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Correlation of Clinical presentation and Angiographic Morphology in patients with Coronary Artery Disease in Ahmed Gasim Hospital-Sudan

By

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ABSTRACT

Background: This study was done in Ahmed Qasim Hospital, from January to June 2005.

Objectives: We studied the correlation between clinical presentation and angiographic findings in patients with coronary artery disease.

Method: We studied 105 patients who underwent coronary angiography in Ahmed Qasim Hospital , from January to June 2005.

56% were males, 44% were females. Ages 30-85 (mean: 59).

The lesions were classified into simple (34%) and complex (66%) according to Ambrose's modified criteria, and into single, two or three vessel disease.

Results: 87 patients had angina; of this group 41 had established angiographic findings.

There was no difference in lesion morphology or number of diseased vessels in those with stable and unstable angina.

30 patients had diabetes, 75 were not diabetics. Complex lesions were more common in diabetics (70%) against (63%) for non diabetics. Three vessel disease was more prevalent in diabetics (43%) against (22%) for non diabetics.

In 16 patients with history of MI the presence of three vessel disease was significant (75%).

Conclusion: The morphology of the lesion was not correlated to type of angina in our study. Diabetes is associated with more extensive coronary involvement.

Myocardial infarction is more common in patients with three vessel disease.

ملخص الأطروحة

أجريت هذه الدراسة بمستشفى أحمد قاسم في الفترة من يناير حتى يونيو 2005 .
هدفت الدراسة إلى معرفة العلاقة بين طبيعة الاعراض السريرية و نتائج قسطرةالشرايين التاجية عند مرضى إقفار القلب.

تمت دراسة 105 مريض من مرضى إقفار القلب. مثّل الذكور 56% و الإناث 44% وتراوحت أعمارهم بين 30 و 85 عاماً.
و تم تقسيم إصابات الشرايين التاجية إلى بسيطة 34% و مركبة 66% وفقا لتصنيف أمبروس وايضا حسب عدد الشرايين المصابة.
إحتوت الدراسة على 87 مريض يعانون من الخناق الصدري، 41 مريض فقط لديهم إصابات واضحة بالشرايين التاجية.

في هذه الدراسة لم يوجد فرق بين نسبة الإصابات البسيطة و المركبة في حالات الخناق الصدري المستقرة و تلك غيرالمستقرة.
ثلاثون مريضاً يعانون من إرتفاع السكر في الدم و هؤلاء كانت لديهم نسبة أكبر من الإصابات المركبة 70% مقابل 63% لغير مرضى السكري. و أيضاً نسبة أعلى 43% للإصابة الثلاثية للشرايين مقابل 22%% لغير مرضى السكري.
في 16 مريض مصابون بإحتشاء القلب سابقاً كانت نسبة الاصابة الثلاثية 75%.
خلصت هذه الدراسة الى عدم وجود علاقة بين شكل الا صابة بالشرايين و نوع الخناق الصدرى. و إلى أن الاصابات المركبة و الثلاثية أكثر شيوعاً بمرضى السكري. و الإحتشاء القلبي أكثر شيوعاً لدى المصابين لدى المرضى أصحاب الإصابات الثلاثية.

Abbreviations

CAD: Coronary Artery Disease.

Cx: Circumflex artery.

EF: Ejection fraction.

IHD: Ischaemic heart disease.

LAD: Left anterior descending.

LM: Left main stem.

MI: Myocardial Infarction.

PTCA: Percutaneous transluminal coronary angioplasty

RCA: Right coronary artery.

SVD: Single vessel disease.

2VD: Two vessel disease.

3VD: Three vessel disease

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CHAPTER ONE

INTRODUCTION
& LITERATURE REVIEW

Coronary artery disease comprises a wide spectrum of conditions, ranging from chronic stable angina to acute myocardial infarction.

Several studies in the past 15 years have described the angiographic morphology of coronary lesions in acute coronary syndromes. [1-5]

In unstable angina or acute myocardial infarction eccentric, irregular, with possible presence of thrombus lesions are more frequent and constitute the so-called **complex lesions.**

They are usually due to the fissuring or rupture of atherosclerotic plaque and sometimes cause a lower degree of stenosis in the coronary arteries.

In chronic stable angina, concentric and regular stenoses are the most frequent lesions and are called **simple lesions.** Usually, these lesions cause a greater degree of stenosis in the coronary arteries.

There are several studies in the international literature, which describe the correlation of the coronary lesion morphology with clinical presentation. [6-10]

Coronary Artery Disease

Coronary artery atherosclerosis is the principal cause of coronary artery disease (CAD) and is the single largest killer of both men and women [11].

CAD should be suspected in a patient with any evidence of cardiac ischemia, which commonly manifest as chest pain. This finding is especially suggestive when it is triggered by exertion, exposure to cold, or stress and when it radiates to left arm, jaw or epigastric area.

Cardiac ischemia also may present without chest pain. Patients may have palpitations or unexpected or disproportionate dyspnoea triggered by exertion. Ischemia may also be asymptomatic, with or without ECG changes.

Intervention before symptoms manifest is termed primary prevention; afterwards, it is termed secondary prevention.

