University of Khartoum

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The correlation of clinical and positive exercise test findings with coronary angiographic Results in Sudanese patients-study

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قال تعـالى :

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صدق الله العظيم

Dedication

To my father, mother, who gave me great

support and motivation…

To all patients, who suffered a lot, praying

that God will grant them health and

happiness…

CONTENTS

Acknowledgement

No words of thanks can convey my deep gratitude to ***Dr.Faisal*** *whose sustained care and unstinting support have been instrumental in bringing this work to a successful completion.*

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ABSTRACT

This study was done in Sudan heart center from the year 2001-2004.

***Objectives**:*

The purpose of this study was to see the mode of clinical presentation of Ischemic heart disease and to correlate it to both the exercise test and coronary angiography in patients suspected to have ischaemic heart disease.

Methods:

This study was a retrospective analysis, for patients with positive exercise test who were referred for coronary angiography; patients with history of acute coronary syndromes and negative exercise test were excluded from the study.

Results:

103 patients were studied, males represented 61.2% of the study population and female were (38.8%).

History of diabetes was obtained in 27 patients (26.7%), 54 patients (52%) were hypertensive, 31 patients (31.1%) gave history of smoking and 24 patients (24.2%) had positive history of IHD. 62 patients had serum cholesterol level estimated, eleven patients (17.7%) had normal levels, 38 patients (61.3%) had high normal levels and 13 patients (21%) had high levels.

History of chest pain was found in 89 patients (86.4%).

Conclusions:

Patients presented with chest pain and had normal coronary angiography findings were (51.9%), the false positive results were more associated with females.

Diabetics and poorly controlled hypertensive patients were associated with more severe coronary diseases.

Patients presented with chest pain and had normal coronary angiography findings were (51.9%), so chest pain as a presenting symptom need to be more evaluated and specified especially in females.

Smokers had certain coronary arteries involvement that is the left anterior descending followed by the right coronary artery.

Resting ECG had limited utility in diagnosing coronary artery disease.

False positive exercise test results were found in (52.6%) of patients. The left anterior coronary artery was the most coronary vessel affected (32.4%). The left main was affected in (3.9%).

The presence of high normal and high cholesterol levels was associated with more affection of the coronary arteries.

Recommendations:

The recording system and especially the presenting symptoms should be given the enough attention and evaluation especially the low risk group patients so as to limit the need for more invasive procedures.

Hypertension should be tightly controlled.

Every patient suspected to have IHD should have full lipid profile as abase line.

Good evaluation and classification of patients to low, intermediate and high risk groups should be done before referral for coronary angiography.

ملخص الأطروحة

هذه الدراسة أجريت بمركز السودان للقلب في الفترة من 2001-2004م.

الأهداف:-

الهدف من هذه الدراسة هو معرفة طبيعة الأعراض السريرية لمرضى إقفار القلب ومحاولة ربط ذلك بإختيار الجهد القلبي وقسطرة الشرايين التاجية في المرضى المتوقع لديهم حالات إقفار القلب.

هذه الدراسة تمت عن طريق الرجوع إلى الملفات للمرضى ذوي النتائج الإيجابية لإختبار رسم القلب بالجهد والذين حولوا لقسطرة الشرايين التاجية، تم استبعاد المرضى الذين لديهم تاريخ مرضي بحالات إحتشاء القلب الحاد.

النتائج:-

- مثل الذكور 61.2% من الدراسة وبينما الإناث مثلن 38.8%.
- التاريخ المرضي للسكري وجد في 27 مريضاً (26.7%) بينما اتفاع ضغط الدم سجل في 54 مريضاً (52%) نسبة المدخنين بلغت 31.1% (31) مريضاً والمرضى الذين لديهم تاريخ ايجابي لمرض إقفار القلب بلغوا 24 مريض (24.2%). سجلت نسبة الكوليسترول في الدم في 62 مريض، 11 منهم (17.7%) وجدت لديهم نسبة طبيعية ، 38 مريض وجدت لديهم نسبة طبيعية قصوى و 13 مريضاً كانت لديهم نسبة عالية. ألم الصدر سجل في 89 مريضاً (86.4%).

الخلاصة:-

- وجود نسبة عالية من الكوليسترول ارتبط بإصابة أكثر حدة للشرايين التاجية.
- مرضى السكري وضغط الدم الغير متحكم به إرتبطوا بحالات إصابة بالغة للشرايين التاجية.
- المرضى الذين لديه ألم بالصدر وفي نفس الوقت شرايين تاجية طبيعية مثلوا 51.9% مما يدل على أهمية معرفة طبيعة ألم الصدر وتحليلها جيداً خاصةً عند الإناث.
- المدخنين لديهم إصابات معينة للشرايين التاجية الشريان التاجي الأيسر الأمامي والشريان التاجي الأيمن.

التوصيات:-

- يجب وجود نظام دقيق بسجلات المرضى مع إعطاء الأعراض التي يتقدم با المريض الاهتمام والدقة الكافيين حتى نقلل من الحوجة لطرق التشخيص الأكثر تعقيداً.
- مرض ارتفاع ضغط الدم يجب أن يجد المتابعة الدقيقة والتأكد من محافظة المريض على العلاج.
- تحليل نسبة الدهون في الدم يجب أن يوفر لكل المرضى الذين يتوقع لديهم حالات إصابة الشرايين التاجية.
- التقييم الدقيق ومحاولة تصنيف المرضى إلى مرضى ذوي خطورة عالية أو متوسطة أو بسيطة له أهمية كبرى ويجب أن يسبق تحويل المريض لقسطرة القلب.

ABBREVIATIONS

- **SVD**: single vessel disease
- **2VD**: two vessel disease
- **3VD**: three vessel disease
- **CAD**: coronary artery disease
- **IHD**: Ischaemic Heart disease
- **BP**: blood pressure
- **LAD**: left anterior descending
- **LM**: left main
- **RCA**: right coronary artery
- **CX**: circumflex
- **PTCA**: percutanious transluminal coronary angioplasty

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Introduction

Exercise is a common physiological stress used to elicit cardiovascular abnormalities not present at rest and to determine adequacy of cardiac function [1] Exercise stress testing is one of the most frequent modalities used to assess patients with suspected or proven cardiovascular disease. It is used to estimate prognosis, to determine the functional capacity, the extent and likelihood of coronary artery disease (CAD) and the effects of therapy [1].

Exercise physiology:

Anticipation of dynamic exercise results in an acceleration of ventricular rate due to vagal withdrawal, increase in alveolar ventilation and increase in venous return primarily as a result of sympathetic vasoconstriction [2]. In a normal person, the net effect is an increase cardiac resting out put before the start of the exercise. The magnitude of haemodynamic response depends on the severity and amount of muscle mass involved. In the early phases of the exercise the upright cardiac output is increased by an augmentation in stroke volume mediated through the use of the Frank Starling law and the increase in heart rate, the increase in cardiac output in the latter phases of exercise is primarily due to a sympathetic mediated

increase in ventricular rate. At fixed sub maximal workload below anaerobic threshold, steady state condition are usually reached after the second minute of exercise, following which heart rate, cardiac output, blood pressure and pulmonary ventilation are maintained at reasonably constant levels[3]. During strenuous exertion sympathetic discharge is maximal and parasympathetic stimulation is withdrawn, resulting in vasoconstriction of most circulatory body systems, except in the exercising muscles and in the cerebral and coronary circulation.

Venous and arterial nonepinephrine release from sympathetic post ganglionic endings, as well as plasma levels is increased, catecholamine release enhances ventricular contractility. As exercise progresses, skeletal muscle blood flow is increased, oxygen extraction increases by as much as threefold, total calculated peripheral resistance decreases, and systolic blood pressure usually increases, mean central blood pressure and pulse pressure usually increases. Diastolic blood pressure does not change significantly. The pulmonary vascular bed can accommodate as much as six fold increase in cardiac output with only modest increase in pulmonary artery pressure, pulmonary capillary wedge pressure and right atrial pressure. In normal individuals this is not a limiting determinant of peak exercise capacity.

Cardiac out put increases by four-to six – fold above basal levels during strenuous exertion in the upright position. Depending on genetic

endowment and level of training [4] .The maximum heart rate and cardiac output are decreased in older individuals partly because of decreased B-beta-adrenergic responsiveness [2]. Maximum heart rate can be estimated from the formula heart rate = (220-age years) with standard deviation of 10-12 beats/min. The age predicted maximum heart rate is a useful measurement for safety reasons. However, the wide standard deviation in the various equations used and the impact of drug therapy limit the usefulness of this parameter in estimating the exact age predicted maximum for an individual patient.

In the post exercise phase, haemodynamics return to base line within minutes of termination. Vagal reactivation is an important cardiac mechanism after exercise and is accelerated in well-trained athletes but blunted in patients with chronic heart failure [2]. The total oxygen uptake in excess of the resting oxygen uptake during the recovery is the oxygen dept.

Patient's position:

At rest, the cardiac output and stroke volume are higher in the supine than in the upright position, with exercise in normal supine persons, the elevation of cardiac out put results almost entirely from an increase in heart rate with little augmentation of stroke volume. A change from supine to upright positions causes a decrease in venous return, left ventricular end diastolic volume and pressure, stroke volume and cardiac

index. Renin and norepinephrine levels are increased. End-systolic volume and ejection fraction are not significantly change. The net effect on exercise performance. Is an approximate 10 % increase in exercise time, cardiac index, heart rate, and rate pressure product at peak exercise in the upright as compared with the supine position.

Exercise protocols:

The main types of exercise are isotonic or dynamic exercise, isometric or static exercise and resistive (combined isometric and isotonic) exercise. Dynamic protocols, most frequently are used to assess cardiovascular reserve, and those suitable for clinical testing should include a low intensity warm-up phase in general, 6 to 12 minutes of continuous progressive exercise during which the myocardial oxygen demand is elevated to a level which is optimal for diagnostic and prognostic procedure [1]. The protocol should include a suitable recovery or cool down period. If the protocol is too strenuous for an individual patient early test termination results and this will not allow an opportunity to cause clinically important responses. Thus exercise protocols should be designed to accommodate patient's limitations.

Static exercise:

This form of exercise generates force with little muscle shortening and produces a greater blood pressure responses than with dynamic exercise, cardiac out put does not increase as much as with dynamic exercise

because increased resistance in active muscle groups limits blood flow in a common form of static exercise, the patient's maximal force on a hand dynamometer is recorded. The patient then sustains 25 to 33 percent of maximal force to 3 to 5 minutes while ECG and blood pressures are recorded. The increase in myocardial $V0_2$ is often insufficient to initiate an ischaemic response.

Electro-cardiographic measurements:

The Mason – Likar modification of the standard 12-leads ECG requires that the extremity electrodes shoud be moved to the torso to reduce motion artifact. The arm electrodes should be located in the most lateral aspects of the infra clavicular fossae, and the leg electrodes below the ribcage. This arrangement results in a right-axis shift and increase voltage in the inferior leads and may produce loss of Q waves and development of new Q in the AVL lead, thus it could not be used to interpret a diagnostic test 12 lead ECG. The more cephalad the leg electrodes are placed, the greater is the degree of change and the greater is the augmentation of R wave amplitude, potentiating exercise induced ST segment changes.

Types of ST segment Displacement:

In normal persons, The PR, QRS and QT intervals shorten as heart rate increases. P amplitude increases, and PR segment becomes progressively more down sloping in the inferior leads, J point, or junctional, depression

is a normal finding during exercise. In patients with myocardial ischaemia the ST segments usually becomes more horizontal (Flattens) with the progression of exercise the depth of ST segment depression may increase involving more leads and the patient may develop angina. These changes may persist 5-10 minutes in the immediate post recovery phase. With down sloping ST segment and T wave inversion. Ischaemic ST segment displacement may be seen during exercise, but in about 10% of patients this may appear only in the recovery phase, this is mainly seen in asymptomatic patients. Patients should not leave the exercise laboratory area until the post exercise ECG has retuned to base line.

Measurement of ST segment displacement:

For purposes of interpretation, the PQ junction is usually chosen as the isoelectric point. The TP point represent the true isoelectric point but impractical choice for most routine clinical measurement. The development of 0.1 mV (1mm) or greater of J point depression measured from the PQ junction with a relatively flat ST segment slope (<1 mV/sec), depressed greater than or equal to 0.1 mV 80 ms after the J point (ST80). In three consecutive beats with a stable base line is considered to be an abnormal response. The ST segment at rest may be occasionally depressed when this occurs. The J point and ST segment should be depressed an additional 0.1 mV or greater to be considered abnormal. When the degree of resting ST segment depression is 0.1 mV

or greater, the exercise ECG becomes less specific and myocardial imaging modalities should be considered [5]. In patients with resting ST segment elevation, return to the pa junction is normal; therefore, the magnitude of exercise induced ST segment depression should be determined from the Pq junction and not from the elevated position of the J point before exercise.

Exercise induced ST segment depression does not localize the site of myocardial ischaemia, nor does it provide a clue about which coronary artery is involved[81]. Exercise induced ST segment elevation is relatively specific for the territory of myocardial ischaemia and the coronary artery involved[81].

Up-sloping ST segment:

Junctional or J point depression is a normal finding, during maximal exercise, and a rapid up sloping of a depression (<1mV) should be considered as abnormal. Occasionally, however, the ST segment is depressed 0-15 mV (1.5 mm) or greater at 80 m sec after the J point. This type of slow up sloping ST segment may be the only ECG finding in patients with well defined obstructive CAD and may depend on the lead set used. In patients' subsets with a high CAD prevalence, a slow up sloping ST segment of depressed (0.15 mV) or greater at 80 m sec, after the J point should be considered to be abnormal. Increasing the degree of ST segment depression at 80 m/sec after the J point to 0.20 mV (2.0mm)

or greater in patients with slow up sloping St segment increases the specificity but decreases sensitivity [6].

