THE PATTERN OF FINDINGS BY STRESS MYOCARDIAL PERFUSION SPECT SCAN IN SUSPECTED OR KNOWN CORONARY ARTERY DISEASE – NAIROBI EXPERIENCE

A dissertation to be submitted in part-fulfilment for the degree of Master of Medicine in Diagnostic Radiology of University of Nairobi.

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DECLARATION

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This dissertation is my original work and has not been presented for a degree in any other university.

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This dissertation has been submitted for examination with my approval as a university supervisor.

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ABBREVIATIONS	FULL DESCRIPTION
CAD	Coronary Artery Disease
CT	Computerized Tomography
CVS	Cardiovascular System
ECG	Electro cardiogram
I.V	Intravenous
KeV	Kilo – Electron - Volts
LAO	Left Anterior Oblique
LOCM	Low Osmolality Contrast Media
MBq units	Mega – Becquerel units.
MITC	Medical Imaging and Therapeutic Centre
M-Mode	Motion mode
MRI	Magnetic Resonance Imaging
NaI	Sodium iodide
PET	Positron Emission Tomography
PHA	Pulse Height Analyzer
PMT	Photo Multiplier Tube
RAO	Right Anterior Oblique
SPECT	Single Photon Emission Computerized
	Tomography
U/S	Ultra sound
2-D	Two dimensional
^{99m}Tc	Metastable 99 Technetium

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SUMMARY

Context: Coronary artery disease (CAD) is a major cause of morbidity and mortality in the developed world. This has also been found to be true in the developing countries although minimal statistics are available to support this.

Objective: To establish the demographics, common clinical presentation and predictive value of stress myocardial perfusion Single Photon Emission Computerized Tomography (SPECT) scan in suspected and known CAD in Nairobi and thus describe its role in management of the same.

Design: Prospective study from April 2005 – February 2006.

Methodology and participants: Single day stress – rest protocol with SPECT acquisition using ^{99m}Tc- tetrofosmin was carried out on all patients referred for this investigation by their primary care physician. A correlation of the perfusion scan findings with angiographic data (where available) and clinical follow-up, was made. The clinical end points were furnished by referring physicians.

Results: There was a male preponderance (65.7%) with the mean age of presentation being 60 years and standard deviation 11.4. Male: Female was 1.9:1. Chest pain and abnormal stress electrocardiogram (ECG) were the common reasons for referral for nuclear perfusion imaging. Of the patients studied 66.7% showed concordance of the myocardial perfusion scan and angiographic findings. In reference to clinical outcome, myocardial perfusion SPECT scan had a sensitivity of 93.5% and a specificity of 97.5%. Positive predictive value of SPECT was 83.3% and its negative predictive value was 50% in this study.

Conclusion: Stress myocardial perfusion SPECT scan is a valuable non-invasive imaging modality in assessment of coronary artery disease which has a good sensitivity and specifity and correlates with clinical outcome data. It reliably assesses the likelihood of a future cardiac event.

INTRODUCTION

Coronary Artery Disease (CAD) is increasingly becoming a health problem owing to dietary habits, stressful lifestyles, a rise in the incidence of smoking and sedentary lifestyles, among other things. Fortunately, there has been an increased awareness to the possibility of existence of the disease. This has prompted a good proportion of the informed population to seek medical help enabling early detection and management (including prevention) of the said condition.

Coronary Artery Disease is a major leading cause of morbidity and mortality in Western countries and this is fast catching up with the developing countries as explained above. It has serious health consequences, which may often be fatal.

Coronary angiography has remained the gold standard in assessment of CAD, however it has some limitations, most obvious being its invasiveness, which calls for other modes of investigations. Cardiovascular nuclear imaging has been a rapidly advancing field over the last three decades, especially for assessing cardiac function. and myocardial perfusion. These developments have occurred due to improvement in instrumentation and radiotracers. The development and continuing refinement of the Anger scintillation camera, introduction of short – lived radiopharmaceuticals and technological improvements on computer hardware and software have been fundamental[1]. The use of these developed imaging equipment and techniques to reach an accurate diagnosis requires properly trained personnel and this includes physicians, technicians or radiologists.

Planar Imaging has been replaced by tomographic studies in assessing various cardiovascular functions[2]. This includes myocardial perfusion studies, ventricular function determination, myocardial infarction imaging and myocardial metabolism studies. Single photon emission computerized tomography (SPECT) is routinely used for myocardial perfusion studies. Stress myocardial perfusion SPECT scan has acquired a significant role in detection and management of CAD due to its three-dimensional representation, improved contrast of image, with potential for quantification of tracer uptake[1]. A study done to compare the sensitivity and specifity of modern SPECT techniques to exercise ECG in suspected coronary artery disease, concluded that the

SPECT techniques had a good accuracy (91% sensitivity and 89% specificity) much better than that of exercise ECG[2]. CAD symptoms are due to myocardial ischemia. The site and extent of myocardial ischemia can be accurately defined with modern SPECT techniques.

Perfusion studies can assess the likelihood of a future coronary event. Prognosis is influenced by the extent and severity of inducible perfusion abnormality; this guides the need for invasive investigation and revascularization[3]. Myocardial perfusion imaging is a more powerful indicator of prognosis than clinical assessment, exercise ECG or coronary angiography. This was deduced from a study done to determine the long term prediction of major ischemic events by exercise thallium – 201 SPECT[2].

In Kenya nuclear imaging has not been regarded as a valuable tool in assessing CAD, much as the disease is present in significant numbers especially among the affluent. Most clinicians still rely on the stress ECG and catheter coronary angiogram despite their limitations. This study is thus geared to finding out what role nuclear imaging has in the detection and management of CAD in Nairobi. Information provided from this study is often pivotal in determining whether patients with known or suspected CAD are managed medically or referred for coronary angiography in preparation for revascularization if technically feasible.

LITERATURE REVIEW

Anatomy and physiology of the heart

Anatomy

The heart is a conical, hollow muscular organ situated in the middle mediastinum. It is enclosed within the pericardium. The heart is placed obliquely behind the body of the sternum and adjoining parts of the costal cartilages so that $^1/_3$ of it lies to the right and the rest to the left of the median plane[4, 5].

The right border of the heart is formed by the right atrium. The superior venacava enters the upper posterior aspect of the right atrium. The atrial septum forms the posteromedial wall of the right atrium, lying in the left anterior oblique plane. The left border of the heart is formed by the auricular appendage of the left atrium and the left ventricle.

The right ventricle forms the bulk of the anterior surface. The pulmonary valve, at the top of right ventricular infundibulum lies above and in front of the aortic root and on its left. The diaphragmatic surface consists of the right and left ventricles separated by the posterior interventricular groove and the position of the right atrium, which receives the inferior vena cava. The base or the posterior surface is formed mainly by the left atrium with openings of the pulmonary veins and to a lesser extent by the right atrium.

The atrial and ventricular septa lie in approximately the same plane (left anterior oblique) forming the septal plane of the heart. The obliquity of the atrioventricular valves and cardiac septa, virtually perpendicular to each other, is of great importance when choosing the best projections to profile these structures.