EPIDEMIOLOGY

Prevalence

For men, the reported prevalence of coronary heart disease increases with age from 7% at ages 40 to 49 years to 13% at 50 to 59 years, 16% at 60 to 69 years, and 22% at 70 to 79 years. The corresponding estimates for women are substantially lower than for men: 5, 8, 11, and 14%, respectively.

Incidence • For persons aged 40-60 years, the lifetime risk of development CHD is 49 percent in men and 32 percent in women. For those reaching age 70 years, the lifetime risk is 35 percent in men and 24 percent in women. • For total coronary events, the incidence rises steeply with age, with women lagging behind men by 10 years.

Mortality Coronary heart disease is the leading cause of death in adults in the United States, accounting for about one-third of all deaths in subjects over age 35 [12]. The death rate is higher in men than in women (three times higher at ages 25 to 34, falling

to 1.6 times at ages 75 to 84) and in blacks compared to whites, an excess that disappears by age 75.

PATHOGENESIS OF ATHEROSCLEROSIS

– Atherosclerosis is responsible for almost all cases of CHD. This insidious process begins with fatty streaks which are first seen in adolescence; these lesions progress into plaques in early adulthood, and culminate in thrombotic occlusions and coronary events in middle age and later life.

HISTOLOGY – The initial lesion in atherosclerosis involves the intima of the artery and begins in childhood with the development of fatty streaks.

Fatty streaks – The first phase in atherosclerosis histologically presents as focal thickening of the intima with an increase in smooth muscle cells and extracellular matrix [13]. These smooth muscle cells migrate and proliferate within the intima. This is followed by accumulation of intracellular lipid deposits or extracellular lipids or both, which produce the fatty streak.

The smooth muscle cells within the fatty streak are susceptible to apoptosis which is associated with further macrophage infiltration and cytoplasmic remnants that can calcify, perhaps contributing to the transition of fatty streaks into atherosclerotic plaques [14].

Fibrous plaque – The fibrous plaque evolves from the fatty streak via accumulation of connective tissue with an increased number of smooth muscle cells ladened with lipids and often a deeper extracellular lipid pool.

Plaque rupture – Atherosclerosis is generally asymptomatic until the plaque stenosis exceeds 70 or 80 percent which can produce a critical reduction in flow). These large lesions can produce typical symptoms of angina pectoris. However, clinical reports suggest that acute coronary syndromes (are due to rupture of plaques with less than 50 percent stenosis [15]. Thus, recent studies have focused on the anatomic aspects of these smaller lesions that render them unstable and likely to fissure, rupture, or dissect with resulting thrombosis [15-18] .Coronary angiography

often delineates an irregular surface of the plaque in patients with unstable symptoms [17].

(Multiple factors contribute to the pathogenesis of atherosclerosis including abnormalities in lipid metabolism, endothelial dysfunction, inflammatory and immunologic factors, plaque rupture, and smoking.)

RISK FACTORS

Risk factors for CAD are classified as modifiable or unmodifiable. **Modifiable risk factors** include smoking, active or passive; hypertension; hyperlipidemia; (high total cholesterol and LDL-cholesterol, low high HDL, and high triglyceride levels); diabetes; abdominal obesity; sedentary lifestyle. High homocysteine level is suspected to be another risk factor. **Unmodifiable risk factors** include age, male sex, and family history.

Aggressive lowering of cholesterol levels has reduced individual morbidity and mortality rates but not the overall cardiovascular death rate.

ESTABLISHED RISK FACTORS FOR CORONARY HEART DISEASE

Lipids – The serum total cholesterol concentration is a clear risk factor for coronary heart disease, the risk of CHD progressively increased with higher values for serum total cholesterol.

More recent data emphasize the advantages in estimating lipid fractions, such as LDL and HDL, in addition to total cholesterol. Higher LDL cholesterol concentrations have been associated with an increased incidence of coronary artery disease in a large number of studies [19]. The following criteria are used for serum LDL-cholesterol concentrations [20]:

- High-risk - Above 160 mg/dL (>4.1 mmol/L)
- Borderline high-risk - 130 to 159 mg/dL (3.4 to 4.1 mmol/L)
- Desirable - Below 130 mg/dL (<3.4 mmol/L)

On the other hand, serum HDL-cholesterol is inversely associated with coronary heart disease incidence [21] .Data from the Framingham Heart Study suggest that the

risk for myocardial infarction increases by about 25 percent for every 5 mg/dL (0.13 mmol/L) decrement below median values for men and women.

The total cholesterol-to-HDL-cholesterol ratio represents a simple, efficient way to estimate coronary disease risk [22]:

- Among men, a ratio of 6.4 or more identified a group at 2 to 14 percent greater risk than predicted from serum total or LDL-cholesterol
- Among women, a ratio of 5.6 or more identified a group at 25 to 45 percent greater risk than predicted from serum total or LDL-cholesterol

The roles of hypertriglyceridemia and elevated levels of Lipoprotein(a) as determinants of cardiovascular risk are less clear.

