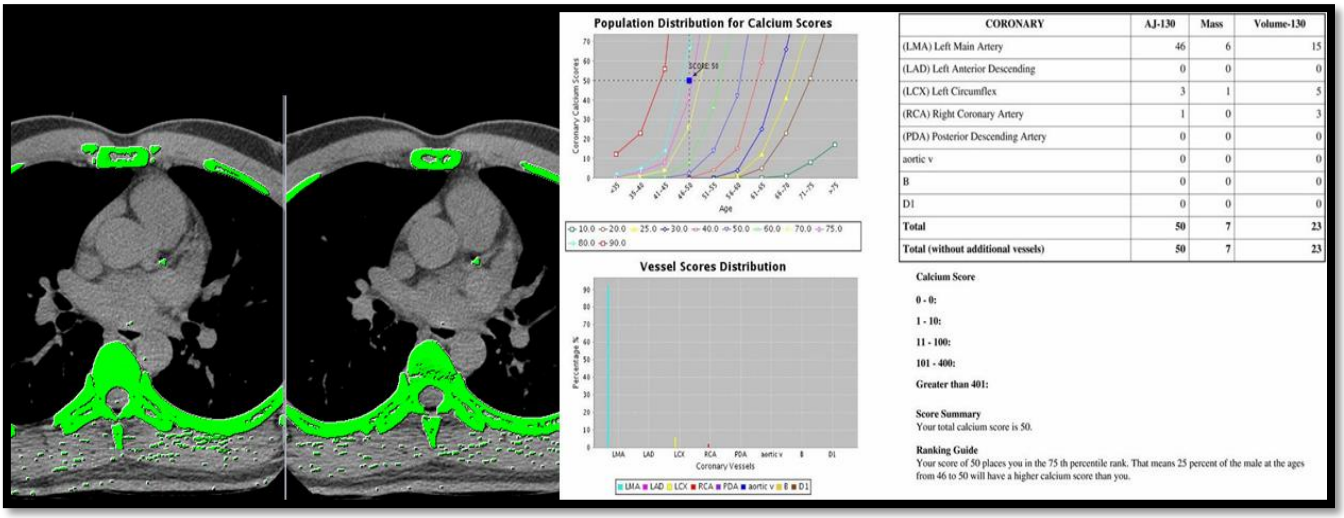


Figure 21:Semiautomated calcium scoring software segments calcific foci (any focus>130HU) on unenhanced CT scans and provides a total score based on Agaston's scoring

2. Transverse/ axial image stack was scrolled through for an overview of the coronary artery anatomy and image quality. Also, identification of plaques on axial images was done
3. MIP and MPR images were used to identify, demonstrate and study plaques in longitudinal and perpendicular planes. The presence of plaques on transverse images was confirmed.

4. In case of no obvious plaques, segment based analysis of the RCA, LAD and the LCx was done to avoid false negatives
5. If plaque was found, or there is a point of coronary artery stenosis, in order to avoid false positives due to motion artifacts, it was essential that the plaque be identified on at least two reconstruction time points.

6. The vessels involved by plaque were documented.

7. *Segment involvement scores(SIS):* SIS was calculated for each segment, which basically denotes the number of segments affected by plaque. A segment was scored 0 when there was absent and scored 1 for any amount of plaque present. The score of each segment was totaled to arrive at a total segment involvement score for the patient. The total SIS was further classified into grades of severity as zero if not involved, 1–2 as mild, 3–4 as moderate, and more than 4 as severe or heavy.

8. *Segment plaque score (SPS):* For all plaques that were identified, the amount of plaque whether calcified or not was graded visually as none or trace (0), mild (1), moderate (2), or heavy (3). The total score was obtained from a sum of individual segment scores. The total SPS was further classified into grades of severity as zero if no or trace plaque, 1–3 as mild, 4–7 as moderate, and 8 or more as heavy plaque burden.

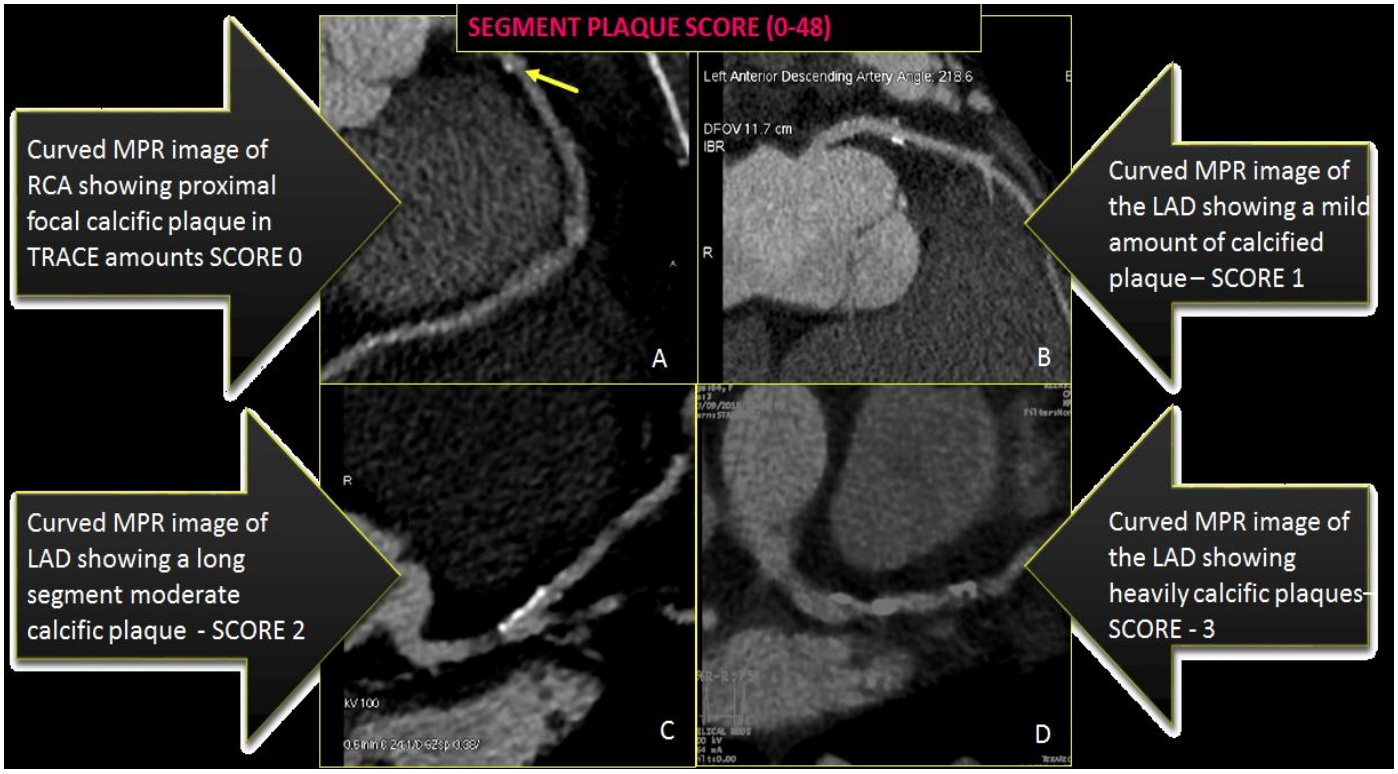


Figure 22:Grading of segment plaque score (SPS)

9. *Segment stenosis score:* For all identified plaques, the resultant luminal narrowing at that level was quantified by measuring the degree of stenosis. This was done by calculating the ratio of the diameter of residual lumen at the site of stenosis to a proximal or distal normal-appearing reference site.

10. Degree of stenosis was measured using semi-automated softwares which allowed optional manual correction of boundaries of the lumen at the normal appearing reference site and at the point of maximum stenosis to arrive at an accurate quantification of stenosis.

11. The degree of stenosis was graded as very mild < 30%, mild 30-50%, moderate 50-69%, or severe >=70%, scored as 0, 1, 2, and 3 respectively. The sum of the scores of each of the segments gave the total segment stenosis score. The total SSS was further classified into grades of severity as zero if no stenosis, 1–3 as mild, 4–7 as moderate, and 8 or more as severe.

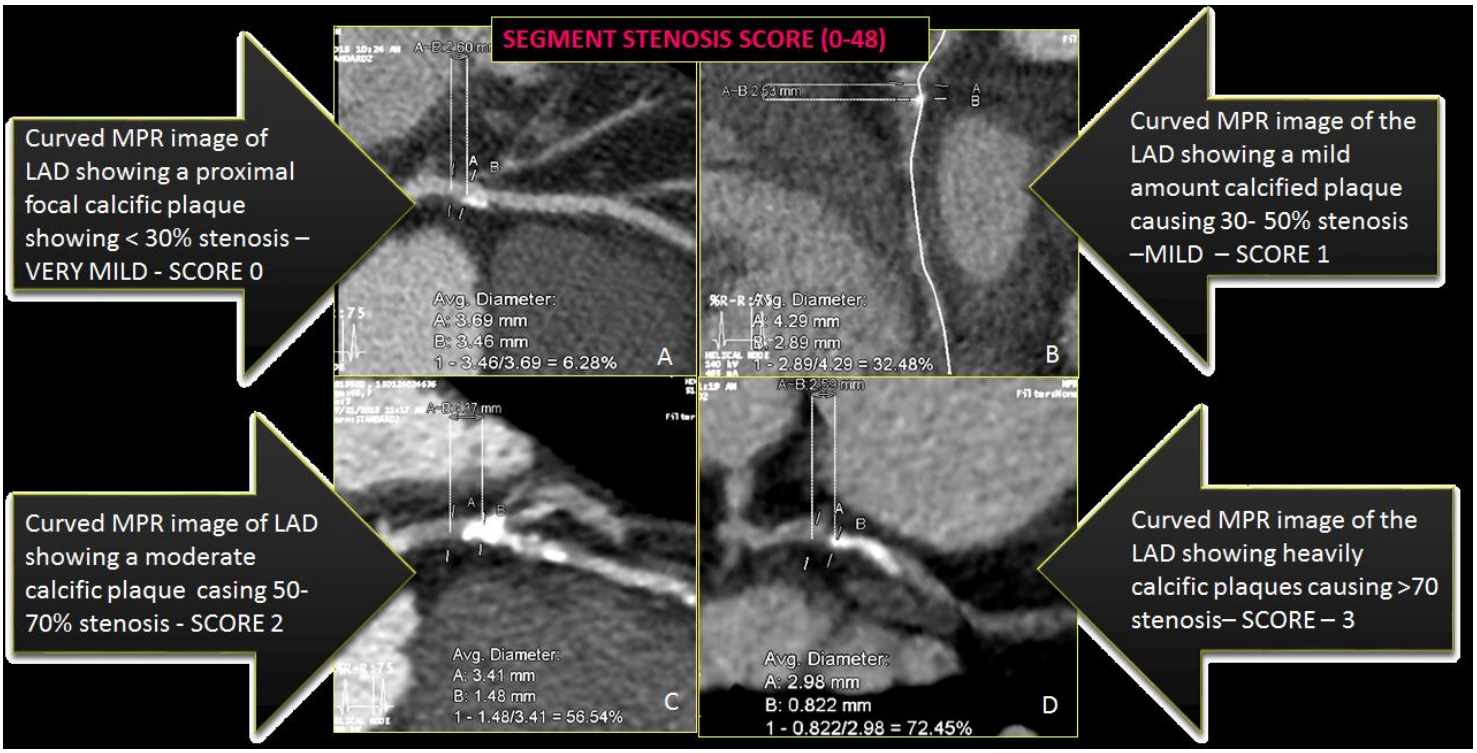


Figure 23: Grading of segment stenosis score

12. *Modified Duke's prognostic index:* Based on the site and severity of the vessel involved and the number of measurable stenosis, each patient was placed under one of the 7 categories (Duke 0 – Duke 6) of the Modified Duke's prognostic index. The Modified Duke's prognostic index was further classified as Category 0 as 0, Category 1 a mild, Category 2 as moderate, and more than 2 as severe.

13. Each of the identified plaques were characterized using semi-automated software called PlaqID, offered by AW Server, GE Healthcare. The software segmented the plaques based on predefined fixed attenuation values (HU values). The fixed cut off values used were <30HU for lipid rich plaque, 30-150HU for fibrous plaque and >150HU for calcified plaque. various components of the plaque was identified and their volumes were quantified.

    Based on the quantified volumes, classification of plaques into non calcified, mixed and calcified was done.

    A plaque was defined as non-calcified when it was of lower attenuation than the luminal contrast with HU values of less than 150HU and no calcification. A plaque with calcification was classified as calcified plaque when more than 50% of the plaque volume was calcium. A plaque with both calcified and non-calcified content was defined as mixed plaque when the volume of calcium was less than 50% of the total plaque volume.

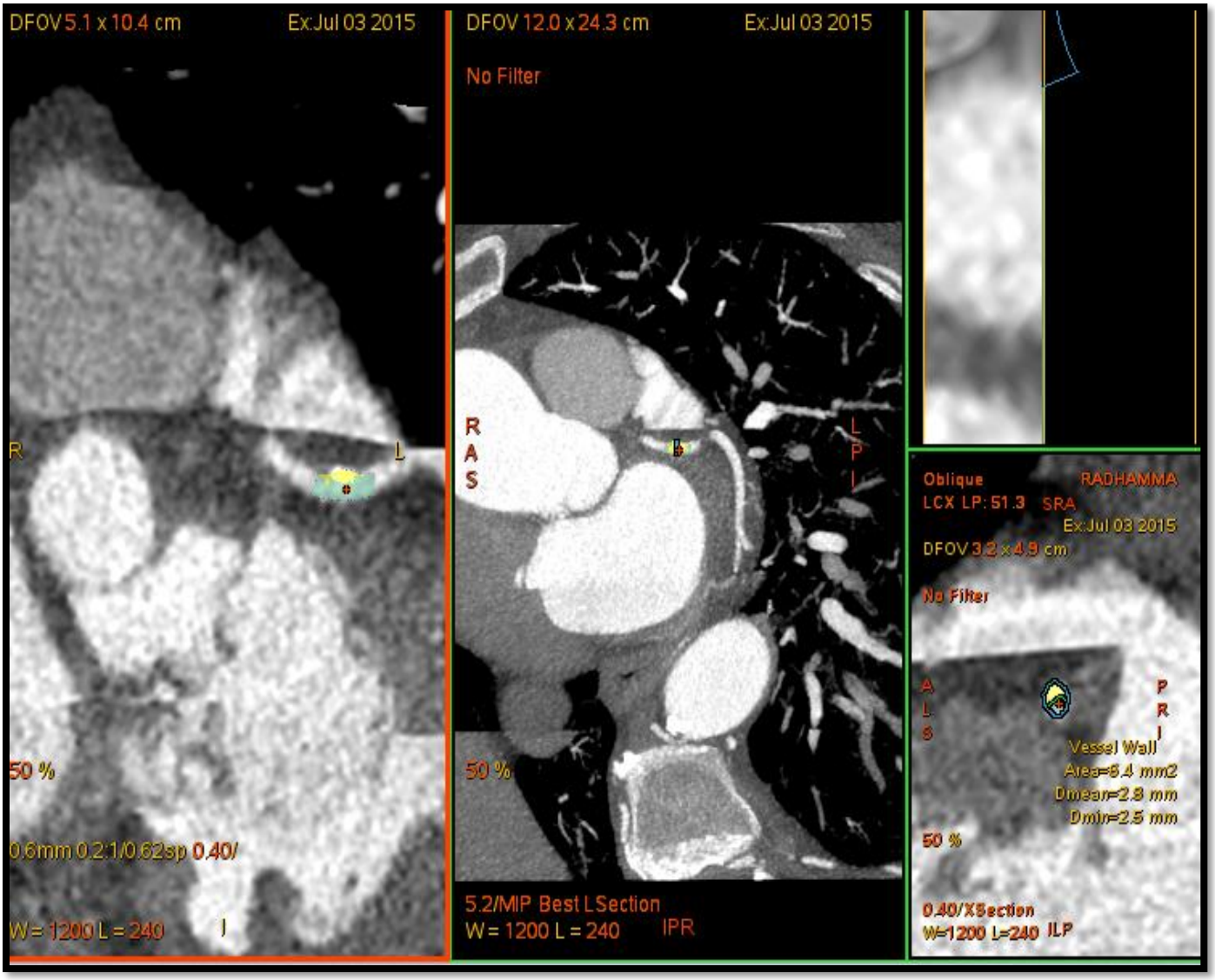
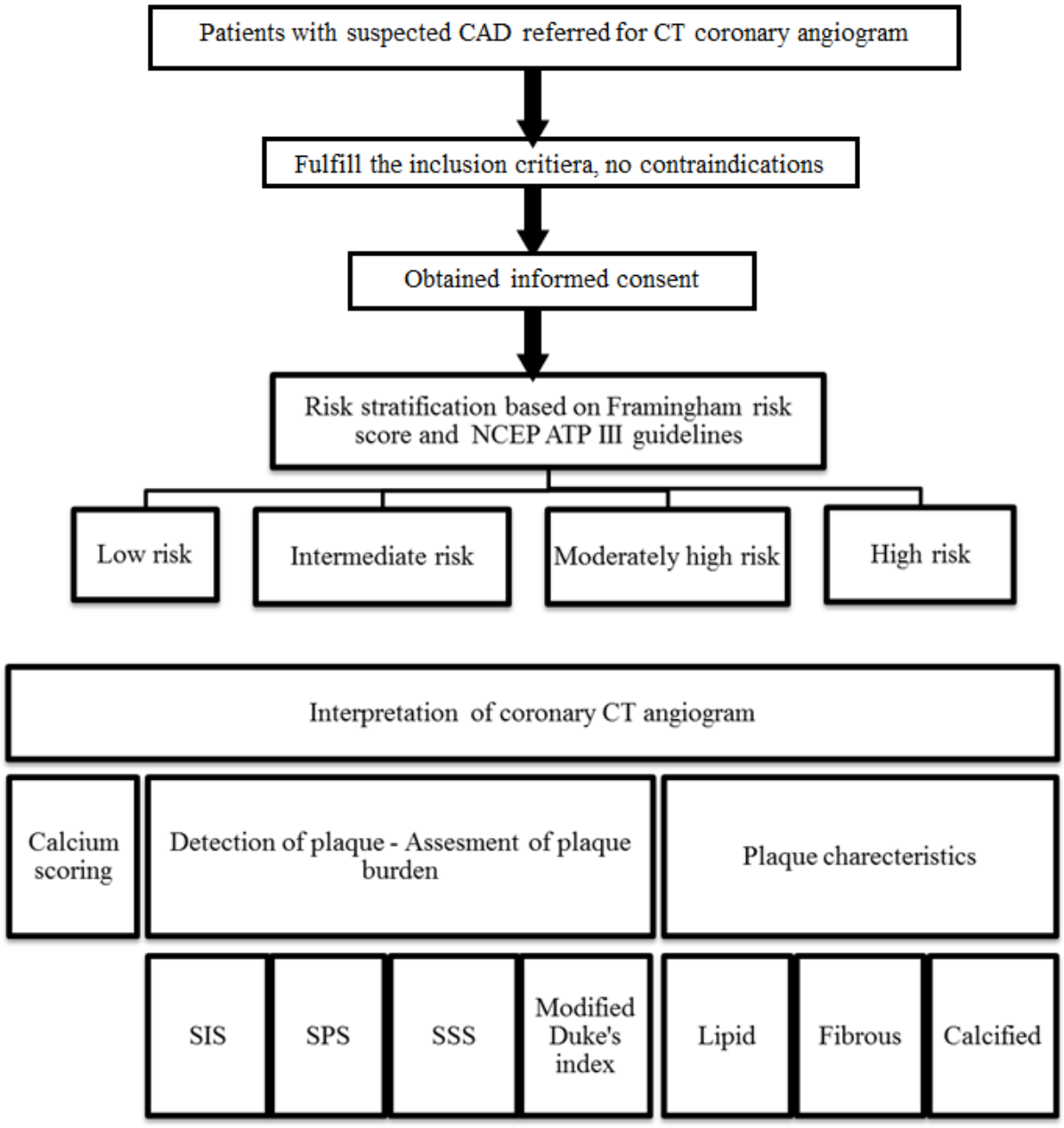


Figure 24: Example of semi-automated plaque segmentation.

69-year-old lady with atypical chest pain and inconclusive TMT, underwent CT coronary angiography for evaluation of cardiac status with the following findings. The curved MPR of the LAD showed an eccentric calcified plaque in the proximal LAD (yellow – calcium, green – lumen). The plaque has been auto segmented based on attenuation values by PlaqID software on AW server provided by GE Healthcare. The outline of the plaque and the residual lumen is verified on the axial view of the LAD obtained from the curved MPR images.

SUMMARY OF METHODOLOGY



Abbreviations:
NCEP – National Cholesterol Education Program; ATP – Adult Treatment Panel; CAD – coronary artery disease; SIS – Segment Involvement Score; SPS – Segment Plaque Score; SSS – Segment Stenosis Score

Figure 25:Flow chart shows summary of methodology of recruitment, risk stratification and coronary CTA interpretation

Statistical analysis

Data entry was performed using Epidata Entry version 3.1, a dedicated data entry software. Statistical analysis was performed using SPSS version 20.0 software. A p value of less than 0.05 indicated statistical significance.

- Discrete variables are reported as proportions.
- Continuous variables are reported as Mean ± SD or median and interquartile range.
- ROC curve analysis was done to demonstrate the predictive value of Framingham risk estimate to identify coronary artery disease.
- A second model for ROC curve analysis was performed using both FRE and calcium score to study the predictive value of combined FRE and calcium score for CAD.
- Pearson's correlation test was used to analyze the correlation between Framingham risk estimates and each of the plaque burden scores.
- In order to demonstrate the association between the four NCEP risk categories and plaque burden scores, contingency tables were generated.
- Pearson's chi-square goodness of fit test was used to analyze the correlation between NCEP risk categories and plaque burden scores.

RESULTS AND ANALYSIS

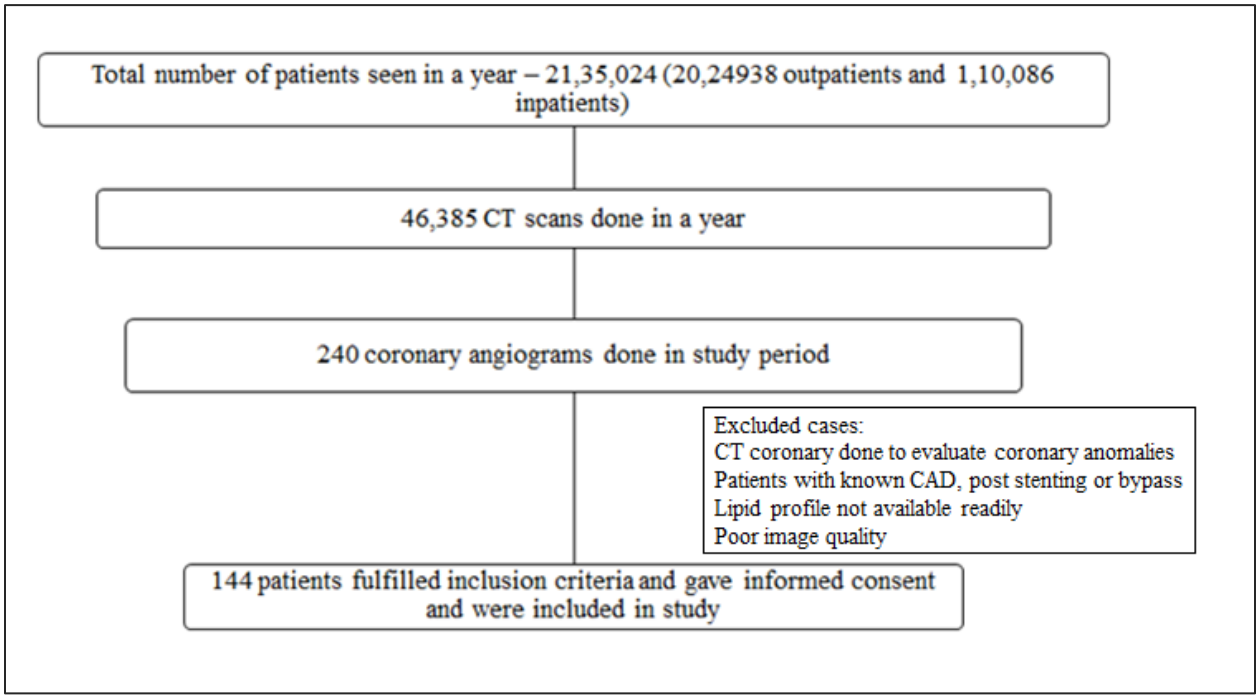


Figure 26:STROBE flow chart representing recruitment process for study.