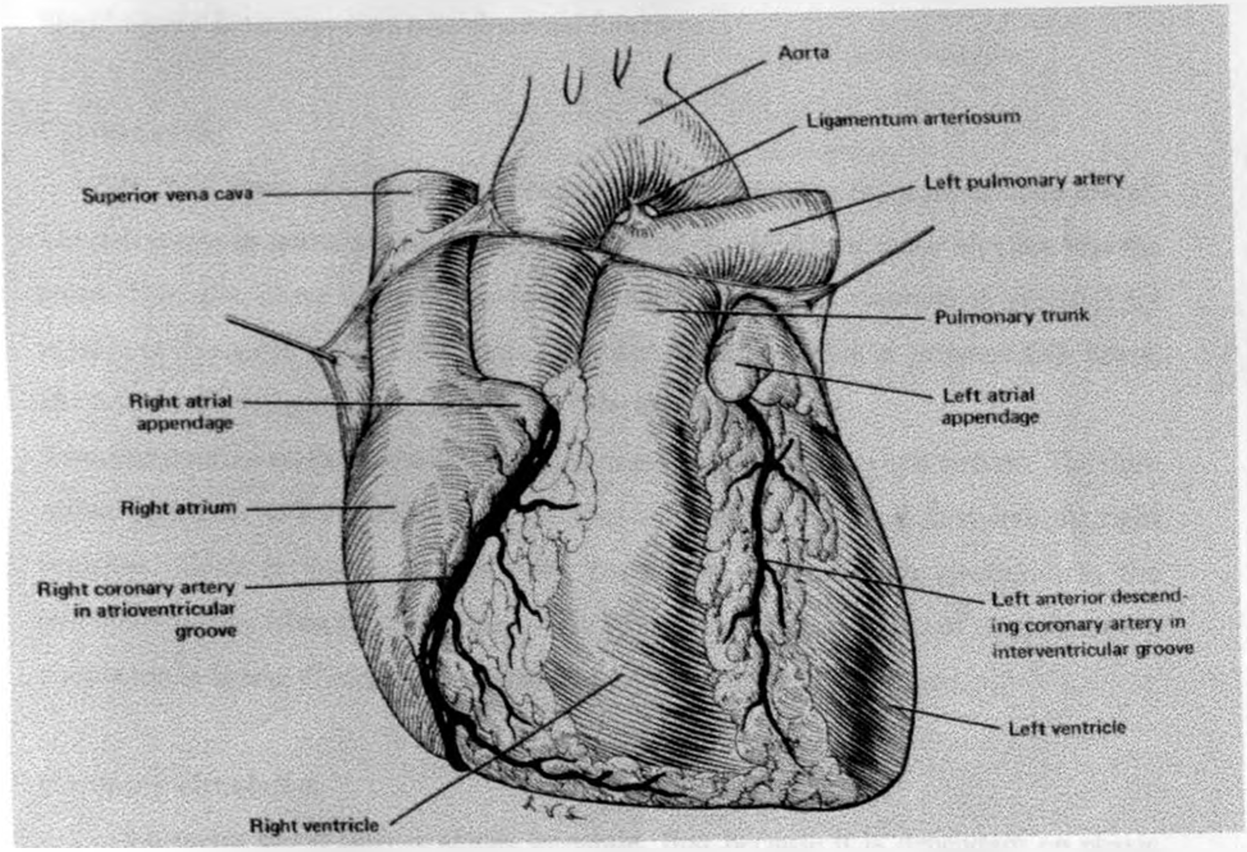
Coronary circulation

The heart is supplied by the right and left coronary arteries[4].

The left coronary artery arises from the left posterior coronary sinus of the ascending aorta. It gives rise to three large divisions namely; The left anterior descending artery which courses down the anterior interventricular sulcus, left circumflex artery which courses into the left atrioventricular sulcus and the diagonal left ventricular branches (one to three in number). The right coronary artery arises from the anterior coronary sinus of the ascending aorta. Its major branches are the marginal artery and the posterior interventricular artery.

Coronary Veins

The coronary sinus is the largest vein of the heart situated in the left posterior coronary sulcus. It opens into the posterior wall of the right atrium. It receives the following tributaries; The great cardiac vein, middle cardiac vein, small cardiac vein, posterior vein of the left ventricle, oblique vein of the left atrium and the right marginal vein. The venae cordis minimae are numerous veins present in all four chambers of the heart, which open directly into the cavity. They are more numerous on the right side of the heart.



ANTERIOR VIEW OF THE HEART

Normal physiology

The cardiovascular system has three basic functions; to transport oxygen and other nutrients to the cells of the body, remove metabolic waste products from the cells and carry substances such as hormones from one part of the body to another. The heart and blood vessels have important neurohumoral functions.

Cardiac cycle

The first phase of ventricular systole is the isovolumetric myocardial contraction[6]. There is a rise in left ventricular pressure followed by rapid ventricular ejection into the aorta. The next phase of isovolumetric relaxation of the left ventricle is signified by closure of the aortic valve - this phase lasts until the left ventricular pressure falls below the left atrial pressure and blood begins to flow into the ventricle.

Deoxygenated blood from systemic circulation is emptied into the right atrium . The right atrium contracts with the opening of tricuspid valve and subsequent flow into the right ventricle. There is then a rise in right ventricular pressure with ejection into the pulmonary artery when the pulmonary valve opens. The basic function of the pulmonary circulation is uptake of oxygen and release of carbon dioxide by the blood.

Coronary circulation

Coronary blood flow is phasic in nature, first because it is dependant on phasic aortic pressure and secondly because the myocardium offers a variable degree of resistance to flow during systole. Coronary flow is also regulated by changes in small vessel resistance. Coronary collateral vascular pathways serve as alternative and sometimes solitary routes of blood flow around stenotic or occluded arteries. Resting coronary flow is normal until the luminal cross-sectional area of the coronary artery is reduced to approximately 85%. Resting ischaemia occurs when the artery is virtually occluded[6,7].

General classification of coronary artery disease

CAD has the following identifiable clinical entities according to the Framingham study (1976)[7]. Asymptomatic coronary disease, angina pectoris, unstable angina, acute myocardial infarction and cardiac failure.

Aetiology and risk factors

Approximately 99% of cases of CAD are due to atherosclerotic changes[8]. Other rare causes include various forms of arteritis including that resulting from syphillis, coronary embolism, connective tissue disorders such as systemic lupus erythematosus, isolated coronary spasm or that which complicates coronary atherosclerosis.

The major risk factors for CAD include hypertension, hyperlipidemia, diabetes mellitus and a positive family history. Others are obesity, decreased physical activity, cigarette smoking and stressful lifestyles. The mentioned risk factors are additive and perhaps synergistic when combined with one or more other risk factors.Disease statistics indicate a male preponderance in the prime of life, women are spared 10 years relative to men.[7]

Pathology and pathophysiology

Atheroma formation within the coronary arteries leads to occlusive thrombosis with resultant myocardial infarction. Coronary artery spasm with or without thrombus formation has been documented as a cause of myocardial ischemia and infarction [7].

A typical atheroma, histologically is a fibrous plaque, which impinges on the lumen of the artery. As it enlarges it may calcify, undergo necrosis, or haemorrhage and develop a superimposed mural thrombus and in these ways partially or completely occlude the artery.

Clinical features

Patients commonly present with chest pain, sweating, weakness, apprehension, light-headedness, dyspnoea and hypotension. Complications of acute myocardial infarction include left ventricular aneurysm, papillary muscle rupture and Dressler's syndrome.

Electrocardiogram (ECG) application in CAD

A normal ECG does not rule out myocardial infarction especially in the early stages of onset of the symptoms.[9] ECG is routinely done during resting and after stress. Typical features of infarction are an abnormal Q wave and ST – T wave abnormalities. Characteristic ST wave changes show depression of the segment. If the ECG is normal at rest, ECG characteristics typical of myocardial ischemia may be induced by exercise.

The significance of exercise-induced ST segment depression, should be interpreted based on time course and the degree of depression and not merely according to whether the test is negative or positive (Selzer, Circulation, 1978). The criteria for diagnosis of CAD with exercise-stress test (assuming normal rest ECG) are; horizontal down sloping ST depression $\geq$ 2mm, duration of ST depression > 3 minutes, angina pectoris during or immediately after the test and exercise associated with hypotension or systolic blood pressure less than 130mmHg[10].

Chest X-ray

The chest X-ray in majority of uncomplicated CAD is normal. In the small minority pulmonary changes may be identified with no specific cardiac changes[11].

Coronary arteriography

It delineates the anatomy of the coronary arteries. Coronary arteriography requires selective injection of contrast medium into the right and left coronary arteries. Percutaneous femoral arterial catheterisation is the usual approach. Percutaneous transbranchial or transradial approaches are being used with increasing frequency [12].