Treatment of hyperlipidemia – Recommendations for lipid evaluation and therapy in adults were formulated by an expert committee of the National Cholesterol Education Program and published in 1993[23]. Stepped care for abnormal lipid levels includes dietary restriction of fat and cholesterol, and recommends medications when certain LDL cholesterol levels are exceeded despite dietary interventions and other lifestyle modifications .

A number of clinical trials have demonstrated that reductions in total and LDL-cholesterol levels reduce coronary events and mortality when given for primary prevention[24,25] and equally in secondary prevention (after MI), including those with average levels of total, LDL and HDL cholesterol of 209 mg/dL, 139 mg/dL, and 39 mg/dL (5.4, 3.6, and 1.0 mmol/L) [26]

.

Hypertension – Hypertension and left ventricular hypertrophy are well-established risk factors for adverse cardiovascular outcomes, including CHD, CHD mortality, stroke, congestive heart failure, and sudden death [27-28]. Systolic blood pressure is at least as powerful a coronary risk factor as the diastolic blood pressure [29] and isolated systolic hypertension is now established as a major hazard for coronary heart disease and stroke [30] .

However, while controlled trials have demonstrated clear benefits with blood pressure reduction in terms of stroke and heart failure risk, they have not consistently demonstrated a benefit in coronary events, particularly in patients with mild hypertension [31] .

Glucose intolerance and diabetes mellitus – Insulin resistance, hyperinsulinemia, and glucose intolerance appear to promote atherosclerosis .And are powerful contributors to cardiovascular events, particularly in women[32].

Diabetics have a greater burden of other atherogenic risk factors than nondiabetics, including hypertension, hypertriglyceridemia, increased total-to-HDL-cholesterol ratio, and elevated plasma fibrinogen.

Thus, the guidelines published by the National Cholesterol Education Program and the sixth Joint National Committee have provided a framework to treat coronary risk factors aggressively in diabetics [23,27]. In addition, there is increasing evidence of the value to aggressive blood pressure control in diabetics.

Estrogen deficiency – The incidence of CHD increases in women after menopause, an effect that is thought to be secondary to hypoestrogenemia. Hormone replacement with low-dose exogenous estrogens and a progestin has a cardioprotective effect [33].

Lifestyle factors – A diet rich in calories, saturated fat, and cholesterol contributes to other risk factors that predispose to coronary heart disease. As noted above, weight gain promotes the major cardiovascular risk factors and weight loss improves them .

Exercise – Exercise of even moderate degree has a protective effect against coronary heart disease and all-cause mortality [34] .The improvement in survival with exercise is equivalent and additive to other lifestyle measures such as cessation of smoking, control of hypertension, and avoidance of obesity

Exercise may have a variety of beneficial effects including an elevation in serum HDL-cholesterol, a reduction blood pressure, less insulin resistance, and weight loss.

Cigarette smoking – Cigarette smoking is an important and reversible risk factor for CHD. The incidence of a myocardial infarction is increased six fold in women and threefold in men who smoke at least 20 cigarettes per day compared to subjects who never smoked [35] .On the other hand, the risk of recurrent infarction in a study of smokers who had a myocardial infarction fell by 50 percent within one year of

smoking cessation and normalized to that of nonsmokers within two years[36] . The benefits of smoking cessation are seen regardless of how long or how much the patient has previously smoked.

Diet – In addition to the role of dietary lipids in the development of CHD, there is growing evidence suggesting that fruit and vegetable consumption and a high fiber diet are inversely related to the risk of coronary heart disease (CHD) and stroke . High fiber intake is associated with a 40 to 50 percent reduction in the risk of CHD and stroke compared to low intake [37] .

ROLE OF FLAVINOIDS AND ANTIOXIDANTS

Flavonoids are polyphenolic antioxidants naturally present in vegetables, fruits, and beverages such as tea and wine. They have been shown to have anti-inflammatory, anti-thrombotic, and vasodilatory activity. In vitro, flavonoids inhibit oxidation of low-density lipoprotein and reduce thrombotic tendency,

In a study by **Hertog MG** et al Flavonoid intake was significantly inversely associated with mortality from coronary heart disease and showed an inverse relation with incidence of myocardial infarction,

Flavonoids in regularly consumed foods may reduce the risk of death from coronary heart disease in elderly men [38].

Obesity – Obesity is associated with a number of risk factors for CHD. These include:

- Hypertension
- Glucose intolerance
- Insulin resistance
- Hypertriglyceridemia
- Reduced HDL-cholesterol
- Elevated fibrinogen

Data from many studies have documented the risk in coronary heart disease associated with being overweight .Patients with abdominal (central) obesity are at greatest risk [39].

Significantly increased risks of death from cardiovascular disease were found at all indices of more than 26.5 kg/m2 in men and 25 kg/m2 in women. The risk is increased with a high waist to hip ratio. It was greater for whites than blacks.

Plasma fibrinogen – Plasma fibrinogen levels are important predictors of cardiovascular disease and there is a linear relationship between fibrinogen and traditional cardiovascular risk factors including age, smoking, diabetes, body mass index, total and LDL cholesterol, and triglycerides. Data from the Framingham Offspring study suggested that measurement of fibrinogen is a useful adjunct screening tool to identify individuals at increased thrombotic risk [40].