ST Segment Elevation:

Exercise induced ST segment elevation may occur in an infract territory where Q waves are present or in a non infract territory. The development of 0.1 mV (1 mm) or greater of J point elevation, persistently elevated greater than 0.1 mV at 60 m sec, after the J point in three consecutive beats, with a stable base line is considered an abnormal response. This finding occurs in approximately 30% of patients with anterior myocardial infractions and 15% in patients with inferior ones tested early (within 2 week) after the index event and decreases in frequency by 6 weeks. As a group post infracts patients with exercise induced ST segment elevation have a lower ejection fraction than those without, a greater severity of resting wall motion abnormalities, and a worse prognosis. When ST segment elevation develops during exercise in a non-Q wave lead in a patient without a previous history of acute myocardial interaction, the findings, should be considered as likely evidence of transmural myocardial ischaemic caused by coronary vasospasm or high grade coronary narrowing but it's a rare finding occurring approximately in 1% of patients with obstructive CAD.

T wave changes:

The morphology of the T wave is influenced by body position, respiration, hyperventilation, drug therapy and myocardial ischaemic necrosis in patients population with a low CAD prevalence, pseudo normalization of T waves (inverted at rest and becoming upright with exercise) is a non diagnostic finding but in a rare instances it could be a marker for myocardial ischaemia in a patient with documented CAD and it needs to be, substantiated by other techniques.

Other electrocardiographic markers:

Changes in R wave amplitude during exercise are relatively non specific and none related to the level of exercise performed- when the R wave amplitude meets voltage criteria left ventricular hypertrophy, the ST segment response can not be used reliably to diagnose CAD even in the absence of LV strain pattern. Loss of R wave amplitude commonly seen after MI, reduces the sensitivity and the ST segment response in that lead to diagnose obstructive CAD.

Mechanism of ST segment Displacement:

Pathophysiology of the myocardium Ischaemic response:

Myocardial oxygen consumption (MO_2) is determined by heart rate, systolic blood pressure, left ventricular end-diastolic volume, wall thickness and contractility [7]. The rate pressure or double product (heart rate X systolic blood pressure) increases progressively with increasing work and can be used to estimate the myocardial perfusion requirement in

normal persons and in many patients with coronary artery disease. Oxygen extraction is maximal at rest and consumption is only increased by increasing perfusions, and there is a linear relationship between MO_2 and coronary blood flow. The principal mechanism for increasing coronary blood flow during exercise is to decrease resistance at coronary arteriolar level [8]. In patients with progressive narrowing of the epicardial vessels, an ischaemic threshold occurs and exercise beyond this threshold can produce abnormalities in diastolic and systolic ventricular function, ECG changes and chest pain. The sub-endocardium is more susceptible to ischaemia because of increase wall tension. Dynamic changes in coronary artery tone at the site of atherosclerotic plaque may result in diminished blood flow during static or dynamic exercise i.e. perfusion pressure distal to the stenotic plaque actually falls during exercise resulting in reduced sub-endocardial blood flow [2]. Thus myocardial ischaemia may result also from a limitation of blood flow.

Nonelectrocardiographic observations:

Blood pressure:

The normal exercise response is to increase systolic BP progressively to a peak response ranging from 160-200 mm Hg – with the higher range of the scale in older patients with less compliant vascular system [2]. Africans Americans groups tend to have a higher systolic BP response than do whites [9]. At high exercise load it is difficult sometimes to obtain a

precise –determination of systolic BP by auscultation [10] usually systolic BP does not increase significantly. Failure to increase systolic BP beyond 120 mmHg or a sustained decrease greater than 10 mmHg repeatable within 15 seconds, or a fall in systolic BP below standing rest values is abnormal and indicates either inadequate elevation of cardiac output and systolic dysfunction or excessive reduction in systemic vascular resistance [11].

An abnormal systolic BP response in patients with a high prevalence of CAD is associated with more extensive CAD and more extensive myocardial perfusion defects[81]. Exertional hypotension is higher in patients with three vessels and left main stem diseases, and many other conditions associated with failure to increase or actual decrease in systolic BP like cardio myopathy, left ventricular flow tract obstruction, use of antihypertensive drugs, hypovolaemia, and prolonged vigorous exercise.

It is important to distinguish between a decline in blood pressure in the post exercise phase and a decrease or failure to increase systolic blood pressure during progressive exercise. The incidence of post exercise hypotension was about 1.9 percent in 78 asymptomatic volunteers in the Baltimore longitudinal study, most hypotensive episodes were symptomatic and only two patients had hypotension associated with bradycardia and vagal symptoms. Although ST segment abnormalities

suggestive of ischaemic occurred in one-third of the patient with hypotension, none of the patients had a cardiac event during 4 years follow up.

Maximal work capacity:

This variable is one of the most important prognostic features or measurements obtained from an exercise test [12]. maximal work capacity in normal individuals is influenced by familiarization with the exercise test equipment, level of training, and environmental conditions at time of testing. In patients with known or suspected CAD, a limited exercise, capacity is associated with increased risk of cardiac events, and in general, the more severe the limitation, the worse the CAD extent and prognosis. In estimating functional capacity, the amount of work performed (or exercise stage achieved) should be the parameter measured not the duration of exercise.

A serial comparison of functional capacity in individual patients to assess significant interval change requires a careful examination of exercise protocol used during both tests of drug therapy and time of ingestion, of systemic blood pressure and of other conditions that might influence test performance. Major reductions in exercise capacity usually indicates significant worsening of cardiovascular status, modest changes may not*.

Exercise testing in determining prognosis:

Exercise testing provides not only diagnostic information, but also more importantly prognostic data and its value should be considered in light of what already known about a patient risk status, LV dysfunction, CAD extent, electrical instability and coronary (Co morbid conditions) especially when estimating long term outcome.

Asymptomatic population:

The prevalence of an abnormal exercise ECG results in middle-aged asymptomatic men ranges from 5-12% [13] and the risk of developing a cardiac event is nine times greater when the test result is abnormal as when it is normal. Also the risk is slightly increased when the result is strongly positive. In the[81] LRC prevention trial a strongly positive test result was defined as one in which the ST response was 0.2mV (2mm) or greater or occurred during the first 6 minutes of exercise or at heart rate at or below (163-0.66 x age). A positive test result was not significantly associated with non-fatal myocardial infarction. this indicates the difficulty in identifying patients destined to develop abrupt changes in plaque morphology.

In Seattle Heart Watch, Bruce[81] noted that an abnormal ST response to exercise in an asymptomatic man did not increase the likelihood of developing cardiac events within six years in the absence of conventional risk factors. However this likelihood increased when the patient had any conventional atherosclerotic risk factor and two or more

abnormal responses to exercise. The abnormal response to exercise defined as chest-discomfort during the exercise, exercise duration less than 6 minutes or ≤ 2 stages, failure to achieve 90% of age-predicted maximum heart rate, or 0.1mV (Imm) or greater of horizontal or down sloping ST segment depression with exercise or in early recovery, only 1.1 percent of the a symptomatic healthy men were in a high-risk category [14].

Serial change of a negative exercise ECG result to a positive one in asymptomatic person carries the same prognostic importance as an initially abnormal test result [13].

The prevalence of an abnormal exercise ECG result in middle-aged asymptomatic women ranges from 20 to 30 percent [1]. In general, the prognostic value of an ST segment shift in women is less than in men. Although the use of multivariate scores to predict CAD in women has improved diagnostic accuracy, false positive results continue to be a problem in many patients and supplemental imaging techniques are often necessary to enhance the diagnostic performance of the test [15].

Symptomatic patients :

Exercise ECG should be performed routinely (unless there is contraindication or it is not feasible) in patients with chronic ischaemic heart disease before coronary angiography. Patients who have excellent exercise tolerance (e.g. > 10 minutes) usually have an excellent prognosis

regardless of the anatomical extent of CAD[81]. It estimates the functional significance of angiographically documented coronary artery stenosis. The impact of exercise testing in patients with suspected or proven CAD was studied by Weirn and colleagues in 4083 medically treated patients in the CASS Study [16]. A high risk patient subset was identified. (12 percent of the population) with an annual mortality of 5 percent a year when exercise work lead was less than Bruce's stage 1 (<4 minutes) and there is 0.1 mV (1mm) or greater ST segment depression. A low risk patients subset (34 percent of the population) who were able to exercise into Bruce's stage III or greater with a normal exercise ECG result had an annual mortality less than 1 percent per year over 4 years of follow up.

Silent Myocardial Ischemia:

In patients with documented coronary artery disease the presence of exercise-induced ST segment depression confers increased risk of subsequent cardiac events regardless of whether angina occurs during the test (17). The magnitude of the prognostic gradient in patients with an abnormal exercise ECG result with or without angina varies considerably in the published literature. In the CASS data bank, 7 years survival in patients with silent or symptomatic exercise induced myocardial ischaemia was similar in patients stratified by coronary anatomy and left ventricular function. With the worst survival in patients with the most extensive CAD. In the CIP trial, coronary revascularization, was a more

effective treatment strategy to reduce exercise induced myocardial ischaemia than was medical therapy [18].

Unstable Angina:

The incidence of exercise-induced angina or ischaemic abnormalities in patients who had unstable angina and who undergo predischarge low-level protocol is about 30-40 percent[81]. The findings of ischaemic ST segment changes or limiting chest pain is associated with a significantly increased risk of subsequent cardiac risk in men and postmenopausal women [19] the absence of these findings identifies a low-risk patients.

Myocardial infarction:

Exercise testing after myocardial infarction is useful to determine:

- Risk stratification and assessment of prognosis
- Functional capacity for activity prescription after discharge
- Assessment of adequacy of medical therapy and need to use supplemental diagnostic or treatment options [3], the incidence of fatal or nonfatal cardiac events associated with it is low. A low level exercise test achievement of 5 to 6 minutes or 70-80 percent of age-predicted maximum is frequently performed before discharge to establish the haemodynamics response and functional capacity [20]. The ability to complete 5-6 minutes or 70-80 of age predicted maximum in the absence of ECG or blood pressure abnormalities is associated with

one-year mortality of 1-2 percent and may help guide the timing of early hospital discharge [21]. Inability to perform low level test, poor capacity, inability to increase, or a decrease in systolic blood pressure, and angina or ST segment changes one all associated with increased risk. Although B blockers may attenuate the ischaemic response, they do not interfere with poor functional capacity and should be continued. There is a trend towards early pre-discharge exercise testing (within 3 to 5 days) in uncomplicated cases (good prognostic value). A 6-week test is useful in clearing patients to return to work and to provide a better estimate of cardiovascular reserve at peak exercise performance.

Risk stratification in the emergency department:

Patients who present to the emergency department are heterogonous population with a large range of pretest risk for CAD. Clinical assessment can identify, lower risk patients who can safely be further risk stratified using exercise testing. The cost-effectiveness of this approach has been demonstrated in both low and intermediate-risk patients.

Exercise testing in the emergency department should not be performed when:

- New or evolving ECG abnormalities are noted in the resting ECG tracing
- The levels of cardiac enzymes are abnormal.

- The patient can not adequately perform exercise
- The patients reports worsening or persistent chest pain symptoms or
- Clinical reports indicate imminent coronary angiography is likely. Several series of clinically low-risk subjects reported 6-month cardiac event rates less than 1 percent with normal exercise test result [22].

Preoperative risk stratification before non-cardiac surgery:

Exercise ECG before elective non-cardiac surgery provides an objective measurement of functional capacity and the potential to identify likelihood of preoperative myocardial ischaemia. In patients with a low ischaemic threshold the risk of perioperative cardiac events and adverse long term out come is significantly increased. In patients with an abnormal exercise ECG result at low work loads, coronary angiography with revascularization should be considered when feasible before non-cardiac operative intervention [23]

Congestive heart failure:

There is a wide range of exercise capacity in patients who have a markedly reduced ejection fraction, with some patients having near-normal peak exercise capacity. Symptoms in patients with congestive heart failure are related to excessive increase in blood lactate during low exercise levels, reduction in quantity of oxygen consumed at peak exertion and disproportionate increase in ventilation at sub maximal and peak workloads. This lead to increase pulmonary dead space and rapid

shallow breathing during exercise . Dyspnoea and fatigue are the usual reasons for exercise termination

Cardiac Arrhythmias and conduction disturbances:

The genesis of cardiac arrhythmias includes reentry, triggered activity, and enhanced automaticity. Increased catecholamines during exercise accelerate impulse conduction velocity, shorten the myocardial refractory period, increase the amplitude of after potentials and increase the stage of depolarization of action potentials. Other potentials include metabolic acidosis and exercise induced myocardial ischaemia. Ventricular premature complexes occur frequently during exercise and increase with age, (0-5%) of asymptomatic patients without suspected cardiac disease and are not associated with increased risk of cardiac death, it is not a useful marker of ischaemic heart disease in the absence of ST segment depression. In patients with a recent myocardial infarction, the presence of exercise induced repetitive forms is associated with subsequent increased risk of cardiac events.

Exercise induced ventricular arrhythmias tend to be more frequent in the recovery phase and Beta-adrenergic blocking agents may suppress them. Exercise testing is also useful in the assessment of patients with ventricular arrhythmias and has an adjunctive role along with ambulatory monitoring and electrophysiological studies. In approximately 10-15 % of

such patients, spontaneously occurring arrhythmias are observed only during exercise*.

Supraventricular arrhythmias:

Supraventricualr premature beats induced by exercise are observed in 4-10 % of normal persons and 40 % of patients with underlying heart disease they are not useful in the diagnosed of IHD.

Atrial fibrillation:

Patients with chronic atrial fibrillation tend to have rapid ventricular response in the initial stages of exercise and 60-70% of the total change in heart rate usually occurs within the first few minutes of exercise. Pharmacological control of the ventricular rate does not necessary result in a signification increase in exercise capacity, which is usually related to the underlying cardiac disease.

Sick sinus syndrome:

Patients with sick sinus syndromes in general have a lower heart rate at submaximal and maximal workloads compared with control subjects. However, 40 -60 % will have a normal exercise heart rate response.

Atrioventricular Block:

Exercise testing may help determining the need for atrioventicualr sequential pacing especially in congenital AV block.

Left bundle branch block:

Exercise-induced ST segment depression is found in most patients with LBBB and can not be used as a diagnostic or prognostic indicator regardless of the degree of St segment abnormality, but the new development of exercise induced LBBB, which occurs in about 0.4 % increased the relative risk of death or major cardiac events by three-folds[81].