Percutaneous Femoral Arterial Catheterization Approach

This technique requires; digital angiography with C-arm (biplane fluoroscopy and cine radiography) - C-arms facilitate axial projections, pressure recording device with ECG monitor and Judkins or Amplatz catheters. The left and right coronary artery catheters are of different shapes due to the different orientations of the left and right coronary arteries. These catheters have one end hole with no side holes.

The catheter is introduced using the Seldinger technique and advanced until its tip lies in the ostium of the coronary artery. Low – osmolality contrast media, 370(LOCM) are safest in that their haemodynamic and ECG effects are low. The contrast media is administered by hand injection, typically 3-10mls for each projection. Filming is done with images being recorded using cine film at 25-60 frames per sec or digital imaging usually with fewer images per second.

Beam direction is extremely important in recording coronary artery images without overlap or foreshortening. Angiographic equipment must have the facility not only to apply rotation of the under couch tube around the patient, but also to angle the beam along the length of the patient producing a cranio –caudal tilt. Typical projections are: Right Coronary Artery ; 60° LAO , 30° RAO and right lateral. Left Coronary Artery ; 30° RAO, 60° LAO,and left lateral.

Coronary arteriography may be preceded by left ventricular angiography in the 30° RAO position to assess left ventricular function. Left ventriculography requires a pigtail catheter with a pump injector for administration of contrast media. The pigtail catheter has one end hole and twelve side holes. The side holes are important due to the large volumes of contrast media injected. They increase the rate of injection; reduce chances of arterial dissection and recoiling of catheter. The dose of contrast media administered is

1.0 – 1.25 ml/kg at the rate of 0.5 – 1.0 ml/ second. Assessment of left ventricular function is useful in evaluation of patients with ischemic heart disease. Non–invasive coronary arteriography with CT Angiography and MR Angiography has been substantially evolving over the last decade. Complications of cardiac catheterisation can be grouped as generalized vascular complications, cardiac complications and those related to contrast media.

Echocardiography of the coronary arteries

The ostia of the main coronary arteries can be imaged by cross-sectional echocardiography in adults. The proximal right and left coronary arteries can often be imaged by transthoracic or trans oesophageal US. Proximal coronary flow as measured by Doppler during stess may detect CAD.

Echo studies may be used to evaluate left ventricular function in ischemic heart disease. Attempts to utilize M-mode echo for assessment of left ventricular function in patients with ischemic heart disease have yielded poor results. [13] Estimation of left ventricular volume by a variety of mathematical manipulations of the left ventricular internal dimension has demonstrated good correlation with angiographically determined ejection fraction, when the ventricular geometry is normal. When there is abnormal regional wall motion and shape as is in IHD, these formulas breakdown. Because M-mode beam traverses the more basal portions of the left ventricle, the body and the apical segments which are most often abnormal in both reversible myocardial ischemia and acute myocardial infarction, are not visualized and thus the calculated ejection fraction may be inaccurate.

Functional and structural hall-marks of IHD are abnormal regional wall motion and shape, thus 2-D echo is ideally suited for the non-invasive evaluation of regional and global left ventricular function. There is evidence that regional wall motion abnormalities detected by 2-D echo correlate well with angiographic findings. One can also assess left ventricular systolic thickening using 2-D echo. It is thus possible with 2-D echo, to assess the extent and location, as well as the presence of left ventricular dysfunction. Two dimensional echo methods, consistently underestimate left ventricular values by approximately 30%. One reason for the relative underestimation of volume is that with 2-D echo, the endocardial surface is measured from echoes of the innermost trabeculae, whereas with angiographic measurements contrast medium obscures these trabeculae and fills the outermost recess between them. Under resting conditions, in the absence of permanent myocardial damage and if the ventricle is not ischemic at the time of examination, left ventricular function may be normal even in the presence of severe coronary artery disease. However, during exercise, ischemia may be produced as oxygen demand increases. Echo studies demonstrating wall motion abnormalities immediately after exercise appear to be highly specific for identifying ischemic disease, although sensitivity of this technique may be limited. [14]

STUDY JUSTIFICATION

Coronary artery disease is a major leading cause of morbidity and mortality in Western countries and this is catching up fast with developing countries.
The objective of this study was to emphasize the role of this non-invasive revolutionary imaging modality for diagnosis and management of CAD. This awareness is not only beneficial to the clinician but also for patients with suspected CAD. as it provides a relatively quick and fairly accurate means of assessing prognosis and future management.To the best of my knowledge no similar study has been done in Kenya.

GENERAL OBJECTIVE

To determine the pattern of findings on Stress Myocardial perfusion SPECT scan in suspected or known CAD and its subsequent role in management.

Specific objectives

To determine the demographics (age, sex, race) of CAD and any associated socioeconomic factors, establish the most common presenting symptoms in patients with features of CAD on Myocardial perfusion SPECT scan and to correlate SPECT scan findings with coronary angiographic data (where the two examinations have been performed) as well clinical follow-up, and thus assess the predictive value of stress SPECT Myocardial perfusion imaging.

STUDY DESIGN, MATERIALS AND METHODOLOGY

Study area

The study was carried out at Medical Imaging and Therapeutic Centre, Nairobi. Follow-up of patients was done in respective hospitals.

Study population

The study population consisted of patients who had been referred for stress myocardial perfusion studies to reinforce/confirm or rule out a clinical diagnosis of CAD, as well as patients known to have CAD and were on follow-up for the same.

Study Design

This was a prospective descriptive study.

Materials and Methodology

Patients' clinical summary (age, sex, serial number, ECG diagnosis etc) were obtained from the request form and filled into the data collection form. Angiographic findings , clinical follow-up data and stress myocardial perfusion scan findings were recorded into the data collection sheet.

A single day stress-rest protocol using ^{99m}Tc- tetrofosmin was employed. Those patients in a position to perform adequate physical exercise were exercised on a bicycle ergometer.The exercise protocol used involved increasing the resistance by 25watts every three minutes.The end points for exercise included attainment of 85%of age-predicted maximum heart rate, limiting angina, severe fatigue, a systolic blood pressure of over 230mmHg or a diastolic blood pressure of over 130mmHg, significant ST segment changes or arrhythmia. Pharmacologic stress using dobutamine infusion was used in those patients in whom adequate exercise was not possible.The tracer was injected at peak stress and exercise continued for one minute thereafter.

Of those on pharmacological stress, the tracer was injected at peak dobutamine infusion. 250MBq of tracer was injected for stress images. Stress images were acquired

45 minutes later on with a single –head Siemens Diacam Gamma camera with a high resolution collimator. A planar image was acquired in the anterior projection followed by SPECT imaging which involved the standard 180 degrees acquisition using a 64x64 image matrix size.This was followed one hour later by injection of 750MBq of tracer at rest and imaging using the same protocol as for stress images one hour later.

Planar images were reconstructed into transaxial tomograms by filtered back projection for data processing. The transaxial slices in a three dimensional data set were re-oriented into oblique slices. The most useful oblique planes were the vertical long axis (VLA) horizontal long axis (HLA) and the short axis (SA) . The myocardium consists of nine segments.The extent of a defect was described as mild (involving one or two segments) moderate (involving three or four segments) and severe if five or more segments were involved. Severity was also described as mild, moderate or severe. This classification of extent and severity assesses future cardiac risk. A variety of normal appearances arising from variation in size and position of the heart, relating to body habitus and tomographic acquisition were seen. Inferior wall attenuation was frequently observed due to diaphragmatic attenuation. Abnormalities of perfusion were classified as fixed or reversible indicating infarcted and reversibly ischaemic myocardium respectively.