C-reactive protein – This is an association rather than a risk factor. It is positively associated with future cardiovascular events in healthy as well as high risk individuals.

PRESENTATION OF CAD

The spectrum of presentation includes symptoms and signs consistent with the following conditions:

- Asymptomatic state (subclinical phase)
- Stable angina pectoris
- Unstable angina (i.e., ACS)
- Acute MI
- Chronic ischemic cardiomyopathy
- Congestive heart failure
- Sudden cardiac arrest

ANGINA PECTORIS

PATHOPHYSIOLOGY OF ANGINA

Angina is caused by myocardial ischemia which occurs whenever myocardial oxygen demand exceeds oxygen supply.

Any clinical setting or pathologic situation which results in a reduction in myocardial oxygen supply can cause ischemia. The most frequent cause is coronary

atherosclerosis, but others include coronary artery vasospasm and embolism. In addition, stimulation of the esophagus by acid can cause coronary artery vasoconstriction and a reduction in coronary blood flow via a neural cardioesophageal reflex [41].

Angina can also occur after eating. Postprandial angina results from a redistribution of blood flow, away from territories supplied by severely stenosed coronary arteries and to those supplied by less diseased or normal arteries [42] .This may be due to sympathetic activation from food ingestion and norepinephrine-induced vasoconstriction in diseased vessels.

CLINICAL PRESENTATION OF ANGINA;

HISTORY – The patient with angina often has a fairly typical history [43]:

• **Quality of the chest pain** – Angina is often characterized more as a discomfort than pain, and may be difficult to describe. Terms frequently used by patients include squeezing, tightness, pressure, etc. In some cases, the patient cannot qualify the nature of the discomfort, but places his or her fist in the center of the chest, known as the "Levine sign."

Angina is typically gradual in onset as the intensity of the discomfort increases over several minutes. In contrast, noncardiac pain is often of greatest intensity at its onset.

The discomfort does not change with respiration or position and is generally not sharp, dull-aching, knife-like, stabbing, or pins and needles-like.

• **Location** –It is not felt in one specific spot, but rather is a diffuse discomfort that may be difficult to localize. The patient often indicates the entire chest, rather than a specific area, when asked where the discomfort is felt.

• **Radiation** – It often radiates to other parts of the body including the upper abdomen, shoulders, arms, wrist, fingers, neck and throat, lower jaw and teeth, and rarely to the back.

• **Associated symptoms** – It is often associated with other symptoms. The most common is shortness of breath, which may reflect mild pulmonary congestion resulting from ischemia-mediated left ventricular dysfunction [44]. Other symptoms may include belching, nausea, indigestion, diaphoresis, dizziness, lightheadedness, clamminess, and fatigue.

- **Provoking factors** – Angina is often elicited by activities and situations which increase myocardial oxygen demand, including physical activity, cold, emotional stress, sexual intercourse, meals and cocaine use.
- **Timing** – Angina occurs more commonly in the morning due to a morning diurnal increase in sympathetic tone. Enhanced sympathetic activity raises heart rate, blood pressure, vessel tone and resistance, and platelet aggregability.

- **Duration of symptoms** – Angina generally lasts for two to five minutes. It does not lasts only for a few seconds or less than a minute, and it generally does not last for 20 to 30 minutes, unless the patient is experiencing an acute myocardial infarction.
- **Relief of discomfort** – Factors that reduce oxygen demand or increase oxygen supply will result in relief of angina. These include cessation of activity, use of nitroglycerin, sitting up (which reduces venous return and preload).

PHYSICAL EXAMINATION – Ischemia can produce myocardial function abnormalities which may result in the following findings:

- **Increase in heart rate** – Ischemia can raise the heart rate which may occur even if the patient is receiving a beta blocker or calcium channel blocker. This is induced by reflex sympathetic nervous system activation as a response to discomfort.
- **Elevation in blood pressure** – Ischemia often causes a hypertensive response. This is induced by both sympathetic activation and stimulation of the LAD chemoreceptor.
- **New heart sounds** – The second heart sound may become paradoxically split due to delayed relaxation of the left ventricular myocardium and delayed closure of the aortic valve. There may also be a third or fourth heart sound. These changes are typically transient and disappear upon resolution of ischemia.
- **New murmurs** – Impaired myocardial function may result in a new mitral regurgitation murmur (transient papillary muscle dysfunction) or changes in preexisting murmurs.
- **Precordial movements** – Palpation of the chest wall may reveal abnormal pulsations which correlate with transient left ventricular dysfunction. These reflect disease of the LAD.

Palpation of the left anterior chest wall at the anterior axillary line may reveal an abnormal tapping in systole, which reflects the presence of an area of dyskinetic contraction or aneurysm. Transient right ventricular dysfunction may also manifest as a transient right ventricular heave.

UNSTABLE ANGINA

This refers to angina of recent onset (less than one month), worsening angina or angina at rest [45].Post-myocardial infarction (MI) angina, and angina after a revascularization procedure are regarded as part of the spectrum.