Right Bundle Branch Block:

The resting ECG in right bundle branch block (RBBB) is frequently associated with T wave and ST segment abnormalities. In early anterior leads (V1-V3). Exercise induced St segment depression in leads V1-V4 is a common findings and is non-diagnostic.

The new development of exercise induced St segment depression in leads V5 – V6 or leads 2 and AVL, reduced systolic blood pressure are useful in detecting patients who have CAD who had and a high pretest risk of disease(5). The presence of RBBB decreases the sensitivity of the test(24).

Preexcitation syndrome:

The presence of Wolf Parkinson syndrome (WPW) invalidates the use of ST segment analysis of a diagnostic method for detecting CAD; false ischaemic changes are frequently registered.

Cardiac pacemakers and implantable cardioverter-defibrillator devices:

The exercise protocol used to assess chronotropic responsiveness in patients before and after cardiac pacemaker insertion should adjust to the

fact that many such patients are older individuals and may not tolerate exercise workloads. An optimal physiological pacemaker should normalize the heart rate response to exercise in proportion to O2 uptake.

When testing patients with an implantable cardioverter-defibrillator devices (ICD) device, the program detection interval of the device should be known. If the ICD device is implantable for ventricular fibrillation or fast ventricular tachycardia, the rate will normally exceed that attainable during sinus tachycardia and the test can be terminated as the heart rate approaches 10 beats/min below the detection interval of the device.

Specific clinical applications:

Influence of drugs and other factors:

Patients with CAD demonstrate individual variability in time to onset of exercise-included angina, time to onset of ST segment. Depression and cardiovascular efficiency during the test [24].

Variability can be reduced by patients' familization with the exercise protocol and equipment, controlling for antianginal therapy and stable test performance conditions.

Women:

The sensitivity and specificity of exercise included ST segment depression for obstructive CAD is less in women than in men. The decreased diagnostic accuracy results in part from a low prevalence and extent of CAD in young and middle aged women, women tend to have a

greater release of catecholamines during exercise, which could potentiate coronary vasoconstriction and augment the incidence of abnormal exercise ECG results. False positive results have been reported to be more common during menses or preovulation. In a series of 976 symptomatic women referred for exercise testing and coronary angiography; a low, moderate and high risk Duke treadmill score were associated with CAD of 79 % or greater in 19.1, 34.9 and 89.2 % respectively. The frequency of three-vessel disease 75% or greater or left main coronary artery disease was 3.5, 12.4 and 46% respectively [25]. Alexander and colleagues compared the Duke treadmill score in 976 women and 2249 men, the 2-years mortality for women was 1, 2.2 and 3.6 for low – moderate and high risk scores, compared with 1.7, 5.8 and 16.6 % in men. They have similar frequency of angina but exertional angina in women was less often correlated with CAD presence. [26].

Hypertension:

Exercise testing has been used in an attempt to identify patient who have an abnormal blood pressure response and are destined subsequently to develop hypertension, severe systemic hypertension may interfere with subendocaridal perfusion and cause exercise induced ST segment depression in the absence of arthrosclerosis, even when the rest ECG does not show significant or T wave changes [27]. Exercise tolerance is decreased in patients with poor blood pressure control [28].

Elderly patients:

The frequency of abnormal exercise ECG pattern is greater in older than younger individual, and the risk of cardiac events is significantly increased because of a concomitant increase in prevalence of more extensive CAD[29]. The greater test sensitivity of the exercise is accompanied by slight reduction in capacity.

Diabetes Mellitus:

Coronary atherosclerosis and peripheral vascular disease are significantly increased in diabetic as compared with non-diabetics and this correlates closely with duration of diabetes. In patients with autonomic dysfunction and sensory neuropathy anginal threshold may be increased and abnormal exercise induced, heart rate and blood pressure responses are common [30]. The probability of an adverse cardiac outcome in a diabatic as compared with a non diabetic individual for a similar abnormal exercise results are likely to be increased because of the increased risk of dyslipidaemiea, impaired fibrinolysis and hypertension.

Safety and risks of exercise testing:

Exercise testing has an excellent safety record. The risk is determined by the clinical characteristic of the patient referred for the procedure. In non-selected patients the mortality is less than 0.01 percent and morbidity less than 0.05 percent [31]. The risk is greater when the test is performed sooner after an acute ischaemic event.

The risk of incurring a major complication during exercise testing can be reduced by performing a careful history and physical examination before the test and observing patients closely during exercise with monitoring of the ECG, BP and symptoms and the contraindications are well defined. Patients with critical obstruction to left ventricular out flow are at increased risk of cardiac events during exercise.

Termination of exercise:

The use of standard test indications to terminate an exercise test reduces risk.

Termination of exercise test should be determined in part by the patient's recent activity level. The rate of perceived patient exertion can be estimated by the Bonges scale. The scale is linear with values of 9, very light, 11 fairly light [13], somewhat hard 13, hard with values of 15, very hard with values of 17 and very very hard with values of 19. It is useful to grade exercise induced chest discomfort *on 1 to 4* scale with 1 indicating the initial onset of chest discomfort and 4 the most severe chest pain the patient has ever experienced. The test should be stopped when the patients reports grade 3 chest pain.

- Contraindications to exercise ECG test.
- Acute MI (<2days).
- Unstable angina with recent chest pain.
- Untreated life threatening arrthythmies.

- Acute myocarditis or pericarditis.
- Critical aeortic stenosis.
- Severe hypertrophic obstructive cardiomyopathy.
- Uncontrolled hypertension.
- Severe systemic illness (pulmonary embolism, aeortic dissection).

Risk factors for atherosclerotic disease:

Cardiovascular disease is the single most common cause of death in the developed would and accounts for almost 1 million fatalities in the United States alone each year.

For an epidemiological perspective a "risk factor " is a characteristic or feature of an individual or population that is present early in life and its associated with an increased risk of developing future disease.

Pathogenesis of various coronary syndromes:

The progression of early atherosclerotic lesion to clinically manifest, enlarging atherosclerotic plagues, such as those causing exertional angina, is often more in people with coronary risk factors.

In some plagues progression is slow, and probably a continuation of the complex biological process initiated by chronic endothelial injury or damage responsible for the early lesion. In most growing lesions, however progression is probably rapid and follows recurrent minor fissures of the most fatty or atheromatous plague with subsequent thrombus formation, and fibrotic organization causing coronary stenosis.

If these are significant, exertional or silent ischaemia commonly result from increase in myocardial oxygen demand that out strips the ability of stenosed coronary artery to increase oxygen delivery.

Vascular biology of risk factors:

Lipoproteins:

Lipoprotein are high molecular weight complexes of lipids and proteins that circulate in the blood. Their physiological functions include transport of lipids to cells for energy, growth requirements and storage.

The role of cholesterol in the pathogenesis of atherosclerotic heart disease remained controversial until recently. Early experiments by *Antis Chow*[81] on cholesterol fed animals and the later identification of cholesterol as an important constituent of the plaque furnished land mark clues in the case against cholesterol in the pathogenesis of cardiovascular disease [32]

The importance of serum or plasma cholesterol emerged not only from the large epidemiological studies conducted afterwards but also from the large body of the epidemiological data that include the seven country study, the Ni-Hon-San study the Northwick park study and more recently, the prospective cardiovascular Munster (Brocam) Study [33].

Lipoproteins are also metabolic precursors of biologic regulators such as prostaglandin, thromboxanes and leukotriens.

LDL (low density lipoprotein) promotes athrogenesis by affecting one or several of the processors of influx and efflux of the vessel wall. Elevated. LDL also promote thrombosis.

HDL (heavy density lipoproteins) promote cholesterol efflux from atherosclrotic lesions, possibly through a receptor mediated mechanism, observational data and experiments in vitro suggest that HDL containing apo A.I is protective.

Evidence is going that triglyceride rich lipoproteins are important contributors to the development of coronary disease.

Smoking:

Cigarettes smoking constitutes the single most important modifiable risk factor in the coronary artery disease and the leading preventable cause of death in the United States where it accounts for over 400,000 deaths annually [34]. Smoking has a particularly staggering impact in the third world, almost one-half billion individuals worldwide will eventually die of smoking related complications [35]. Even among non-smoker inhaled smoke also greatly increase coronary risk [36].

Land mark studies in the early 1950 first reported strong positive association between cigarette exposure and coronary heart disease, over the next 40 years, an exceptionally consistent series of prospective studies have clearly documented the effects of smoking on coronary risk, these studies suggest that, compared with non-smokers, those who consume 20

or more cigarettes have a two-three folds increase in total coronary artery disease risk [36].

Smoking affects atherothrombosis by several mechanisms inducing an elevation in blood fibrinogen concentration, enhancing platelets activity and increasing whole blood viscosity by inducing secondary polycythaemia. In addition to accelerating atherosclerotic progression[37], long-term smoking may enhance oxidation of LDL-c and reduces levels of HDL-C[38]. It also impairs endothelium dependent coronary artery vasodilation[39], has multiple adverse haemostatic effects[49], increases inflammatory markers such as CRP, *soluble intercellular adhesion . Molecule -1 (ICAM-1) and Fibrinogen [40].* Compared with non-smokers, smokers have an increased prevalence of coronary spasms,[41] and may have reduced thresholds for ventricular arrhythmia.

Hypertension:

In contrast to cigarette smoking, hypertension is often a silent cardiovascular risk factor, elevated levels of blood pressure consistently correlate with elevated risks of stroke and myocardial infarction and an early metanalysis that evaluated over 5500 cardiovascular events found a 27 % increase in risk of coronary heart disease and 42 % increase in risk of ischaemia for every 7mm Hg elevation of diastolic blood pressure[42].

Even among individuals without diastolic hypertension, isolated increases in systolic pressure are risk factor. It increases the risk for non-fatal

myocardial infarction and cardiovascular death among both general population samples [29] and apparently low risk groups. [43]

With regard to treatment, blood pressure reduction greatly reduces risk, even among individuals with mild to moderate hypertension. In an over view analysis, pharmacological reductions in diastolic blood pressure of 5 to 6 mmHg appear to reduce the risk of stroke by over 40%, and the risk of vascular mortality by 21 % and the risk of coronary heart-diseases by 14 percent [44].

Insulin resistance and diabetes:

Three-fourth of all deaths among diabetic patients result from coronary heart disease [45]. Compared to unaffected individuals, diabetic patients have a greater atherosclerotic burden both in the major arteries and in the micro vascular circulation, not surprisingly, diabetic patients have substantially increased rates of atherosclerotic complications in the setting of both in the primary prevention and after coronary interventional procedures [46]. Thus insulin resistance and diabetes mark among the major cardiovascular risk factors.

Patients with diabetes have three to five folds increased rates of further cardiovascular events [47] with even higher rates reported among diabetic women [48]. However, although hyperglycemia is associated closely with micro vascular disease, insulin resistance itself promotes atherosclerosis even before it produces frank diabetes [49]. This finding has promoted

recommendations for increased surveillance for the insulin resistance syndrome a cluster of glucose intolerance and hyper insulinaemia accompanied by hypertriglyceridaemia, low HDL levels and a predominance of small dense LDL particles. It also produces a prothrombotic state due to increased levels of PAI-1 and fibrinogen[50].

In addition to these systemic metabolic abnormalities hyperglycemia causes accumulation of advanced glycation end products inculpated in vascular damages[51]. Furthermore, diabetic patients have markedly impaired endothelial and small muscles function [52] and appear to have increased leukocyte adhesion to vascular endothelium, a critical early step in athrogenesis, and diabetic nephropathy accelerates these adverse processes

Despite evidence concerning pathophysiological abnormalities associated with diabetes and epidemiological data describing increased hazards associated with hyperglycemia few clinical trials have evaluated whether improved glycaemic control improves cardiovascular risk. The diabetes complications and the control trials of strict glycaemic control among (IDDM) reported benefits on micro vascular end points but did not find significant benefits on coronary events rates[53] Similarly, the United Kingdom prospective Diabetes study found only marginal benefit for improved glycemic control among non-insulin dependent diabetics[54]. Thus as outlined later, exercise, diet, avoidance of obesity and aggressive

control risk factors remain primary targets for risk reduction in type II, populations[54].

Exercise and Obesity:

Regular physical exercise reduces myocardial oxygen demand and increases exercise capacity, both of which are associated with lower levels of coronary risks[55] . A consistent series of prospective studies have demonstrated an association between levels of physical activity and reduced rates of cardiovascular morbidity and all-cause mortality[56], for example, in a prospective evaluation of Harvard Olumni initially free of apparent cardiovascular disease, those men with the highest level of activity at baseline had a 40% reduction in non-fatal cardiovascular events , and 24% reduction in cardiovascular death compared with those with sedentary life styles. [56] whereas the level of exercise in early life predict long term exercise pattern, significant reductions in subsequent risk also applied to individuals who were initially sedentary but later increased exercise levels [57]. Thus, increasing exercise levels even in mid to late life reduces coronary risk in men [58] and women[55], The American heart Association has recommended an exercise energy expenditure approaching 2000 calaries each week, a level of exercise that can be achieved with modest daily exertion [59].

The mechanisms by which exercise lowers cardiovascular risk remain uncertain but likely include favorable effects on blood pressure[60], weight

control , lipid profiles [61], and improved glucose tolerance [62] exercise also improves endothelial function, enhances fibriolysis, reduces platelets reactivity and reduces propensity for in situ thrombosis[63]

It is important to recognize that obesity itself is associated with substantially increased cardiovascular risk, regardless of activity levels. For example, the Nurses Health Study revealed a direct linear relation between body mass index and subsequent risk of coronary heart disease[64] as does the distribution of body fat. Recent studies indicate that the index to hip ratio, or abdominal obesity is an independent marker of vascular risk both in women and older men[65.] .

Controversy remains as to whether obesity itself is a free risk factor for cardiovascular disease or whether its impact on vascular risk is mediated solely through interrelations with glucose intolerance, insulin resistance, hypertension, physical in activity and dyslipidaemia.

Mental stress and cardiovascular risk

The adrenergic stimulation of mental stress can clearly augment myocardial oxygen requirements and aggravate myocardial ischemia .