A total of 144 patients with suspected coronary artery disease participated in the CT coronary angiography study.

Baseline patient characteristics:

1. **Age distribution:**

   The mean age of patients included in the study was 50 years.

2. Gender:

43% (63) of the patients were men and 55% (81) of the patients were women

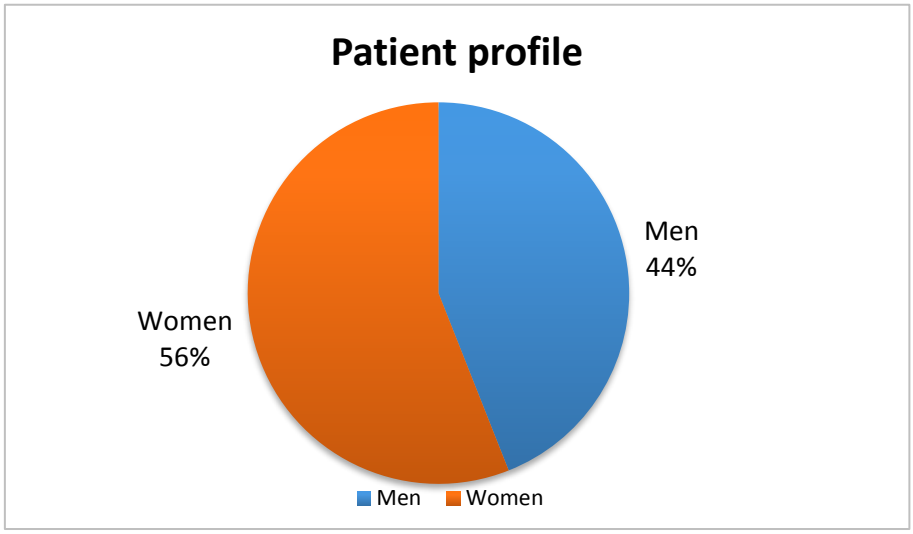


Figure 27: Gender distribution among study population

3. Indication for referral for CCTA:

CCTA was performed in the study population for the following specific indications (Figure 28)

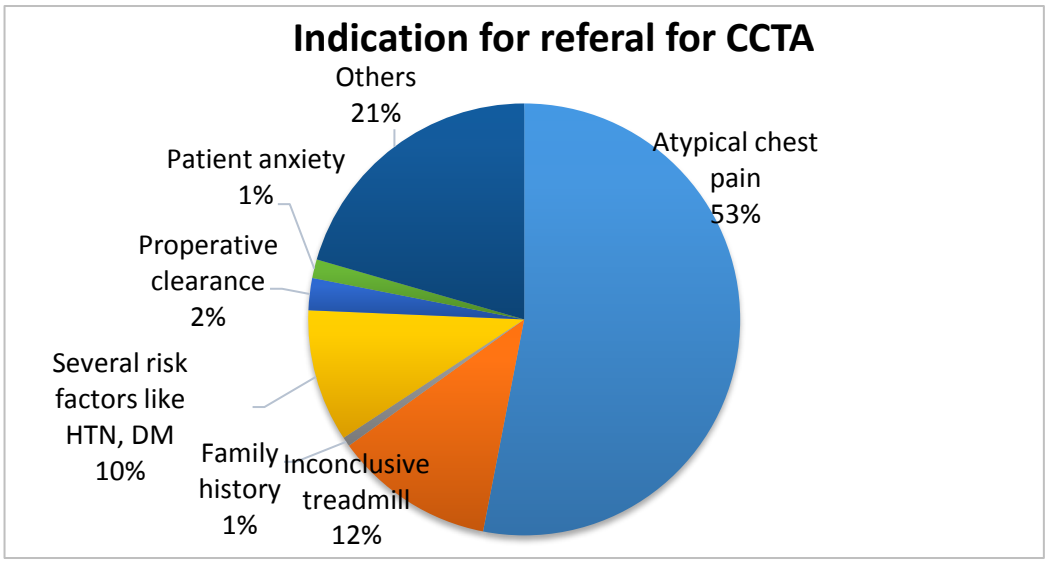


Figure 28: Various reasons for referral of patients for CCTA

The most common indication for referral for CTCA was atypical chest pain and inconclusive treadmill test results. Other miscellaneous indications like for coronary CT angiography such as dyspnea on exertion, false positive thallium studies, ischemia on SPECT formed the other significant proportion of cases referred.

4. Risk profile:

The most prevalent risk factor among the study population was hypertension and dyslipidemia. The least prevalent risk factor was positive family history and smoking.

Table 3: Risk factor profile among the study population

Risk factor	Frequency	Percentage
Smoking	5	3.5%
Hypertension	67	46.5%
Diabetes	33	22.9%
Dyslipidemia	61	43.9%
Significant family history	2	1.4%

Parameters of risk stratification

The risk scoring systems used in the study were the Framingham risk scoring system and the NCEP risk categories.

1. **Framingham risk estimate:**

   The median 10 year Framingham risk estimate (FRE) was 5.8% with an interquartile range of 3 – 12

2. **NCEP core risk categorization:**

   Risk stratification of the study population based on FRE and NCEP risk categories revealed that approximately half the study population (54%, n=77) of the patients fell into the low risk category and approximately one- fourths of the study population fell into the high risk category (26%, n= 38)

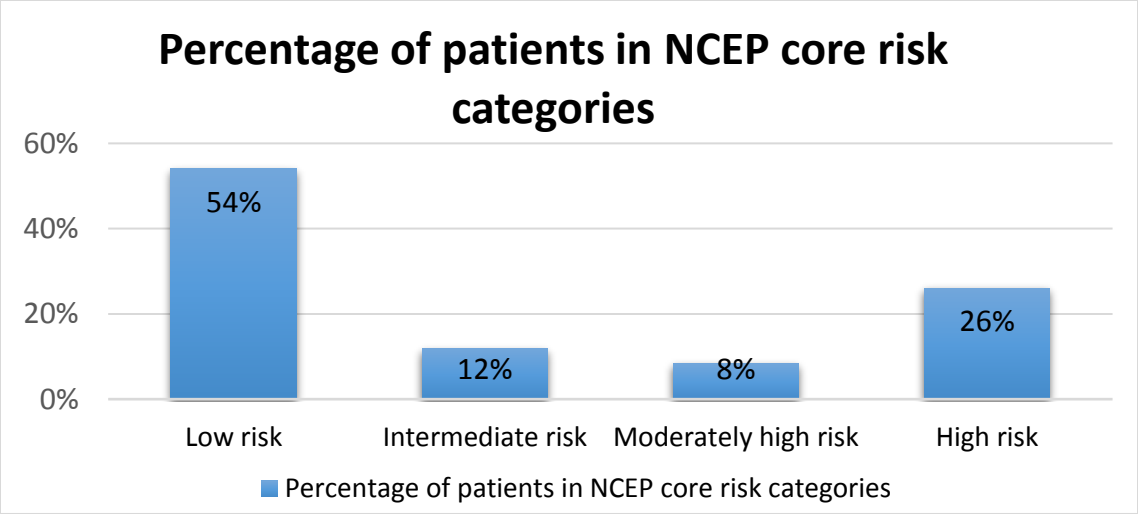


Figure 29:Distribution of risk categories among the study population

Findings on coronary CT angiogram

1. **Presence of coronary artery plaque:**

Out of the 144 patients who underwent coronary CT angiography, coronary artery disease was present only in 22% of patients (n=31). The rest of the 113 patients had no coronary artery plaque.

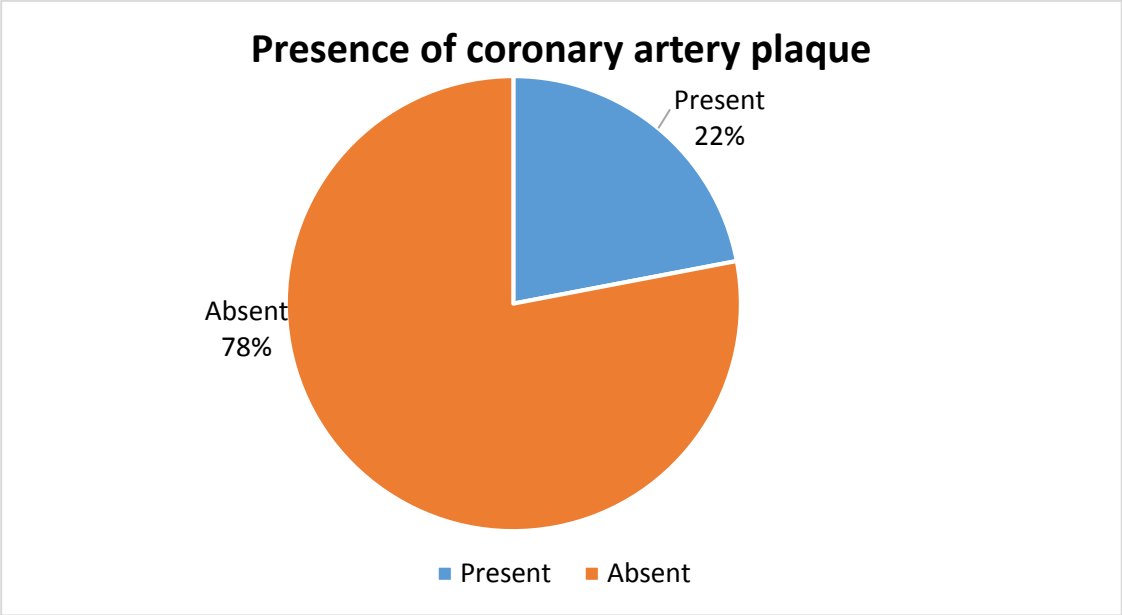
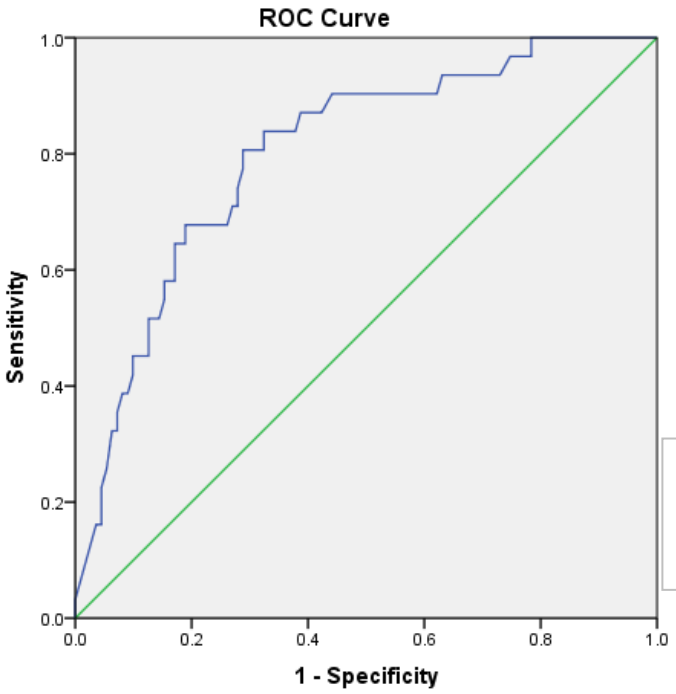


Figure 30: Prevalence of coronary artery plaque in study population

2. **Predictive potential of Framingham risk estimate (FRE):**

ROC curve analysis was done to test the potential of Framingham risk estimate to predict the presence of subclinical atheroma. Figure 31 indicates that FRE is a good

indicator of the presence of coronary artery plaque. The area under the curve was 0.80 (95% CI: 0.71- 0.88, p <0.001).



Area under curve	95% C.I.
0.801	0.71- 0.88

: Figure 31: Predictive potential of FRE for coronary artery plaque – ROC curve analysis

3. Arteries involved by plaque

Among patients with coronary artery plaque (n=31), the left anterior descending artery (LAD) was the most commonly involved vessel (80.6%) followed by the right coronary artery (51.6%).

Table 4: Distribution of atherosclerotic plaque in the coronary arteries among patients with coronary artery disease

Vessel involved	Frequency	Percentage (%)
RCA	16	51.6
Left main	6	19.4
LAD	25	80.6
LCx	9	29
Diagonal	3	9.7
Marginal	3	9.7
PDA	1	3.2
RI	1	3.2

4. Risk categories among patients with coronary artery plaque

51% of patients with coronary artery plaque were belonged to the high risk category. Most of these patients had diabetes and hence were categorized into high risk category. (9 out of 14 patients in the high risk category).

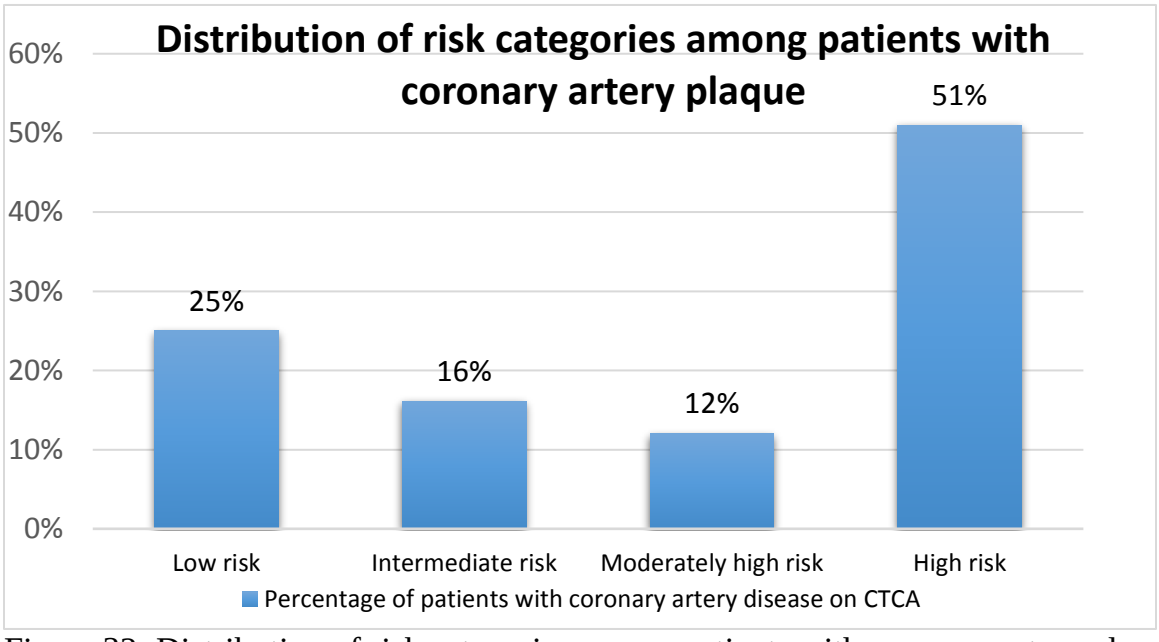


Figure 32: Distribution of risk categories among patients with coronary artery plaque on CCTA

5. Calcium scoring (CACS):

a. Of the 144 patients who underwent a CCTA as part of the study, as shown in figure 33, on the non-contrast CT, majority of them (78%, n=113) did not have any coronary calcification (calcium score=zero).

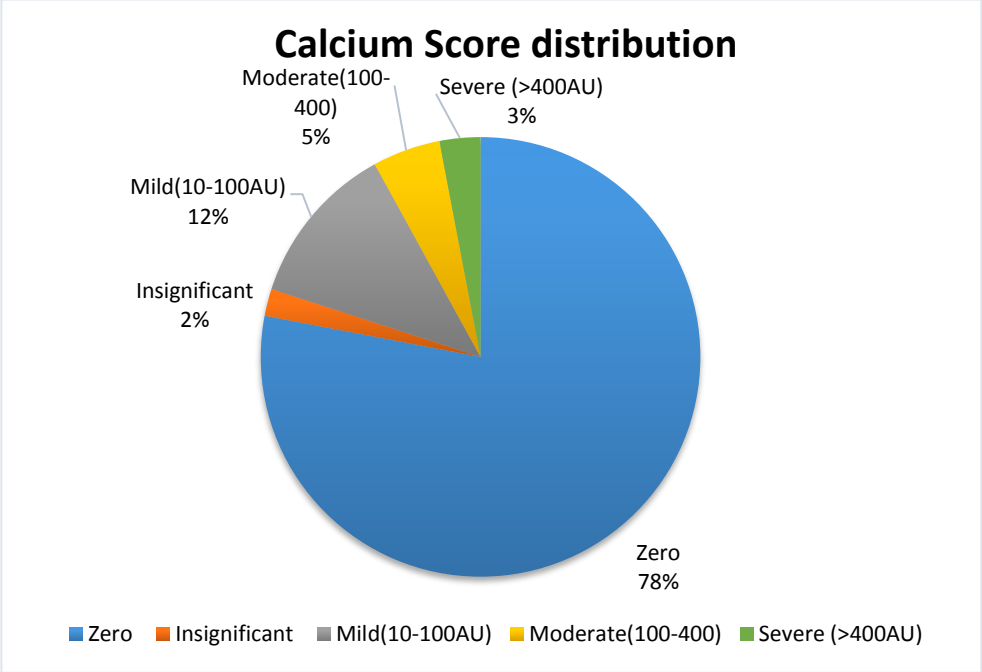


Figure 33: Distribution of calcium score among study population

6. Risk categories versus calcium scoring:

i. Among patients with calcium score of zero, 62% belonged to the low risk category and 20% to the high risk category (Figure 34).

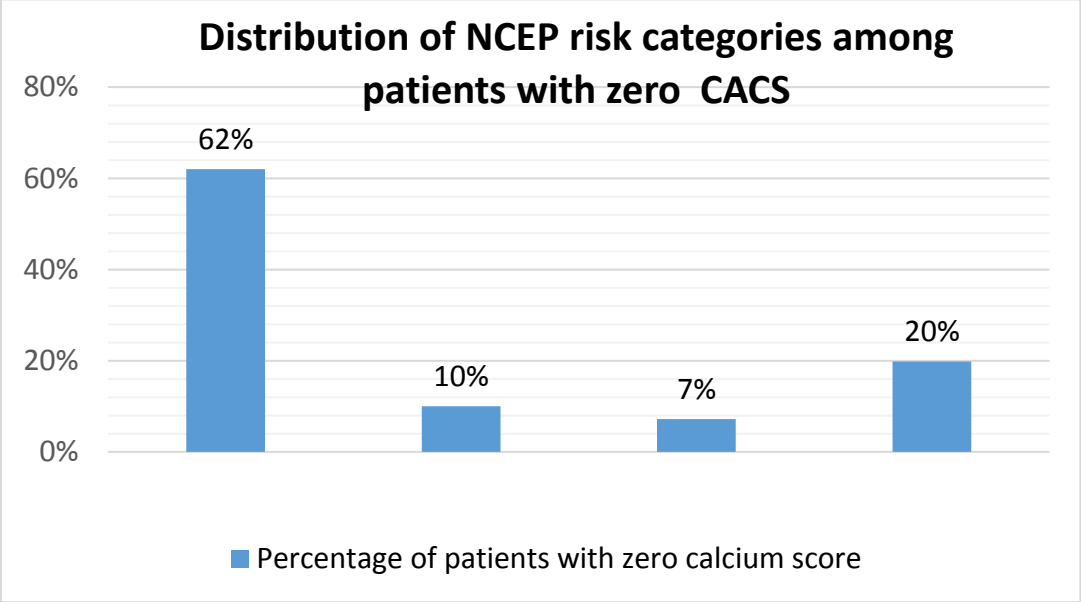


Figure 34: Distribution of risk categories among patients with CACS of zero

ii. Among the 31 patients with calcium score of more than zero, the distribution of risk categories is as follows:

Table 5: Distribution of calcium score among various risk categories

Risk category	Insignificant	Mild	Moderate	Severe
Low risk	0%	62.5%	37.5%	0%
Intermediate risk	40%	40%	0%	20%
Moderately high risk	25%	75%	0%	0%
High risk	0%	50%	29.%	21%

None of the patients with low risk scores had severely high calcium scores. High calcium scores were seen in patients with both high risk and those patients with intermediate risk.

7. Potential of combined Framingham risk estimate and coronary calcium score to predict coronary artery disease:

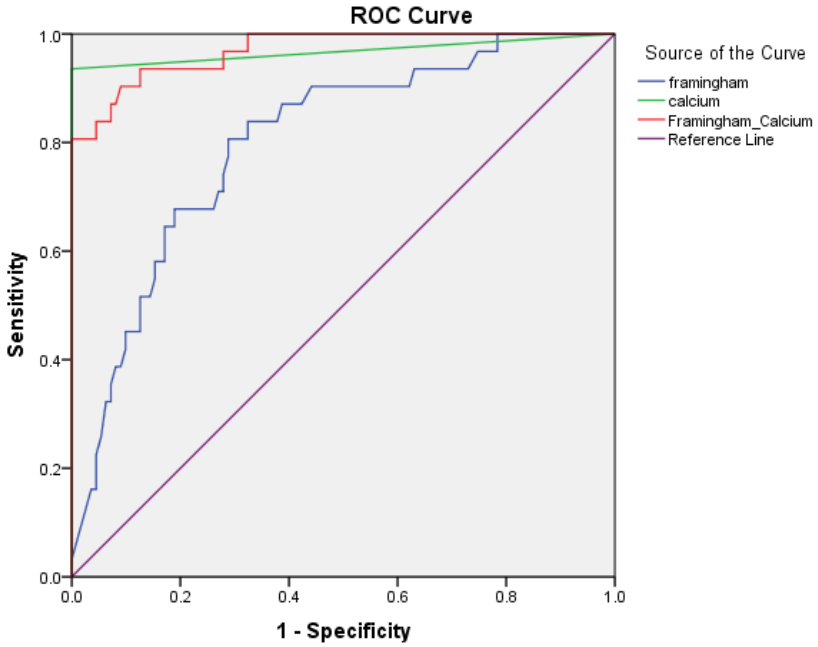


Figure 35: ROC of Framingham risk estimate(FRE), calcium score (CACS) and FRS combined CACS to predict coronary artery disease

Table 6: The area under curve of the possible coronary artery disease predictors

Variables	Area under the curve	95% confidence interval	p value
Framingham risk estimate (FRE)	0.801	0.717-0.886	0.000
Calcium score (CACS)	0.968	0.917 – 1.000	0.000
Framingham risk estimate + calcium score	0.970	0.941 – 0.999	0.000

These results show that by FRE when combined along with calcium score is a superior indicator than using FRE or calcium score as a sole indicator to predict the presence of coronary artery disease.

8. Coronary artery plaque burden

a. Out of the total of 144 patients recruited, 31 patients (22%) had atherosclerotic plaque.

Plaque burden as assessed by each of the four CT scores was categorized into 0, mild, moderate and severe. Their distribution within the study population has been represented in Table 7.

Major proportion of patients had a score of zero across all different plaque burden scoring systems.

Table 7: Distribution of study population across the grades of severity of atherosclerotic disease burden assessed by the four CT scores

Plaque burden scores	Distribution of severity among study population			
	0	Mild	Moderate	Severe
Segment involvement score (SIS)	78%	13%	7%	2%
Segment plaque score (SPS)	83%	10%	4%	3%
Segment stenosis score (SSS)	90%	6%	1%	3%
Modified Duke's prognostic index (MDPI)	81%	9%	6%	4%

Association of conventional risk scoring models and coronary artery plaque

1. Correlation between Framingham risk estimate and plaque burden scores:

There was moderate positive correlation between Framingham 10-year risk estimate and the various CT scores assessing atherosclerotic plaque burden (all, p value <0.001) as elaborated in Table 8.

Table 8: Correlation between Framingham 10-year risk estimates and atherosclerotic plaque burden scores as assessed by CCTA

Variables	Pearson's correlation co-efficient	P value
Segment involvement score (SIS)	0.401	<0.001
Segment plaque score (SPS)	0.356	<0.001
Segment stenosis score (SSS)	0.345	<0.001
Modified Duke's Prognostic Index (MPDI)	0.436	<0.001

Pearson's correlation co-efficient for each of the plaque burden scores fall between 0.3-0.5, suggestive of moderate positive correlation.

The results have been graphically represented using scatter plots (Figure 36). This shows moderate correlation between the Framingham risk estimates and each of the plaque burden scores.