Thallium has been the mainstay of nuclear cardiac imaging for more than two decades. It has limitations, which favour the use of 99_m technetium– labelled tracers. These include; relatively long physical half-life of seventy three hours which increases the patient's radiation burden, relatively low injected doses of thallium result in low signal to noise ratio giving suboptimal images and low energy emission leads to low resolution images and significant attenuation by soft tissue especially in obese patients.
Technetium – labelled tracers are especially useful if the patient is quite obese or has large breasts preventing satisfactory imaging by low energy thallium photons.
Technetium based tracers have a short half-life of six hours and this significantly reduces the patient's radiation burden. They are fixed in the myocardium with no redistribution.

SPECT (Single Photon Emission Computerized Tomography)

Parts of the equipment include a Gamma – camera (one or two camera heads) and a computer [15].

The gamma camera consists of;

a) A scintillation crystal made of sodium iodide. The crystal absorbs incident gamma photons and produces light.

b) Photomultiplier tubes (PMTs), which detect the light output from the sodium iodide crystal. Signals from PMTs generate information about where each photon interacted(spatial data). The position of the gamma ray is determined by the relative strength of the signal received by several PMTs.

c) The pulse height analyzer (PHA) is an electronic device used to determine which portion of the detected spectrum is to be used for creating the image. It is placed between the detector and counting portion of the camera system.

The computer is for reconstruction of images of activity distribution in sections through the patient. SPECT provides computed tomographic views of three-dimensional distribution of radioisotopes in the body. The gamma camera rotates 180 or 360 degrees around the patient acquiring data that allows the tomographic images to be generated. Typically 64 or 128 projections are taken. Scan profiles from these projections are mathematically reconstructed to generate transverse, sagittal, oblique and coronal images. Multiheaded cameras are used to increase system sensitivity and reduce scan times. Major benefit of SPECT is the improved contrast that results from the elimination of overlapping structures.

Sample Size Determination

The sample size was all the patients that availed themselves for stress myocardial perfusion SPECT scan within the period of ten months extending from April 2005 to February 2006. The sample size was determined using the following formula;

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

Where

n=desired sample size

z=standard normal distribution (1.96)

p=known prevalence rate for the factor of interest under study (7.5%)

d=level of significance desired (0.05)

Minimum sample size was 100. However a total of 105 patients was studied

Control of selection bias

No myocardial SPECT scan done within the study period was excluded. Only patients referred for the study were included. Reporting was done by a nuclear medicine consultant in collaboration with interventional radiologists.

Data Management

Data analysis was done using software programme for social science research (SPSS), systat version 11 and excel computer software. Results were presented in form of frequency distributions and descriptive statistics.

Stastical Analysis

Descriptive statistics were used to examine differences in demographic charasteristics, risk factors associated with CAD as well as presenting symptoms and signs.

P <0.05 was considered significant and adjustments was made for multiple comparisons and where the conditions of Chi square were not met, by use of Fishers exact probability.

Ethical considerations

Patient's name was not recorded during the study to maintain confidentiality and the information acquired was not used for any purpose other than research. For referral purposes only patient's number was required. The information was acquired from the respective institutions/ departments; as such there was no need for signed consent from the patient. No examination was done on a patient apart from the one requested by the primary physician hence there was no need for signed consent from the patient. Before commencement of the study a request was submitted together with the proposal copy to the ethical and research committee for approval.

RESULTS

The total number of patients studied was one hundred and five. Males were 65.7% while females comprised 34.3%. Male: Female ratio was 1.9:1. (Table 1).The youngest and eldest were 36 and 82 years respectively. The mean age of presentation was 60 years and the standard deviation was 11.4 (Table 2). Asians comprised 68.6% of the total population, while the Caucasians and Africans had an equal distribution with 15.2% each of the total population. The most common presenting symptom was chest pain, seen in 54.4% of all the patients. A sizeable proportion of patients presented for stress myocardial perfusion stress imaging because they had an abnormal stress ECG examination on routine physical examination, but had no clinical symptoms. This comprised 20.2% of the total number. Dyspnoea was a presenting symptom in about 18.4% of all patients either in isolation or in association with the other symptoms previously mentioned. Only one patient presented with diaphoresis.

Four patients had a positive history of smoking, none of whom were positive on myocardial perfusion imaging with p =0.9 (Table 3). Eighteen patients (17.1%) had a positive family history of coronary artery disease, three of whom were positive on perfusion imaging p=0.272 (Table 4). Fifty one patients (48.6%) were hypertensive and of these ten had a positive perfusion scan with p=0.021 (Table 5). Thirty two patients comprising 30.5% of the total population had diabetes mellitus and eight were positive on perfusion imaging, p=0.06 (Table6). Twenty seven patients had dyslipidaemia but only four of whom had a positive perfusion scan with p=0.688 (Table 7).

Twenty one patients had a positive myocardial perfusion SPECT scan for stress induced ischaemia and of these 47.6% were hypertensives, 38.1% had diabetes mellitus and 19% had dyslipidaemia. Positive family history of coronary artery disease was present in 14.3%. Of those with a positive stress myocardial perfusion scan for CAD, 75% were of Asian origin, 15.0% were Africans while 10% were Caucasians. The mean age of patients with a positive perfusion scan was 62 years. Of those positive for ischaemia on myocardial perfusion imaging 66.7% were male, while 33.7% were females. (Table8). Of the patients with a positive myocardial perfusion scan 81% presented with chest pain

(p= 0.042) and 42% with dyspnoea (p= 0.45). Twenty-three patients had features of fixed perfusion defects (infarcts) on SPECT scanning. Fifty seven scans were normal. (Table 9). On stress ECG twenty-five patients were positive for ischaemia, seventy one were negative and eight were borderline.Thirty eight percent (38.1%) of those positive on stress ECG were positive on perfusion imaging while 61.9% of patients who were negative on stress ECG had a positive perfusion scan.

Twelve patients went ahead to have a coronary angiogram done. Eight patients had a positive coronary angiograms while four were negative, 66.7% showed concordance with the results of myocardial perfusion imaging while four were discordant i.e. one patient who was positive on myocardial perfusion had a normal coronary angiogram while three patients who had normal myocardial perfusion scans had severe stenosis on angiography.

One of the patients who was positive on angiogram and negative on SPECT developed myocardial infarction after six months. Compared to the gold standard angiogram,the sensitivity of myocardial perfusion SPECT scan was 62.5% while the specificity was 75% in this study. The positive predictive value of SPECT was 83.3% and negative predictive value was 50%. (Table 10). Seventy two patients had clinical follow-up. The mean duration for clinical follow-up was 6 months, with a range of 1 to 13 months. Fifty-one of these patients had negative perfusion scans two of whom developed coronary artery disease on follow-up.Twenty-one patients had a positive myocardial perfusion scan.(ischaemia). All except one patient had a cardiac event. (Table 11). In reference to clinical outcome Myocardial perfusion SPECT scan had a sensitivity of 93.5% and a specificity of 97.5%.

Known cases of CAD were twenty-seven comprising 26% of the total population. Fifteen had had intervention- 8 angioplasty and 7 Coronary artery by-pass grafting. Five of these had a positive perfusion scan for stress induced ischaemia while twenty-two were negative for the same.

Table 1: Sex Distribution

Gender	Frequency	Percentage
Male	69	65.7
Female	36	34.3
Total	105	100.0

Results show male preponderance amongst patients presenting with clinical features of CAD.

Table 2: Age distribution

Age (in Years)	Frequency	Percentage
30 – 40	5	4.8
41 – 50	17	16.4
51 – 60	28	26.6
61 – 70	37	35.3
71 – 80	16	15.6
81 – 90	2	1.9
Total	105	100.0

Majority of the population were elderly with a mean age of 60years and a standard deviation of 11.4.

Table 3: Myocardial perfusion SPECT scan findings Vs smoking

		Smoker		**Total**
		Yes	**No**	
Myocardial perfusion findings	Positive	0	21	21
	Negative	4	80	84
Total		4	101	105

None of the patients who had a history of smoking had a positive scan. p=0.9.