Mental stress can cause coronary vasoconstriction, particularly in atherosclerotic coronary arteries and hence can influence myocardial oxygen supply as well[66], Myocardial ischemia provokable by mental stress can predict future coronary events[67]. Catecholamine can also promote alterations in thrombosis and coagulation that might favor clot

formation and stability. These factors may well trigger complications of preexisting atherosclerotic lesions. The increase in coronary death documented during missile attacks or natural disasters such as earthquakes support this concept [68].

what remains uncertain is the effect of mental stress per se on the development of atherosclerosis[69]. Studies in this regard have proved challenging because the metrics for mental stress lend themselves less well controlled than other more readily quantified risk factors.

Estrogen status:

Before menopause, women have lower age –adjusted incidence and mortality rates for coronary heart disease than men. Gender-specific incidence rates converge after menopause, suggesting a major role for estrogen in delaying progression of atherosclerosis, much of this effect results from beneficial actions of estrogen on lipid fractions. In studies of exogenous oral estrogen replacement therapy such as the Post mengrpousal menopausal Estrogen Progestion Intervention (PEPI) Trial progesterone intervention, estrogen reduced LDL-L by 10 to 15 % while increased HDL-L, $apoA_1$, and triglycerides[70] the mechanism of this effect results partly from a first –pass action in the liver that augments LDL catabolism while reducing activity of hepatic lipase with subsequent promotion of hepatic HDL ,Uptake [71].

The lipid effects of estrogen, however explain only part of the apparent cardiovascular benefits enjoyed by premenupousal women and women taking hormone replacement therapy[71].

Estrogen must therefore have other potentially beneficial effects[72]. These likely include direct vascular mechanisms such as improved endothelial dependent vasomotion[73], altered adhesions molecules levels, increased libindytic capacity [74] and enhanced glucose metabolism [75].

Despite those data, exogenous estrogen use among young women as form of contraception is associated with increased rates with intravascular thrombosis including deep venous thrombosis, pulmonary embolism as well as myocardial infiltion and stroke. These effects are particularly prominent within smokers so they should use alternative forms of contraceptives[76].

By contrast, among post-menopausal women using hormone replacement therapy, prospective observational studies suggest that estrogen use reduces cardiovascular risk by 35 to 45 % [77]. In one study estrogen users had an adjusted relative risk of coronary heart disease 40% lower than that of nonusers [78]. However, the clinical utility of estrogen replacement therapy remains controversial.

None-Atherosclerotic risk factors:

Despite the importance of blood lipids, half of all myocardial infarctions occurs among individuals without overt lyprlipodemia. Several novel

markers of atherothrombotic risk have emerged from low epidemiological studies and might prove useful clinically. However when considering adoption of screening for any new cardiovascular risk factor, clinicians need to consider. Whether there is a standardized and reproducible assay for the marker of interest [79] whether there is a consistent series of prospective studies demonstrating that baseline of a given parameter predict further risk, and whether the novel marker adds to the predictive value of lipid screening [80]. There are five promising novel markers of cardiovascular risk; total plasma homocysteine, fibrinogen, LP(a) fibrinolytic functions as ascertained by E-PA or PA-1 antigens, and markers of low grade inflammation such as CRP, physicians should also consider the relative magnitude of novel markers in terms of risk prediction particularly in comparison to lipid screening.

Cardiac Cathetarization :

Angiography provides detailed evaluation of both the anatomy and the haemodynamics of the heart and remains the gold standard of assessment of coronary arteries. It gives valuable prognostic information that can be gathered from the haemodynamic assessment at the time of cardiac catheterization.

Cardiac catheterization is most commonly performed to determine the nature and extent of coronary insufficiency in the symptomatic patient in who surgical or interventional therapy is contemplated. It is also used to

exclude the presence of significant disease when findings from other modalities such as stress test or echocardiography are equivocal, or when the patient continues to be severely symptomatic and definite diagnosis is important in the patient management

Because coronary angiography is the only technique capable of accurately defining the severity and the extent of coronary disease, it is important in the assessment of patients being considered for revascularization.

It is also indicated in patients with high risk for adverse outcome based on non invasive testing, in patients with severe angina on medical therapy, in unstable angina, in chest pain of undetermined origin when noninvasive testing is equivocal and in high risk patients undergoing cardiac surgery.

In acute MI cardiac catheter is indicated in:

Primary reperfusion with angiography.

Recurrent ischaemic episodes during hospitalization. Shock or haemodynamic instability.

Mechanical complications such as mitral regurgitation or ventricular septic defect.

OBJECTIVES

The objective of the study is:

- To see the mode of clinical presentation of coronary heart disease and
- To correlate it to both the exercise test and coronary angiography in patients suspected to have ischaemic heart disease.

Patients and methods

This is a retrospective study, which is conducted in Sudan Heart Centre.

Inclusion criteria:

The study selected patients who fulfilled the following criteria.

Sudanese patients with (+ve) exercise tolerance test who were referred for coronary angiography.

Exclusion criteria:

- Patients with (-ve) exercise test.
- Patients known to have acute coronary syndromes or patients who had pervious myocarial infarction.

Methodology:

A. Questionnaire designed to show patients risk factors and symptoms of IHD and ECG and echocaridoghraphic findings.

B. Information also taken from patients notes and records.

C. Investigations:

   - ECG.
   - Echocardioghraphy.
   - Lipid profile.
   - Cardiac catheter.
   - The BP levels were divided into 5 groups:

- Normal: $\rightarrow < {}^{130}/_{85}$.
- Heigh normal: ${}^{130}/_{85} - {}^{139}/_{89}$.
- Mild: ${}^{140}/_{90} - {}^{150}/_{99}$.
- Moderatic: ${}^{160}/_{100} - {}^{179}/_{109}$.
- Severe: $> {}^{180}/_{110}$.

Cholesterol levels was chividal in to 3 groups:

- Normal: 100-149.
- High normal: 150-199.
- Heigh: >200.

Triglecerides were divided into 2 group:

- Normal < 150.
- Heigh > 150.

Results

103 patients were studied. The distribution of age within the study group was 8 patients < 40 years (7.608%) and 95 patients > 40 years (92.2%) .40 patients were females (38.8%) and 63 were males (61.2%).[fig 1,2].

Concerning risk factors diabetes was obtained in 27 patients (26.7%), 54 patients (52.9%) were hypertensive, 31 patients (31.1%) gave history of smoking and 24 patients (24.2%) patients have positive family history of Ischaemic heart disease. [Fig 3,4,5,6] respectively.

62 patients had serum cholesterol level estimated: 11 patients had normal readings (17.7%), 38 patients had high normal readings (61.3%), 13 patients had high readings (21%).

Regarding the clinical presentation 89 patients (86.4%) presented with chest pain,[Fig 7] 40 patients (38.8%) gave history of palpitations, 47 patients (46.5%) complain of dyspnoea, 3 patients (3%) experienced lower limb swelling and history of cough was found in 12 patients (11.7%).

The distribution of patients with regards to blood pressure was as follows:

Normal 43 patients (44.8%)

High normal 12 patients (12.5%)

Mild hypertension 15 patients (15.6%)

Moderate hypertension 12 patients (12.5%)

Severe hypertension 14 patients (14.6%)

In correlating the degree of hypertension with angiographic findings: for the first group which recorded as normal 20patients have normal coronary study (50%), 10 had single vessel disease (25%), 5 had two vessel disease (12.5%) and 5 had three vessel disease (12.5%).

In patients with high normal blood pressure 5 patients had normal study (50%), 2 had single vessel disease (20%) and 3 had three-vessel disease (30%)

In those with mild hypertension 6 patients (42.9%) had normal study 3 had single vessel disease (21.4%), 2 had two vessel disease (14.3%) and three had three vessel disease (21.4%)

In patients with moderate hypertension 6 had normal study (60%), 3 had single vessel disease (30%) and 1 had two-vessel disease (10%).

In those with severe hypertension 8 patients had normal study (57.1%), 2 had single vessel disease (14.3%) and 4 patients had three-vessel disease (28.6%) [P value 0.720 not significant] [Fig 8].

Cardiovascular examinations revealed normal findings in all patients; with exception of the BP. Other signs were also normal except 3 patients who were found to have lower limb oedema.

The resting electrocardiogram (ECG) was done in 87 patients and it was normal in 36 patients (41.4%) with voltage criteria of left ventricular

hypertrophy (LVH) in 5 patients (5.7%). T-wave inversion and ST segment depression were found in 26 patients (29.9%). 20 patients (23%) had left axis deviation.

The Echocardiogram was recorded in 53 patients (51.5%) in whom 24 patients (45.3%) patients has normal studies. LVH in 20 patients (37.7%) and hypo or akinetic wall motion was found in 9 patients (17.0%) patients.

Concerning the coronary angiography, the left main coronary artery was involved in 4 patients (3.9%) [Fig 9]

For the left anterior descending coronary artery, 60 patients had normal study (67.4%) 14 had stenosis < 70% (15.7%) 15 had > 70% stenosis (16.7%). [Fig 9]

Regarding the left circumflex artery, 70 patients (79.5%) had normal study and 7 patients had < 70% stenosis (8%)and 11 patients had have > 70% stenosis (12.5%) [Fig 9]

70 patients had normal right coronary artery study (77.8%), 6 patients had < 70% stenosis (6.6 %) and 14 had > 70% stenosis (15.6%) [Fig 9].

Ejection fraction was recorded in only 12 patients of whom it was less than 50% in 4 patients (33.3%) and more than 50% in 8 patients (66.7%)

The diagnosis was recorded as normal study, single vessels disease, 2-vessele diseases or 3-vessel disease.

Patients recorded as normal study were 50 patients (52.6%).

Single vessel disease (SVD) was 21 patients (22.1%), 2 vessels disease (2VD) were 8 patients (8.2%) and 3 vessels disease (3VD) were 16 patients (16.8%).[Fig 10]

The treatment options were either medical, surgical or percutanious transluminal coronary angioplasty (PTCA). The percentages were as follows, patients for medical follow up were 11 patients (11.8%), patients for PTCA were 9 patients (9.7%) and patient for surgical intervention were20 patients (21.5%). The report was missing concerning 63patients (47%).

Concerning the coronary angiographic findings in diabetic diabetics; [27 patients] 11 patients (44%) had normal study, 4 patients (16%) had SVD, 3 patients (12%) had 2VD and 7 patients (28%) had 3VD. [p value 0.295 not significant]. [Fig 11]{Table 2}

The percentages within smokers were; 12 patients with normal studies (42.9%), 8 patients (28.6%) with SVD, 2 patients (7.1%) with 2VD and 6 patients (21.4%) with 3VD. [P value 0.339 not significant].{Table 3}

In patients with +ve family history of IHD [24 patients], 11 patients (52.4%) had normal coronary studies, 2 patients (9.5%) had SVD, 4 patients (19%) had 2VD and 4 patients (19%) had 3VD.{Table 4}

In patients with normal cholesterol level, 4 patients (40%) had normal coronary studies, 2 patients (20%)had SVD, 1 patient (10%) had 2VD and 3 patients (30%)had 3VD.

In patients with high normal cholesterol level, 16 patients (48.5%) had normal study, 12 patients (36.4%) had SVD, 1 patient (3%) had 2VD, and 4 patients (12.1%) had3VD.

In those with high cholesterol level, 6 patients (46.2%) had normal study, 2 patients (15.4%) had SVD, 3 patients (23.1%) had 2VD, and 2 patients (15.4%) had3VD. [P value 0.268 not significant]{Table 10}

Regarding the triglyceride, in patients with values<150mg/dl.

9 patients had normal study (60%), 5 patients had SVD (33.3%), 1 patient had 3VD (6.7%).

In patients with values >150mg/dl 4 patients (40%) had normal study, 5 patients (50%) had SVD and 1 patient (10%) had 3VD.[p value 0.618 not significant].[Fig 12]{Table 5}

Concerning the clinical presentation in correlation to the diagnosis, in patients presented with chest pain 42 patients (51.9%) had normal study, 17 patients (21%) had SVD, 7 patients (8.6%) had 2VD and 15 patients (18.5%) had 3VD. 8 patients with no history of chest pain had normal study (57.1%), 4 patients (28.6%) had SVD, 1 patient (7.1%) had 2VD and another 1 patient (7.1%) had 3VD.

Regarding the ECG findings in comparison to the coronary angiography results, in patients with normal resting ECG; 20 patients (58.8%) had normal coronary study, 9 patients (26.5%) had SVD, 2 patients (5.9%)

had 2VD and 3 patients (8.8%) had 3VD. [P value 0.252 not significant].[Fig 13]

In patients with LVH 3 patients (60%) had normal studies, no patients had SVD, 1 patient (20%) had 2VD and another 1 patient (20%) had 3VD.

For ST segment T wave changes 14 patients had normal studies (61.%), 3 patients (13%) had SVD, 3 patients reported with (13%) 2VD and another 3 patients (13%) had 3VD.

Concerning the Echocardiography, in patients with normal Echo (23 patients), 17 patients had normal coronary study (73.9%), 3 patients (13%) had SVD, 1 patient (4.3%)had 2VD and 2 patients (8.7%)had 3VD.

In patients with LVH (18 patients), 6 patients (33.3%) had normal study, 3 patients (16.7%) had SVD, another 3 patients had 2VD and 6 patients had 3VD (33.3%).

In whom reported as having wall dyskinesia or akinesia 3 patients had normal study (37.5%), 3 patients had SVD (37.5%), 1 patient (12.5%) had 3VD. [p value 0.101 not significant]. One patient had 2VD (12.5%).

Regarding the ejection fraction, in patients with EF<50% no patients reported as having SVD, 2 patients with 2VD (50%) 2 patients with 3VD (50%). In patients with EF> 50% 4 patients has SVD (50%), 1 patient had

2VD (12.5%), 3 patients has 3VD (37.5%). [P value 0.165 not significant].[Fig 14] {Table 1}

Age was divided into groups:

In males:

Age group (30-39 years) 2 had normal coronary study (50%), 1 had single vessel disease (25%), 1 had three-vessel disease (25%).