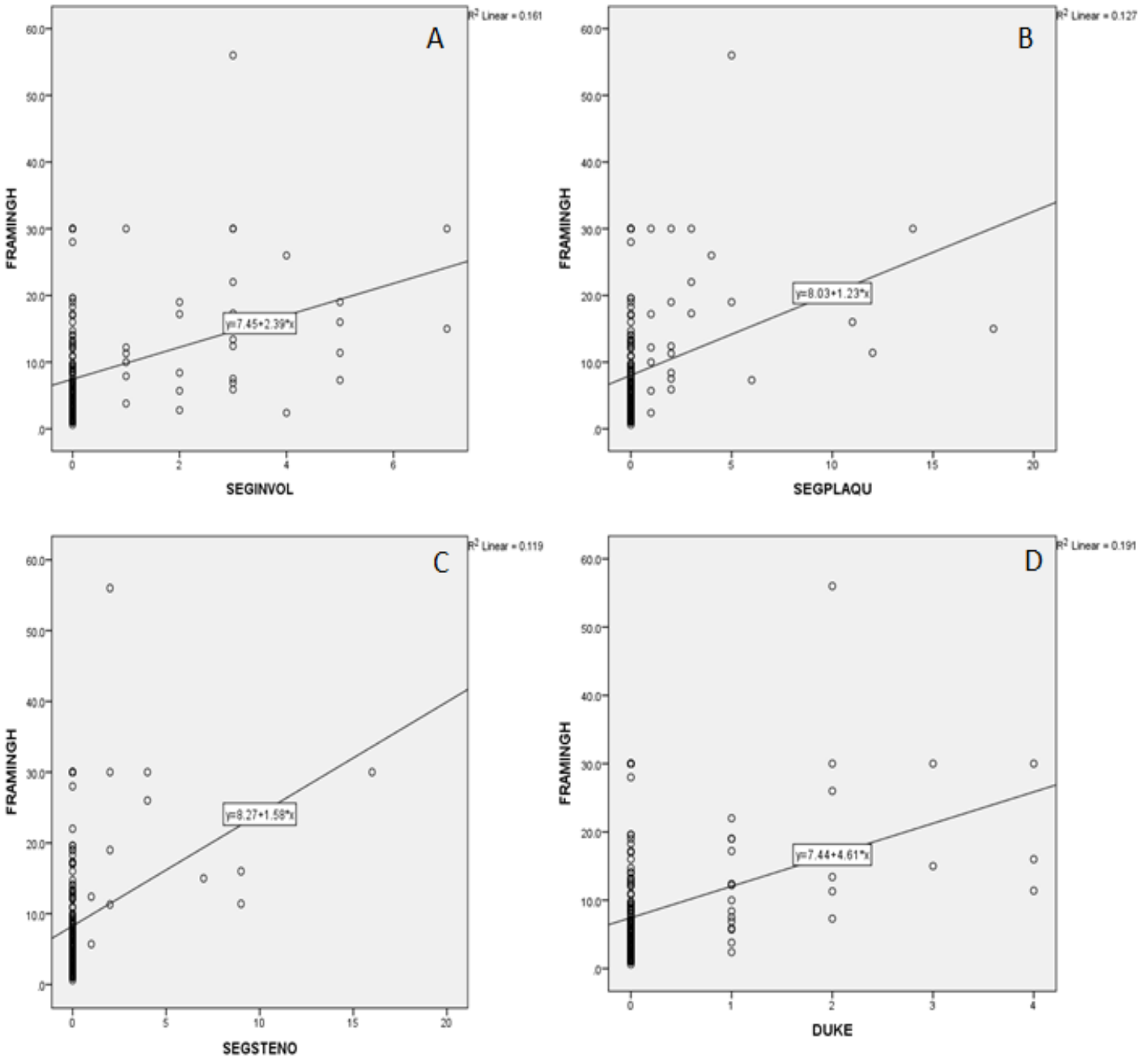


Figure 36: Correlation between Framingham risk estimate and the four plaque burden scores; A - FRE versus SIS, B - FRE versus SPS; C- FRE versus SSS; D- FRE versus Modified Duke's prognostic index

2. NCEP risk categories versus plaque burden scores:

Contingency tables generated between NCEP risk categories and various plaque burden scores showed an association between the two variables (X^2 (9) = 20.1, 24.9, 34.1, 26.2 for SIS, SPS, SSS and Modified Duke's prognostic index respectively; all p<00.1) (Table 9).

Table 9: NCEP risk categories versus four measures of coronary plaque burden

Risk Variables	Severity of plaque burden				N (Total)	p – value
	0	Mild	Moderate	Severe		
	n (%)	n (%)	n (%)	n (%)		
Segment involvement score						
Low risk	69 (89.6%)	3 (4%)	5 (6%)	0 (0%)	77	0.017
Intermediate risk	12 (70.6%)	4 (24%)	0 (0%)	1 (6%)	17	
Moderately high risk	8 (66.6%)	4 (33%)	0 (0%)	0 (0%)	12	
High risk	24 (63.1%)	7 (18%)	5 (13%)	2 (5%)	38	
Segment plaque score						
Low risk	71 (92%)	5 (6%)	1 (1%)	0 (0%)	77	0.003
Intermediate risk	13 (76%)	0 (0%)	3 (18%)	1 (6%)	17	
Moderately high risk	8 (67%)	4 (33%)	0 (0%)	0 (0%)	12	
High risk	27 (71%)	6 (16%)	2 (5%)	3 (8%)	38	
Segment stenosis score						
Low risk	75 (97%)	2 (3%)	0 (0%)	0 (0%)	77	0.000
Intermediate risk	13 (76%)	1 (6%)	3 (18%)	0 (0%)	17	
Moderately high risk	10 (83%)	2 (17%)	0 (0%)	0 (0%)	12	
High risk	31 (82%)	4 (11%)	1 (3%)	2 (5%)	38	
Modified Duke's prognostic index						
Low risk	70 (91%)	5 (6%)	2 (3%)	0 (0%)	77	0.002
Intermediate risk	13(76%)	0 (0%)	2 (12%)	2 (12%)	17	
Moderately high risk	8 (67%)	3 (25%)	1 (8%)	0 (0%)	12	
High risk	26 (69%)	5 (13%)	4 (10%)	3 (8%)	38	

a. NCEP risk categories versus Segment Involvement Score (SIS):

Though there were patients from all 4 risk categories who had segment involvement score of 0, the greater proportion (89.6%) of patients belonged to the low risk category

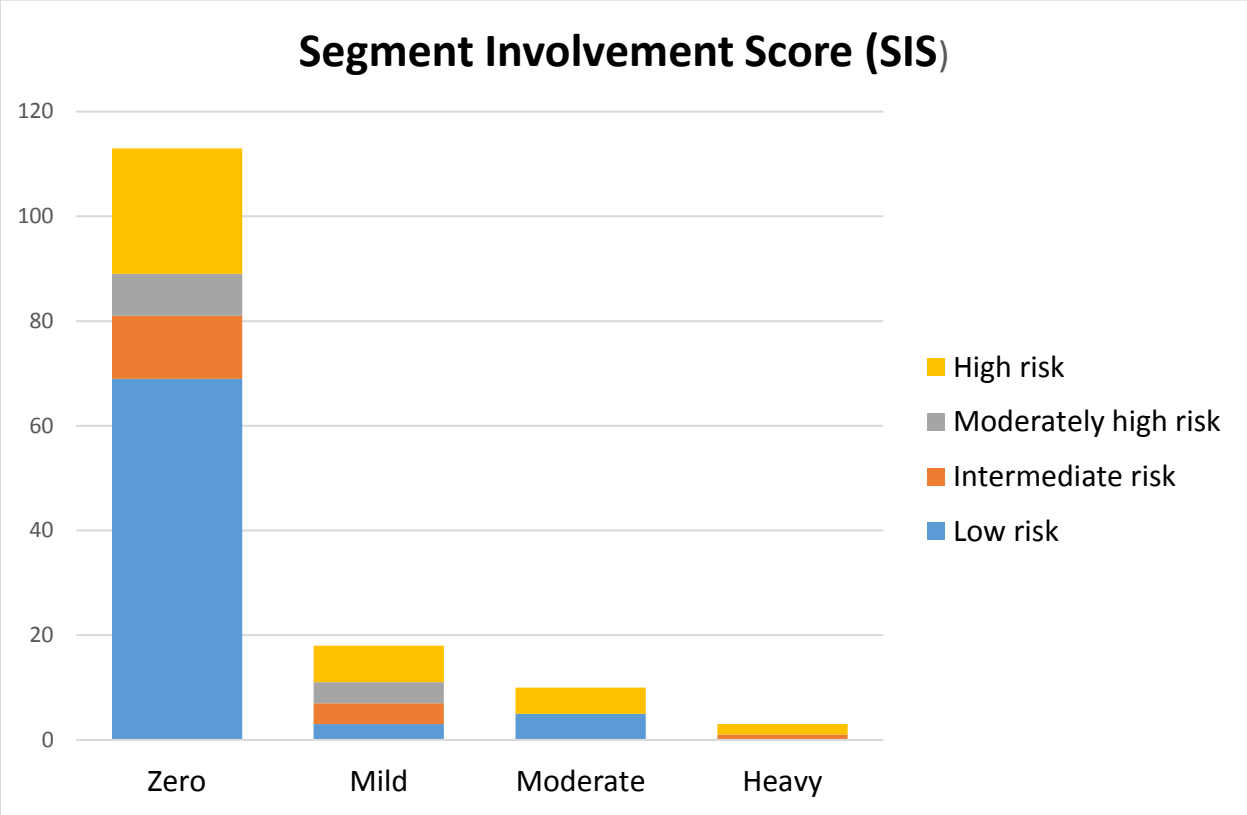


Figure 37: Comparison of NCEP risk categories with segment involvement scores (SIS); NCEP versus SIS in all patients recruited in study; n=144

Among those with coronary artery disease on CCTA, 38% with mild SIS, 50% of patients with moderate SIS and 50% of patients with heavy SIS belonged to the high risk category. Therefore, patients with higher risk showed involvement of more number of segments.

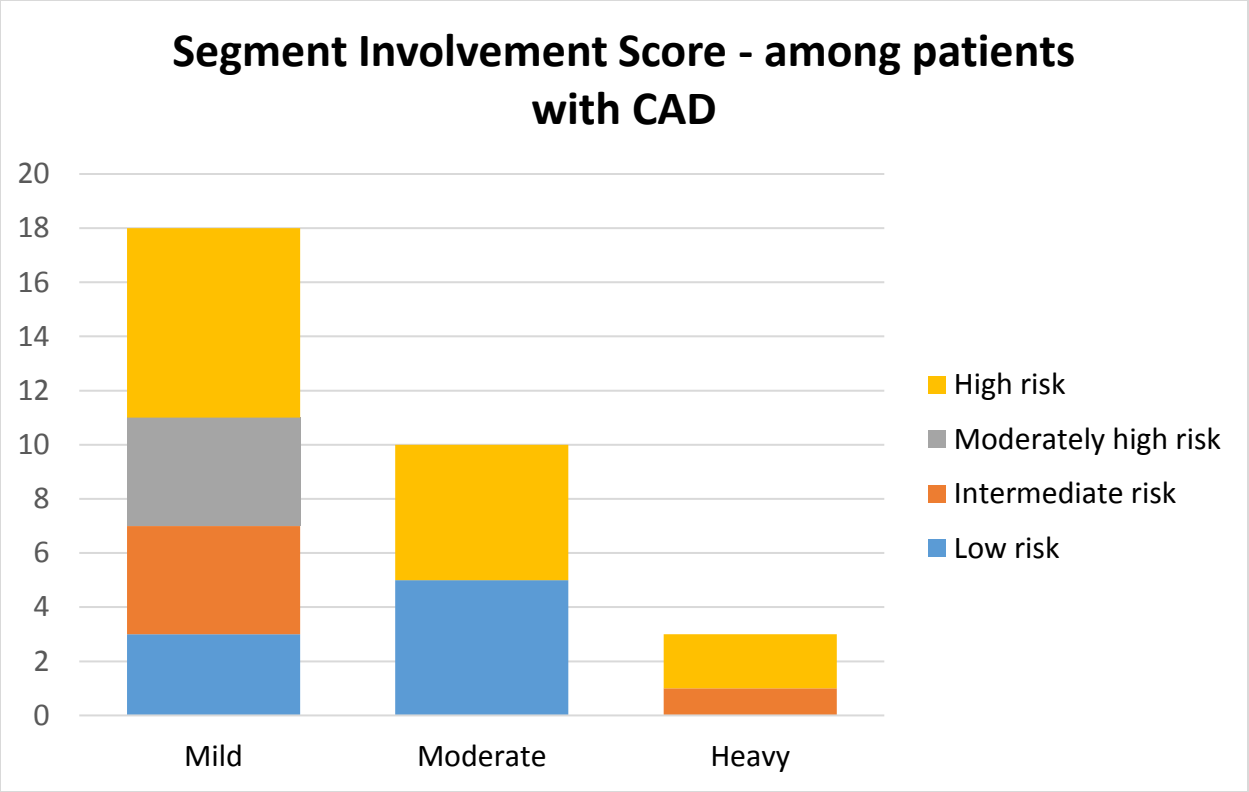


Figure 38: Comparison of NCEP risk categories with segment involvement scores in patients with coronary artery disease

b. NCEP risk categories versus Segment Plaque Score (SPS):

92% patients in the NCEP low risk category had zero segment plaque score. None of the patients in the low risk category had a heavy plaque and only one patient from the low risk category had moderate plaque burden. Therefore, overall, good correlation was seen between NCEP low risk category and low plaque burden assessed by segment plaque score (SPS) (Figure 39).

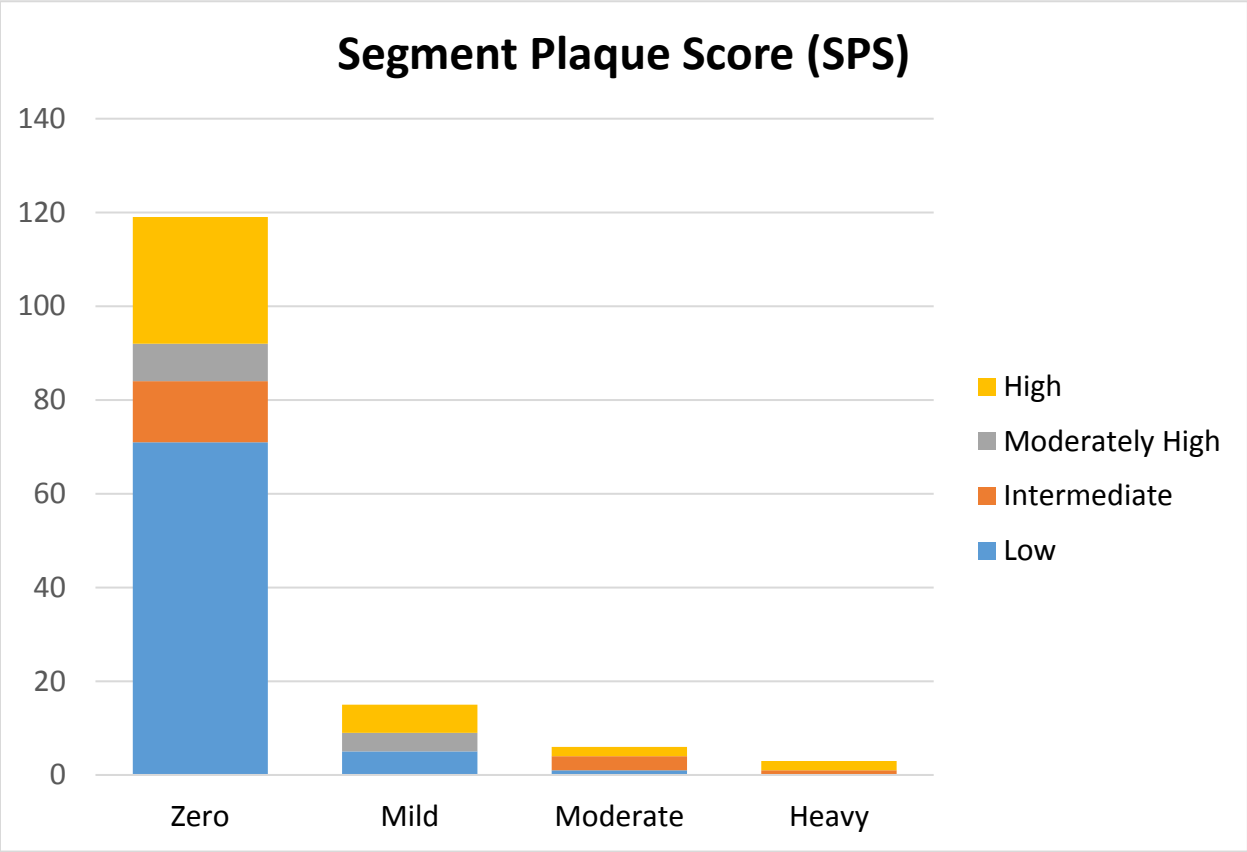


Figure 39: NCEP risk categories compared with segment plaque (SPS) among all patients recruited in study; n=144

Analysis of SPS among the subset of patients with coronary artery plaque on CCTA showed that patients who had heavy plaque (SPS score >8) fell into matching NCEP high risk category. 60% of patients who fell into the intermediate risk category had moderate plaque burden. 20% of the remaining patients had heavy disease and 20% of them has insignificant plaque burden. Overall, there is poor correlation between intermediate NCEP risk category and coronary artery plaque burden as assessed by SPS.

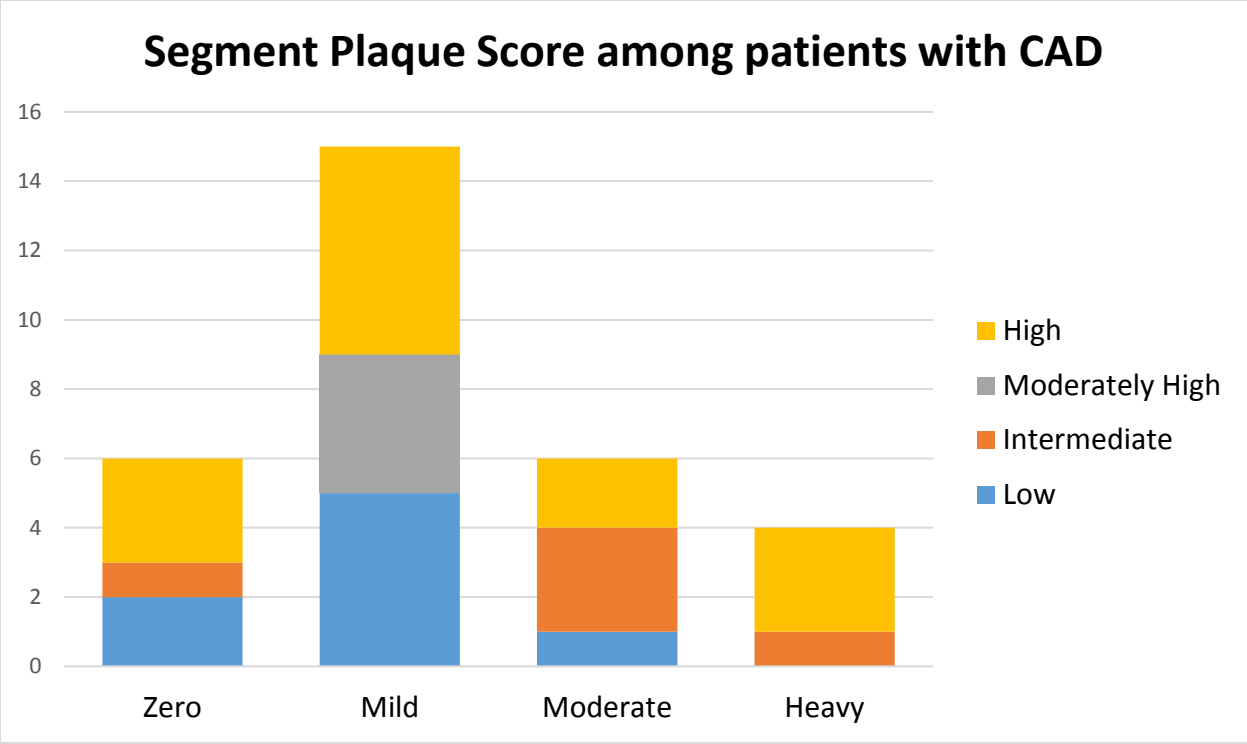


Figure 40: NCEP risk categories compared with segment plaque scores (SPS) in patients with coronary artery disease; n= 31

c. NCEP risk categories versus Segment Stenosis Score (SSS):

Segment Stenosis Score may not correlate with segment plaque score because an eccentric moderate plaque may not cause significant stenosis.

Among 144 patients, only 12 patients had plaque that caused quantifiable stenosis of the coronary artery ranging from mild stenosis (30-50%) to severe stenosis (>70%).

97% patients in the low risk category had a SSS of zero. 3% of them had SSS of 1-3 which was classified as mild. None of them had moderate or severe stenosis and

this suggests that there is good correlation between NCEP category and segment stenosis score in the low risk group.

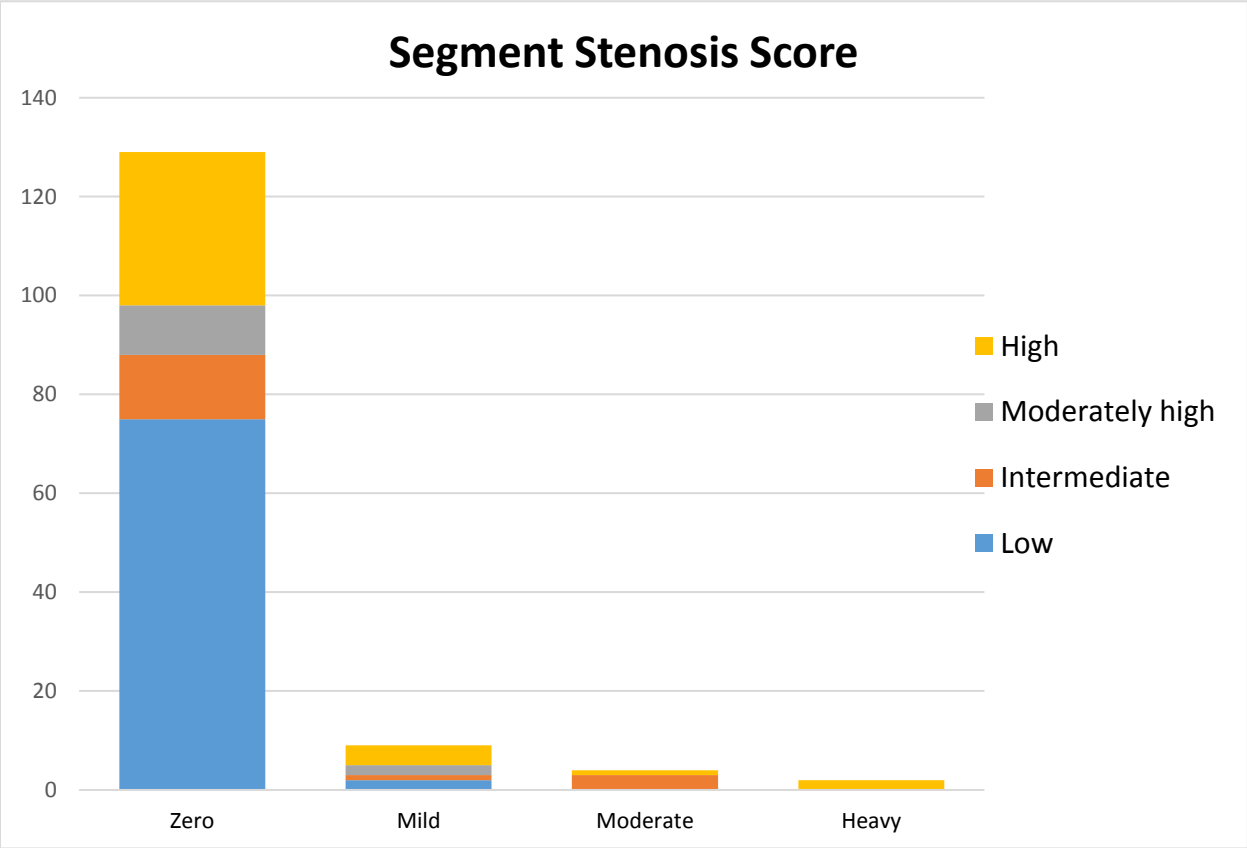


Figure 41:NCEP risk categories compared with segment stenosis scores (SSS) in all patients recruited in study; n=144

Stenosis less than 30% was considered as insignificant and given a score of zero. So, out of 31 patients with coronary artery disease, 16 patients (~50%) had less than 30% stenosis. Significant stenosis of more than 70% was seen only among patients belonging to the high risk category, suggestive of good correlation between high NCEP risk category and coronary artery plaque burden quantified using segment stenosis score.