Table 4: Myocardial perfusion SPECT scan findings Vs a positive family history of CAD

		Positive Family Hx of CAD		**Total**
		Yes	**No**	
Myocardial perfusion findings	Positive	3	18	21
	Negative	15	69	84
Total		18	87	105

Of the total number of patients with a positive family history of CAD only three had a positive perfusion scan p=0.272.

Table 5: Myocardial perfusion SPECT scan findings Vs hypertension

		History of hypertension		Total
		Yes	No	
Myocardial perfusion findings	Positive	10	11	21
	Negative	41	43	84
Total		51	54	105

47.6% of patients with a positive scan had hypertension.
P=0.021.

Table 6: Myocardial perfusion SPECT scan findings Vs diabetes mellitus

		Diebetes Mellitus		Total
		Yes	No	
Myocardial perfusion findings	Positive	8	13	21
	Negative	24	60	84
Total		32	73	105

Only eight patients with diabetes mellitus had a positive scan.
p=0.06.

Table 7: Myocardial perfusion SPECT scan findings Vs dislipidaemia

		Dislipidaemia		Total
		Yes	No	
Myocardial perfusion findings	Positive	4	17	21
	Negative	23	61	84
Total		27	78	105

Four patients with a positive scan had abnormal lipid profiles
p=0.688.

Table 8: Myocardial perfusion SPECT scan findings Vs gender

		Sex		Total
		Yes	No	
Myocardial perfusion findings	Positive	14	7	21
	Negative	55	29	84
Total		69	36	105

Two-thirds of the patients with a positive scan were male while the rest were female. p=0.011

Table 9: Myocardial Perfusion SPECT findings

Findings	Frequency	Percentage
Positive for Ischaemia	21	20.0%
Infarction	27	25.7%
Normal	57	54.3%
Total	105	100.0%

The majority of patients were shown to obtain a nonnal scan. Those with infarction were most likely due to a previous cardiac event.

Table 10: Myocardial perfusion SPECT scan findings Vs coronary angiography findings

		Coronary angiography findings		Total
		positive	negative	
myocardial perfusion SPECT scan findings	positive for Ischemia	5	1	6
		83.3%	16.7%	100.0 %
		62.5%	25.0%	50.0%
	Negative	3	3	6
		50.0%	50.0%	100.0 %
		37.5%	75.0%	50.0%
Total		8	4	12
		66.7%	33.3%	100.0 %
		100.0%	100.0%	100.0 %

Sensitivity of SPECT scan compared to angiography was 62.5% while specificity was 75%. The positive predictive value of the former was 83.3% while the negative predictive value was 50%.

Table 11: Myocardial perfusion SPECT Scan findings Vs clinical outcome

	Clinical outcome		
Perfusion Scan findings	Cardiac event/+ve angiography	No cardiac event/-ve angiography	
Positive	20	1	21
Negative	2	49	51
TOTAL	22	50	72

Most of the patients with a positive scan had a future cardiac event on follow -up while only one patient with a negative scan developed coronary artery disease.

Reversible ischaemia with left anterior descending artery stenosis

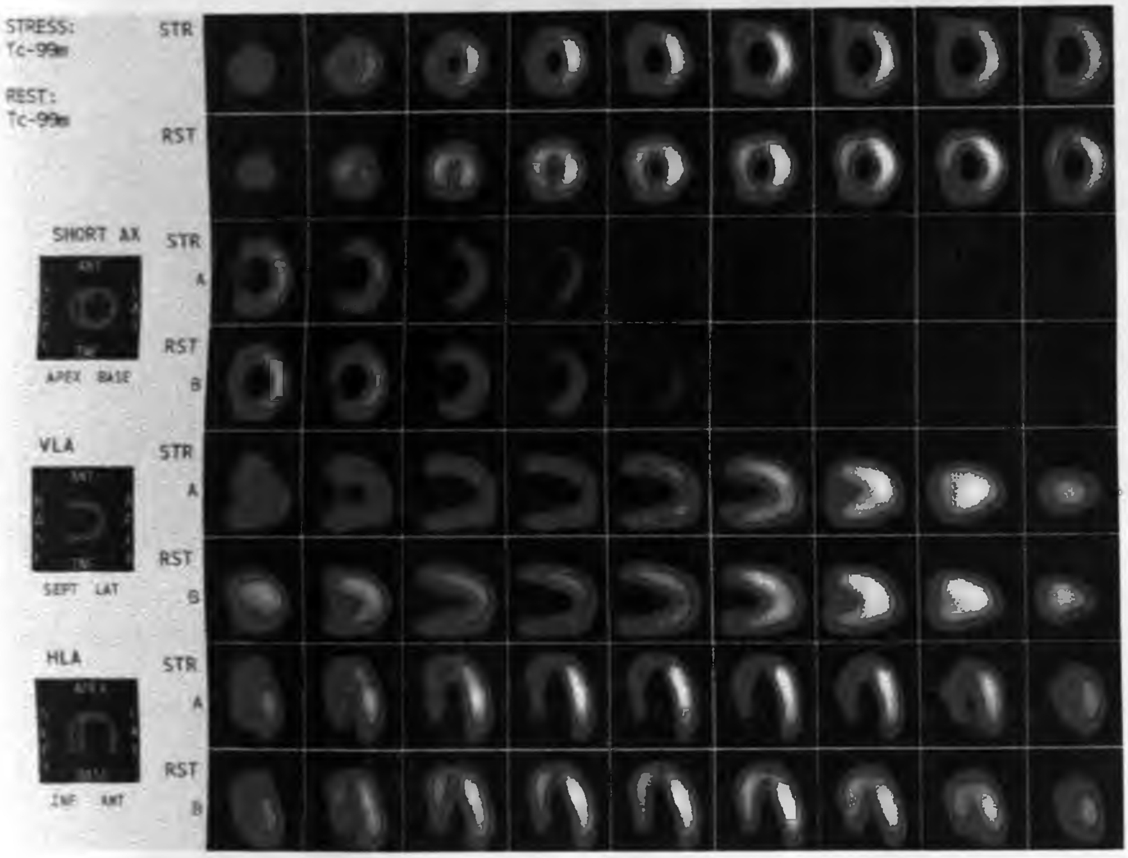


Fig. 1a. **77years old male with chest pain. He was a known hypertensive and diabetic for over 15years. ECG showed depression of the ST segment suggestive of myocardial ischaemia.**

The scan shows a perfusion defect in the stress images involving the anteroseptal wall and the apex which is reversible on rest images. This is due to ischaemia following left anterior descending artery stenosis. Corresponding coronary angiogram next page.

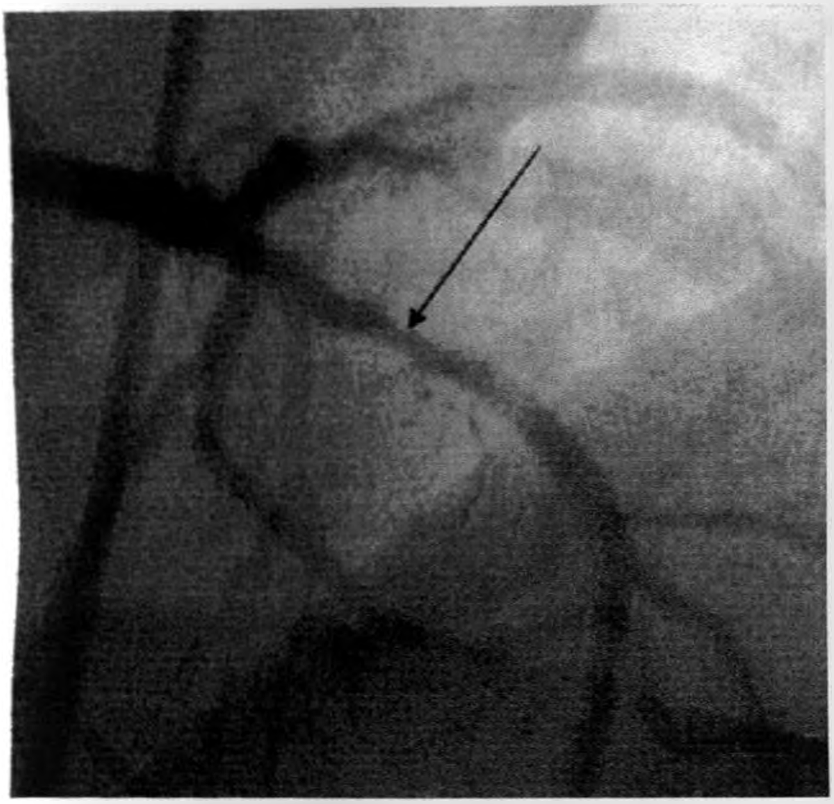


Fig. 1b. Coronary angiogram of previous patient (Fig. 1a.)