(40-49 years) 5 had normal coronary study (45.50%), 4 had single vessel disease (36.4%), 2 had two-vessel disease (18.2%)

(50-59 years) 7 had normal coronary study (38.9%), 8 had single vessel disease (44.4%), 2 had two-vessel disease (11.1%) and 1 had three-vessel disease (5.6%)

>60 years 6 had normal coronary study (25%), 8 had single vessel disease (25%), 2 had two-vessel disease (8.3%) and 10 had three-vessel disease (41.7%) [P value 0.161 not significant].{Table 6,7}

In females:

Age group (30-39) 3 patients had normal coronary studies with no patients reported as SVD, 2VD, and 3VD.

In the age group of (40-49) years 13 patients had normal coronary study (86.7%), no patients reported as SVD or 2VD and 2 patients (13.3%) have 3VD.

In the age group of (50-59) 7 patients reported as normal study (70%) 2 patients has SVD (20%), 1 patient has 2VD (10.0%) and no patient has 3VD.

In the group of (60-69) 4 patients (66.7%) had normal study and 2 patients have 3VD (33.3%).

In the age group >70 3patients has normal study (75%); 1patient has 2VD (25%) and no patients reported as SVD or 3VD. [P value 0.209 not significant]. [Fig 15] {Table 8,9}.

The distribution of patients by occupation was as follows:

- House wives were (32.2%)
- Government employee (28.7%).
- Skilled laborers (24.8%)
- Retired (14.9%)

Table 1: The effect of ECHO findings on diagnosis

Echo findings	Diagnosis			
	Normal	**SVD**	**2VD**	**3VD**
Normal	17(73%)	3(13%)	1(4.3%)	2(8.7%)
LVH	6(33.6%)	3(16.7%)	3(16.7%)	6(33.3%)
Dys, Hypokinesia	3(37.5%)	3(37.5%)	1(12.5%)	1(12.5%)

(P value 0.101)

Table 2: The effect of diabetes on diagnosis

	Diagnosis			
Diabetes	**Normal**	**SVD**	**2VD**	**3VD**
Yes	11(44%)	4(16%)	3(12%)	7(28%)
No	39(57.4%)	15(22.1%)	5(7.4%)	9(13.2%)

(P value 0.295)

Table 3: The effect of smoking on diagnosis

	Diagnosis			
Smoking	**Normal**	**SVD**	***2VD***	**3VD**
Yes	12(42.9%)	8(28.6%)	2(7.1%)	6(21.4%)
No	37(58.7%)	10(15.9%)	8(8.8%)	10(15.9%)

(P value 0.399)

Table 4: The effect of family history of IHD on diagnosis

Family history	Diagnosis			
	Normal	**SVD**	**2VD**	**3VD**
Yes	11(52.4%)	2(9.5%)	4(19%)	4(19%)
No	39(54.9%)	16(22.5%)	4(5.6%)	12(16.9%)

(P value 0.186)

Table 5: The effect of triglycerides level on diagnosis

	Diagnosis			
Triglycerides	**Normal**	**SVD**	**2VD**	**3VD**
Normal	9(60%)	5(33.3%)		1(6.7%)
High	4(40%)	5(50%)		1(10%)

(P value 0.618)

Table 6: The effect of male age on diagnosis

	Diagnosis			
Age group	Normal	SVD	2VD	3VD
30-39	2(50%)	1(25%)		1(25%)
40-49	5(45.5%)	4(36.4%)	2(18.2%)	
50-59	7(38.9%)	8(44%)	2(11.1%)	1(5.6%)
>60	6(25%)	6(25%)	2(8.3%)	10(41.7%)

(P value 0.161)

Table 7: Distribution of male patients by age groups

Age group	%
30-39	6.8
40-49	26.2
50-59	29.1
>60	37.9

Table 8: Distribution of female patients by age groups

Age group	%
30-39	7.5
40-49	40
50-59	25
60-69	17.5
>70	10

Table 9: The effect of female age on diagnosis

	Diagnosis			
Age group	**Normal**	**SVD**	**2VD**	**3VD**
30-39	3(100%)			
40-49	13(86.7%)			2(13.3%)
50-59	7(70%)	2(20%)	1(10%)	
60-69	4(66.7%)			2(33.3%)
>70	3(75%)		1(25%)	

(P value 0.209)

Table 10: The effect of cholesterol level on diagnosis

Cholesterol level	Diagnosis			
	Normal	**SVD**	**2VD**	**3VD**
Normal	4(40%)	2(20%)	1(10%)	3(30%)
High normal	16(48.5%)	12(36.4%)	1(3%)	4(12.1%)
High	6(46.2%)	2(10.4%)	3(23.1%)	2(15.4%)

(P value 0.225)