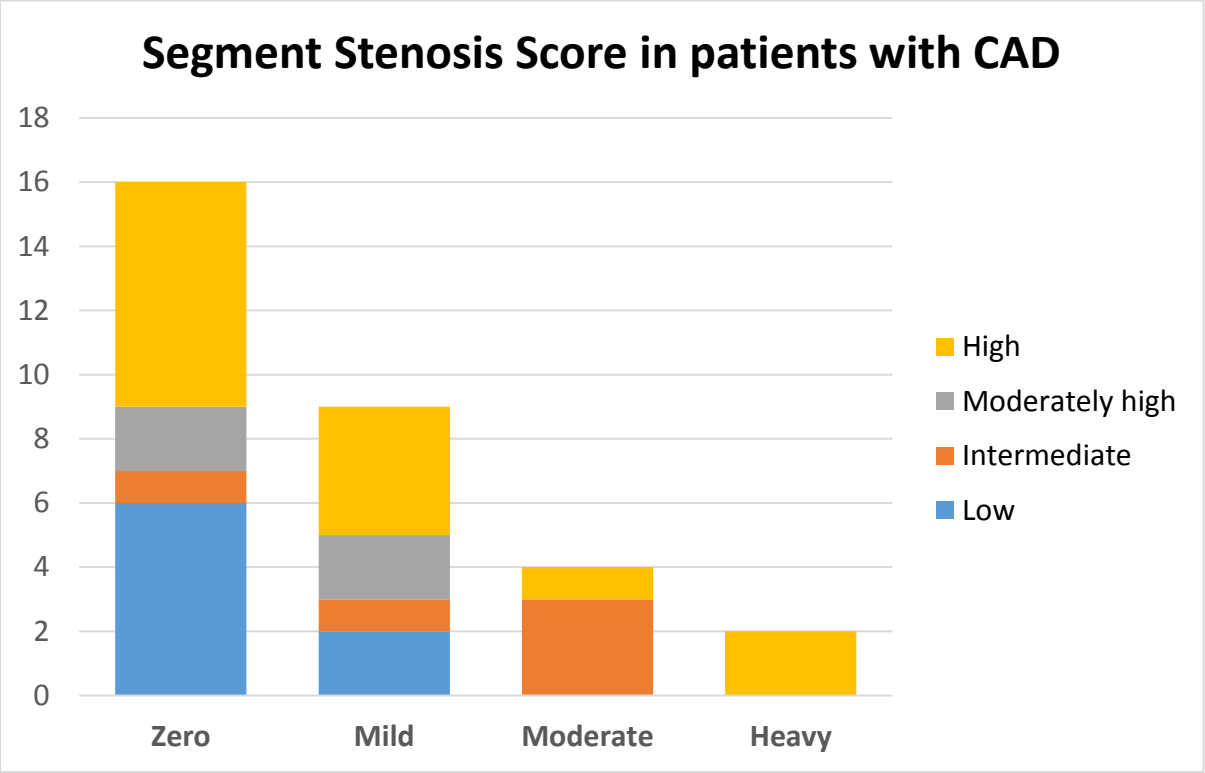


Figure 42:NCEP risk categories compared with segment stenosis scores (SSS) in patients with coronary artery disease; n=31

d. NCEP risk categories versus Modified Duke's Prognostic Index:

Patients falling into Duke category 3 and above were classified as heavy due to the presence of at least 2 moderate stenosis. 81% (117 out of 144 patients) of patients were categorized into Duke category 0 as they had no plaque or insignificant trace amounts of plaque. Among patients in Duke 0 category, 60% of patients belonged to the NCEP low risk category.

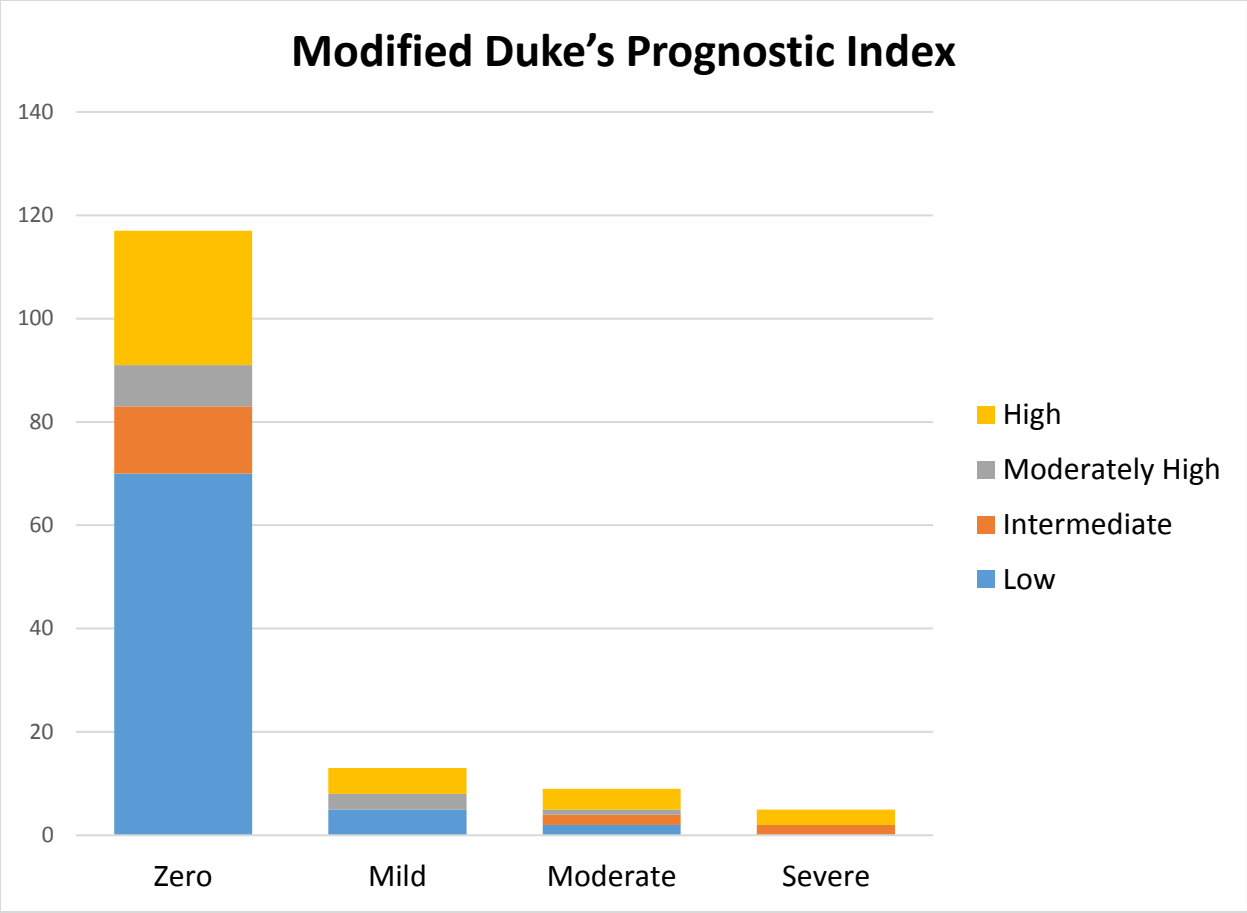


Figure 43:NCEP risk categories compared with Modified Duke's Prognostic index (MDPI) in all patients recruited in study; n=144

Similar to SPS, 60% of patients with Duke category score of more than 3 (2 or more moderate stenosis) belonged to the high risk group. The remaining 40% patients belonged to the intermediate group. But no patient with low risk had a Modified Duke's index of more than 3, thereby suggestive of good correlation between NCEP low risk group and Modified Duke's prognostic index. Hence, it demonstrates the low likelihood of patients in the low risk group from developing a cardiac event in the next 5 years.

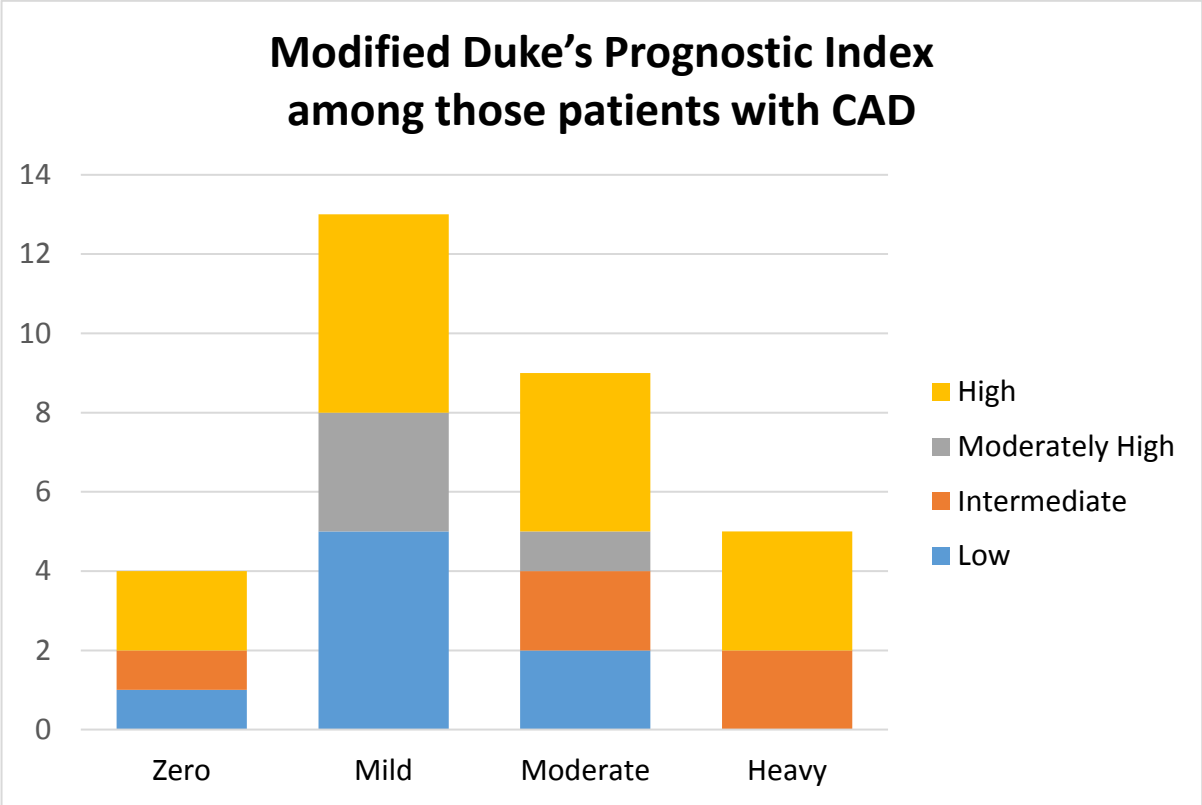


Figure 44: NCEP risk categories compared with Modified Duke's Prognostic index (MDPI) in patients with coronary artery disease; n=31

Plaque characterization using CCTA:

a. Distribution of plaques among study population:

Of 2592 segments studied, 79 segments (4%) had evidence of plaque. The remaining 2513 segments (96%) had no plaque.

Of the 79 segments involved, 62 segments had calcified plaques, 14 segments had mixed plaque and 3 segments had non calcified plaque.

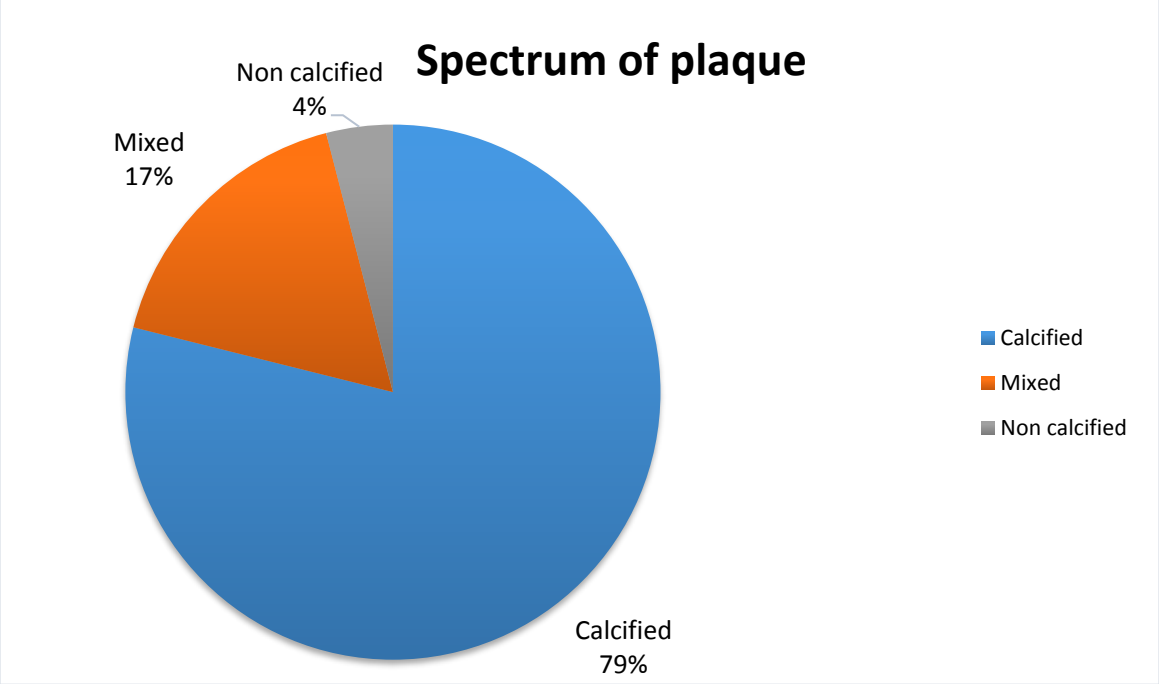


Figure 45:Distribution of subtypes of coronary artery plaque in the study population

b. NCEP risk categories and plaque type

Comparison of the NCEP risk category versus type of plaque present in a segment revealed the presence of calcified plaque across all risk groups. Mixed plaque was also seen across all risk groups in similar proportions (17-24%). Non calcified plaque, which is considered the most vulnerable for plaque rupture or thrombosis, resulting in a coronary event was seen only in 3(4%) of the 79 segments involved. All segments with non-calcified plaque were of patients in the intermediate risk group (Figure 46).

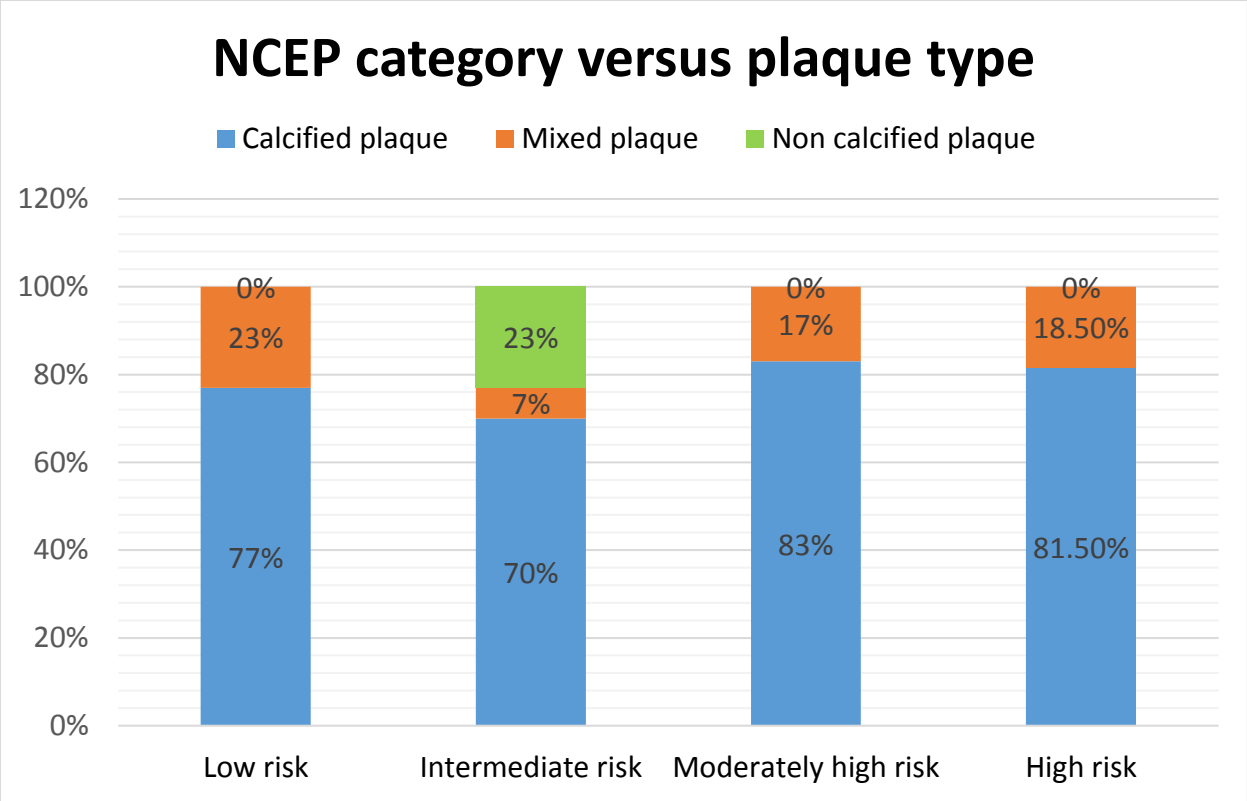
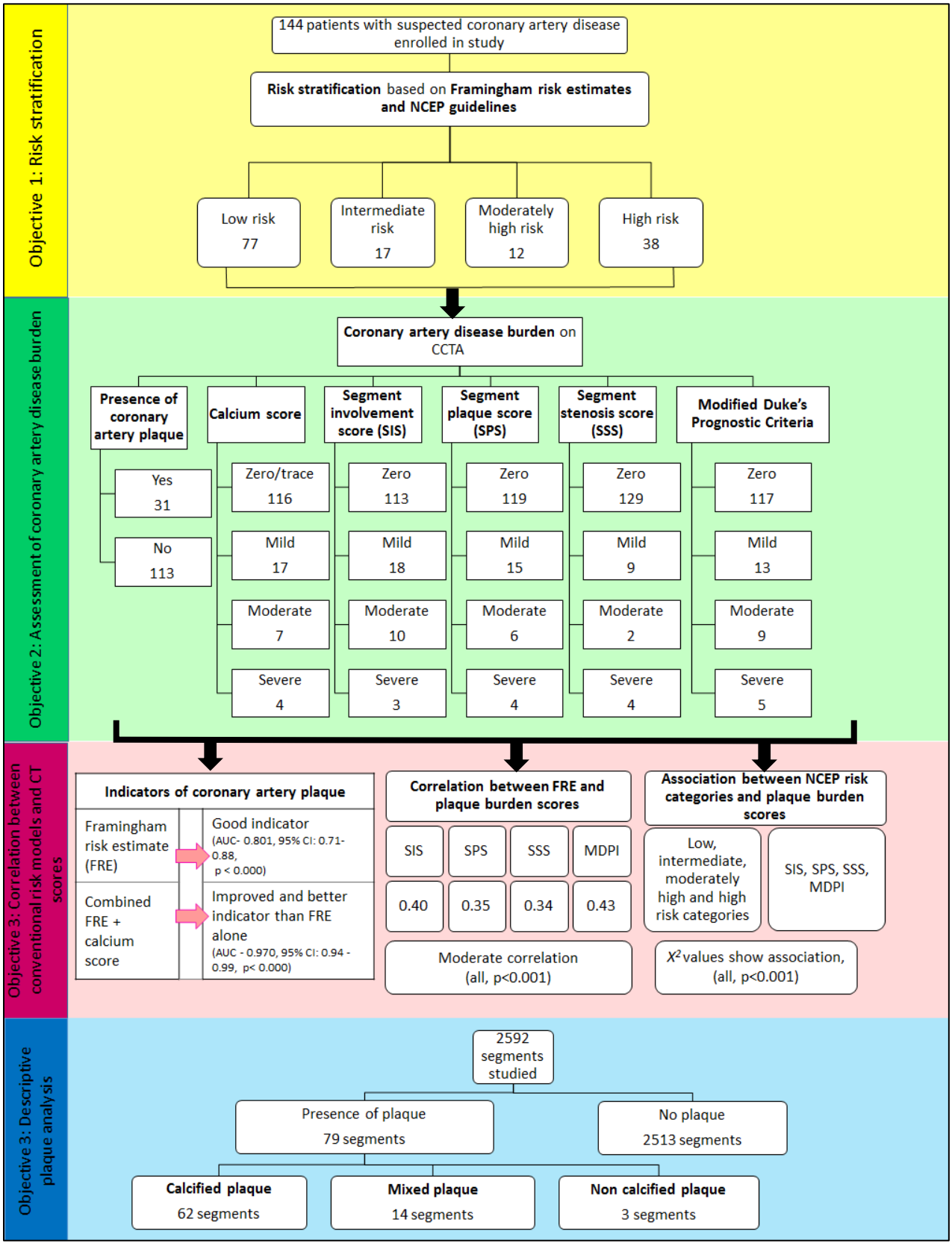


Figure 46: NCEP risk categories versus prevalence of plaque subtypes

SUMMARY OF RESULTS



DISCUSSION:

In this cross sectional study of 144 patients who underwent coronary CT angiography (CCTA) for suspected coronary artery disease, the percentage of patients who fell in the NCEP low, intermediate, moderately high and high risk categories were 54, 12, 8 and 26% respectively.

This study found a trend towards good correlation in the Indian population between Framingham risk estimates and presence of coronary artery plaque on CCTA (AUC of 0.801, 95% CT 0.71- 0.88, $p<0.001$).

This is of value in the background of the disagreement that exists regarding the predictive value of conventional risk models like the Framingham risk estimate (FRE) and the NCEP risk categories in the prediction of the risk of developing a future coronary disease event (23). FRE and NCEP risk categories are epidemiological tools which were developed for assessing risks in populations and are considered to have limited value in risk prediction when applied to individual patients(38). Therefore, a good correlation between conventional risk scores and coronary artery disease burden on CCTA validates use of these conventional scoring systems as the starting point in the management of patients especially with respect to primary prevention strategies.

We found that calcium scoring performed using the algorithm developed by Agatston et al correlated with risk categories as well as atherosclerotic plaque burden as assessed by CCTA. 62% patients with zero plaque belonged to the low risk category.

Higher calcium scores were seen in patients in the high risk category and they also had higher SIS, SPS, SSS and belonged to higher categories in Modified Duke's prognostic index. It has been established that non contrast computed tomography for calcium scoring is robust in predicting plaque burden and has been used for risk stratification along with conventional risk scoring systems. In our study, combined use of FRE and calcium score together to predict coronary artery disease was shown to be more robust than using FRE alone (AUC 0.907 versus AUC 0.801 respectively, both p value <0.001)

Calcium scoring however cannot quantify vascular stenosis or assess non calcified and mixed plaque which may have features that render the plaque as vulnerable or at high risk for rupture due to presence of a lipid core or spotty calcifications. This underestimates the actual plaque burden. Contrast enhanced study of the coronaries gives us this additional information regarding plaque burden and degree of stenosis.

Plaque burden:

The study revealed moderate correlation between Framingham risk estimates ($p<0.001$) and each of the CT scores used to assess plaque burden (Pearson's correlation co-efficient (r) = 0.401, 0.35, 0.34, 0.43 for SIS, SPS, SSS, MDPI respectively, all $p<0.001$).

Contingency tables between NCEP risk categories and plaque burden scores showed that the association between the low, intermediate, moderately high and high risk

categories and the four CT scores assessing plaque burden score was significant (p value <0.001). It was observed that 10% patients in the low risk category, 30% in the intermediate risk category had coronary artery disease. Patients belonging to high risk group however showed higher plaque burden scores.

Attention needs to be paid to the observation that 80% patients in the intermediate group, among those with coronary artery disease, had either moderate or heavy segment plaque scores. This is similar to findings in other studies that report conventional risk scoring systems underestimate coronary atherosclerotic plaque in intermediate risk population(39)(38). These results point out that even in the absence of known risk factors, that is in the low to intermediate risk groups, there is potential for development of cardiovascular events due to the presence of coronary artery plaque. This is the group of patients for whom, in the absence of an imaging evaluation, aggressive treatment strategies or lifestyle modifications would not be indicated.

Plaque characterization:

It was observed in this study that calcific plaque represented 77, 70, 83 and 81.50% in the low, intermediate, moderately high and high NCEP risk category patients respectively. This study showed that a higher proportion of patients in the intermediate risk group had non calcified plaque (23%). Non calcified plaque, along with large volume plaque are associated with a higher likelihood of complications like plaque rupture

resulting in an acute coronary event. These patients will therefore benefit from earlier interventions towards risk factor modification.