This confirms the stenosis of the left anterior descending artery.

Myocardial infarction of the left anterior descending artery territory

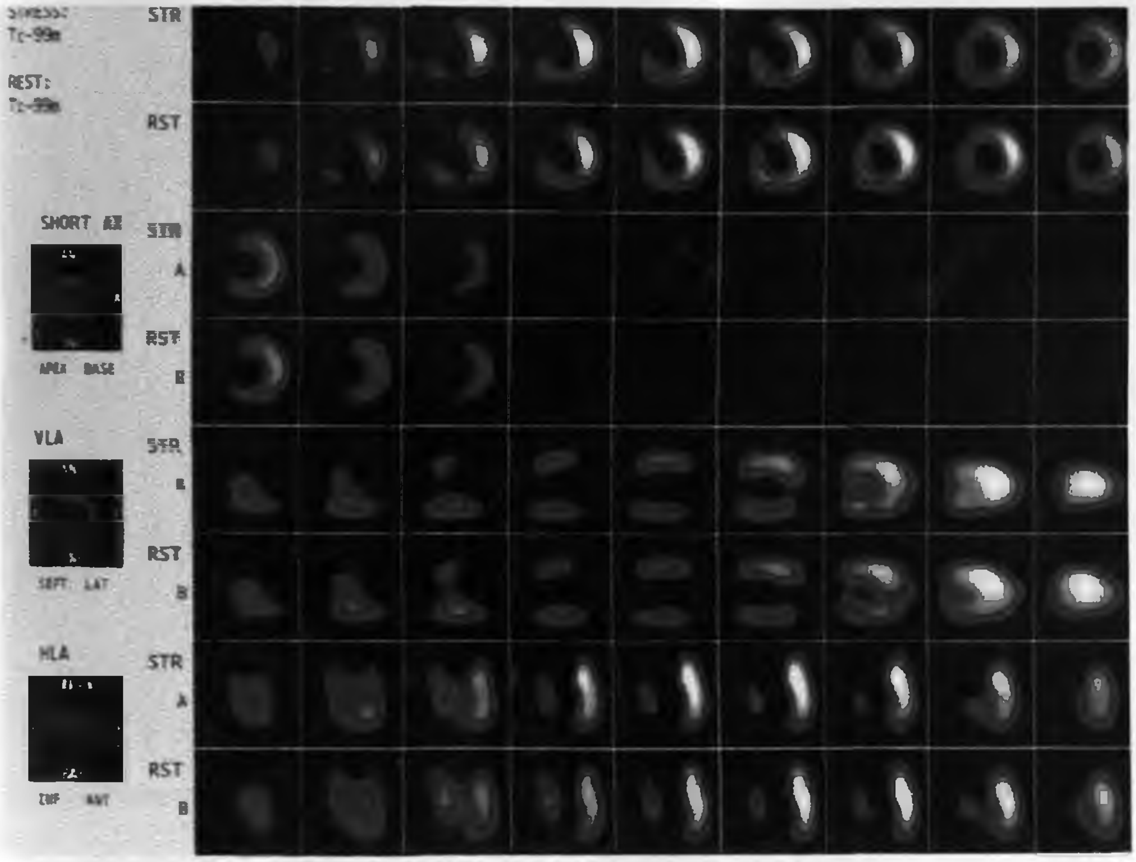


Fig. 2a. 64years old male known to have CAD. He had had a previous angioplasty. Now presented with recurrent acute excruciating chest pain.

The scan shows a fixed perfusion defect on both the stress and rest images involving the antero-septal region and apex. This is infarction in the territory of the left anterior descending artery. Corresponding coronary angiogram next page.

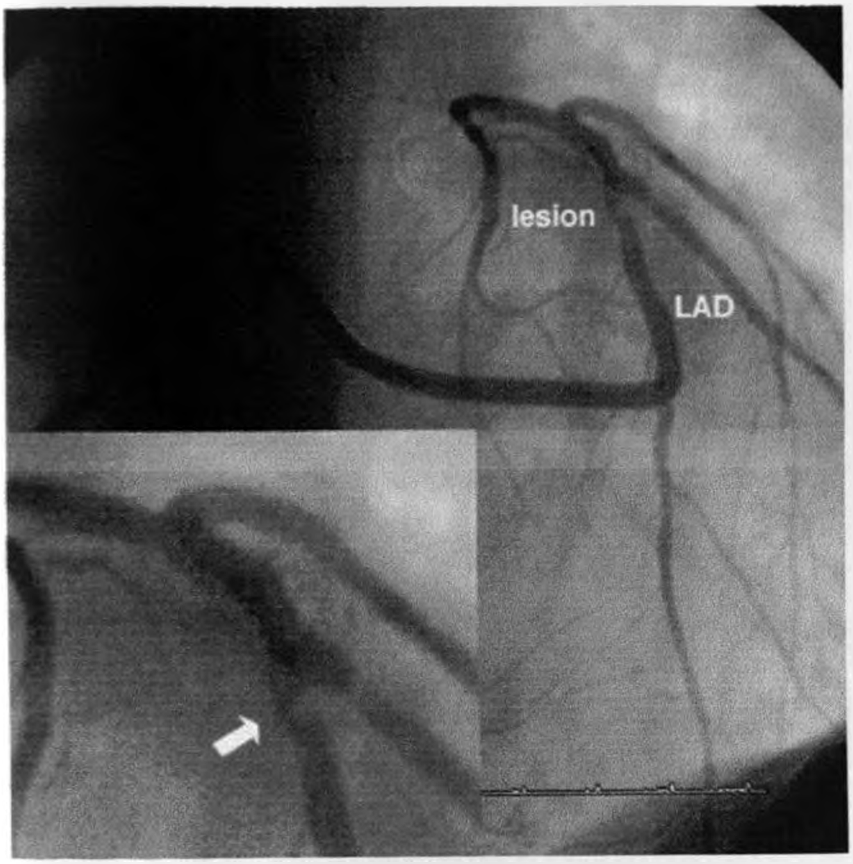


Fig. 2b. Coronary angiogram of previous patient. (Fig. 2a)

This demonstrates the stenosis in the proximal left anterior descending artery.