Fig (1):Distribution of patients by age group

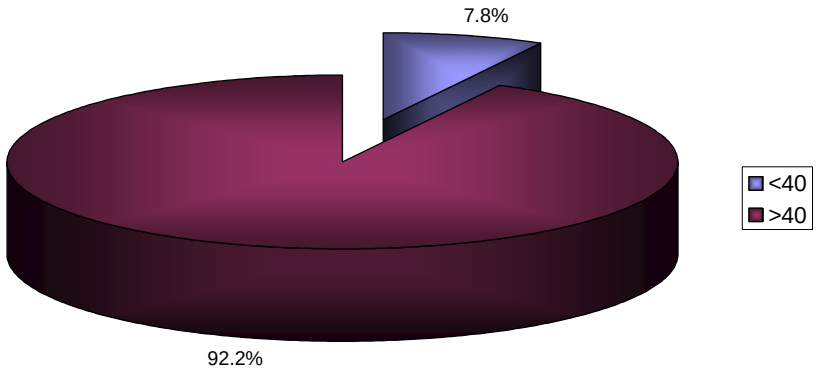


Fig (2): Distribution of patients by gender

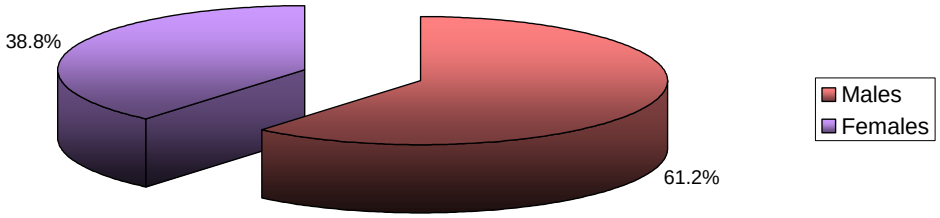


Fig (3):Distribution of patients by history of diabetes

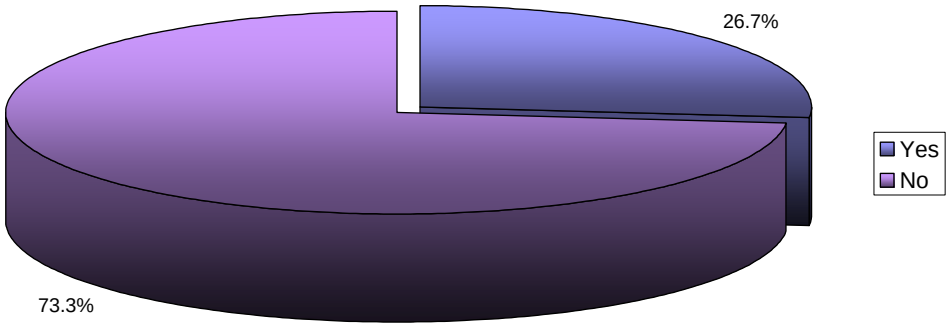


Fig (4):Distribution of patients by history of hypertension

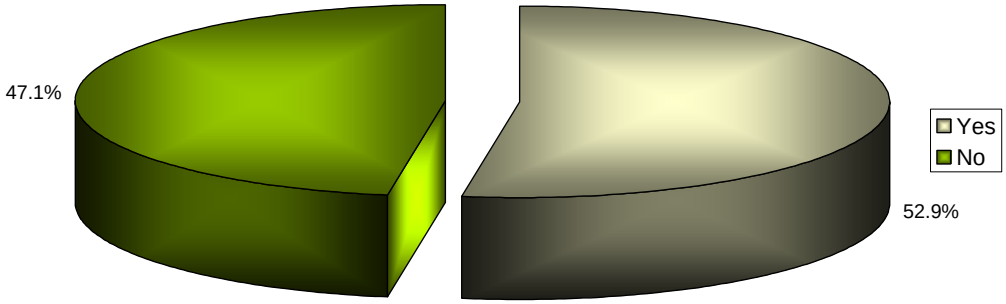


Fig (5):Distribution of patients by history of smoking

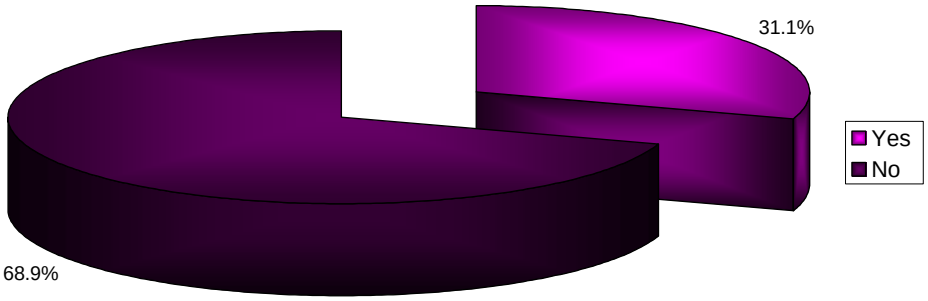


Fig (6):Distribution of patients by family history of IHD

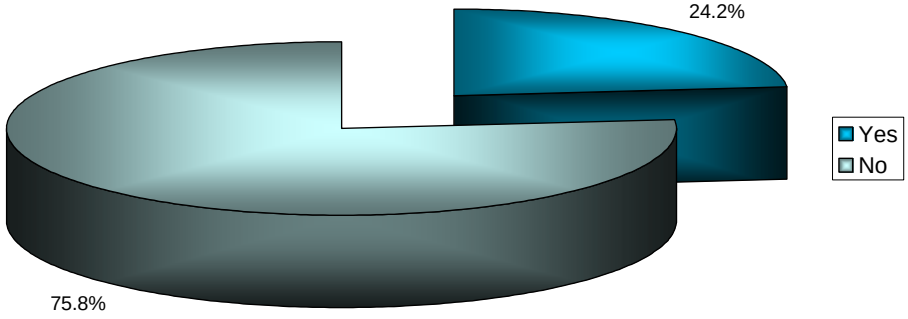


Fig (7):Distribution of patients by history of chest pain

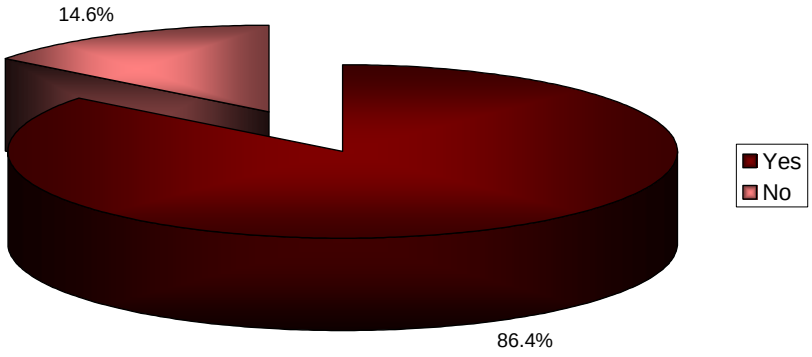


Fig (8):The correlation between blood pressure and diagnosis

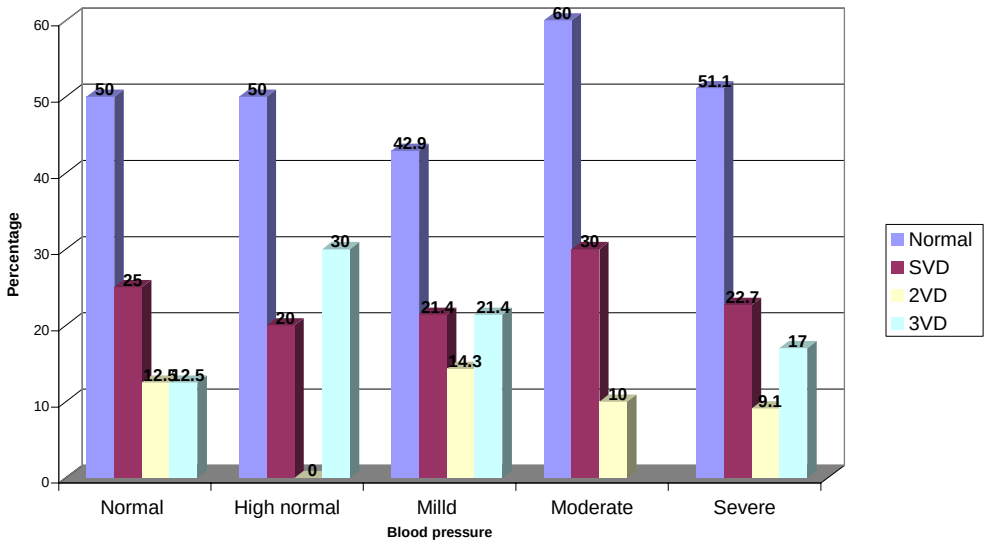


Fig (9):The distribution of coronary arteries involvement

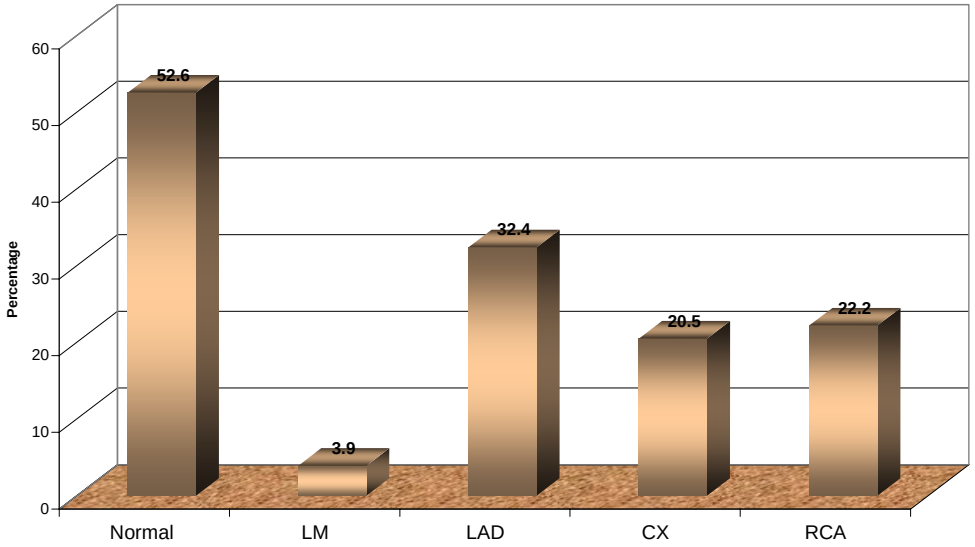


Fig (10): The percentage of different diagnosis in coronary findings

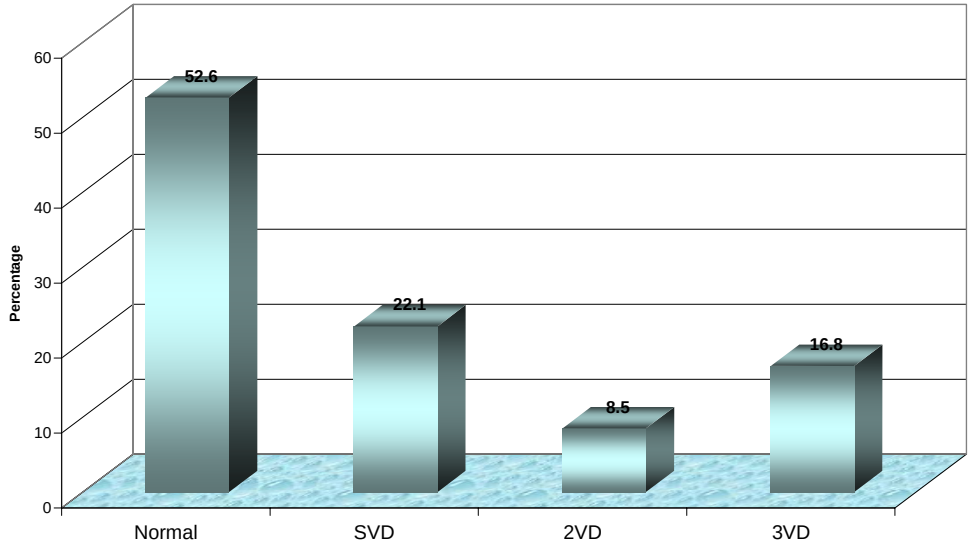


Fig 11: The effect of diabetes on diagnosis

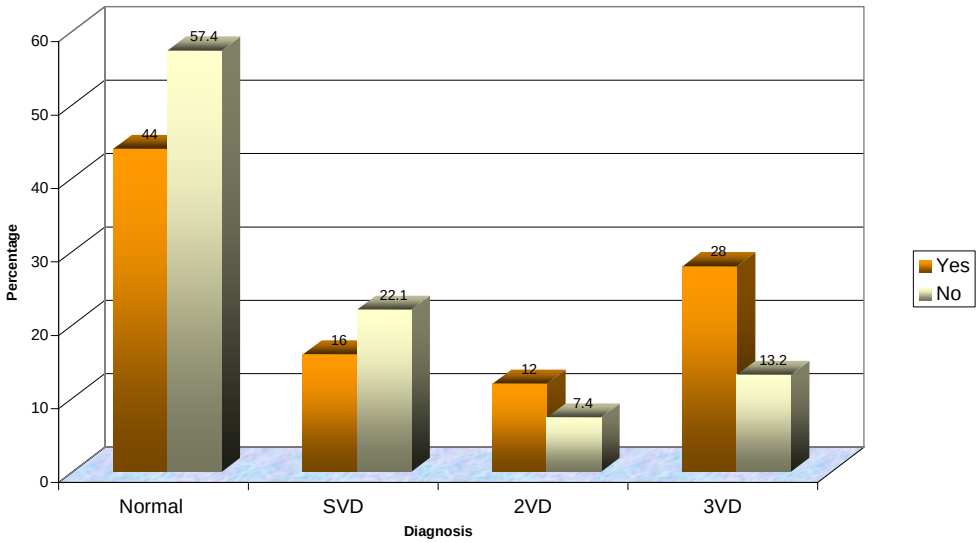


Fig (12): The effect of triglycerides level on diagnosis

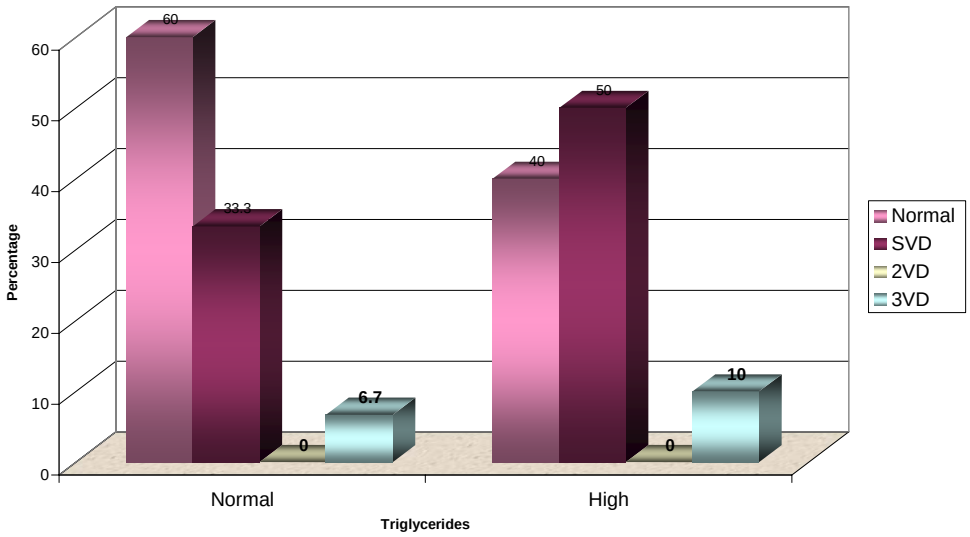


Fig (13):The effect of ECG findings on diagnosis

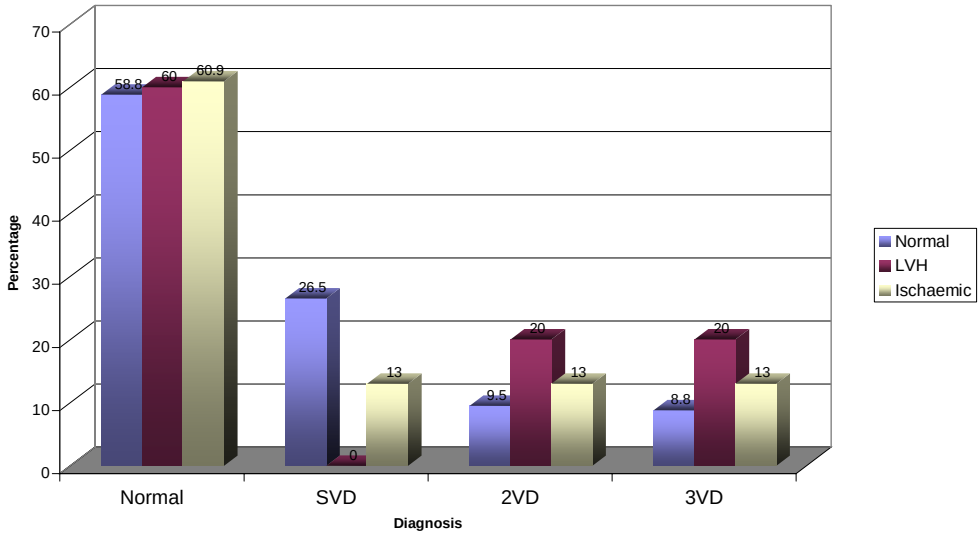


Fig (14): Distribution of patients by ECHO findings

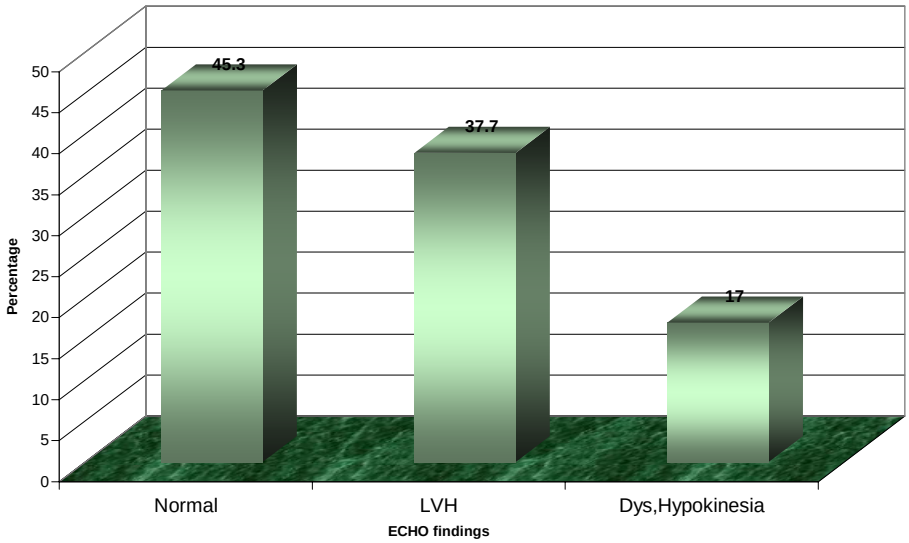


Fig (15):The effect of female age on diagnosis

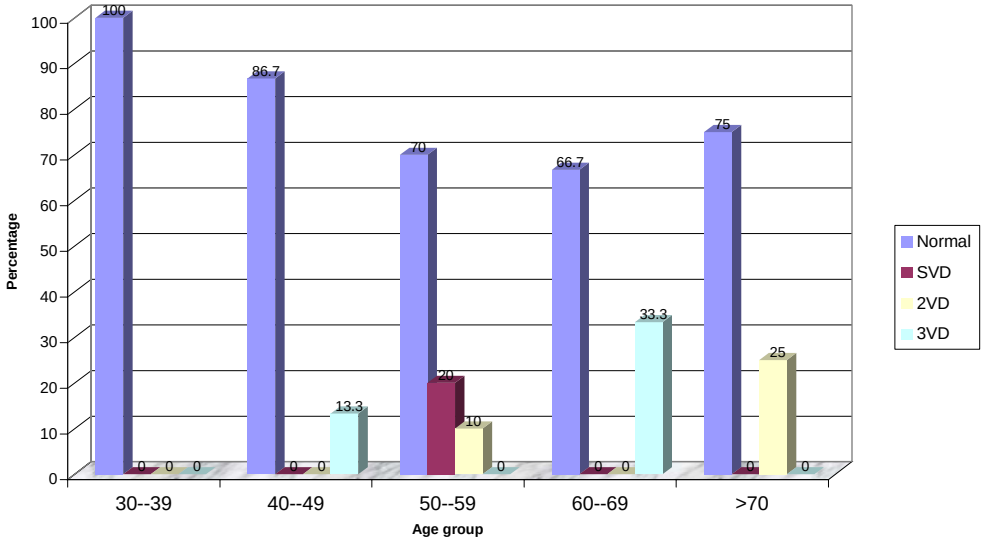
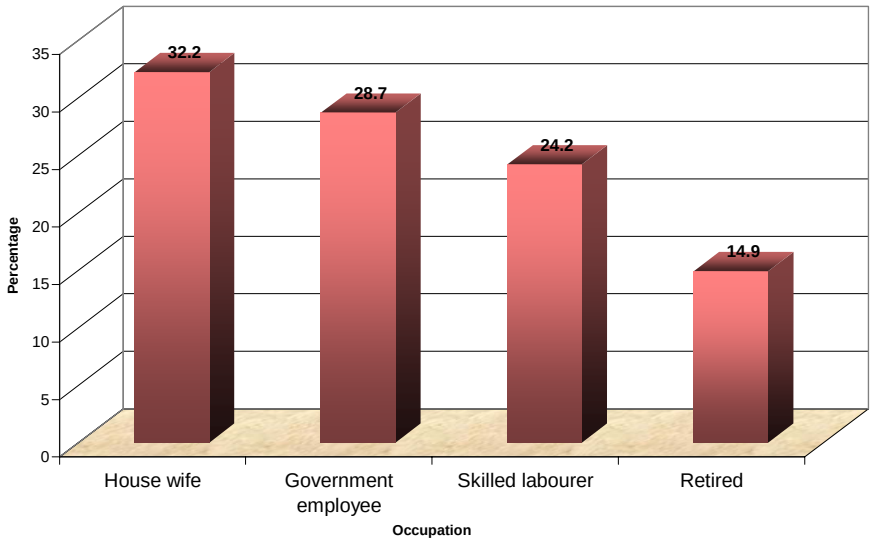


Fig (16):Distribution of patients by occupation



DISCUSSION

In our study population females were 40 patients (38.8%). The presence of false positive exercise test results in females was 60% where it was 40% in males. And this might correlates with the (CASS) study done by DAWeiner et al [82] ,they studied 1465 males and 580 females and they

found that the false positive results differed between males and females.(12+/-1 present versus 53+/-3) and the increased frequency of false positive results in both sexes in our study may be due to the small number of patients or to the coronary angiography done for low risk group of patients, or may be because the description of chest pain was not very accurate in females. Another study done by Debe R, Juclelson et al [83] for examination of the gender bias in evaluating coronary artery disease in females found that false positive stress testing was associated with 40% in female versus fewer than 10% in males. They found that the sensitivity and specificity of exercise induced ST segment depression for obstructive CAD are less in females than in males, the decreased diagnostic accuracy results partially from a lower prevalence and extent of CAD in young and middle aged females. Females tend to have a greater release of catecholamines during exercise, which could potentiate vasoconstriction and augment the incidence of abnormal exercise ECG results (the P. value in our study in this correlation was highly significant P 0.0001).