Classification of unstable angina

In 1989, a classification of unstable angina was introduced [46]; this classification is based on the **clinical history** (accelerated exertional angina or rest pain, the timing of the latter in respect to presentation, and the clinical circumstances in which unstable angina developed), on the presence or absence of **ECG changes**, and on the intensity of **anti-ischemic therapy**. (see table)

Table 1. Classification of Unstable Angina [16]

	Clinical Circumstances		
Severity	A—Develops in Presence of Extracardiac Condition That Intensifies Myocardial Ischemia (Secondary UA)	B—Develops in Absence of Extracardiac Condition (Primary UA)	C—Develops Within 2 wk of AMI (Postinfarction UA)
I—New onset of severe angina or accelerated angina; no rest pain	IA	IB	IC
II—Angina at rest within past month but not within preceding 48 h (angina at rest, subacute)	IIA	IIB	IIC
III—Angina at rest within 48 h (angina at rest, acute)	IIIA	**IIIB-T_{neg} IIIB-T_{pos}**	IIIC

UA indicates unstable angina; AMI, acute myocardial infarction.

Although the development of this classification was based on clinical experience, it has been validated in a number of prospective studies. For example, Calvin et al [48] studied 393 patients with unstable angina and reported that a history of a myocardial infarction within 14 days (class C) and ST-segment depression on the presenting ECG were both markers of increased risk or complications.

Miltenburg-van Zijl et al[49] classified 417 patients with unstable angina and followed them up for 6 months. Death or myocardial infarction occurred more frequently in those with recent rest pain (class III) and in postinfarction patients (class C). The presence of ECG changes and the need for maximal antianginal therapy were also independent risk factors. A high unstable angina class (IIIB or IIIC) led to a high rate of coronary revascularization.[50]

However, this classification also has a number of weaknesses including substantial overlap between the groups and difficulty in identifying very low risk patients. In addition, a number of important clinical considerations are not included, such as the presence or absence of electrocardiographic (ECG) changes, age, gender, and the presence of comorbid illness known to increase the risk of coronary disease such as diabetes or peripheral vascular disease.

In attempt to correct these weaknesses, a recent prospective study separated 1387 patients into four different classes on the basis of chest pain pattern and ECG findings [51] :

- Class IA – accelerated angina without ECG changes
- Class IB – accelerated angina with ECG changes
- Class II – new onset exertional angina
- Class III – new onset rest angina
- Class IV – protracted rest angina with ECG changes

Follow-up demonstrated a progressive increase in cardiac events rate from class I to class IV with mortality limited to patients in classes III and IV .

Taken together with the other clinical and patient variables mentioned, these classifications provide a valuable background for approaching a patient with unstable angina.

DIAGNOSTIC WORKUP

Following proper clinical assessment, patient with suspected CAD ideally should undergo an array of investigations to establish the diagnosis of CAD.

RESTING ECG:

The electrocardiogram (ECG) remains a mainstay in the diagnosis of acute and chronic coronary syndromes. The findings depend upon the **duration**, **extent** (transmural versus subendocardial), and **localization** of ischemia or infarction.

ECG-coronary syndromes – There are four major types of acute coronary artery syndromes, in which myocardial ischemia leads to different ECG manifestations [52]:

- Noninfarction subendocardial ischemia (classic angina), manifested by transient ST segment depressions and T wave inversion.
- Noninfarction transmural ischemia (Prinzmetal's variant angina), manifested by transient ST segment elevations.
- Non-Q wave infarction, manifested by ST depressions or T wave inversions without Q waves.
- Q wave infarction, manifested by Q waves which are usually preceded by hyperacute T waves and ST elevations, and followed by T wave inversions.

LOCALIZATION OF ISCHEMIA OR INFARCTION –

The pattern of involvement of ECG leads helps in localizing regions of ischemia.

- Involvement of precordial leads (V1-V6), leads I and aVL indicates anterior wall ischaemia ,
- Leads V1 to V3: anteroseptal ischemia,
- Leads V4 to V6 : apical or lateral ischemia
- Leads II, III, and aVF: inferior wall ischemia
- Right-sided precordial leads : right ventricular ischemia.

Posterior wall infarction can induces ST elevations in leads placed over the back of the heart, and can be recognized by reciprocal ST depressions in leads V1 to V3.

When the resting ECG is normal or non conclusive in patients who are highly suspected to have myocardial ischaemia, exercise ECG is indicated.

EXERCISE ECG

Main indications:

- Evaluation of patients with symptoms suggestive of IHD.
- Assessment of level of exercise at which ischaemic manifestations occur in a patient with known IHD.

Contraindications:

- Recent MI (4-6 weeks) except for submaximal test,
- Angina at rest,
- Rapid arrhythmias,
- Uncompensated heart failure,
- Advanced atrioventricular block,
- Severe aortic stenosis,
- Bp> 170/100 before the onset of exercise.

Procedure:

Multistage protocols are used that use dynamic exercise on a treadmill up to a predicted maximal heart rate for age. These differ in the speed of the treadmill and in the duration of each stage of the test.

ECGs are performed at each stage, immediately post exercise and at 2 minutes intervals thereafter for 6-10 minutes.