Our results are similar to findings reported by Schneer et al in the Israeli population(40) and Allajbeu et al in the Albanian population(39) that conventional risk scoring systems used in clinical practice predict fairly well the overall atherosclerotic plaque burden. In certain proportion of low and intermediate risk groups however, these risk scoring systems were inaccurate in predicting plaque burden. Our results differ from findings from Johnson et al (41) which state that traditional risk scoring systems are weak predictors of coronary artery plaque burden. Therefore, in most patients, conventional risk scoring systems can be used to guide therapy. This avoids unnecessary radiation exposure and risk related to intravenous iodinated contrast administration. However, CCTA can add significant and crucial details with regards to the coronary status in patients which will direct the treating clinician to the most appropriate treatment strategy.

Our results show that there is reasonable correlation between these risk groups and atherosclerotic disease burden that thereby suggests that low risk patients most often presents with lower plaque burden and severity and high risk patients present with higher plaque burden and severity. The intermediate risk group however shows association with both higher segment plaque scores and presence of vulnerable plaque. Therefore, patients in the intermediate NCEP risk categories would benefit from CCTA as it provides significant additional details regarding coronary artery plaque volume, degree of stenosis and plaque type, thus guiding further management.

CONCLUSION:

In conclusion, it is evident that coronary CT angiography is an accurate, reliable noninvasive imaging tool, especially in patients in low and intermediate risk groups, for the diagnosis of early, subclinical CAD. It also has additional benefits of quantifying plaque burden and detecting the presence of vulnerable low density plaques.

It has been demonstrated that there is moderate correlation between Framingham risk estimates and NCEP risk categories and presence of coronary artery plaque and the coronary artery disease burden in our study population, especially among the low risk and high risk groups.

But among intermediate risk patients, the correlation of conventional risk scoring systems with plaque burden and vulnerable plaque was observed to be less robust. The results of our study suggests that coronary CT angiography should be considered in the intermediate risk group to guide planning of optimal therapy and preventive strategies.

LIMITATIONS

The relatively small sample size is an obvious limitation of this study.

The study was confined to a specific population of patients whose clinical condition did not warrant an invasive catheter angiography. So there is an obvious selection bias as patients with a higher suspicion for coronary artery disease are taken up directly for invasive catheter angiography over coronary CT angiography.

Spectral imaging using use two X-ray tubes with different voltages to thus further characterize plaque composition was done as the study was started during the initial phases of computed tomographic imaging of the coronary arteries. This is an exciting new arena that we hope to venture into.

This was a cross sectional study and the relationship between risk estimates and plaque burden and its progression along with long term cardiovascular outcome and prognosis requires further investigation.

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ANNEXURES

ANNEXURE 1a: Consent form and patient information sheet in English

Format for Informed Consent Form for Subjects

Study Title: Study title: A comparative study of conventional risk models and CT coronary angiography

Study Number: _____

Subject's Initials: _____ Subject's Name: _____

Date of Birth / Age: _____

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____ Signature:

Or

Representative: _____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____

For any querries, kindly contact Dr. Geethu Elizabeth Punnen, PG Registrar, department of Radiology, CMC, Vellore.Mobile – 9994982024

PATIENT INFORMATION SHEET

Study title: A comparative study of conventional risk models and CT coronary angiography

The following information is provided to inform you about this study and your participation in it. Please read the information carefully and you are free to ask questions regarding the study and the information given. Participation in this study is purely voluntary and you are free to withdraw from the study anytime.

What is coronary CT angiography?

Coronary computed tomography angiography (CCTA) is a heart imaging test that helps determine if plaque buildup has narrowed a person's coronary arteries, the blood vessels that supply the heart.

What is the purpose of this study?

It is a non-invasive test which is useful for looking at the coronary arteries to assess if there is any block to the normal flow of blood to the heart. The results of this scan will help your doctor to know more about your disease condition and treat you better. The results of this study may reveal the usefulness of this test to identify coronary artery disease and will also help to treat other patients with similar illnesses better.

What are the risks involved while being a part of this study?

Your participation in this study is not associated with any added risks.

Confidentiality

Your participation in this study will remain confidential and shall be known only to the investigators. The results of the study will be published in medical journals, but your personal identity such as name and address will not be disclosed to anyone.

Withdrawal from the study

Participation in this study is purely voluntary and you can withdraw from the study anytime without explaining any reasons. It will not compromise your treatment in any way.

Detailed information about the procedure

Before the test

You have to give your consent in writing prior to the test.

You will have to meet the doctor in CT Room 22 two days prior to your test, who will then record your heart rate and blood pressure. It is essential that during the test your heart rate is at a controlled rate to avoid blurring of pictures that are acquired by the machine. To keep your heart rate under control the doctor will give you medication, T Ivabradrine 5mg, for one and a half days. The doctor will also make sure it is safe for you to undergo the test after taking done your past medical history

The day of the test

The actual test takes only about 10 to 15 minutes. However, make arrangements to stay for 2- 3hours from the time you arrive to the time you leave.

Please arrive at CT Room 22 in the Radiology department one hour prior to the scheduled test time.

You will be asked to change into a hospital gown and remove all jewellery.

During the test

The test takes only about 10 to 15 minutes.

You will be asked to lie down on a table that goes into the CT scanner and connected to a machine that monitors your heart beat.

Once the test starts, you will hear various sounds as the machine takes pictures.

We will also prompt you with instructions. For example, we may ask you to hold your breath for 8 to 10 seconds at a time.

It is important that you stay as still as possible because movements can create glitches in the pictures.

After the test

You may resume your normal activity immediately after the test.

The test results will be sent to the doctor who is treating you in OPD by the following day.

You will need to contact your treating doctor to discuss the results of your test.

Keep any scheduled follow-up appointments with your primary doctor.

ANNEXURE 1b: Consent form and patient information sheet in Tamil

ஒப்புதல் படிவம்

ஆய்வின் பெயர்: காரொநரீ சி. டி. அஞ்ச்சியோகிராப்பியில் இத யரத்த நாளங்களைப் பற்றிய பரிசோதனை

நான் _____ அவர்களின் மகன் / மகள் -ஆகிய _____

1. இந்த ஆய்வு குறித்து எனக்கு வழங்கப்பட்ட தகவல் தாளை படித்து என் சந்தேகங்களையும் தெளிவுபடுத்தினேன் என்று அறிவிக்கிறேன். [ ]
   (தயவு செய்து பெட்டிகளை குறிக்கவும்)
2. இந்த ஆய்வில் என் பங்கு முற்றிலும் தன்னார்வமானது. மேலும் என் வழக்கமான சிகிச்சை அல்லது என் சட்ட உரிமைகளை பாதிக்கும் எந்த நேரத்திலும் பங்கேற்பை நிறுத்த எனக்கு அனுமதி உண்டு என்று புரிந்துக்கொண்டேன். [ ]
3. நான் ஆய்விலிருந்து விலகினாலும். ஆய்வாளர்கள் என் சிகிச்சை விவரங்களை பரிசீலிக்க உரிமை உண்டென்று அறிகிறேன். [ ]
4. மருத்துவ ஆராய்ச்சிக்காக உதவக்கூடும் என்னுடைய எந்த தகவலையும் பயன்படுத்த நான் தடைகூர மாட்டேன். [ ]
5. இன்னை பற்றிய சொந்த தகவல்களையோ, அடையாளத்தையோ யாருக்கும் தெரியப்படித்துவதில்லை அன்று அறிகிறியன். [ ]
6. என் சொந்த விருப்பத்தினால் இந்த ஆராய்ச்சியில் பங்கேற்கிறேன். [ ]

ஆய்வில் பங்குபெறுபவரின் கையொப்பம்(அல்லது கை நாட்டை):

தேதி: _____ / _____ / _____

பெயர்: _____

கையொப்பம்:

உங்களுக்கு மேலும் கேள்விகள் இருந்தால் தொடர்பு கோள்ள வேண்டிய தொலைபேசி எண்: Dr. கீத்து புன்னன். 9994982024

ஆய்வின் பெயர்: இதயரத்த நாளங்களைப் பற்றிய பரிசோதனை (சி. டி. ஸ்கேன்)

இந்த பரிசோதனையின் முழுவிவரங்கள் இந்த ஒப்புதல் படிவத்தின் மூலம் ஆக உங்களுக்கு அறிவிக்க படுகிறது. இந்த பரிசோதனைக்கு ஒப்புதல் தருவதோ அல்லது ஏற்க மறுப்பதற்கோ உங்களுக்கு முழு உரிமை உண்டு.

காரொநரீ சி. டி. அஞ்ச்சியோகிராப்பி என்றால் என்ன?
ரத்தநாளங்களின் அமைப்பு அல்லது அதன் குறைபாடுகளை கண்டறிய மேற்கொள்ளும் சோதனை.

பரிசோதனையின் பக்கவிளைவுகள் பற்றிய விவரம்:
க. கதிர்இயக்ககருவி உபயோகித்தல்
உ. இதயத்துடிப்பை கட்டுப்படுத்தும் மருந்து ஐவபிராதின் உபயோகித்தல்
ங. கான்ட்ராஸ்ட் எனப்படும் ரத்த நாளங்களை துல்லியம்மாக படம் பிடிக்க உதவும் மருந்து உபயோகித்தல்

மேற்கூறியவற்றை உபயோகம் செய்யும் சில நேரங்களில் சதை, நாளங்கள், நரம்புகள் பாதிப்பு அடைய சில வாய்ப்பு உள்ளது.

ஆராய்ச்சியின் முடிவு என்ன?
இது உங்கள் வியாதியை கண்டறிய உதவக்கூடும்.இதனால் மற்றவர்களும் பயன் அடைவார்கள்.

உங்கள் விவரங்கள் பாதுகாக்கபடுமா?
இந்த ஆராய்ச்சி மருத்துவ இதழ்களில் வெளிவரலாம். ஆனால் உங்கள் பெயரோ, சொந்த விவரங்களோ யாரிடவும் அறிவிக்கப்படாது. உங்களை பற்றிய தகவல்கள் அனைத்தும் ஆய்வாளர்களுக்கு மட்டும் தெரிந்திருக்கும். வேறு யாரிடமும் தெரிவிக்கப்படாது.

சோதனையில் இருந்து விலகுதல்:
நீங்கள் எந்த நேரத்திலும் இந்த சோதனையில் இருந்து விலகலாம், இது உங்கள் தொடர்ச்சியான சிகிச்சையை எந்த வகையிலும் பாதிக்காது.

சோதனையின் விரிவான விவரங்கள்:

உங்களுக்கு மேலும் கேள்விகள் இருந்தால் தொடர்பு கோள்ள வேண்டிய தொலைபேசி எண்: Dr. கீத்து புன்னன். 9994982024

சோதனையின் முன்:

க. சி.டி. அறை எண் 22இல் உள்ள மருத்துவரை சந்தித்து இதயத்துடிப்பு, ரத்தஅழுத்தும் பரிசோதனை செய்து சரிபார்க்கவேண்டும். இங்கு இருந்து மருந்துகள் தரப்படும். ஏனெனில் சோதனை நாளன்று இதய துடிப்பு சரியான அளவு இருக்கவேண்டும்.

சோதனையின் நாள் அன்று:

சோதனையின்போது ஒரு மணிநேரத்திற்கு முன்பு சி. டி. அறை 22இல் வரவேண்டும்.அங்கு வந்த பிறகு துணி மாற்றிக்கொள்ள வேண்டும். இந்த சோதனை10 -15 நிமிடங்கள்தான் இருக்கும்.

சோதனையின் போது:

- அசையாமால் படுக்க வேண்டும் சொல்லும்போது மூச்சி பிடித்து வைக்கவேண்டும்

சோதனையின் பின்:

உடனே சாதாரண நிலைக்கு வந்துவிடலாம்
இந்த சோதனையின் ரிபோர்ட் உங்கள் மருத்துவரிடம் அனுப்பப்படும். நீங்கள் உங்கள் மருத்துவரை பார்த்து உங்கள் ரிபோர்ட்டை பற்றி தெரிந்துகொள்ளலாம்.

உங்களுக்கு மேலும் கேள்விகள் இருந்தால் தொடர்பு கோள்ள வேண்டிய தொலைபேசி எண்: Dr. கீத்து புன்னன். 9994982024

ANNEXURE 1c: Consent form and patient information sheet in Telugu

పార్టిసిపెంట్ యొక్క పేరు:

పుట్టిన / వయసు తేదీ (సంవత్సరాలలో):

I_____, కొడుకు / కూతురు _____

నేను చదివాను / ఈ అధ్యయనం గురించి నాకు అందించిన సమాచారం షీట్ చదివి చేయబడింది మరియు నేను కలిగి ఉన్న అనుమానాలను వివరించారు చేసిన ప్రకటిస్తాయి. [ ]

(దయచేసి టిక్ పెటండి)

నేను కూడా ఈ అధ్యయనంలో నా పాల్గొనడం పూర్తిగా స్వచ్ఛంద మరియు నా సాధారణ చికిత్స లేదా నా చట్టపరమైన కు ప్రభావితం లేకుండా ఏ సమయంలోనైనా పాల్గొనేందుకు కొనసాగించడానికి అనుమతి ఉపసంహరించుకోవాలని ఉచిత అని అర్థం [ ]

నేను విచారణ నుండి వెనక్కి కూడా అధ్యయనం సిబ్బంది మరియు ఎథిక్స్ కమిటీ సభ్యులు సంస్థాగత నా ఆరోగ్య రికార్డులను కు నా అనుమతి అవసరం లేదు అని అర్థం. నేను ఈ యాక్సెస్ అంగీకరిస్తున్నారు [ ]

అటువంటి ఒక ఉపయోగం అందించిన ఈ అధ్యయనం ద్వారా ఉత్పన్నమయ్యే ఏ డేటా లేదా ఫలితాల ఉపయోగం పరిమితం అంగీకరిస్తున్నారు మాత్రమే శాస్త్రీయ ప్రయోజనం [ ]

మీ గుర్తింపును మూడవ పార్టీలు విడుదల లేదా ప్రచురించబడిన ఏ సమాచారాన్ని బహిర్గతం చెయ్యబడదు అర్థం.

నేను స్వచ్ఛందంగా ఈ అధ్యయనంలో పాల్గొనేందుకు మీరు అంగీకరిస్తున్నారు[ ]

పేరు:

సంతకం:

తేదీ:

రోగి సమాచార పత్రం

పరిశోదన పేరు : సి.టి. కొరొనరి యాంజియోగ్రఫి మరియు సాధారణ రిస్క్ మోడల్స్ మధ్య పోలిక గురించి.

జ. క్రింద మీకు తెలుపబడిన సమాచారం, మీకు పరిశోధన గురించి అందులో మీరు పాల్గొనడం గురించి తెలియజేయును. కాబట్టి మీకు అందించిన ఈ సమాచారాన్ని మీరు జాగ్రత్తగా చదివి ఏవైనా ప్రశ్నలు తలెత్తినచో వాటిని మిమ్ము అడుగవలెనని తెలియజేయుచున్నాము. ఈ పరిశోధనలో మీరు పాలుపంచుకొనడం పూర్తిగా మీ యొక్క ఐచ్చికం, దీని నుండి మీరు ఎప్పుడైననూ తప్పుకోగలిగిన స్వేచ్ఛ మీకు ఇవ్వబడుతుంది.

కొరొనరి సి.టి. యాంజియోగ్రఫి అనగా నేమి ?

జ. ఇది మీ గుండె యొక్క రక్తనాళాలలో ఏమైనా అడ్డుపడినచో, దానిని ఛాయా చిత్రం ద్వారా తెలుపగల పరీక్ష.

ఈ స్టడీ యొక్క లక్ష్యం ఏమిటి/ దీనిని ఎందుకు చేయ గోరుచున్నాము ?

జ. ఇది శరీరానికి గాయం ఏర్పరచకుండా, ఒక మనిషి యొక్క గుండెకు చెందిన రక్తనాళాలలో ఏర్పడేటటువంటి అడ్డుపొర గురించి తద్వారా రక్త సరఫరా యొక్క హెచ్చుతగ్గుల గురించి తెలియజేయు పరీక్ష. ఈ పరీక్ష ననుసరించి మీ వైద్యుడు మీకు మరింత మెరుగుగా చికిత్స చేయగలడు. ఈ స్టడీ యొక్క ఫలితాలు ఈ పరీక్షను మిగిలిన రోగులలో కూడా చేసి వారి యొక్క రోగ స్థితిని త్వరగా తెలుసుకొనుటకు తద్వారా చికిత్స చేయుటకు ఉపయోగపడును.

ఈ పరీక్ష చేయించుకొనడం వల్ల రోగికి కలుగు హాని ఏమైనా వుందా?

గోప్యత :

ఈ పరిశోధనలో మీరు పాల్గొనడం రహస్యంగా ఉంచబడుతుంది. పరిశోధకులకు మాత్రమే మీ గురించి తెలుస్తుంది.

పరిశోధన నుండి వైదొలగుట :

ఈ పరిశోధనలో మీరు పాలుపంచుకోవడం అనేది మీ యొక్క ఐచ్ఛికం కాబట్టి మీరు ఏ సమయంలోనైనా ఈ పరిశోధన నుండి కారణం చెప్పవలసిన అవసరం లేకుండానే వైదొలగవచ్చు. ఇది ఏవిధంగాను మీ చికిత్సకు రాజీకాజాలదు.

పరీక్ష విధానం యొక్క వివరములు :

పరీక్షకు ముందు:

మీరు ఈ పరిశోధనకు ఒప్పుకుంటున్నట్లుగా ప్రాత పూర్వక పత్రం సమర్పించాలి.
మీరు గది నెం. 22 లోగల డాక్టరు గారిని పరీక్షకు రెండురోజుల ముందు కలవాలి. అక్కడ మీ డాక్టరు గారు మీ యొక్క గుండె వేగాన్ని, మరియు రక్తపోటుని నమోదు చేసుకుంటారు.
ఇది పరీక్ష జరుగు సమయంలో తీయదలచిన చిత్రాలు స్పష్టంగా రావడానికి దోహదపడుతుంది. మీ యొక్క గుండె వేగాన్ని నియంత్రించడానికి వైద్యుడు "ఇనాప్రడిన్" అను 5 మిల్లీ గ్రాముల మాత్రను ఒకటిన్నరరోజుల పాటు మీకు ఇస్తారు. డాక్టరు గారు మీ యొక్క పూర్వ వైద్య చరిత్రను కూడా తెలుసుకొని అంతా బాగానే ఉంది అనుకున్న తర్వాత మాత్రమే మీకు ఈ పరిక్ష చేయడానికి అనుమతి ఇస్తారు.

పరీక్ష రోజు :

పరిక్ష సమయం కేవలం 10-15 ని॥లు మాత్రమే అయినసూ మీరు రెండు నుండి మూడు గంటలు వేచి ఉండగల సమయానికి తగు జాగ్రత్తలు తీసుకుంటారు.
మీకు నిర్దేశించిన పరీక్ష సమయానికి ఒక గంట ముందు రేడియాలజి విభాగములో గల సిటి గది నెం. 22 వద్దకు రావలెను. మీరు మీ యొక్క బట్టలను మార్చుకుని ఆసుపత్రి గౌను ధరించి మీ యొక్క ఆభరణాలు అన్ని తీసివేయాలి

పరీక్ష జరుగు సమయము :

పరీక్ష సమయం కేవలం 10-15 ని॥లు మాత్రమే
మీరు ఒక టేబులో పై పరుండి, సిటి స్కానర్ యంత్రం లోనికి వెళ్ళవలసి వుంటుంది మరియు మీ యొక్క గుండె వేగాన్ని తెలుసుకోవడానికి ఒక యంత్రం మీకు తగిలించబడి వుంటుంది.
పరిక్ష మొదలవగానే మీకు యంత్రం పనిచేయు కొన్ని శబ్దాలు వినబడగలవు మరియు ఈ క్రమంలోనే యంత్రం మీ యొక్క గుండె ఛాయాచిత్రాలు బంధించును.
మేము మీకు కొన్ని ఆదేశాలు ఇస్తాము. దానికి అనుగుణంగా మీరు నడచుకోవలసి వుంటుంది. ఉదా॥ శ్వాస తీసుకోవడం, 8-10 సె॥ ఆపడం వంటివి.
ఒక ముఖ్యవిషయమేమనగా, పరిక్ష జరుగు సమయంలో మీరు సాధ్యమైనంత వరకు కదలకూడదు.

పరిక్ష తర్వాత :

మీరు మీ దైనందిన పనులను పరీక్ష మరుక్షణం చేసుకొనవచ్చును.
మీ పరీక్ష ఫలితాలు మీ డాక్టరు గారికి మరుసటి రోజు చేరును. మీరు పరీక్ష ఫలితాల కొరకు మీ యొక్క వైద్యుని సంప్రదించవలెను.

ఏదైనా అనుమానము ఉంటే దయచేసి సంప్రదించండి : డా. గీతం ఎలిజబెత్‌వున్నేస్
పి.జి రిజిస్ట్రార్, రేడియాలజి విభాగము, సియుంసి, వెల్లూరు.మో. 9994982024

ANNEXURE 1d: Consent form and patient information sheet in Hindi

अध्ययन सख्या:

प्रततभागी का नाम:

जन्म / Age की तारीख (र्वों में):

हचपताल नंबर:

मे_____ बेरा / बेरी

_____

एलान करता हूकी मैने जानकारी पत्र को पढा है / इस जानकारी पत्र को मेरे ललये पढा गया है,

तथा मेरे सन्देहोंका चपचरीकरण क्रकया गया है

मैंयह भी समजता हूँक्रक इस अध्ययन मेंमेरी भागीदारी परी तरह चवैस्छकि हैऔर
मझु`मेरेसामान्य उपरि

और अपनेकाननू ी अधधकारों का ज्ञान है. मैंजनताा हूकी एस अनमतत ु को वापस लेनेके ललए
मेंचवतंत्र

हुऔर इससे मेरे इलाज पर कोई असर नहीं होगा

मैंसमझता हूँक्रक अध्ययन कमटारिरयों और संचथागत नैततकता सलमतत के सदचयों को मेरे
उपरि ररकॉटि

को देखने के ललये मेरी अनमु तत की जरूरत नहीं हैऔर उसका ऊपयोग करने के ललय सहमती
देता हू

मैंसमजता हूकी इस अध्यन के पररनाऊ पर मेरा होई अधधकार नहीं होगा

मैंसमझता हूँक्रक मेरी पहानि क्रकसी तीसरेपक्ष को जारी या प्रकालति जानकारी मेंखुलासा नहींक्रकया जाएगा

मैंचवेछा इस अध्ययन मेंभाग लेनेके ललए सहमती देता हू

नाम:

हचताक्षर / अगं ठूेका तनानि

ततधथ:

गवाह का नाम:

भागीदार के संबंध:

ततधथ:

अन्वेक का हचताक्षर:

ततधथ:

किसी भी प्रकार की अधिक जानकारी के लिये कृपया संपर्क करे डाक्टर गीतू पुण्णन (९९९४९८२०२४) या email: gpunnen@gmail.com

अध्ययन का नाम: कोरोनरी धमनी की बीमारी की जाँच मे हृदय के सी. टी स्कान की भूमिका

निम्न जानकारी इस अध्ययन और उस में अपनी भागीदारी के बारे में सूचित करने के लिए प्रदान की जाती है। ध्यान से जानकारी पढ़ सकते हैं और आप को दी गई जानकारी के बारे में सवाल पूछ सकते है।। इस अध्ययन में भागीदारी पूरी तरह स्वैच्छिक है और आप अध्ययन से कभी भी वापस लेने के लिए स्वतंत्र हैं।

कोरोनरी सी.टी. एंजियोग्राफी क्या है?

कोरोनरी सीटी एंजियोग्राफी हृदय की खून की नालियों की जाँच की एक सुलभ विधि है जिसके द्वारा रक्त की प्रवाह की बाधा को आसानी से देखा जेया सकता है और चिक्तिसा मेई सुधार किया जा सकता है। इस अध्यन से प्राप्त जानकारी का उपयोग अन्य रोगियों की चिकित्सा मे मद्द कर सकति है।

क्या कोरोनरी सी टी आंजियोग्रफी से किसी प्रकार की खतरा है?

अन्य प्रक्कआर की स्ट्रीट टी के मुकाबलाए मे इस जाँच से आपको कोई अतिरिक्त खरा नहीं है।

क्या आपका व्यागततगत विवरण गोपनीया रखा जायेगा?