In our study females were divided into five groups, in the first group (30-39) the presence of false +ve exercise results was 100%, in the second group (40-49) it was 86.7%, and in the third group (50-59) it was 70%. So with the increase in age the false positive results decreased and the correlation was not statistically significant (P 0.209). Dtch Med

Wochencher [84] studied exercise ECGs in 252 females aged 20-49 without evidence of organic heart disease, the frequency of false positive results increased with increase in age. In group I (20-29) it was 5% and in group II (30-39) it was 20% and in group III (40-49) it was 38%, so the contradiction with our results and this study may be due to the increase awareness within young age groups here in Sudan specially these educated generation in whom seeking of medical advise is more than in older patients in addition to difficulty in evaluating chest pain in females in general.

Sex differences in pathophysiologic treatment and cause of coronary artery disease (CAD) have been described extensively and accurate diagnosis of CAD in females remains challenging, the Framingyham study was among the first to describe discrepancies in the number of males and females reporting followed by acute MI. This display is in part due to the difficulty in evaluating chest pain in females, whose assessment often are characterized by an increased prevalence of false positive exercise test, false positive radionuclide tests and substantial sex bias.

Concerning history of chest pain in correlation to coronary angiography findings, 42 patients (51.9%) had normal coronary artery study while 39

patients (48%) had abnormal study ranging from SVD, to 2VD and 3VD. In a similar study done by Bartel et al [85] ,They studied a group of patients who presented with the various types of chest pain and they were tested using both exercise test and coronary angiography and they assumed angiography indicates patients true status whether there is coronary artery stenosis of at least 70%, they found that patients with abnormal coronary artery study were 137 and 148 patients with true positive test were (92.5%) while patients with false positive test were (7.3%).They also studied patients with negative exercise test and they found that patients with false negative results were 90(44.5%) and patients with true negative tests were 112(55.4%),so they concluded that if a patient with chest pain , like those in this study has a positive exercise test , the probability of significant coronary artery stenosis goes from 65 before the test to 93 if the exercise test is positive (the predictive value of a positive test) and if the test is negative the probability decreased from 65 to 55 (the predictive value of a negative test).

The absence of correlation in our study may be because the history of chest pain was not clearly specified and there could be a proportion of patients without typical anginal pain and also the females in whom there is a great difficulty in evaluating chest pain. Another problem is the deficiency in records as there were some patients in whom definite diagnosis was not specified and also the small sample size.

In patients with diabetes the presence of angiographic CAD was 56%, 4 of them (16%) with SVD and 3(12%), 7(28%) were with 2VD and 3VD respectively. The most common lesion in diabetes concerning diagnosis was 3VD, which could be considered as severe coronary artery disease. In a study done by David P. Lee et al[86] they studied the utility of the exercise test in diabetic patients ,they found that 38% had an abnormal exercise test and the presence of angiographic CAD was 69%, they also found that the number of diseased vessels is significantly increased in diabetic patients. The P value in our study was not statistically significant (0.295) may be because diabetics represented only 27 patients of the study group (26.7%)and the diagnosis was not labeled clearly in a proportion of patients (2 patients) and also the small number of patients studied.

Severe systemic hypertension may interfere with subendocardial perfusion and causes exercise induced ST segment depression in the absence of atherosclerosis, even when the resting ECG does not show significant ST or T wave changes[87]. In our study 60% of the patients with voltage criteria of LVH shown in the ECG had a normal coronary angiographic study and this point to the significance of LVH as one of the important causes of false positive exercise ECG test. IN this study hypertensive patients were divided in to five groups of normal, high normal, mild, moderate and severe hypertension. In correlating the degree

of hypertension with coronary angiography findings, the presence of normal coronary study was more in patients with normal blood pressure and 15 patients of those labeled as having severe hypertension had 3VD, so 3VD is more associated with patients with poorly controlled hypertension and this reflects the need for aggressive control of the blood pressure and that hypertension is one of the modifiable risk factors. The correlation is again not statistically significant and this may be because as mentioned previously that false positive results are more common in patients with LVH and hypertensive patients represented 52.9% of the study group (54 patients) but mainly the small sample size.

Dyslipidemia is one of the most important modifiable risk factors in ischaemic heart disease. In this study the serum cholesterol was estimated in only 60.1% of the patients (62patients) and they were divided into normal and high normal and high cholesterol level. Coronory artery lesions were associated with high normal and high cholesterol level but the total number of the affected vessels in high normal and normal levels was equal and this was not statistically significant (P 0.268) may be because cholesterol level was not estimated in all patients (only in less than half of the patients). In the study done by Ubbink J B, Vermeiak W J< Bennet J M et al, [88] they studied the prevalence of hypercholesteraemia in angiographicaly defined coronary heart disease and they found that the prevalence of hypercholesteraemia was 34.9% ,in

our study it was 34.8% but no graded strength of association between the number of stenotic coronary arteries could be demonstrated and this correlates with our findings in that number of patients with 3VD is equal in patients with high normal and high cholesterol levels.

Triglycerides levels were also estimated but in only 13 patients and the results in correlating patients with normal or high levels were equivocal with the same number of patients who had abnormal coronary angiography findings and those with normal findings and this was not statistically significant. Triglycerides as a risk factor for coronary artery disease is still a matter of research and till now the results are equivocal. Unfortunately other parameters of lipid profile (LDL, HDL) are not routinely done because full lipid profile is an expensive investigation and most of the patients can not afford to do it, and may be this is one of the factors that affected the correlation and gave rise to insignificant results.

For many years general practitioners have been suspecting that coronary heart disease runs in families, but it is only recently epidemiological and genetic studies have provided scientific evidence for this, this is significant because family history information enables the identification of individuals who are at risk. In our study only 24 patients (24.2%) gave family history of IHD, and in correlating positive family history with the coronary angiographic findings 11 patients (52.4%) had normal coronary study, and 10 patients (54.16%) had had coronary artery lesions ranging

from SVD, 2VD and 3VD and 3 patients were not labeled with a definite diagnosis.

In a study done by Grech E D, Ramsdole et al[89] for the family history as an independent risk factor for coronary artery disease , they studied the relation between the family history of IHD and the presence of coronary heart disease in 387 patients undergoing coronary angiography and they found that 107 patients (27.6%) had a family history of IHD , 52(48.6%) had significant coronary artery disease, so the overall severity and extent of coronary artery disease is more in those patients with positive family history. More over the incidence of significant coronary disease increases as the number of relatives with IHD also increased. Multiple logistic regression analysis suggest that family history is an independent predictor of the presence of significant coronary artery disease and the European guidelines emphasizes that close relatives of patients with early onset of CHD (less than 55 years in males and 65 in females) are apriority group for risk identification and monitoring. In our study the results were not statistically significant (P0.186) may be because of the small number of the patients with positive family history (24 patients) and here many of the patients can not give a definite family history of IHD for their relatives because no regular check up or good records are available and history of sudden death which may be due to IHD may passed unnoticed.

History of smoking was obtained in 31 patients (31.1%) of them 12 patients (42.9%) had normal study, 8 patients (28.6%) had SVD, 2 patients (7.1%) had 2VD and 6 patients (21.4%) had 3VD and this was not statistically significant (P0.399) may be because of that only one third gave history of smoking and usually females in our community denied completely history of smoking as it is against our conservative community. Furtherly we tried to see whether smoking has favorable effect on certain coronary arteries and we found that left coronary artery is not affected within smokers, 11 patients had left interior descending lesions, 6patients had their left circumflex artery affected and another 7 patients had their right coronary artery affected. Results from a large study suggest an association between smoking and specific location of blockages in coronary vessels. The blockages were located with the electron beam computed tomography (EBCT) anon –invasive imaging technique to detect coronary artery calcification, which was thought to be related to atherosclerotic plague burden (smoking is an independent predictor of the development of sub clinical coronary disease and follows atherosclerotic pattern of development) this was proved by said Julie Hoff et al.[90] They studied 22,204 persons between 30 and 93 years old who voluntarily presented for EBCT screening between 1993 and 1997, compared to non-smokers, smokers were more likely to develop lesions in the left anterior descending vessels and right coronary artery. In our

study the left anterior descending coronary artery was more affected than the other coronary arteries within smokers followed by the right coronary artery.

The resting ECG was done in 84.4% of the patients concerning the correlation between the ECG and the coronary angiography findings 58.8% of the patients with normal ECG had normal coronary artery study and 26.5%, 5.9% and 8.8% had SVD, 2VD and 3VD respectively. In patients who had a resting ECG with ST segment depression or T wave inversion 40% had normal study and this was not statistically significant (P0.252). In study done by Aust NZJ et al (1977)[91] the reader performance in resting ECG reading and case summary interpretation was investigated, 8 cardiologists were asked to read independently 105 ECG summary case sheets, the results showed low levels of inter and intra reader reliability when physicians reported on ECG traces. Reference to the coronary artery angiography information confirmed that the resting ECG has limited utility in the detection of coronary artery disease.

A proportion of patients were found to have more than one risk factor. 16 patients were found to have history of hypertension and diabetes and the frequency of coronary angiography findings was 7 patients with normal study (50%) and 7 with abnormal coronary artery findings (50%) of them 5 patients (35.7%) had 3VD. 4 patients presented with history of hypertension, diabetes and cigarette smoking. In 2 patients (50%)

coronary angiography findings was normal and in 1 patient (33.3%) the finding was SVD, while the other 1 patient was not labeled with specific diagnosis. 2 patients had history of hypertension, diabetes, smoking and positive family history one of them had a normal study and the other had SVD. SO we concluded that the presence of 3VD was more associated with patients presented with history of hypertension and diabetes, but in the other groups presented with history of hypertension, diabetes, smoking or in addition positive family history the presence of 3VD was not recorded and this could be explained by the small number of patients, the fact that positive family history was obtained in small number of patients and also cigarette smoking, and the deficiency of a clear diagnosis for some patients was another contributing factor.

Conclusions

The conclusions of this study are: -

- The false positive exercise results were more associated with females rather than males.
- Chest pain as the main presenting symptom in most of the patients was not clearly specified or evaluated especially in females and this may contribute to the insignificant results in correlation with the presence or absence of IHD.

- The presence of high normal and high chlolesterol levels was associated with more affection of the coronary artery but not with the number of coronary arteries involved and this correlates with the international studies. The other parameters of lipid profile could have a significant effect as a part of hyper or dyslipidaemia.
- The most common lesion within diabetics was 3VD more than SVD and 2VD.
- Hypertension specially if poorly controlled is associated with more severe coronary artery disease (3 VD) and left ventricular hypertrophy is one of the contributing factors that gave rise to false positive results.
- WE agreed with the international studies in that smoking may preferentially follows a certain anatomical distribution in the affection of coronary vessels.
- The resting ECG has limited utility in the detection of coronary artery disease.
- In patients presented with history of hypertension and diabetes together as multi risk factors the presence of 3VD is more than SVD or 2VD.

Recommendations

- During the data collection we noticed that there was deficiency in the recording system and usually the presenting symptoms were not given the enough attention and evaluation, so there should be good evaluation specially in low risk group and females so as to limit the need for more invasive procedures and every single patient should be labeled with a clear and specific diagnosis.
- Hypertension should be controlled properly with good follow up and check of the patients' response and compliance to treatment.
- If it is possible, screening of at least the first degree relatives of patients with positive family history of IHD should be done and more evaluation in history of sudden or unexplained death may be useful.

- Although full lipid profile is expensive but we cannot ignore its significance as a modifiable risk factor that may affect the survival of patients with IHD, so it is better to do a base line for every patient after explaining the importance of this estimation.
- Good evaluation and classification of patients to low, intermediate and high-risk groups should be done before the referral for coronary angiography.

References

1. Ellestad MH. Stress testing. Principles and Practice. In: Braunwald E, Zipes D, Libby P, (editors). Braun Wald Zipes Libby, 6th ed. Philadelphia: FA Davis; 1995. p. 129.
2. Guaton AC,(editorial). Exercise physiology. Textbook of Medical Physiology, 9th ed. Phladelphia: Saunders;1995.p. 129
3. Fletcher GF, Balady GJ, Froelicher VF. Exercise standards. A statement for health care professionals from the American Heart Association. Writing Group. Circulation 1995; 91: 580.
4. Hachamovitch R, Berman DS, Shaw LJ. Program value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: Differential

stratification risk of cardiac death and myocardial infarction. In: Braunwald E, Zipes D, Libby P, (editors). Braun Wald Zipes Libby, 6th ed. Philadelphia: Saunders; 1998. p. 129.

5. Glibbons RJ, Balady GJ, Beasley JW. ACC/AHA guidelines for exercise testing. A report of the American Collage of Cardiology/American Heart Association Task Force on practice guidelines (Committee in exercise testing). Am Coll Cardiol 1997; 30:260.

6. Chaitman BR. Exercise electrocardiographic stress testing. Chronic Ischaemic Heart Disease. In: Braunwald E, (editor). Series of Heart Diseases. Vol V. Philadelphia: Saunders; 1995. p2.1-2.30.

7. Froelicher VF, Myer J. Exercise stress testing. Exercise and The Heart, 3rd ed. Philadelphia: W.B. Saunders; 1999.p. 135.

8. Berdeaux A, Ghaleh b, Dubois-Rande JL. Role of vascular endothelium in exercise-included dilation of large epicardial coronary arteries in conscious dogs. Circulation 1994; 89:2799.

9. Ekelund LG, Suchindran CM. Karon JM. Black-white differences in exercise blood pressure. Circulation 1990; 31: 1568.

10. White WB, Lund-Johansen P. Omvik P. Assessment of four ambulatory blood pressure monitors and measurements by clinicians versus intra-arterial blood pressure at rest and during exercise. Am J Cardio J 1990; 65:60.

11. Reman A. Zelos G, Andrews NP. Blood pressure changes during transient myocardial ischemia: Insight into mechanisms. J Am Coll Cardiol 1997; 30:1249.

12. Chaitman BR, Mc Mahon RP, Terrin M. Impact of treatment strategy on predischarge exercise test in the Thrombolysis in Myocardial infraction (TIMI) II trial. Am J Cardiol 1993.; 71:131.

13. Ekelund LG, Suchindran CM, McMahonr R. Coronary heart disease morbidity and mortality in hypercholesterolemic men predicated from an exercise test: The lipid Research Clinics Coronary Primary: Prevention Trail. J Am Coll Cardiol 1989; 14: 556.