Normal tetrofosmin cardiac scan

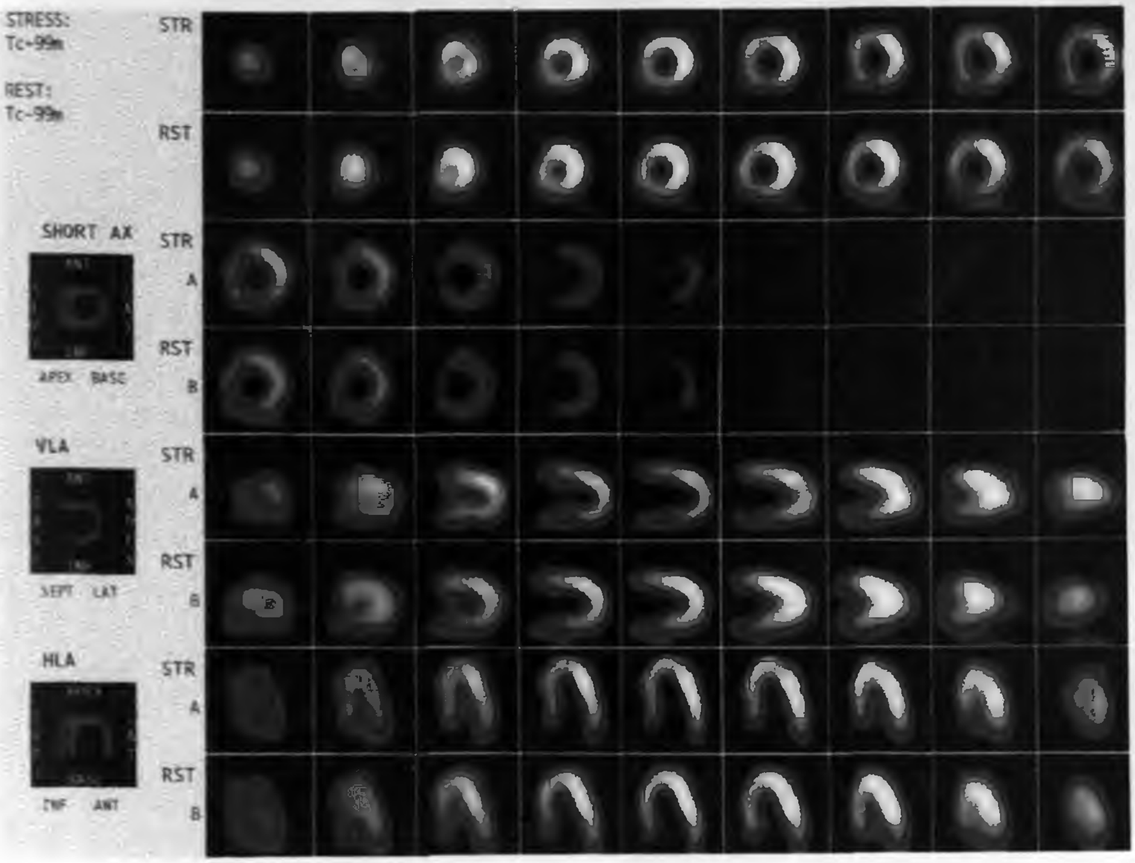


Fig. 3. **36 years old male with chest pain and a strong positive family history of CAD. ECG was equivocal for ischaemic changes.**

The perfusion scan was normal after stress and rest injections. No reversible ischaemic or fixed perfusion defects were noted.

Normal tetrofosmin scan with inferior attenuation

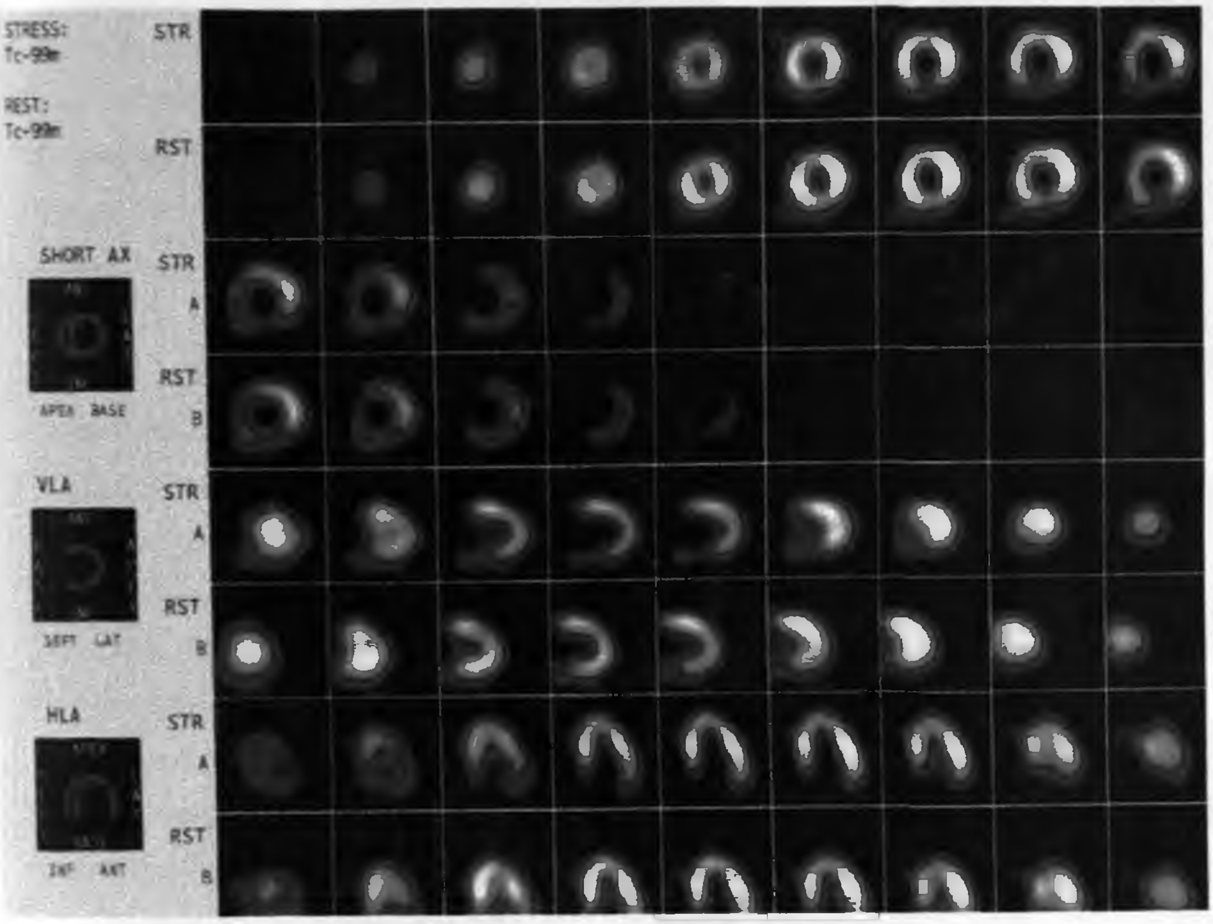


Fig. 4. **66year old obese man who presented with acute chest pain. He was a known hypertensive for over a decade. ECG showed depression of the ST segment suggestive of myocardial ischaemia.**

This study showed normal myocardial perfusion after the stress and rest injections. There is inferior wall attenuation particularly affecting the basal inferior segment. This is common especially in men and is thought to be due to increased attenuation of photons from the deeper myocardium. Care should be taken not to interprete this as abnormal especially if there is no other reason to suspect disease.

DISCUSSION

Demography

The mean age of presentation of 60years and male preponderance is comparable to what is in literature where the majority are elderly males[6,7] This is related to the atheromatous changes within the vessels which increase in frequency with advancing age and are commoner in males. The majority affected in this study were of Asian origin. In the existing literature no race is particularly predisposed as is contrary to what my data potrays. This discrepancy could be attributed to a particular community's sensitization coupled with affordability for medical care hence presenting a comparatively larger sample size.

Clinical presentation

Chest pain was of value in predicting an abnormal outcome on perfusion imaging and this was statistically shown to be so, $P<0.05$. Of the patients with a positive perfusion scan, 81% presented with chest pain , 42% with dyspnoea and 1% with diaphoresis. In literature over 60% of patients with proven CAD will present with a major complaint of excruciating chest pain.[9,26]

Dyspnoea and diaphoresis are quoted by many authors as frequent presentations of CAD[7]. This was not so in this study. This could possibly be explained by the fact that most of the patients were not particularly very sick and could still achieve adequate oxygenation to the myocardium at rest.

SPECT scan findings in smoking

Smoking as an independent risk factor was not a strong predictor of an abnormal perfusion scan as was statistically shown- $p=0.9$. This does not tally with what is in literature. Studies done documented that approximately 20% of the patients with features of CAD have a positive history of smoking [8,21]. The difference could be explained by the fact that a good number of those patients had no clinical symptoms or signs but either had abnormal stress ECG or did the perfusion imaging as part of routine medical exam on their own request or that of their primary care doctor.