इस अध्यन से मिले परिणाम को किसी भी जर्नल मे प्रकाशित किया जायेगा, पर आपका नाम किसी भी जगह पर नहीं लिया जायेगा। परंतु आपके चिकित्सालय के रिकॉर्ड की समीक्षा हो सकते है उन लोगो के द्वारा जो इस अध्यन से जुड़े है, और ये आपकी जानकारी के बेगार हो सकता है।

क्या आप इस अध्यन से अपना नाम वापस ले सकते है?

इस अध्यन स्वेचक है, आप इस अध्यन से अपना नाम कभी भी वापस ले सकते है। इस से आपका कोई भी नुकसान नहीं होगा।

जाँच की बारे मे जानकारी

टेस्ट के पेहले:

आपको सहमती पत्र पर हस्ताक्षर करने होगे।
रूम २२ की डॉक्टर को टेस्ट की दो दिन पेहेले मिलना होगा। वहाँ आपका पल्स और बी.पी. ले जायेगा। स्कान के दो दिन पेहेले से हृदय का गति धीमी करने के लिये एवाब्रेडिन दवा खाना पड़ता है।

टेस्ट के दिन:

इस टेस्ट को पूरा होने के लियए १० से १५ मीनेटोका वक्त लगता है।
कृपया टेस्ट के समय से एक घंटा पेहेले आप सी टी रूम २२ मे पहुंचे
आप को आसपाताल के कपड़े पेहनने होंगे

टेस्ट के दौरान:

आपको सी टी स्कान तबले पर लेटना होगा। इसके बाद आपके हृदय धडकनोका रेकॉर्डिंग किया जायेगा। सी.टी. स्कान चालू होनेपे आपको अलग अलग तरह की आवाज सुनाई देंगे।

आपको अलग अलग सूचनाये दिया जायेगी, जैसे की आप को ८ से १० सेकंड के लिये सांस बंद करेने को कहा जायेगा
इस टेस्ट के दौरान आपको बिल्कुल हिलना नहीं है।

टेस्ट के बाद:

इस टेस्ट के बाद तुरंत आपका रोजका काम चालू कर सकते है।
टेस्ट के रिपोर्ट आपके डॉक्टर के पास भेजे जायेंगे।
आप आपके दोटॉर से मिलके इस टेस्ट के रिज़ल्ट के बारे मे जानकारी प्राप्त कर सकते है।

किसी भी प्रकार की अधिक जानकारी के लिये कृपया संपर्क करे डाक्टर गीतू पुण्णन (९९९४९८२०२४) या email: gpunnen@gmail.com

ANNEXURE 2: Data collection form

1. Name Hospital no
2. Referring unit:
3. Reason for referral:
    1. Atypical chest pain
    2. Inconclusive treadmill
    3. Family history
    4. Several risk factors – smoking/ alcohol/obesity
    5. Pre-operative clearance screening
    6. Patient anxiety
    7. Others (please specify) _____
4. Age: ☐☐ Date of birth ☐☐ ☐☐ ☐☐

5.	Sex	1. Male	2. Female
6.	Do you smoke?	1. Yes	2. No
7 a.	Do you have hypertension?	1. Yes	2. No
7 b.	If yes: are you on medications for hypertension:	1. Yes	2. No
8.	Do you have diabetes?	1. Yes	2. No
9. a.	Have you checked your cholesterol levels?	1. Yes	2. No
9. b.	If yes , are your cholesterol levels high	1. Yes	2. No
9. c.	Are you on treatment for high cholesterol levels	1. Yes	2. No
10. a.	Does anyone in your immediate family have heart disease	1. Yes	2. No

B. If yes, who had heart disease and at which age

1. Father (specify age) ☐ 2. Mother (specify age) ☐
3. Brother (specify age) ☐ 4. Sister (specify age) ☐

C. Is the history significant? 1. Yes 2. No

11. Weight (kg): 12. Height(cm):

13. Blood Pressure (mm Hg):

Systolic	Diastolic

14. BMI

1. Underweight <18.5
2. Normal weight =<18.5 – 24.9
3. Overweight 25 – 29.9
4. Obesity >=30

15. Total cholesterol (mg/dl)

16. LDL (mg/dl)

17. Triglycerides (mg/dl)

18. HDL (mg/dl)

19. Framingham risk score:

20. NCEP core risk category:

21. Coronary artery disease - any plaque:
    1. Present 2. Absent
22. Calcium score:
    1. <10AU (nonsignificant)
    2.10-100AU (mild
    3.101-400(moderate)
    4. >400 (severe)
    No of vessels involved:
23. Vessels involved:
    1. RCA 2. Left Main 3. LAD 4. LCX 5. Marginal 6. Diagonal 7. Other

24. Segment plaque score (0- 48)
    0 – trace
    1- Mild
    2- Moderate
    3- Heavy

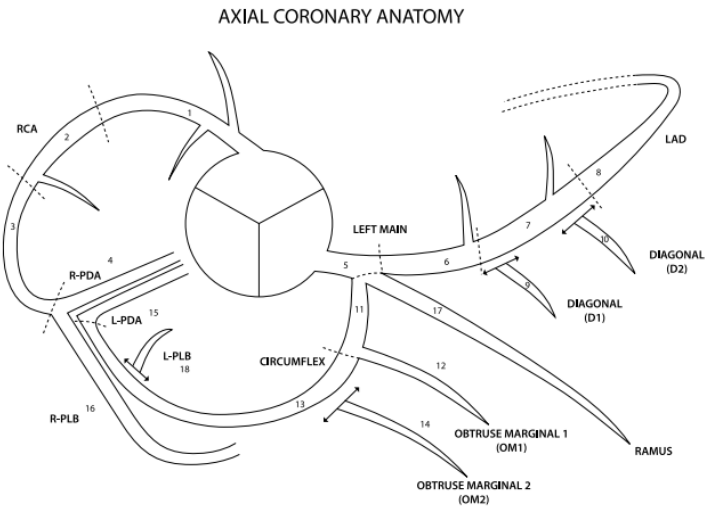

Figure 1 SCCT Coronary Segmentation Diagram. Axial coronary anatomy definitions derived, adopted, and adjusted from WG Austen, JE Edwards, RL Frye, GG Gensini, VL Gott, LS Griffith, DC McGoon, ML Murphy, BB Roe: A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. Circulation. 1975;51:5–40.

25. Segment involvement score (0-16)
    0- Absent, 1- Present

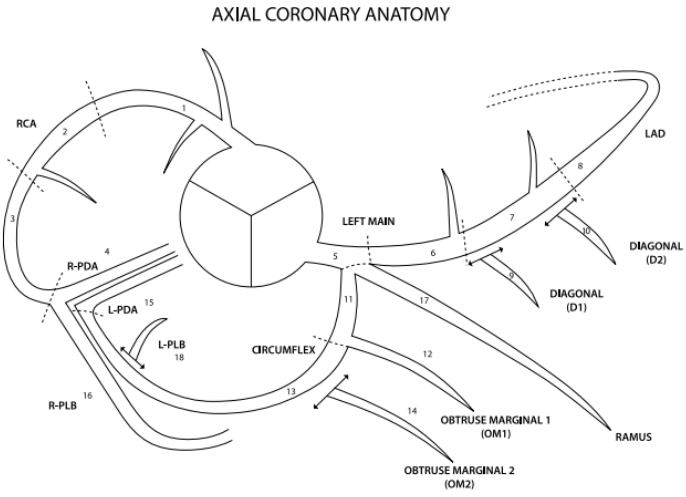

Figure 1 SCCT Coronary Segmentation Diagram. Axial coronary anatomy definitions derived, adopted, and adjusted from WG Austen, JE Edwards, RL Frye, GG Gensini, VL Gott, LS Griffith, DC McGoon, ML Murphy, BB Roe: A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. Circulation. 1975;51:5–40.

26. Segment stenosis score:
    <30%- very mild - 0
    30- 49%- mild - 1
    50-69% - moderate - 2
    >=70% severe - 3

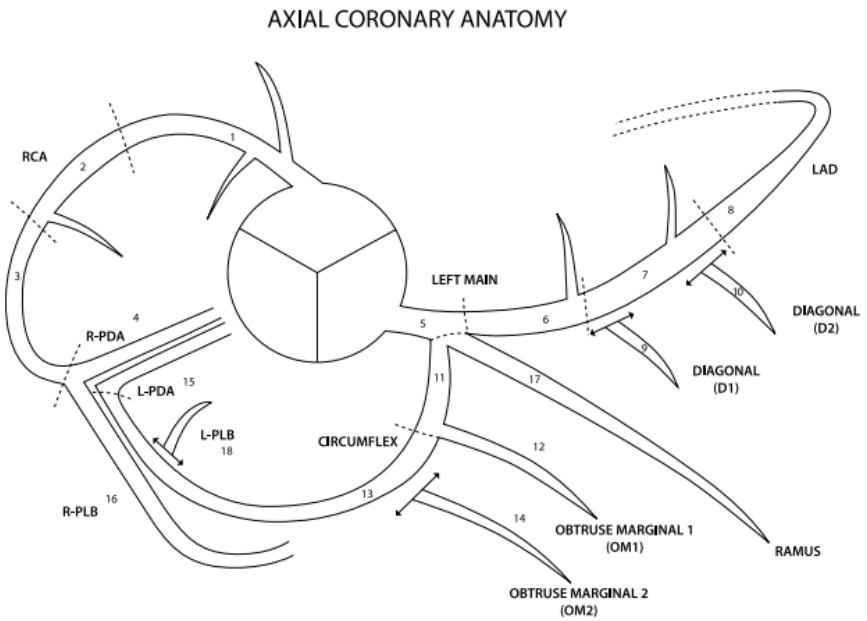

Figure 1 SCCT Coronary Segmentation Diagram. Axial coronary anatomy definitions derived, adopted, and adjusted from WG Austen, JE Edwards, RL Frye, GG Gensini, VL Gott, LS Griffith, DC McGoon, ML Murphy, BB Roe: A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. Circulation. 1975;51:5–40.

	Total score
Segment involvement score	
Segment plaque score	
Segment stenosis score	

27.Modified duke's prognostic criteria

Modified Duke's prognostic criteria		Tick as appropriate
Duke 0	No stenosis	
Duke 1	Very mild/ Mild stenosis	
Duke 2	Two or more mild stenoses with one proximal or one moderate stenosis	
Duke 3	Two moderate stenoses or one severe stenosis	
Duke 4	Three moderate stenoses, two severe stenoses, or one severe stenosis of the proximal left anterior descending (LAD) coronary artery	
Duke 5	Three severe stenoses or two severe stenoses with the proximal LAD involved	
Duke 6	Moderate or severe left main artery stenosis.	

28.Coronary plaque characteristics:

Plaque	Non calcified (1)	Mixed (2)	Calcified (3)
PI			
P2			
P3			
P4			
P5			

ANNEXURE 3: IRB Protocol

APPLICATION FOR IRB APPROVAL OF OBSERVATIONAL

(CASE-CONTROL / COHORT/ CROSS-SECTIONAL) STUDIES

CHRISTIAN MEDICAL COLLEGE, VELLORE

(Please complete Sections **I to III** and submit with all supporting documents)

SECTION I

Fluid Research Funding

Title of Research: A comparative study of conventional risk models and CT coronary angiography

Title of Study (for lay public): To compare the scores of CT based coronary artery tests and conventional clinical risk factors for coronary artery events such as heart attack and death due to heart attack

Acronym if any: nil

Unique Protocol ID, if any: nil

Name of the Principal Investigator: Dr. Geethu Elizabeth Punnen

Designation / Department / Unit / of Principal Investigator:

PG Registrar

Department of Radiodiagnosis and Imaging

Christian Medical College

Employment Number:29376

Address for communication (including telephone and fax numbers and email id):

Dr. Geethu Elizabeth Punnen

PG registrar

Department of Radiodiagnosis and Imaging

Christian Medical College

Vellore -632004

Tamil nadu

Phone no: 9994982024

E-mail: gpunnen@gmail.com

If Post Graduate Registrar / Fellowship:

Enrollment date of PG Course: 05/2014

Completion date of PG Course: 04/2017

6. Name of Guide (for Post-Graduate Registrar / Fellowship): Dr. Elizabeth Joseph

Employment Number: 20071

Address for communication

Dr. Elizabeth Joseph

Professor

Department of Radiology

Christian Medical College & Hospital

Vellore Tamil Nadu

Mobile: 09488934984

Radiology Office: 0416-228-3012/2027

Email: josephg@cmcvellore.ac.in

Name and Designation of Co-Investigator(s), Employment Number and Address :

Dr. Aparna Irodi

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Department of Radiology

Christian Medical College & Hospital

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Employment no: 28382

Dr. Binita Riya Chacko

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Dr. Leena R. V.

Assistant professor

Department of Radiology

Christian Medical College & Hospital

Vellore Tamil Nadu

Radiology office: 0416-228-3012/2027

Employment no: 28374

Dr. Paul V George

Professor of Cardiology

Department of Cardiology

Christian Medical College & Hospital

Vellore Tamil Nadu

Employment no:

Department of Institution where the research will be carried out: Department of Radiology, Christian Medical College, Vellore

Names and addresses of other institutions where research will be carried out: nil

Duration of the Scheme: 15 months

Source/s of Monetary or Material Support

Internal - Fluid /Major Research Grant : FLUID RESEARCH GRANT

External : nil

Departmental fund : nil

Objectives and aims of study

AIM:

To study the degree of correlation between conventional risk models as assessed by the National Cholesterol Education Program (NCEP) - Adult Treatment Panel (ATP) III guidelines and coronary atherosclerotic disease burden as well as risk prediction as estimated on Coronary CT Angiography (CTCA) in a tertiary care hospital in South India

Primary objectives:

5. To determine the NCEP Core risk category among patients referred for a coronary CT angiography

6. To assess the calcium score (CACS), segment plaque score (SPS), segment involvement score (SIS), segment stenosis score (SSS) and Modified dukes prognostic score, based on coronary CT angiography in the same group of patients

7. To describe plaque characteristics as lipid rich, fibrous, fibrocalcific and calcified plaques

8. To correlate the risk prediction of Modified Duke's score with the NCEP core risk score.

Secondary objectives(long term):

1. To describe the change in medical management, in the referred patients, post coronary CT angiography.

Summary of the proposed research scheme (250 words).

STUDY PERIOD: Study will be conducted in the Department of Radiology and Cardiology between January 2015 to April 2016

Using a retrospective review, a sample of 144 (72 cases and 72 controls)was arrived at to detect 20% difference in high risk (i.e above 20% of Framingham risk score) among those with coronary artery disease and those without coronary artery disease, with a power of 80% and

5% type 1 error using two tailed chi square test, assuming that 30% of patients are high risk group among those with coronary artery disease on CT angiogram and 10% of patients are of high risk group in those with no coronary artery disease on CT angiogram

All consecutive adult patients advised to undergo coronary CT angiography for suspected coronary artery disease will be recruited for the study, assuming they have no contraindication for the same.

Informed consent will be obtained by the principal investigator.

The cost of the study will be arranged by the patient themselves when affordable. If they are unable to afford the scan, provision for the scan can be arranged for them through the grant for the research project.

Demographic details of the patient with relevant history of risk factors, along with lipid profile values will be collected and the Framingham risk score will be calculated. Risk stratification of each patient according the NCEP core risk score will be performed.

The coronary CT angiography will be performed in CT Room 22 in the Radiology department in the GE HD 750 machine using standardized protocol for coronary artery imaging. The scan will be analyzed on 3D workstation and reported by the principal investigator in a standardized format and checked by a radiologist of professor grade (Guide).

Calcium score, the total plaque burden as assessed by the segment plaque score, segment involvement score, segment stenosis score and Modified duke's prognostic index, and the plaque characteristics will be assessed on each scan. Examinations which are of poor image quality will be excluded from the study.

Analysis will include the assessment of the above mentioned scores among the patient group as well as the degree of correlation between the NCEP core risk score and the Modified Duke's prognostic index in predicting a coronary event

Present Knowledge and relevant bibliography

Cardiovascular disease is the leading cause of mortality in the world. (1)Also, Indians have been shown to have a higher risk factor burden at younger ages compared with Western populations; thereby risk prediction models developed in Western countries may

underestimate CHD risk. A high short-term risk (≥10% 10-year risk or diabetes) for CHD was prevalent in more than one-fifth of the population.(2) There is a substantial lack in evidence regarding risk based coronary artery disease prediction models in the Indian population.

Risk factors for atherosclerosis and cardiovascular disease (CVD), including age, sex, lipid levels, smoking and blood pressure, are incorporated in risk algorithms that are used to predict an individual's absolute risk for CVD in the general population. Widely used risk assessment tools like the Framingham risk score (FRS) or the National Cholesterol Education Program guidelines guide initial management of patients at risk for coronary artery disease. Although these risk factors are useful to predict risk in populations, their accuracy in predicting cardiovascular risk in individuals varies considerably across populations(3). This can potentially lead to patients in high risk CHD group with limited or no plaque to be treated to life-long drug therapy, and those with low risk CHD but with significant plaque might be undertreated or not treated at all. Also the FRS does not incorporate family history and many of the components of metabolic syndrome, both of which are important risk factors for coronary heart disease(3). It is also known to underestimate subclinical atherosclerotic risk in women(4).

Imaging is considered superior to risk estimation of risk charts since:

- Direct detection of atherosclerosis is better than identifying only risk factor exposure
- Re-classification of low-risk subjects into higher strata may guide therapy
- The identification of high-risk subjects might improve adherence to risk-modifying therapy(4).

Coronary CT angiography (CCTA) has emerged as an accurate non invasive method for the evaluation of coronary artery disease (CAD), stenosis severity, extent, and distribution. It provides direct visualization of plaques, enabling its characterization, an advantage over conventional coronary angiography.

Calcium score (CACS):

The quantitative CACS protocol was introduced by Arthur Agatston and his colleagues in 1990 and has still remained the standard method in CACS. Any structure which has densities of 130 Hounsfield units (HU) or more and having an area of 1 mm2 or more will be segmented as calcified focus and those foci overlying the anatomic site of coronary arteries will be considered to represent calcified plaques. . The stratified density scores 1, 2, 3 and 4 represent the highest densities 130-199 HU, 200-299 HU, 300-399 HU and ≥ 400 HU, respectively.

The total Agatston score (AS) of each individual is calculated by summing the scores of every calcified focus through all of the coronary arteries (5)

It is established that coronary artery calcium scoring is a strong tool for prediction of coronary events.(6).

The CCTA is of more important role than CACS for CAD assessment; therefore, following CACS, patients may undergo CCTA to assess CAD likelihood. Hence, CACS has been considered to be a "gatekeeper" for CCTA(7)

There is increasing data to suggest that contrast enhanced computed tomography of the coronary arteries which help detect both calcified and non calcified plaques, thus giving a more accurate estimate of the burden of atherosclerosis

Segment plaque score(SPS):

The segment plaque score is an indicator of plaque burden. For each segment, the amount (volume) of plaque, whether calcified or not will be scored as none or trace (0), mild (1), moderate (2), or heavy (3).In case of multiple lesions in a given segment, the amount is classified by considering the segment as a whole. The SPS for each patient is calculated as the sum of individual segments' burdens.

Segment stenosis score (SSS):

Segment stenosis score is similar to segment plaque score but it uses an estimate of the diameter of the stenosis per segment rather than volume of plaque. It is scored as very mild < 30%, moderate 50-69%, or severe >=70%. Sum of all the individual segments is called the segment stenosis score.

Segment involvement score (SIS):

Each segment is scored according to the its involvement as absent or trace or as present, (1)absent, (2) present

Modified Duke's prognostic index:

Modified Duke's prognostic index has been derived from conventional angiographic data and is shown to correlate with cardiac mortality. Higher the Duke's score, higher is the risk.

The stenosis is visually graded with the varying combination of plaque in different vessels. The area a total of six Modified Duke's criteria(8)

Plaque characteristics:

Plaques can be divided as calcified, mixed or non calcified plaques. But with advance in analysis workstations, based on Hounsefeild units plaques are now classified as lipd(fatty -100 to 29HU), fibrous (30-189), fibro-calcific (190-349), calcified(>350) plaque.

Calcified plaque(CAP) represents only approximately 20% of the total atherosclerotic plaque burden and is thought to be present in the advanced stages of atherosclerosis within an individual plaque whereas non calcified plaques(NCAP) is considered to be a feature of early atherosclerosis. Furthermore, there is growing evidence suggesting that NCAP might be associated with acute coronary syndrome. However, whether the relation of CAP to NCAP is dependent of age, and whether the presence and extent of NCAP, mixed coronary atherosclerotic plaque (MCAP), and CAP are similarly associated with cardiovascular risk factors remains unclear.(9)

There is recent evidence which suggests that Coronary risk stratification using a risk factor only–based scheme is a weak discriminator of the overall atherosclerotic plaque burden in individual patients (8) The Framingham and NCEP core risk categories do not reflect the amount of coronary atherosclerotic disease detected at coronary CTA in individual patients. The study by Johnson et all (8) confirms the observations of others who used calcium scoring and extends the conclusion to include all plaque, calcified and uncalcified, detected at coronary CTA. Coronary CTA may provide incremental information beyond risk factors and may significantly influence therapeutic decisions regarding prophylactic therapy for CAD (8).

The purpose of this study will be to evaluate the degree of correlation between the conventionally used risk models such as the Framingham risk score, along with the NCEP Core risk score and the Modified Duke's score in predicting a coronary event as well as the severity of coronary artery disease as assessed by various scores on coronary CT angiography

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3. Hwang Y, Kim Y, Chung I-M, Ryu J, Park H. Coronary heart disease risk assessment and characterization of coronary artery disease using coronary CT angiography: comparison of asymptomatic and symptomatic groups. Clin Radiol. 2010 Aug;65(8):601–8.

4. Peters SAE, Ruijter HM den, Bots ML, Moons KGM. Improvements in risk stratification for the occurrence of cardiovascular disease by imaging subclinical atherosclerosis: a systematic review. Heart. 2012 Feb 1;98(3):177–84.

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6. Arjmand Shabestari A. Coronary Artery Calcium Score: A Review. Iran Red Crescent Med J [Internet]. 2013 Dec [cited 2014 Nov 22];15(12). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3955514/

7. Van Werkhoven JM, de Boer SM, Schuijf JD, Cademartiri F, Maffei E, Jukema JW, et al. Impact of clinical presentation and pretest likelihood on the relation between calcium score and computed tomographic coronary angiography. Am J Cardiol. 2010 Dec 15;106(12):1675–9.

8. Johnson KM, Dowe DA, Brink JA. Traditional Clinical Risk Assessment Tools Do Not Accurately Predict Coronary Atherosclerotic Plaque Burden: A CT Angiography Study. Am J Roentgenol. 2009 Jan 1;192(1):235–43.

9. 568.full.pdf [Internet]. [cited 2014 Nov 22]. Available from: http://atvb.ahajournals.org/content/28/3/568.full.pdf

Preliminary work already done by the investigator in this problem: nil

List of publications of the investigator in the field: nil

Structured abstract:

AIM:

To study the degree of correlation between conventional risk models and coronary atherosclerotic disease burden s well as risk prediction as estimated on coronary CT angiography in a tertiary care hospital in South India

Primary objectives:

1. To determine the NCEP Core risk category among patients referred for a coronary CT angiography

2. To assess the calcium score (CACS), segment plaque score (SPS), segment involvement score (SIS), segment stenosis score (SSS) and Modified dukes prognostic score, based on coronary CT angiography in the same group of patients

3. To describe plaque characteristics as lipid rich, fibrous, fibrocalcific and calcified plaques

4. To correlate the risk prediction of Modified Duke's score with the NCEP core risk score.

Secondary objectives(long term):

To describe the change in medical management, in the referred patients, post coronary CT angiography.

Design of data collection: Prospective descriptive study

Cases: Patients with suspected/diagnosed coronary artery disease, which are advised to undergo coronary CT angiography in the period between Jan 2015 and April 2016.

Sample size : 144 cases

Methodology:

All consecutive adult patients advised to undergo coronary CT angiography for suspected coronary artery disease will be recruited for the study, assuming they have no contraindication for the same. Informed consent will be obtained by the principal investigator.

Demographic details of the patient with relevant history of risk factors, along with lipid profile values will be collected and the Framingham risk score will be calculated. Risk stratification of each patient according the NCEP core risk score will be performed. These parameters will be compared with findings on CT coronary angiography.