14. Bruce RA, Fischer LD. Exercise-enhanced assessment of risk factors for coronary heart disease in healthy men. J Electrocardiol 1987; 20:162.

15. ESC Working Group on Exercise Physiology. Physiology and Electrocardiography: Guidelines for cardiac exercise testing. Eur Heart J 1993; 14: 969.

16. Weiner DH, Ryan T, Mc cabe CH. Prognostic importance of a clinical profile an exercise test in medically treated patients with coronary artery disease. J Am coll cardiol 1984; 3:772.

17. Benhorin J, Pinsker G. Moriel M. Ischemic threshold during two exercise testing protocols and during ambulatory electrocardiographic monitoring. J Am Coll Cardiol 1973; 22:671.

18. Rogers WJ, Bourassa MG, Andrew TC. Asymptomaic Cadiac Ischemia Pilot (ACIP) study: Outcome at one yea for patients with asymptmatic cardic ischemia randomized to medical therapy or revascularization. The ACIP investigators. J Am Coll Cardiol 1995; 26(3): 594.

19. Safstrom K. Nielsen NE. Bjorkholm A. Unstable coronary artery disease in post-menopausal women. Identifying patients with significant coronary artery disease by basic clinical parameters and exercise test. Eur Heart J 1998; 19: 899.

20. Juneau M, Colles P, Theroux P. Symptoms-limited versus low level exercise testing before hospital discharge after myocardial infarction. J Am Coll Cardiol 1992; 20: 927.

21. Senaraine MP, Lrwin ME, Shaben S. Feasibility of direct discharge. Coll Cardiol 1990; 33: 1040.

22. Stein RA, Chaitman BR, Balady GJ. Safety and utility of exercise testing in emergency room chest pain centers. An advisory from the Committee on Exercise, Rehabilitation, and Prevention, Council on Clinical Cardiology. Circulation 1997; 96:1260-290.

23. Chaitman BR, Miller DD. Perioperative cardiac evaluation for noncardiac surgery noninvasive cardiac testing. Prog cardiovasc Dis 1998;40: 405.

24. Chaitman BR. Stone PH, Knatterud GL. Asymptomatic Ischemia Pilot (ACIP) study: Impact of anti-ischemia therapy week rest ECG and exercise test outcomes. Jj Am Coll Cardio 1995; 26: 585.

25. Melandri G, Semprini F, Cervi V. Benefit of adding low molecular weight heparin to the conventional treatment of stable angina pectoris: A double-blind, randomized. Placebo-controlled trial. Circulation 1993; 88: 2517.

26. Manson JE, Tosteson H, Ridker PM. The primary prevention of myocardial infarction. N Engel J Med 1992; 326:1406-16.

27. The sixth Report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Arch Intern Med 1997; 157:2413-46.

28. Lim PO, MacFayden RJ, Clarkson PB. Impaired exercise tolerance in hypertensive patients. Ann Intern Med 1996; 124(1): 41.

29. Neaton JD, Wentworth D. Serum cholesterol, blood pressure, cigarette smoking and death from coronary heart disease: Overall findings and differences by age for 316099 white men. Multiple Risk Factor Intervention Trial Research Group. Arch Intern Med 1992; 152: 56-4.

30. Mitchll GF, Moye LA, Eraunwald E. Sphygmomanometrically determined pulse pressure is a powerful independent predictor of re current events after myocardial infarction in patients with impaired left ventricular function. SAVE investigator. Survival and ventricular Enlargement, Circulation 1997; 96:1254-4260.

31. Stuart RJ. Ellestad MH. National survey of exercise stress testing facilities. Chest 1980; 77: 94.

32. Anitschkow N, Chalatow S. On experimental cholesterin steatosis and its significance in the origin of some pathological processes (1913). Arteriosclerosis 1996; 3: 178-82.

33. Steinberg D. The cholesterol controversy is over: Why did it take so long? Circulation 1989; 80:1070-78.

34. Centers of Disease Control. The Health Consequences of Smoking: Nicotine Addiction. A Report for the Surgeon General. Rockville, MD, U.S. Department of Health and Human Service. Public Health Service. Centers of Disease Control: 1998.

35. Peto R, Lopez AD, Boreham J. Mortality from smoking worldwide. Br Med Bull 1996; 52: 3-11.

36. Willet WC, Green A, Stampfer MJ. Relative and absolute excess risk of coronary heart disease among women who smoke cigarettes. N Eng J Med 1987; 371: 1303-9.

37. Hward G, Wagenknecht LE, Burke GL. Cigarette smoking and progression of atherosclerosis. The Atherosclerosis Risk in Communities (ARIC) Study. JAMA 1998; 279:119-124.

38. Morrow JP, Frei B. Longmire AW. Increase in circulating products of lipid peroxidation (F2-isoprostanes) in smokers: Smoking as a cause of oxidative damage. N Engl J Med 1995; 332:1198-03.

39. Zeiher AM, Schachinger V, Minners J. Long term cigarette smoking impairs endothelium-dependant coronary atrial vasodilation function.Circulation 1995; 92: 1094-100.

40. Tracy RP, Pasty BM, Mecy E. Lifetime smoking exposure affects the association of C-reactive protein with cardiovascular disease risk factors and subclinical disease in healthy elderly subjects. Arterioscler. Thromb Vasc Biol 1977; 17:2167-1176.

41. Sugiishi M. Takatsu F. Cigarette smoking is a major risk factor for coronary spasm. Circulation 1993; 87:76-9.

42. MacMahon S, Peto R, Cutler J. Blood pressure, stroke, and coronary heart disease: 1. Prolonged differences in blood pressure: Prospective observational studies corrected for the regression dilution bias. Lancet 1990; 335:765-74.

43. O'Donnell CJ, Ridker PM, Glynn RJ. Hypertension and borderline isolated systolic hypertension increase risks of cardiovascular

disease and mortality in male physicians. Circulation 1997; 95: 1132-137.

44. Collins R, Peto R, MacMahon S. Blood pressure, stroke, and coronary heart disease: II. Short term reduction in blood pressure: Overview of randomized drug trials in their epidemiological context. Lancet 1990; 335:827-38.

45. Gu K, Cowie CC, Harris MI. Mortality in adults with and without diabetes in national cohort of U.S population.1971-1993. Diabetes Care 1998; 21:1138-145.

46. Stein B, Weintraub WS, Gebhart SP. Influence of diabetes mellitus on elderly and late outcome after percutaneous transluminal coronary angiography. Circulation 1995; 91:979-89.

47. Kannel W, McGee D. Diabetes and glucose tolerance as risk factors for cardiovascular disease: The Framingham Study. Diabetes Care 1979; 2:120-26.

48. Manson JE, Colditz GA, Stampfer MJ. A prospective study of maturity –onset diabetes mellitus and risk of coronary heart disease and stroke in women. Arch Intern Med 1991; 151:1141-147.

49. Nathan DM: Long term complications of diabetes mellitus. N Eng J Med 1993; 328:1676-685.

50. Reaven GM, Role of insulin resistance in human disease. Nutrition 1997; 13(65) 64-6 .

51. Wautier JL. Gillausseau PJ. Diabetea : advanced glycation end products and vascular disease. Vasc Med 1998; 3:131-37.

52. Stehouwer CD, Nuata JJ. ZeldenrustGC. Urinary albumin excreation , cardiovascular disease ,and endothelial dysfunction in non-insulin dependant diabetes mellitus. Lancet 1992; 340:319-23.

53. The effect of intensive treatment of diabetes on the development and progression of long-term complication in insulin-dependant diabetes mellitus. The Diabetes Control and Complication Trial Research Group. N Engl J Med 1993; 329:977-86.

54. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type -2 diabetes (UKPDS 33). UK.Prospective Diabetes Study (UKDPS) Group. Lancet 1998.; 352:837-53.

55. Fletcher GF, Blair SN. Blumenthal J. Statement on Exercise: Benefits and recommendations for physical activity programmes for all Americans: A Statement for health professionals by the Committee on Exercise and Cardiac Rehabilitation of the Council on Clinical Cardiology. American Heart Association. Circulation 1992; 86:340-44.

56. Paffenbarger RS, Hyde RT, Wing AL. Physical activity, all causemortality, and longevity of college alumni. N Engl J Med 1986; 314:605-13.

57. Peterson ED, Shaw L, Califf RM. Risk stratification after myocardial infraction. Ann Intern Med 1997; 126: 561.

58. Wannamethee SG, Shaper AG, Walker M. Change in physical activity mortality and incidence of coronary artery disease in men. Lancet 1998; 351:1603-608.

59. Fletcher GF, Balady G, Froelicher VF. A Statement for the health care professionals from the American Heart Association. Circulation 1995; 91: 580-615.

60. Kokk PF, Naryan P, Colleran JA. Effect of regular exercise on blood pressure and left ventricular hypertrophy in African-American men with severe hypertension. N Engl J Med 1995; 333:1462-467.

61. King AC, Haskel W, Young DR. Long-term effects of varyingintensities and formats of physical activities on participation rates, fitness, and lipoproteins in men and women aged 50 to 65 years. Circulation 1995; 91:2596-604.

62. Helmirch SP, Ragland DR, Leung RW. Physical activity and reduced occurrence of non-insulin-dependant diabetes mellitus. N Engl Med 1990; 325:147-52.

63. Clarkson P, Montgomery HE, Mullen MJ. Exercise training enhance endothelial function in ypung men. J Am Coll Cardiol 1999; 33:1379-385.

64. Manson JE, Colditz GA, Stampfer MJ. A prospective study of the obesity and the risk of coronary heart disease in women. N Engl J Med 1990; 322: 882-89.

65. Rexrode KM, Carey VJ, Hennekens CH. Abdominal adiposity and coronary heart disease in women. JAMA 1998; 280:1843-848.

66. Yeung AC, Vakshtein VI, Krantz DS. The effect of atherosclerosis on the vasomotor response of coronary arteries to mental stress. N Engl J Med 1991; 325:1551-556.

67. Krantz DS, Santiago HT, Kop WJ. Prognostic value of mental stress testingin coronary artery disease. Am J Cardiol 1996; 84:1651-656.

68. Leor J, Poole WK, Kloner RA. Sudden cardiac death triggered by an earthquake. N Engel J Med 1996; 334:413-19.

69. Krantz DS, Sheps DS, Carney RM. Effect of mental stress in patients with coronary artery disease. JAMA 2000; 283:1800-802.

70. Effect of estrogen or estrogen / progestin regimens on heart disease risk factors in post menopausal women. The postmenopausal estrogen / progestin Interventions (PEPI) Trial. The Writing Group for the PEPI Trial. JAMA 1995; 273: 199-208.

71. Walsh BW, Schiff I, Rosner B. Effect of postmenopausal estrogen replacement on the concentrations and metabolism of plasma lipoproteins. N Engel J Med 1991; 325:1196-204.

72. Stampfer MJ, Ccolditz GA, Willett WC. Postmenopausal estrogen therapy and cardiovascular disease. Ten-year follow-up from the nurse health study. N Engel J Med 1991;325:756-62.

73. Reis SE, Gloth ST, Blumenthal RS. Ethinyl estradiol acutely attenuates abnormal coronary vasomotor responses to acetylcholine in postmenopausal women. Circulation 1994;89:52-60.

74. Koh KK, Micemoyer R. Bui MN. Effects of hormone replacement therapy on fibrinolysis in postmenopausal women. Engel J Med 336:683-90.

75. Espeland MA, Hogan PE, Fineberg SE. Effect of Postmenopausal hormone therapy on glucose and insulin concentrations. PEPI Investigators. Postmenopausal estrogen / progestin investigations. Diabetes Care 1998; 253: 1589-595.

76. Rosenberg L, Kaufman DW, Helmrich SP. Myocardial infarction and cigarette smoking in women younger than 50 years of age. JAMA 1985; 253: 2965-969.

77. Grodstein F, Stampfer M. The epidemiology of coronary heart disease and estrogen replacement in postmenopausal women. Prog Cardiovasc Dis 1995; 38:199-210.

78. Grodstein F, Stampfer M.J, Manson JE. Postmenopausal estrogen and progestin use and the risk of cardiovascular diseases. N Engel J Med 1996; 335:453-561.

79. Sshawaery GT, Vita JA, Kenny JF. Antioxidant protection of LDL by physiologic concentrations of estrogens in specific for 17-beta-estradiol. Atherosclerosis 1998;138:255-62.

80. Ridker PM. Evaluating novel cardiovascular risk factors: Can we better predict heart attacks? Ann Intern Med 1999; 130:933-37.

81. Libby B. Exercise stress testing. Risk factors for ischemic heart disease. In: Braunwald E, Zipes D, Libby P, (editors). Heart Disease, 6th ed. Philadelphia: Saunders; 2001.p.1010-37.

82. Bartel S. ECG for chest pain. Circulation 1974; 44: 348.

83. Davids T, Sheps Z. Sex differences in chest pain in patients with documented coronary artery disease and exercise induced Ischamia results from PIMI study. Am Heart J 2001; 142(5):864-71.

84. Debra R, Judelson M. Examining the gender bias in evaluating coronary disease in women. www.Medscapegeneral medicine.com. 2003.

85. Wener DA, Ryan TJ. Exercise stress testing correlation among history of angina, ST segment response and prevalence of coronary artery disease in the Coronary Artery Aurgery Study (CASS). N Eng J Med 1979; 301: 230-35

86. Grech ED, Ramschale DR, Braycl R. Family history as an independent risk factor of coronary artery disease 1. Eur Heart J 1992; 13 (10): 1311-315.

87. Schuren KP, Behrens R. False positive exercise ECG in women without organic heart disease. (Dtsch Med Wochenshr 1978;12 (103): 816-21.

88. Weston MJ, Bett JH. Consensus opinion and observer accuracy in electrocardiography with reference to coronary arteriographic information. Med J 1976; 6 (5): 429-32.

89. David P, Lee MD. Clinical utility of the exercise ECG in patients with diabetes and chest pain. Chest 2001; 119: 1576-581.

90. Hoff J. Smoking coronary vessel blockage location linked. Med Post 2002; 38(2): 1-2.

91. Weston MJ, Bett Y. Consensus opinion and observer accuracy in electro-cardiography with reference to coronary arteriographic information, Aust J Med 1976; 6 (5): 429-32.