A **horizontal** or **down-sloping ST segment** that is depressed at least 1mm below the isoelectric line at the J point and persists for 80 msec is interpreted as a **positive test**.

The workload, heart rate, blood pressure, presence of arrhythmias and symptoms are recorded.

Decrease in blood pressure, submaximal pulse response, exercise induced pain, ventricular ectopy, early onset and prolonged persistence of ST segment changes: all correlate with more severe disease.[53]

ECHOCARDIOGRAPHY

Echocardiography is a valuable measure in evaluation patients with IHD. Regional wall motion abnormalities, indicating previous ventricular damage, can be visualized within seconds of a coronary artery occlusion, and occurs prior to the onset of electrocardiographic changes or the development of symptoms [54] . Ventricular ejection fraction can be calculated and is useful in determining prognosis.

STRESS ECHOCARDIOGRAPHY – Stress echocardiography can be performed with exercise, or pharmacologically with the administration of dobutamine, dipyridamole or other agents.

Dobutamine echocardiography – Because of the difficulties with exercise 2D echocardiography, dobutamine echocardiography has become increasingly popular. This procedure is based upon the fact that the myocardial regions perfused by arteries with significant stenoses will deteriorate when ischemia is provoked by the inotropic and chronotropic effects of dobutamine[55] .

Dobutamine stress echocardiography may provide additional information in patients with chest pain, a negative initial serum assay for myocardial infarction, a non-ischemic ECG, and a normal resting echocardiogram. One study in 163 such patients found that dobutamine stress echocardiography had a sensitivity, specificity, and negative predictive accuracy of 90, 89, and 99 percent, respectively, versus clinical and catheterization studies[55] .

PERFUSION IMAGING

Myocardial perfusion scintigraphy demonstrates relative myocardial perfusion. It is used in conjunction with exercise to detect ischemia.

The sensitivity of the test in the diagnosis of coronary heart disease (CHD) is approximately 90 percent, greater than that achieved with the exercise electrocardiogram. Scintigraphy is also useful in evaluating myocardial viability, in establishing the "culprit" lesion prior to revascularization, in assessing the

completeness of revascularization, and in the risk stratification of patients with stable CAD, postmyocardial infarction, post-unstable angina, and prior to vascular surgery [56].

The test consists of injecting a radioactive agent (Thallium-201 or Technetium-99) which is distributed into the myocardium according to the coronary blood flow and uptake characteristics.
Regions with decreased blood flow are seen as cold spots. Images taken during rest and following exercise are compared to detect areas of reversible ischaemia.

Pharmacologic stress modalities in conjunction with perfusion imaging are used in patients who are unable to exercise.
Dipyridamole, adenosine, and dobutamine have all been extensively studied and show sensitivity and specificity generally comparable to exercise perfusion imaging [57] Each of these drugs increases myocardial blood flow, the first two by inducing primary vasodilatation without producing any significant hemodynamic effects, and dobutamine via its positive inotropic and chronotropic actions which lead to secondary vasodilatation. This will produce relative hypoperfusion in the myocardium served by stenotic coronary arteries.

(CORONARY ANGIOGRAPHY)

APPROACH TO SPECIFIC CLINICAL SETTINGS

Chest pain at rest – Some patients present with typical chest pain and ECG changes that easily establish the diagnosis of unstable angina. Other patients, however, present with atypical chest pain and nonspecific ECG findings.

Patients with atypical symptoms, no ECG changes at rest and, especially, during an episode of pain, are at a very low risk and can be evaluated on an outpatient basis.

On the other hand, patients with distinct ischemic ECG abnormalities, regional wall motion abnormality, and/or perfusion wall defect constitute a high risk group requiring close observation and intensive medical therapy, frequently including emergent or urgent cardiac catheterization. [58]

New onset angina – Patients with new onset angina, even if only exertional in nature, should be treated as if they have a potentially unstable lesion.

Post-MI angina – Angina occurring shortly after myocardial infarction, either Q wave or non Q wave, places the patient into a very high risk group for subsequent ischemic events and usually requires prompt diagnostic and therapeutic interventions [59].

Post-bypass or post-angioplasty angina – Recurrence of anginal chest pain symptoms after coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA) may signify the development of an acute complication, new lesions, graft failure. or post-angioplasty restenosis.

In both cases, cardiac catheterization is the preferred approach to define the problem and to provide a therapeutic intervention.

The ACC/AHA published recommendations for therapy and the use of coronary angiography in patients with ischemia after revascularization [58].