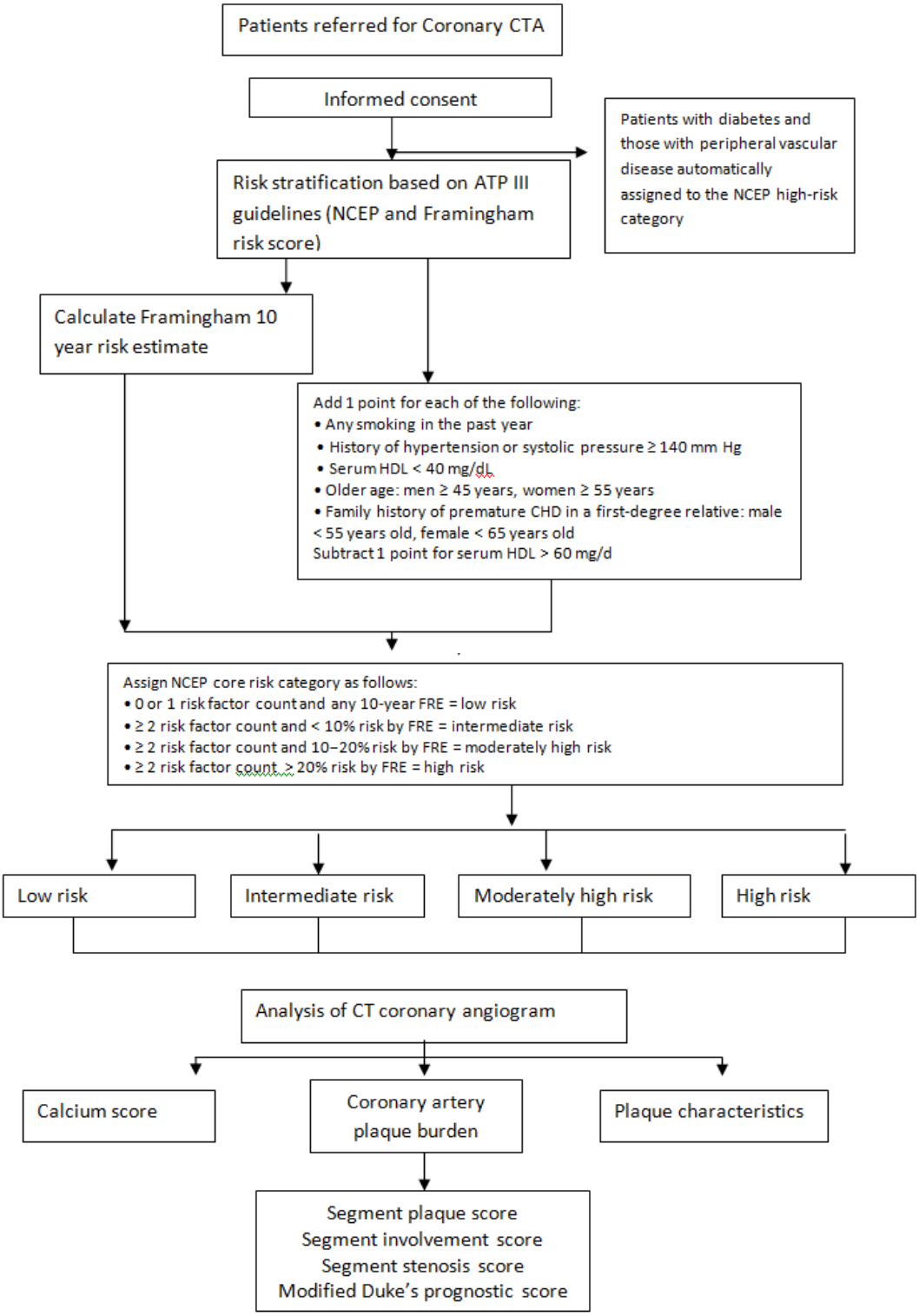
The scores that will be assessed are :

1. Calcium score
2. Segment plaque score
3. Segment involvement score
4. Segment stenosis score
5. Modified Duke's prognostic criteria
6. Coronary plaque characteristics

Outcome measures:

- Burden of coronary artery disease among the NCEP core risk groups as assessed by calcium score, segment plaque score, segment stenosis score, and segment involvement score
- The distribution of plaque characteristics among the risk groups
- The correlation of risk prediction of conventional risk models (NCEP ATP III guidelines) and Modified Duke's prognostic index in predicting a coronary event

Detailed diagrammatic Algorithm of the study



Detailed research plan:

Study population recruitment.

The study will be conducted in the Department of Radiology, Christian Medical College and Hospital, Vellore from the period between Jan 2015 and April 2016.

Sampling strategy

Patients with suspected/diagnosed coronary artery disease, who present to Cardiology services and fulfill the inclusion criteria, have none of the exclusion criteria, and have given consent to be a part of the study will be included

Sample size calculation: Using a retrospective review, a sample of 144 (72 cases and 72 controls)was arrived at to detect 20% difference in high risk (i.e. above 20% of Framingham risk score) among those with coronary artery disease and those without coronary artery disease, with a power of 80% and 5% type 1 error using two tailed chi square test, assuming that 30% of patients are high risk group among those with coronary artery disease on CT angiogram and 10% of patients are of high risk group in those with no coronary artery disease on CT angiogram

Inclusion criteria

Patients with suspected coronary artery disease with the following complaints and are advised to undergo coronary CT angiography in the period between Jan 2015 and April 2016:

8. Atypical chest pain, dyspnea or syncope
9. Inconclusive treadmill
10. Not fit for invasive catheter coronary angiography
11. Family history
12. Several risk factors – smoking/ alcohol/obesity
13. Pre operative clearance screening
14. Patient anxiety

Exclusion criteria

Patients with contraindication to the administration of iodinated contrast

Previous history of myocardial infarction, stenting, coronary artery bypass graft stenting

Poor image quality

Pregnancy

Design of data collection: Prospective descriptive study

CT coronary angiography

This test uses intravenous contrast agents to enable visualization of the coronary arteries and to look for any abnormalities of the coronary arteries such as suspected abnormal anatomy, presence of coronary artery plaques, narrowing of coronary arteries. Calcium score is a standardized score which quantifies the amount of calcified plaque in the coronary artery.

The cross-sectional images generated during a CT scan are then reformatted and reconstructed in multiple planes and reviews. Three dimensional images will be generated as well. These images can be viewed on a computer monitor.

Benefits and risks of the procedure:

Benefits

CCTA is not invasive. An alternative test, cardiac catheterization with a coronary angiogram, is invasive, has more complications related to the placement of a long catheter into the arteries and the movement of the catheter in the blood vessels, and requires more time for the patient to recover.

A major advantage of CT is that it is able to view bone, soft tissue and blood vessels all at the same time. It is therefore suited to identify other reasons for your discomfort.

CT examinations are fast and simple, can be performed even if you have a medical device of any kind, unlike MRI

Risks

There are no added risks to patients enrolling in the study. The risk involved is common to all undergoing a CT scan.

The risks of the procedure are very small and are associated with the use of the drug ivabradine and intravenous contrast agent. When receiving Ivabradine, the patient may have bradycardia which can be symptomatic. It often presents with lightheadedness, dizziness, fainting.

If a large amount of x-ray contrast material leaks out from the vessel being injected and spreads under the skin where the IV is placed, skin damage or damage to blood vessels and nerves, though unlikely, can result.

There is always a slight chance of cancer from excessive exposure to radiation. However, the benefit of an accurate diagnosis far outweighs the risk.

The effective radiation dose for this procedure varies. The reported effective radiation doses for retrospectively gated, single-source, 64-slice CT scanning have ranged from 9.5-21.4 mSv. However, various technologies and techniques have made it possible to lower the dose to less than 5 mSv are possible in some patients.

The ALARA (as low as reasonably achievable) principle applies to all studies. This principle calls for patient-specific adjustment of scanner settings to the patient's body habitus so that the lowest possible tube current setting that still results in a diagnostic study can be chosen.

The risk of serious allergic reaction to contrast materials that contain iodine is extremely rare, and radiology departments are well-equipped to deal with them. Severe complications such as the possibility of heart attack and/or death are extremely rare. The careful monitoring of your blood pressure and continuous heart monitoring serve to minimize the small risks of the test.

Before the test

The patient on being advised by the cardiologist for CT coronary angiography will be sent from the OP booking counter to CT Room22 for receiving an appointment date for the test. The radiographer in CT Room 22 will then inform the primary investigator who will then meet the patient for the test. It is essential that the patient has to be seen at least 2 days before the test in the radiology department. The patient will then be asked questions about his/her medical history and the medication(s) he/she is taking, any history of previous contrast reaction, any history of asthma, allergies. Creatinine values will be checked and recorded. This is to make

sure it is safe to have a contrast enhanced CT coronary angiogram. The procedure will also be explained to the patient in detail and the 'patient information sheet' will be given.

Their pulse and blood pressure will be measured. If heart rate is more than 65 beats/ minute, they will be given T. Ivabradine 5mg, which is a selective heart rate lowering drug. A total of 4 tablets to be taken for one and a half days, in the night 2 days prior to the scan and in the morning and in the night on the previous day of the scan. The last dose will be taken in the morning on the day of the scan.

The patient will be asked to strictly adhere to the following:

- ✓ Have a light meal and water / juice / coffee / tea prior to the appointment.
- ✓ Regular medications as instructed by the treating doctor.
- ✓ All male patients must shave their chest.
- ✓ Avoid wearing jewellery

Day of the test

Including all preparations, the CT coronary angiography scan usually takes about 15 minutes if the heart rate is slow and steady. The patient is to arrive at CT Room 22, one hour prior to the scheduled test time. Patient will be asked to change into a hospital gown and remove all jewellery. One intravenous cannula (usually 20G) will be placed.

Demographic details will be collected. Heart rate, systolic and diastolic blood pressures will be measured in the sitting position at baseline. Height, weight and waist circumference at the level of the umbilicus will be measured. If and when the heart rate is in the acceptable range for CT coronary angiogram, the test will be done.

An individual whose arterial blood pressure is 140/90 mm Hg or more or is taking antihypertensive medications will be classified as having hypertension. An individual with a non-fasting plasma glucose concentration of at least 200 mg/dl, or fasting plasma glucose level of at least 126 mg/dl, or is being treated with anti-diabetic medication will be considered to have diabetes. An individual with a body mass index (BMI) (calculated as weight divided by height squared) of 30 kg/m2 or more will be considered to be obese. A smoker is defined as an individual who smoked at least one cigarette per day or had quit smoking during the previous

year. Hypercholesterolemia is defined as a total serum cholesterol level of 240 mg/dl or more or a serum triglyceride level of 200 mg/dl or more (or both) or use of a lipid-lowering agent. Individuals were considered as having a positive family history, when they had first-degree or second-degree relatives with premature cardiovascular disease.

During the test

Just before the test, when the patient is on the scanning table, an anxiolytic, Inj Midazolam 0.25mg, diluted in 1 ml of saline will be given intravenously along with 1 puff of nitroglycerine spray, a vasodilator.

The technologist will clean three small areas of the patient's chest and place electrodes (small, sticky discs) on these areas. The electrodes are attached to an electrocardiograph (ECG) monitor, which shows the heart's electrical activity during the test.

A non-contrast scan will be done for calcium scoring. Intravenous contrast will be administered using a pressure injector along with a saline chase to remove contrast from the right side of the heart. The scanning table will move in and out of the machine depending on the type of scan done.

After the scan, the technologist will ensure that the images taken are of high enough quality for accurate interpretation. The intravenous cannula will be then removed

Machine: GE Advantage 750 HD 64 slice dual energy CT machine

Imaging protocol: Retrospective or prospective ECG gated CT coronary angiogram will be planned according to the patient's heart rate.

As with all CT applications, the ALARA (as low as reasonably achievable) principle applies. This principle calls for patient-specific adjustment of scanner settings to the patient's body habitus so that the lowest possible tube current setting that still results in a diagnostic study can be chosen.

Image reconstruction

The phase with minimal cardiac motion is preferably chosen for placement of the image reconstruction window. The transverse source images will be initially reviewed to obtain general information about the presence, location, and composition (calcified vs noncalcified) of atherosclerotic lesions. Once lesions are detected, stenosis severity is evaluated by using simple visualization tools that enable a more comprehensive and condensed display of the data set.

Maximum intensity projection and multiplanar reconstruction tools are used, along with dedicated analysis software for grading of lesions

Personnel. The coronary CT angiography studies will be reported provisionally by the principal investigator, which will then be approved by a radiologist of professor grade

Statistical methods.

Categorical variables will be represented using percentages

Continuous variables will be represented using mean and standard deviation, median and inter-quartile range. “Pearson’s correlation coefficient and t test” will be used to determine the correlation between the variables , framingham risk score and the CT scores.

Interpretation. Clinical data will not be taken into consideration while reporting the imaging findings.

Unclear results. Utmost effort will be taken to avoid any artifact or error in the CT scan and its report

Missing data. Utmost effort will be made to get back any missing information with regards to diagnosis and imaging report

Complete budget plan for all studies

Coronary CT angiography is a fairly new imaging avenue in our institution. It is not yet fully incorporated into the routine protocol for diagnosis of patients with intermediate risk of

coronary artery disease due to financial constraints. We would like to request for FLUID research grant to fund for the cost of the Coronary CT Angiography test for the period of this research project so that patients who cannot afford this study can be included as recommended by the referring clinician. We hope that the referring doctors will help in making an accurate judgment regarding patients who deserve concession.

The proposed budget is as follows:

S.no	Item	Cost per patient	No of patient	Total
1	Coronary CT angiogram	11,000	9	99,000
			Total	99,000

Name & designation of the statistician involved in your project for Statistical

Analyses: Dr. Antonisamy B

Informed Consent Documents (patient information sheet, investigator's brochure, drug information etc and informed consent document) : enclosed

Publication Plans: (List all potential authors and their likely contributions)

(Please tick √ appropriate box)

Inter-departmental cooperation: (Please describe the arrangements with institutional diagnostic service units/departments that are being used for this research project, if applicable).

Authors name	**Research & study design**	**Data collection & analysis**	**Lab analysis**	**Interpretation**	**Preparation of manuscript**	**Review of manuscript**	**Guide & critical revision**	**Administration**	**Technical support**
Dr. Geethu Elizabeth Punnen	+	+	+	+	+	+	+	+	+
Dr. Elizabeth Joseph	+	+	+	+	+	+	+	+	+
Dr. Aparna Irodi	+	+	+	+	+	+	+	+	+
Dr. Binita Riya Chacko	+	+	+	+	+	+	+	+	+
Dr. Leena R.V.	+	+	+	+	+	+	+	+	+
Dr. Paul George	+	+	+	+	-	+	+	+	+

Signature of Principal Investigator

Dr. Geethu Elizabeth Punnen

Signature of Guide/~~Head of the Department/ Unit~~

Dr. Elizabeth Joseph

Co-Investigators' Consent (all co-investigators have to sign this form or supply separate letters of consent)

I/We give my/our consent to be a Co-Investigator and provide my/our expertise to the project. I/We have approved this version of the protocol and have contributed substantially to its development.

Name	Department	Signature	Date
Dr. Aparna Irodi	Radiology		24/11/2014
Dr. Binita Riya Chacko	Radiology		24 Nov/2014
Dr. Leena R.V.	Radiology		24/11/2014
Dr. Paul George	Cardiology		24/11/14

Section II

APPLICATION FOR APPROVAL FROM ETHICS COMMITTEE OF THE INSTITUTIONAL REVIEW BOARD OF CMC VELLORE FOR ALL OBSERVATIONAL (CASE CONTROL, COHORT & OBSERVATIONAL) STUDIES IN HUMAN SUBJECTS

1. **Please provide a brief summary of the justification, objectives and methods in lay language, avoiding technical terms.**

Coronary artery disease, also known as ischemic heart disease means that one or few of the many arteries supplying the muscles of the heart are diseased and fully or partially plugged. A substance called plaque builds up in the arteries that supply blood to the heart causing it to get plugged. Plaque is made up of cholesterol deposits, which can accumulate in your arteries. Atherosclerosis is a condition that occurs when too much plaque builds up in your arteries, causing them to narrow.

Heart disease is the leading cause of death in the world and people of all ages and backgrounds can get the condition. Various conditions can increase the risk of developing heart disease, such as high blood pressure, smoking, LDL cholesterol. Not all cholesterol is bad for the heart. Some cholesterol is often termed "good," and some often termed "bad." A higher level of high–density lipoprotein cholesterol, or HDL, is considered "good," and gives some protection against heart disease. Higher levels of low–density lipoprotein, or LDL, are considered "bad" and can lead to heart disease. Several other medical conditions and lifestyle choices can also put people at a higher risk for heart disease, including:

- Diabetes
- Overweight and obesity
- Poor diet
- Physical inactivity

To determine the risk of a heart attack there are scoring systems which employ clinical and lab tests. However the predictability of these tests are uncertain, which means that there is a potential chance that patients in high risk CHD group with limited or no plaque to be treated to life-long drug therapy, and those with low risk CHD but with significant plaque might be undertreated or not treated at all. The gold standard to asses heart vesses is coronary angiogram,which is invasive, has more

complications related to the placement of a long catheter into the arteries and the movement of the catheter in the blood vessels, and requires more time for the patient to recover.

Computed tomography, more commonly known as a CT scan, is a diagnostic medical test that, like traditional x-rays, produces multiple images or pictures, in much greater detail, of the inside of the body Coronary CT scan is a test when the patient receives iodine-containing contrast material (dye) as an intravenous (IV) injection to ensure the best possible images of the heart blood vessels.

The objective of this study is to to compare the CT score used to assess heart disease and the regular widely used clinical assesment scores known as the Framingham risk score and the NCEP Core risk score in predicting cardiac events.

2. **Please describe if the study uses procedures already being performed on patients for diagnosis or treatment or if modified or novel procedures are to be used?**
   Coronary CT angiogram is an established modality of imaging diseases of the heart's blood vessels.

3. **Please describe what benefits might be reasonably be expected by the participant as an outcome of participation**
   The patients taking part in the study will benefit in that the clinician treating them will have a one-step test to assess for coronary artery disease. It may detect severe heart disease in patients who may not have significant symptoms. Awareness of the extent of coronary artery involvement may motivate patients to actively involve themselves in preventive strategies like physical exercise, diet restrictions and good compliance with medication or undergo major procedures.

4. **Please describe what benefits to others or new knowledge might be expected as a result of this study**
   This study may reveal the usefulness of CT coronary angiogram to determine early heart disease. The results of the study will help us understand if the current scoring

systems are adequate or newer scoring systems need to be established to determine initial management of patients based on their risk factors.

5. **Who are to be enrolled?**
   Only those who have been referred for Coronary Ct angiogram, and give informed consent will be enrolled. No vulnerable groups such as women, children will be enrolled.

(If any vulnerable groups (e.g., pregnant women, children) are to be enrolled, please provide a justification for their inclusion).

6. **If any economically disadvantaged individuals are to be enrolled, please provide a justification for their inclusion.**
   Not applicable

What are the potential risks to participants in this study?

There are no added risks to participants who undergo this study. All coronary CT angiograms are associated with exposure to radiation and intravenous contrast agents. Exposure to excessive radiation has a slight risk of developing cancer. Severe intravenous contrast reactions causing anaphylactic shock are very rare and our department is well equipped with a rapid response team and drugs to manage an anaphylactic reaction. Definite protocols for management of minor side effects like flushing, rash , contrast extravasations are already in place. Ivabradine is a selective heart rate lowering drug and it has minimal side effects like flushing, lightheadedness and dizziness. Ivabradine rarely causes visual side effects like phosphenes which are bright spots in field of vision which is very transient and requires no treatment. A study by Tanuj et al in 2008 , visual symptoms were reported by 3% of patients receiving ivabradine 5 mg twice daily.

7. **Are the risks to participants reasonable in relation to the benefits that might reasonably be expected as an outcome to the participant or to others, or the importance of the knowledge that may reasonably be expected to result? Please provide a detailed description of the above.**

   There is no added risk in taking part in the study. The risks associated with all coronary CT angiogram apply. These risk are reasonable in relation to the very high benefits associated with coronary CT angiography, as the extent of the disease involvement is diagnosed. This may change management or specify the need for a major procedure. It enables clinicians to assess if the present method of risk stratifying patients are accurate, or if new guidelines need to be developed.

8. **Regarding informed consent to obtained from research participants or their legally authorized representative(s):**

a. **Does the informed consent document include all the required elements?** Yes

b. **Are the participant information sheet and the consent document in language understandable to participants?** Yes

   Who will obtain informed consent (PI, nurse, other?) and in what setting?

   The informed consent will be taken by the principal investigator when the patient comes to the department of radiology with the referral coronary CT angiogram

c. **If appropriate, is there a children's assent?** Not applicable

d. **Is the EC requested to waive or alter any informed consent requirement?** No

9. **Is there provision of free treatment for research related injury?** No

10. **Is there provision for compensation of participants for disability or death resulting from**

research related injury. No

11. Is the study covered by insurance? No

12. In addition to the overall budget in Section I, please provide details of the following

a. Justification, timing and amount of payments to study participants

b. Justification, timing and amount of payments to investigators/departments

c. Any other study related financial or in kind incentives to participants or study staff

There is no other payment or financial or any other kind of incentive being planned for the participants, the study staff, investigators and their departments.

13. Please describe the plan for maintaining confidentiality of study participant information.

The study participants informatation will be saved in password protected files which will remain highly confidential, accessible to only the investigator and co - investigators

14. Please describe the plans for monitoring the safety of participants, reporting and managing adverse events. If this is an externally funded study with a Data Safety Monitoring Board, please provide the name and contact information of the DSMB chairperson.

There is an already established protocol in place to report contrast reaction which is associated with any contrast enhance CT study. There is no increased risk in patients taking part in this study. The patients who develop contrast reactions will be seen by the doctor posted in the CT room and the necessary medication for the same will be given based on the severity of the reaction. In case of contrast extravasations, Department of Hand surgery will be informed and the patient will be handed over for further management.

15. If applicable; please provide all significant previous decisions (e.g., those leading to a negative decision or modified protocol) by other ECs or regulatory authorities for the

proposed study (whether in the same location or elsewhere) and an indication of the modification(s) to the protocol. Not applicable

16. **If appropriate, has permission from the Drug Controller General of India been obtained?** Not applicable

17. **If this is international collaborative research, has permission from the Health Ministry's Screening Committee been obtained?** Not applicable

18. **For exchange of biological material in international collaborative studies, please provide a Memorandum of Understanding (MOU)/ Material Transfer Agreement (MTA) between the collaborating partners.** Not applicable

Declaration (to be signed by all investigators)

By signing this form we give our consent to provide our expertise to the project. In addition:

We confirm that all investigators have approved this version of the protocol and have contributed substantially to its development.

We confirm that all potential authors are included in this protocol.

We confirm that we shall submit any protocol amendments, significant deviations from protocols, progress reports (if required) and a final report and also participate in any audit of this study, if required.

We confirm that we shall conduct this study in accordance with the Declaration of Helsinki; the ICMR Guidelines for Biomedical Research in Human Subjects 2006, with any subsequent amendments; and all applicable laws of the land.

We also agree to submit for publication to a peer reviewed journal the complete results of this study within two years of completion of this study.

We declare that we have no conflicts of interest that may affect the conduct or reporting of this study (OR) we declare the following conflicts of interest below.

We are aware of the institution's policies regarding scientific misconduct (Falsification/fabrication/plagiarism) and agree to abide by them.

Signature of Principal Investigator

Dr. Geethu Elizabeth Punnen

Signature of Guide/~~Head of the Department/ Unit~~

Dr. Elizabeth Joseph

Co-investigator's Consent (all co-investigators have to sign this form or supply separate letters of consent)

Name	Department	Signature	Date
Dr. Aparna Irodi	Radiology		24/11/2014
Dr. Binita Riya Chacko	Radiology		24/11/2014
Dr. Leena R.V.	Radiology		24/11/2014
Dr. Paul George	Cardiology		24/11/2014

Conflicts of interest if any: none

Section III

CHECKLIST FOR PROTOCOLS SUBMITTED TO IRB OF CMC VELLORE FOR OBSERVATIONAL

(CASE CONTROL, COHORT & CROSS SECTIONAL) STUDIES

Please tick the appropriate boxes below to indicate that the following have been submitted and if not, please explain why:

1. **Form for protocols of Observational Studies with all sections (I, and II) completed [√]**
2. **Informed consent sheet *and participant information sheet* in all relevant local languages (PDF Format) [√]**
3. **Names, affiliations and signatures of all investigators/co-investigators for the declaration [√]**
4. **Signature of the Head of the department or unit as applicable (for interdepartmental studies, an agreement letter from concerned departmental heads is desirable, especially if they are not co-investigators). [√]**
5. **Recent curriculum vitae of all the investigators indicating qualification and experience and relevant publications in the past five years. [√]**
6. **If applicable, proposed compensation and reimbursement of incidental expenses and management of research related and unrelated injury/ illness during and after research period. [NA]**
7. **If applicable (in study-related injuries), a description of the arrangements for insurance coverage for research participants and copy of insurance documents from an India insurance agency. [NA]**
8. **If applicable; all significant previous decisions (e.g., those leading to a negative decision or modified [NA] protocol) by other ECs or regulatory authorities for the proposed study and an indication of the modification(s) to the protocol made on that account. The reasons for negative decisions should be provided. [NA]**
9. **Plans for publication of results - positive or negative - while maintaining the privacy and confidentiality of the study participants, with names of proposed authors and their expected contributions. [√]**

10. **All other relevant documents related to the study protocol like product information and statement of relevant regulatory clearances. [NA]**
11. **If applicable, any material used for advertisement to recruit participants to the study - this may include flyers, brochures, posters, radio and TV advertisements. [NA]**
12. **For externally funded studies, details of Funding agency/ Sponsors and breakdown of fund allocation. [NA]**
13. **One hard copy and a soft copy on CD to research@cmcvellore.ac.in of all the above. [√]**

Please list below all additional documents that are being submitted along with this application including all appendices.