SPECT scan findings in diabetes mellitus

Diabetes mellitus on its own was not found to be a strong predictor of positive ischaemic findings on perfusion scanning p=0.06. This does not rhyme with what is in most studies, where approximately 25% of patients confirmed to have CAD have pre-existing diabetes mellitus. Diabetes mellitus causes hypercholesterolemia leading to atheroma formation. The discrepancy could be explained by the fact that most of these patients had their blood sugars well-controlled. The other possibility is that hyperglycaemia alone may not lead to elevated cholesterol levels but works synergistically with other co-existing abnormalities to lead to this.

SPECT scan findings in hypertension

Hypertension was a strong predictor of a positive perfusion scan, p=0.021. This compares favourably with the existing literature. According to most literature approximately 25% of patients with CAD have pre-existing hypertension with or without diabetes mellitus[6,7].

SPECT scan findings vs positive family history

A positive family history alone was not a strong predictor of an abnormal perfusion scan. P=0.272. This does not tally with what is in literature where over 50% of patients with CAD confirmed on imaging, have a positive family history[7,8]. Again this could be explained by the fact that a number of these patients had no clinical symptoms but had a perfusion scan due to an equivocal stress ECG or as part of routine medical examination.

SPECT scan findings in dyslipidaemia

Only four patients with abnormal lipid profiles had a positive scan. P=0.688. This contrasts what most literature provides where on average 40% of patients with CAD on imaging will have deranged lipid profiles. The difference could be due to that, the deranged levels were not sufficient enough to cause significant occlusion or stenosis so as to present features of CAD.

SPECT scan vs stress ECG

Stress ECG correlated poorly with observations on SPECT scan. This is comparable to what is in literature. In one large series studied, stress ECG was found to have a sensitivity and specificity of 22.5% and 30.0% respectively[26,27].

SPECT scan findings vs coronary angiogram

Compared to the gold standard coronary angiogram , myocardial perfusion scan had a sensitivity of 62.5% while the specificity was 75% in this study. This was lower than quoted by various authors who concluded that SPECT had a good accuracy with 91% sensitivity and 89% specificity [2,18,25]. A plausible explanation could be that fewer patients in my study went ahead to have a coronary angiogram hence only a small fraction were used to reach a conclusion. Coronary angiography as a gold standard is limited in assessment of significant coronary artery disease because it does not demonstrate ischaemic myocardium[26]. It only shows a site of occlusion in the affected vessel(s): Blood may by-pass a small emboli, resulting in no interruption of blood supply to the myocardium and this on myocardial perfusion is normal while a coronary angiogram shows an abnormal pattern.

SPECT scan findings vs clinical outcome

A normal stress –rest myocardial perfusion scan is considered a strong predictor of very low (<1%)likelihood of a cardiac event for at least the next twelve months[29]. This is irrespective of gender, age or symptom status. In my study two patients out of fifty-one(3.9%) with normal scans had a cardiac event in the next six months of follow –up. Patients with mild ischaemia also have a low likelihood of future cardiac events hence managed conservatively. Those with moderate-severe disease as seen on SPECT require coronary revascularization ideally because without this, they have been shown to suffer significant morbidity and mortality sooner or later [2,26].

Myocardial perfusion imaging is useful post angioplasty to confirm improved stress perfusion, early detection of the disturbance of coronary anatomy which may be poorly assessed by coronary angiography,detect restenosis which may require repeat catheterization and in assessment of the need for further culprit lesion angioplasty.

SPECT is also a useful baseline investigation should symptoms recur. It enables differentiation of ischaemic chest pain from non-ischaemic chest pain. However catheterization may be required to differentiate graft occlusion from native CAD [26].

CONCLUSION

The mean age of those presenting for assessment of CAD was 60 years and of those with positive features of coronary artery disease on stress myocardial perfusion imaging the mean age was 62 years. There was a male preponderance both for overall patients presenting for investigation, as well as those with features of coronary artery disease on myocardial perfusion imaging.The Asian race was the majority. The most common presenting symptom was chest pain followed by abnormal stress ECG warranting further investigation for coronary artery disease. The former was a strong predictor of an abnormal stress myocardial perfusion scan. Hypertension was frequent either in isolation or in combination in patients with a positive perfusion scan for coronary artery disease. Smoking and positive family history as independent risk markers were not strong predictors of an abnormal perfusion scan. Stress myocardial perfusion study has a well documented role in the diagnosis and risk stratification of patients with coronary artery disease. A normal stress-rest study is considered a strong predictor of very low likelihood of a cardiac event for at least the next 12 months, as is mild ischaemia. The latter have been shown to be successfully amenable to medical management.

RECOMMENDATIONS

Stress myocardial perfusion SPECT scan imaging should be made more available and affordable for most patients especially those at risk of developing coronary artery disease. Most clinicians should be made aware of the limitations of stress ECG in diagnosing coronary artery disease. The important role of nuclear imaging in assessing cardiac disease should be made clear to the physicians. Clinical symptoms and signs of coronary artery disease may mimic those of many other disease entities and in the event of unequivocal findings on myocardial perfusion imaging coronary angiography should be performed. Long term follow up of patients is necessary especially those with normal stress myocardial perfusion studies but having clinical symptoms and signs coupled with risk factors. This is crucial as those patients may develop coronary artery disease sooner or later.

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10. APPENDIX A

QUESTIONNAIRE (Data collection form)

1) Patients number

2) Age

3a)Sex

3b)Race

4a) Positive family history of CAD **Yes** **No**

4b)Known case of CAD? **Yes** **No**

5a)History of intervention **Yes** **No**

If yes : Angioplasty

or

CABG

5b) Smoker **Yes** **No**

6a)History and duration of a)Hypertension

b)Diabetes Mellitus

c)Dyslipidaemia

6b)History of myocardial infarction? **Yes** **No**

7) (a) Presenting	Symptom	Present	Absent
	- Chest pain acute/chronic		
	- Dyspnoea		
	- Diaphoresis		

b)Myocardial perfusion SPECT scan findings

Percentage of target heart rate achieved;

8) E C G findings/ diagnosis:

9) Coronary angiography findings (where available)

10) Clinical follow-up (where data is available).

APPENDIX B

PATIENT CONSENT FORM

I am Dr. Stella W. a post-graduate student at the Department of Diagnostic Radiology, University of Nairobi. As part of my post-graduate studies, I am required to undertake a research project. I plan to do a study on coronary artery disease as seen on nuclear imaging. With your permission I may need to use the results of this procedure performed on you as part of my study.

This procedure involves injection of dye through a peripheral vein followed by acquisition of images using a camera. Complications include contrast media reaction which is however rare. Your rights will be respected and confidentiality maintained at all times. No names will be mentioned in the study document except the serial numbers. Any useful information that will improve the quality of care and outcome of your problem will be shared with your clinician for appropriate action. It is important that you understand that participation in this study is absolutely voluntary and you can withdraw from the study without losing any of your rights to care. You are now free to ask any questions relating to this study so as to get clarification on any issues that may not be clear to you. Thank you for your co-operation.

I .... have been adequately explained to about the study by Dr. Stella and I voluntarily consent to participate in the study.

Signature ....

Date ....

Number ....

I have adequately explained to the patient all issues touching on this study and he/she has consented to participate in the study.

Dr. Stella W. ....

Signature ....

Date ....

For any issues contact Dr. Stella on Telephone Number 0722 785539

APPENDIX C

PROJECT BUDGET

ACTIVITY	ESTIMATED AMOUNT KSH
i) Literature research	5,000
ii) Computer and Stationery	5,000
iii) Computer data entry and data analysis	5,000
iv) Scanning	6,000
v) Printing and binding of final dissertation	3,000
vi) Travelling	6,000
vii) Patients Procedures	110,000
viii) Incidental expenses	10,000
TOTAL	**150,000**