CORONARY ANGIOGRAPHY

Coronary angiography is an invasive investigation which is used in the diagnosis and management of patients with known or suspected coronary artery disease. It is useful in delineating the exact coronary anatomy especially in those considered for revascularization. At present, there is no alternative investigation to conventional coronary angiography.[60]

Main indications are [11]:

- Angina (refractory and post MI)
- Acute Coronary Syndrome
- Uncertain diagnosis

Procedure

The basic principle of the procedure is to outline the coronary arteries radiographically by transiently filling them with a radio-opaque contrast agent. A sheath is inserted percutaneously into a peripheral artery under local anaesthesia through which a fine hollow coronary catheter is manipulated, under fluoroscopic guidance, into the coronary ostium. Several views are taken, each requiring the hand injection of 5-10 ml of contrast agent into the coronary artery. A film of left ventricular myocardial contraction, a ventriculogram, is often carried out during the procedure by advancing a specific catheter into the left ventricular cavity where a larger volume (35-45 ml) of contrast is mechanically injected. Most patients tolerate coronary angiography well with little or no sedation

Complications

Major complications are rare (~1 in 1000) but do include death, myocardial infarction, stroke, aortic or coronary dissection, cardiac rupture, air embolus, cardiac arrhythmia and peripheral arterial injury. Minor complications are relatively common and include haematoma at the site of arterial puncture, short-lived episodes of angina, vasovagal reactions, and allergies to contrast agents and drugs.

Equipment

In view of the potential complications, the procedure should only be carried out by experienced trained operators in a well-equipped and staffed cardiac catheter

laboratory.. In addition to the *x*-ray equipment, the catheter laboratory must have monitors to allow continuous ECG and intra-arterial pressure recordings as well as full resuscitation equipment including a defibrillator, oxygen, suction, and all appropriate drugs.

Personnel

Staffing of the laboratory requires medical and paramedical personnel including radiographers, physiological measurement technicians and nursing staff as well as trained medical operators. The experience of the operator and laboratory staff has an important influence on the safety and complications of catheter procedures.

Findings:

The extent of coronary artery disease is measured by the **number of vessels** involved and the **severity** of their obstructions.

For each vessel the following are determined:

- **Percentage** of occlusion.
- **Site**, **length** and **shape** of the lesion.
- **Flow,** scored according to **TIMI classification** as follows:

Grade 0:total occlusion, grade 1:slow and incomplete opacification of the artery portion after the lesion, grade 2:slow but complete opacification, grade 3:normal opacification.

The American College of Cardiology has defined significant coronary artery disease as evidence by angiography of at least **50%** narrowing of the lumen of the artery.

ANGIOGRAPHIC MORPHOLOGY

AMBROSE'S MODIFIED CRITERIA.

In patients with either stable or unstable angina, the morphology of coronary artery lesions can be qualitatively assessed at angiography. Each obstruction reducing the luminal diameter of the vessel by 50% or greater can be categorized into one of the following morphologic groups [2] :

1. concentric (symmetric narrowing).
2. type I eccentric (asymmetric narrowing with smooth borders and a broad neck).
3. type II eccentric (asymmetric with a narrow neck or irregular borders, or both).
4. multiple irregular coronary narrowings in series.

Type II eccentric lesions are frequent in patients with unstable angina and probably represent ruptured atherosclerotic plaques or partially occlusive thrombi, or both; whereas concentric and type I eccentric lesions are seen more frequently in patients with stable angina [2] .