1. Consent forms in English, Tamil, Telugu and Hindi
2. Patient information sheet in English, Tamil, Telugu, Hindi
3. Curriculum vitae of principal investigator, guide and co-investigators
4. Data collection sheet

ANNEXURE 4: Raw data

slno	refunit	referral	others	age	dob	sex	smoke	hyperten	hyperyes	diabetes	cholestero	cholesyes
1	crd2	3		44	03/05/1971	1	1	1	1	1	1	2
2	crd3	1		48	07/02/1967	1	2	2	2	2	1	1
3	crd2	1	hypertension	62	16/02/1953	2	2	1	2	2	1	2
4	crd2	5		73	01/07/2042	2	2	2	2	1	1	2
5	crd3	7	postive treadmil	31	05/05/1984	1	2	2	2	2	1	2
6	crd1	7	tredmil false positive	54	16/03/1961	2	2	2	2	2	1	2
7	crd2	1		59	01/07/1956	1	2	1	1	2	1	2
8	crd3	1		53	01/01/1962	1	2	2	2	2	1	1
9	crd1	1	dyspnea	34	01/07/1981	1	2	2	2	2	2	
10	crd2	1		45	01/07/1970	1	2	2	2	2	1	2
11	crd2	1		43	26/08/1972	1	2	2	2	2	1	1
12	crd3	1		51	30/08/1964	2	2	1	1	2	1	1
13	crd1	1		41	18/08/1974	2	2	2	2	1	1	1
14	crd2	7	myocarditis	54	01/07/1961	2	2	1	1	2	1	2
15	crd1	7	dyspnea, TMT false positive	48	11/07/1967	2	2	2	2	2	1	2
16	crd3			42	02/01/1973	2	2	2	2	2	1	2
17	crd3	7	tmt positive inducible ischemi	44	16/05/1972	1	2	2	2	2	1	2
18	crd1			44	01/07/1971	2	2	2	2	2	1	2
19	crd3	1		45	13/05/1970	1	2	1	1	2	1	1
20	med2	1		57	13/12/1958	1	1	1	1	2	1	1
21	crd3	7	tmt positive HTN DM	38	04/05/1977	2	2	2	2	1	1	2
22	med2	1		58	01/07/1957	2	2	1	1	1	1	2
23	crd3	2		69	01/07/1946	2	2	2	2	2	1	2
24	crd3	7	dyslipidemia	44	02/01/1971	1	2	2	2	2	1	1
25	crd2	2		49	16/05/1966	2	2	2	2	2	1	2
26	crd2	2		43	26/01/1972	1	2	2	2	2	1	2
27	crd3	7	tmt positive	48	01/07/1969	2	2	1	1	2	1	1
28	crd2	7	low pretest probablity tmt pos	49	06/10/1966	2	2	2	2	2	1	2
29	crd2	1	hypertension	53	18/02/1962	2	2	1	1	1	1	1
30	ch2	7	chest pain with raised troponi	17	01/07/1998	2	2	2	2	2	1	2
31	crd3	7	LBBB, dyslipidemia	56	14/11/1958	2	2	1	1	2	1	1
32	crd3	1		57	30/11/1957	2	2	1	1	1	1	1
33	crd3	7	dyspnea, tmt positive	44	30/05/1971	2	2	1	1	2	1	2
34	crd3	4		61	25/12/1953	2	2	1	1	1	1	2
35	crd3	7	palpitations SLE	45	01/07/1970	2	2	1	1	2	1	2
36	crd3	1		46	27/09/1969	1	2	2	2	2	1	2
37	crd3	2		50	01/07/1965	1	2	2	2	2	1	1
38	crd2	7	false pasiive thallium study	60	01/06/1955	1	2	2	2	2	1	2
39	crd1	7	dyspnea, TMT positive	36	09/05/1979	2	2	2	2	2	1	2
40	crd1	2		60	25/06/1955	2	2	2	2	2	1	1
41	crd	4		45	01/07/1970	1	2	2	2	2	1	1
42	crd2	1		56	01/07/1959	2	2	2	2	2	1	2
43	crd3	7	postive tmt	64	01/07/1951	1	2	1	1	1	1	1
44	crd3	7		44	06/06/1971	2	2	2	2	2	1	2
45	crd2	7	SPECT ischemia	25	10/06/1990	1	2	2	2	2	1	2
46	crd3	1		48	02/07/1967	2	2	1	1	2	1	2
47	crd1	7	tmt postive	53	01/07/1962	2	2	1	1	1	1	1
48	med1	4		58	12/05/1957	1	2	1	1	2	1	1
49	crd2	1		53	20/05/1962	2	2	1	1	1	1	2

treatchole	heartdisea	whoheartdi	whichage	historysig	weight	height	bp	diastolic	bmi	bmirange	totalchol	ldl	trigly	hdl	framingham
2	1	3	41	1	131	180	120	80	40.43	4	133	86	152	36	26
2	2				66	170	110	80	22.84	2	219	139	175	54	3.2
1	2				82	155	147	90	34.13	4	142	79	148	45	9.1
2	2				62	152	140	90	26.84	3	143	93	270	32	17.3
2	2				57	170	110	80	19.72	2	210	132	126	51	1
2	2				87	159	130	70	34.41	4	95	50	43	47	2.6
2	2				70	170	175	84	24.22	2	145	103	71	27	30
1	2	1			71	174	120	80	23.45	2	88	34	201	27	6.7
	2				61	164	140	90	22.68	2					
2	2				60	160	130	70	23.44	2	181	109	180	36	4.9
1	2				75	170	110	80	25.95	3	127	75	98	35	3.3
2	2				70	157	137	83	28.4	3	184	122	119	49	6.3
1	2				62	150	110	80	27.56	3	309	206	235	45	7.1
2	2				51	160	138	85	19.92	2	260	167	124	66	19.6
2	2				65	155	140	80	27.06	3	169	88	54	69	3.6
2	2				87	156	120	70	35.75	4	164	117	95	36	2
2	2				71	155	110	80	29.55	3	128	74	192	29	2.7
2	2				66	158	120	80	26.44	3	176	104	89	45	2.8
2	2				82	169	120	80	28.71	3	166	110	136	34	3.3
1	2				59	175	140	90	19.27	2	142	86	175	40	14
2	2				62	151	120	80	27.19	3	94	50	161	25	2.8
2	2				72	150	110	72	32	4	179	100	103	52	9.7
2	2				63	162	120	75	24.01	2	220	120	98	68	7.5
1	2				97	178	120	80	30.61	4	248	169	130	54	5.8
2	2				66	160	120	72	25.78	3	180	101	102	46	3.6
2	2				78	170	120	80	26.99	3	163	104	123	39	4.6
2	2				59	160	140	70	23.05	2	151	90	101	43	5.9
2	2				68	170	130	80	23.53	2	90	48	65	38	2.2
1	2				72	160	120	76	28.13	3	185	126	119	42	12.1
2	2				90	150	120	60	40	4	156	101	143	37	0.6
1	2				57	141	150	100	28.67	3	157	83	63	58	8.6
1	2				74	149	152	90	33.33	4	144	85	99	47	18.3
2	2				72	160	164	80	28.13	3	169	88	246	46	8.1
2	2				75	157	170	78	30.43	4	194	112	140	54	30
2	2				71	161	120	75	27.39	3	138	81	40	43	3
2	2				80	175	130	80	26.12	3	107	51	89	46	3.6
2	2				88	172	100	70	29.75	3	114	70	47	39	4.4
2	2				65	158	120	80	26.04	3	105	64	119	29	10
2	2				52	160	120	80	20.31	2	128	73	119	46	1.1
1	2				70	158	124	78	28.04	3	223	146	122	52	14.1
2	2				79	164	110	80	29.37	3	270	165	658	43	7.1
2	2				65	160	110	70	25.39	3	207	136	122	40	3.8
1	2				63	175	140	70	20.57	2	183	66	577	22	30
2	2				65	150	120	80	28.89	3	118	70	101	36	2
2	2				86	183	120	80	25.68	3	197	143	121	33	1.3
2	2				59	148	132	82	26.94	3	202	135	79	48	6.5
1	2				46	145	118	63	21.88	2	226	145	472	32	17.2
1	2				67	165	130	80	24.61	2	224	139	291	58	17.2
2	2				74	156	110	70	30.41	4	179	117	97	50	3.8

ncep	coronary	calcium	rca	leftmain	lad	lcx	marginal	diagonal	pda	ri	sps	sis	sss	duke	p1	p2	p3	p4	p5	p6	p7
4	1	2	2	2	1	1	2	2	2	2	4	4	4	2	4	4	4	4			
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3	1	2	1	2	1	2	2	2	2	2	3	3	0	2	4	3	3				
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4	1	2	2	2	1	2	1	1	2	2	1	3	0	0	4	4	4				
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3	1	1	2	2	2	1	2	2	2	2	1	1	0	1	4						
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3	1	2	2	2	1	2	1	2	2	2	1	2	0	1	3	4					
4	1	2	2	1	2	2	2	2	2	2	0	1	0	1	1						

50	crd3	1		31	03/03/1984	1	2	1	1	2	1	2
51	crd2	1		64	19/10/1950	2	2	1	1	1	1	1
52	crd2	2		56	05/03/1959	2	2	2	2	1	1	2
53	crd	7		54	01/07/1961	2	2	1	2	1	1	2
54	crd	7		47	01/07/1968	2	2	2	2	2	1	2
55	crd	1		33	01/07/1982	1	2	2	2	2	1	1
56	med2	4		68	14/08/2047	2	2	1	1	2	1	2
57	crd	7		44	07/07/1971	2	2	2	2	1	1	2
58	crd	1		61	24/02/1954	2	2	1	1	2	1	2
59	crd1	1		46	07/11/1968	2	2	2	2	2	1	2
60	crd1	1		63	12/12/1951	2	2	2	1	2	1	2
61	crd	1		43	01/07/1971	2	2	1	1	2	1	2
62	crd2	7		54	01/07/1961	1	2	2	2	1	1	2
63	crd2	7		58	01/07/1957	1	2	2	2	2	1	1
64	crd	2		57	19/03/1958	2	2	2	2	2	1	1
65	crd	1	triple rule out	37	22/07/1978	2	2	2	2	2	1	2
66	crd1	2		44	01/07/1971	1	2	2	2	2	1	2
67	crd	2		48	11/10/1967	2	2	2	2	2	1	2
68	crd1	1		57	01/07/1958	1	2	1	1	2	1	2
69	crd	5		76	01/07/2039	1	2	2	2	1	1	2
70	crd2	7	ventricular ectopic	54	04/05/1961	1	2	2	2	2	1	2
71	crd3	1		32	15/02/1983	1	2	2	2	2	1	1
72	crd	5		45	01/07/1970	2	2	1	1	1	1	2
73	crd2	6		37	27/07/1978	1	2	1	1	1	1	1
74	crd	1		25	02/03/1989	1	2	1	1	2	1	2
75	crd1	1		61	01/07/1954	2	2	1	1	2	1	1
76	crd1	1		30	10/03/1986	1	2	2	2	2	1	1
77	crd3	2		55	18/06/1960	2	2	2	2	2	1	1
78	crd3	4		59	01/07/1956	2	2	1	1	2	1	1
79	crd3	1		31	01/01/1984	1	2	2	2	2	1	2
80	crd2	7	tmt positive	53	01/06/1962	1	2	2	2	2	1	1
81	crd1	1		50	01/07/1965	2	2	2	2	2	2	
82	crd3	1		49	01/07/1966	2	2	1	1	2	1	
83	crd3	1		52	03/06/1963	2	2	2	2	2	1	2
84	crd3	1		40	11/02/1975	1	2	2	2	1	1	1
85	crd3	1		59	13/03/1956	2	2	1	1	2	1	1
86	crd2	7	inferior wall mi changes in ecg	32	01/07/1983	1	1	1	1	2	1	2
87	crd1	1		40	01/07/1975	2	2	1	1	2	1	1
88	crd1	2	chest pain to arm	56	05/04/1959	1	2	2	2	2	1	1
89	crd1	2		45	01/07/1970	2	2	1	1	2	1	2
90	crd2	6		60	03/02/1956	1	2	1	1	2	1	2
91	crd1	2		54		2	2	2	2	2	1	2
92	crd1	1		34	15/06/1981	1	2	2	2	2	1	2
93	crd3	1		39	01/01/1976	2	2	2	2	2	1	2
94	crd	1		72	30/04/1943	1	2	1	1	2	1	2
95	crd3	1		41		1	2	2	2	2	1	2
96	crd3	1		47		2	2	2	2	2	1	2
97	crd3	2		36	03/08/1979	1	2	2	2	2	1	2
98	crd2	1		57	10/04/1958	1	2	2	2	2	1	2
99	crd1	1		64	01/07/1948	1	2	1	1	1	1	1

2	2				70	172	140	80	23.66	2	157	78	162	54	1.9
1	2				58	154	130	90	24.46	2	113	66	97	40	13.3
2	2				65	160	120	80	25.39	3	200	127	120	55	9.4
2	2				90	158	120	87	36.05	4	118	581	116	49	6.8
2	2				70	156	110	60	28.76	3	127	76	82	47	1.3
1	2				98	176	120	74	31.64	4	221	161	66	43	3.6
2	2				55	157	160	100	22.31	2	120	54	53	50	12.7
2	2				60	158	120	80	24.03	2	144	98	89	44	5.8
2	2				55	155	130	70	22.89	2	163	109	91	44	8.9
2	2				60	160	130	90	23.44	2	179	110	167	41	4.1
2	2				60	156	104	63	24.65	2	185	101	150	64	3.5
2	2				60	155	116	72	24.97	3	183	123	127	35	4
2	2				62	179	100	80	19.35	2	134	92	88	28	12.2
2	2				72	168	158	87	25.51	3	157	93	155	48	14.7
1	2				65	154	130	70	27.41	3	167	98	138	53	5.2
2	2				75	152	109	73	32.46	4	183	118	73	54	1.3
2	2				63	160	110	70	24.61	2	138	88	87	36	1.9
2	2				67	167	100	63	24.02	2	135	62	71	66	1.1
2	2				60	160	110	70	23.44	2	185	118	236	33	16
1	2				68	170	100	66	23.53	2	145	74	63	71	15
2	2				93	190	120	80	25.76	3	167	110	99	44	8.4
1	2				77	172	120	70	26.03	3	550	409	499	24	19
2	2				114	158	140	90	45.67	4	152	82	245	31	12.4
1	2				74	175	121	73	24.16	2	98	61	113	28	5.5
2	2				68	172	130	86	22.99	2	170	103	213	37	1.6
1	2				64	154	130	90	26.99	3	145	78	114	52	6.9
2	2				60	148	120	70	27.39	3	207	129	121	53	1.2
2	2				87	162	125	79	33.15	4	206	95	84	94	3.7
1	2				74	163	129	80	27.85	3	197	111	179	61	6.6
2	2				88	181	102	63	26.86	3	131	71	183	40	1.3
1	2				80	174	121	71	26.42	3	181	103	154	33	11
	2				73	154	130	80	30.78	4	326	232	76	63	7.5
2	2				83	155	128	90	34.55	4	135	60	131	50	3.4
2	2				100	170	130	80	34.6	4	126	71	283	71	8.5
1	2				58	149	140	80	26.12	3	195	114	104	39	13.4
2	2				100	176	120	80	32.28	4	146	87	153	25	6.5
2	2				70	154	110	80	29.52	3	211	126	85	47	2.8
1	2				70	174	120	80	23.12	2	189	114	155	39	12.4
2	2				65	156	130	80	26.71	3	162	98	163	31	5.7
2	2				70	170	138	78	24.22	2	188	104	76	51	19
2	2				60	145	136	80	28.54	3	187	120	122	40	7.2
2	2				63	174	130	90	20.81	2	126	57	109	67	1.3
2	2				69	151	119	77	30.26	4	147	81	148	43	1.6
2	2				65	170	130	80	22.49	2	202	115	51	52	30
2	2				83	178	145	75	26.2	3	151	96	131	36	5.8
2	2				52	150	108	76	23.11	2	167	94	63	60	1.8
2	2				65	170	100	90	22.49	2	169	114	125	28	2.3
					68	170	120	90	23.53	2	191	108	75	52	9.8
1	2				62	177	107	62	19.79	2	99	47	92	40	28

1	2																				
4	1	3	2	2	1	1	2	2	2	2											
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1	1	2	2	1	2	1	2	2	2	2	0	2	0	0	4	4					
1	1	3	1	1	1	2	2	2	2	2	2	3	1	1	4	3	3				
1	1	2	1	2	1	2	2	2	2	2	1	2	1	1	3	4					
3	1	2	1	2	1	2	2	2	2	2	2	2	2	1	4	4					
1	2																				
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4	1	2	1	2	2	2	2	2	2	2	2	1	2	2	3						
2	2																				
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1	2																				
1	2																				
4	2																				

100	crd3	1		41	25/01/1945	1	2	2	2	2	1	2
101	cd3	1		52	01/07/1963	2	2	1	1	1	1	1
102	crd3	1		46	28/01/2016	2	2	1	1	2	1	2
103	crd2	1		42	02/03/1973	2	2	2	2	2	1	2
104	crd3	1		27	01/07/1988	1	2	2	2	2	1	2
105	crd3	1		50	31/01/1965	1	2	2	2	2	1	1
106	crd3	1		60	10/08/1955	2	2	1	1	2	1	1
107	med5	1		41	01/07/1974	2	2	2	2	2	1	2
108	crd3	1		62	08/04/1953	2	2	2	2	1	1	1
109	med1	7	breathing difficulty	65	01/07/1950	2	2	1	1	1	1	1
110		4		76	10/07/1939	1	1	1	1	2	1	1
111	crd3	1		52	01/07/1963	1	2	1	1	2	1	1
112	med2	1		50	19/07/1965	1	2	2	2	2	1	1
113	crd3	4		71	01/07/1945	1	2	1	1	1	1	1
114	crd3	2		40	06/05/1975	1	2	1	1	2	1	1
115	crd3	1		64	01/01/1952	1	2	1	1	2	1	1
116	crd3	1		50	01/07/1965	2	2	2	2	2	1	1
117	epc	1		68	01/07/1947	1	2	1	1	2	1	2
118	crd2	1		61	01/07/1954	2	2	2	2	2	2	
119	crd2	1		61	21/05/1955	2	2	2	2	2	1	2
120	med2	1		59	01/03/1956	1	1	1	1	2	1	1
121	crd3	4		36	06/10/1979	1	2	1	1	2	1	1
122	crd3	1		54	07/04/1962	2	2	2	2	2	1	1
123	epc	1		60	01/07/1955	1	2	2	2	2	1	2
124	crd3	1		56	24/08/1959	2	2	1	1	2	1	1
125	crd3	1		54	01/07/1960	2	2	2	2	2	1	1
126	epc	1		62	12/11/1953	1	2	1	1	2	1	1
127	crd2	4		68	01/07/1947	2	2	1	1	2	1	1
128	crd3	4		49	01/07/1969	2	2	1	1	1	1	1
129	crd1	1		66	01/07/1947	1	2	1	1	1	1	2
130	epc	1		42	01/07/1973	1	2	2	2	1	1	1
131	crd3	1		38	01/07/1977	2	2	1	1	2	1	2
132	crd1	1		39	02/02/1977	1	2	1	1	2	1	1
133	crd3	1		47	22/05/1969	2	2	2	2	2	1	2
134	epc	1		67	01/07/1949	1	2	2	2	1	1	2
135	crd3	1		53	10/02/1963	2	2	1	1	2	1	1
136	crd3	7	transient ecg changes	35	01/07/1980	1	2	2	2	2	2	
137	crd3	2		41	05/02/1975	2	2	2	2	1	1	1
138	crd3	4		52	05/11/1962	2	2	1	1	1	1	1
139	crd2	1		60	12/09/1955	2	2	1	1	1	1	1
140	crd1	1		45	01/07/1970	2	2	1	1	2	1	2
141	epc	4		68	11/04/1948	2	2	1	1	2	1	2
142	epc	4	family history	56	01/07/1959	2	2	1	1	2	1	2
143	crd3	4		40	10/09/1975	2	2	1	1	1	1	1
144	med2	2		40	19/04/1976	2	2	1	1	2	1	2

2	2				83	175	129	79	27.1	3	151	96	131	36	4.2
2	2				75	155	142	74	31.22	4	145	90	60	38	10.8
2	2				65	150	100	70	28.89	3	185	126	107	38	1.7
2	2				68	159	130	90	26.9	3	158	92	118	43	2.1
2	2				85	170	120	80	29.41	3	175	109	183	34	1.3
2	2				72	180	141	75	22.22	2	217	164	95	39	7.9
1	2				55	156	121	73	22.6	2	246	145	182	40	12.1
2	2				60	164	100	60	22.31	2	128	76	56	59	1
1	2				65	150	120	80	28.89	3	99	42	82	52	5.2
1	2				77	148	140	90	35.15	4	204	134		77	56
1	2				60	166	110	70	21.77	2	226	140	93	53	30
1	2				80	166	123	72	29.03	3	106	56	107	44	5.5
1	2				64	165	130	80	23.51	2	144	75	86	55	5.4
1	2				80	170	129	80	27.68	3	157	92	97	60	30
2	2				79	165	130	80	29.02	3	189	250	53	105	5.3
1	2				68	172	131	73	22.99	2	126	69	152	42	16
1	2				63	154	116	75	26.56	3	189	117	185	35	4.2
2	2				44	161	150	70	16.97	1	180	112	73	45	30
	2				56	158	111	78	22.43	2	207	120	193	57	4.5
2	2				49	145	140	80	23.31	2	194	133	98	49	9.4
1	2				51	155	130	80	21.23	2	153	92	120	33	30
1	2				66	167	121	76	23.67	2	252	161	235	42	5.7
1	2				54	150	100	60	24	2	144	83	91	48	2.4
2	2				90	177	108	73	28.73	3	175	125	159	32	13
1	2				68	160	110	70	26.56	3	174	110	100	54	4.4
2	2				67	152	125	78	29	3	275	178	291	59	7
1	2				69	166	130	78	25.04	3	149	98	90	42	19
1	2				65	154	140	79	27.41	3	160	84	85	72	11.4
1	2				67	156	100	60	27.53	3	147	84	90	51	5.4
1	2				70	173	122	87	23.39	2	93	63	33	51	19.6
1	2				55	162	130	90	20.96	2	168	173	91	45	5.7
2	2				76	160	150	90	29.69	3	217	153	103	50	5.8
1	2				76	170	130	80	26.3	3	201	128	109	48	5.3
2	2				57	157	120	90	23.12	2	125	79	95	35	2.5
2	2				64	170	129	79	22.15	2	119	63	141	40	22
1	2				61	158	137	75	24.44	2	176	119	180	43	8.4
	2				77	176	90	60	24.86	2	138	85	121	34	1.4
1	2				72	166	106	75	26.13	3	266	149	608	47	4.5
1	2				88	164	140	80	32.72	4	175	115	105	42	17
1	2				65	146	114	78	30.49	4	110	67	45	48	7.3
2	2				62	150	140	90	27.56	3	147	78	172	43	4.9
2	2				68	154	136	78	28.67	3	145	78	172	43	11.3
2	1	1	80	2	75	160	110	60	29.3	3	193	117	140	42	5.9
1	2				76	154	106	70	32.05	4	178	110	213	34	5.1
2	2				59	156	100	80	24.24	2	164	112	103	33	2.6

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