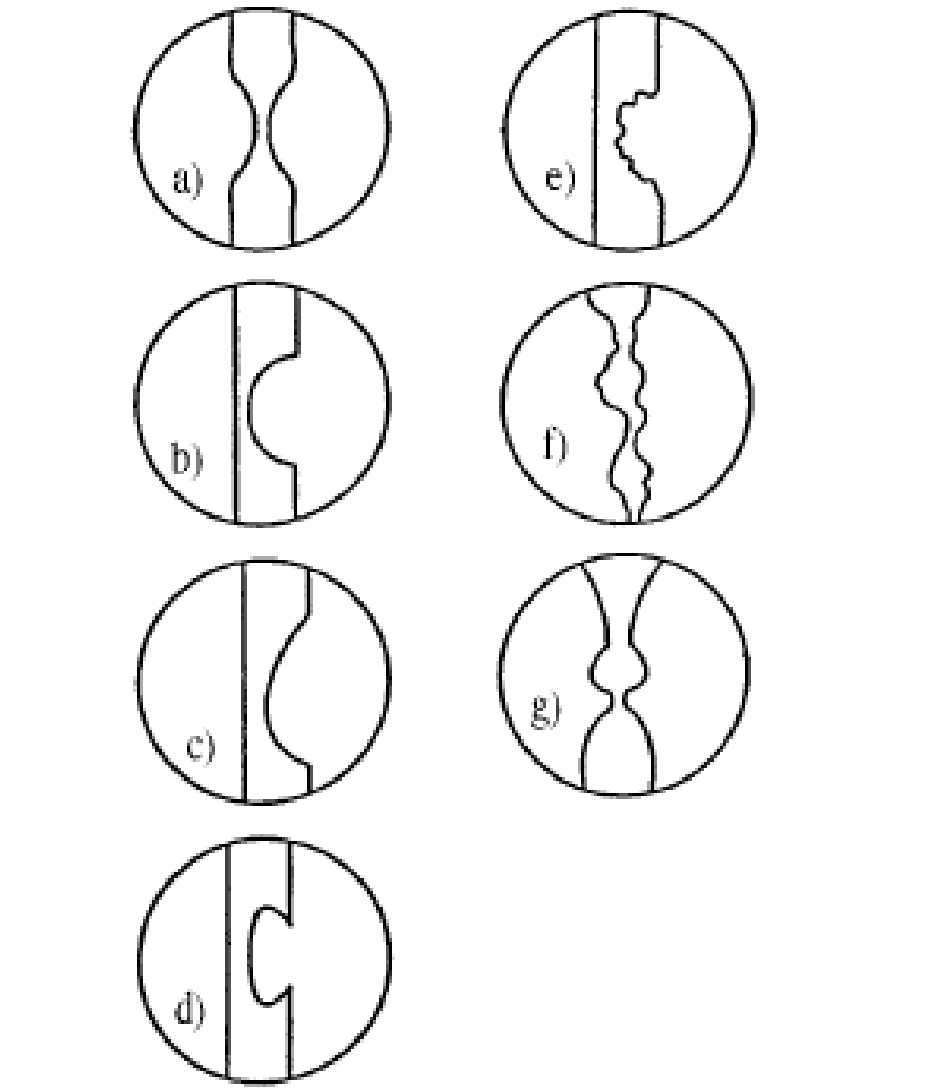


Figure 1. Ambrose's classification of coronary lesion morphology: a) concentric, b) eccentric IA, c) eccentric IB, d) eccentric IIA, e) eccentric IIB, f) multiple irregularities, g) tandem lesions.

THE ACC/AHA GRADING SYSTEM:

This was made mainly to predict rate of success and complications in coronary angioplasty; the more complex lesions has less success rates and more complications.

Characteristics of ACC/AHA Type A, B and C lesions

TYPE A LESIONS: (High success, > 85%; low risk)

Discrete (<10 mm length)	Little or no calcification
Concentric	Less than totally occlusive
Readily accessible	Notostial in location
Nonangulated segment <45 degrees	No major branch involvement
Smooth contour	Absence of thrombus

TYPE B LESIONS (Moderate success, 60 to 85%; moderate risk)

Tubular (10-20 mm length)	Ostial in location
Eccentric	Bifurcation lesions requiring
Moderate tortuosity of prox.segment	double guidewires
Moderately angulated, 45-90°	Some thrombus present
Irregular contour	Total occlusion < 3 months old
Moderate to heavy calcification	

TYPE C LESIONS (low success, < 60%; high risk)

Diffuse (>2 cm length)	Degenerated vein grafts with
Excessive tortuosity of prox.segment	friable lesions.
Extremely angulated, >90 degrees	Total occlusion > 3 months old
Inability to protect major side branch	

CORRELATING ANGIOGRAPHIC FINDINGS WITH CLINICAL PRESENTATION

A correlation between **clinical class and coronary anatomy** has been described. Ahmed et al [6] reported that an "unstable angina score" based on the clinical classification was the most important predictor of intracoronary thrombus and lesion complexity.

Danges et al found that both classes III and C were associated with complex culprit artery lesions and reduced TIMI flow [7].

Rupprecht et al [10] reported that the incidence of the angiographic evidence of complex lesions and/or thrombosis rose progressively with higher unstable angina classes.

Owa et al[61] found that unstable angina class III was associated with both a higher incidence of coronary thrombi on angiography and an increased risk of clinical progression to myocardial infarction.

Angiographic findings and serum troponin T

– Serum troponin T concentrations may be a sensitive marker for lesion severity and TIMI flow. As an example, in the CAPTURE trial of patients with refractory angina, those with elevated serum troponin were more likely to have complex lesion morphology (type B2 or C) (72 versus 54 percent), visible thrombus (15 versus 4 percent), and TIMI flow grade <2 (16 versus 5 percent) than those with negative troponin T levels.

Extent of coronary disease in DM

In addition to the increased clinical incidence of CHD, the extent of the disease in the coronary arteries is also greater among diabetic patients. Autopsy studies have reported that diabetic patients, compared to nondiabetics, have a higher incidence of two and three-vessel disease (83 versus 17 % in one report) and a lower incidence of one vessel disease [62]

Retrospective analyses of patients undergoing elective percutaneous transluminal coronary angioplasty (PTCA) support these data. The diabetic patients had more multivessel disease.

However, not all studies support these findings . One study, for example, compared the angiograms of 55 patients with noninsulin-dependent diabetes with 55 nondiabetic patients of similar age and with similar symptoms [63]; no difference in the severity and extent of CHD was observed between the two groups. One possible explanation for these results is the inclusion of insulin-dependent diabetics in those studies reporting a difference in CHD.

TREATMENT OF CAD

LIFESTYLE MODIFICATION

- Weight loss and a healthy diet (rich in vegetables and fruits, low in cholesterol)
- Exercise: Gradual institution of a regular exercise program results in a lower oxygen requirement and improves exercise tolerance.
- Risk factors modification: This includes treatment of hypertension, cessation of smoking, and correction of hyperlipidemia and controlling diabetes.

MEDICAL TREATMENT

Antiplatelets: Aspirin 75- 300 mg daily to decrease risk of thrombosis plus clopidogril 75 mg in high risk cases.

Nitrates – Nitrates are a first-line therapy for treatment of acute anginal symptoms. They act as venodilators and coronary vasodilators. These effects decrease left ventricular systolic wall stress while increasing coronary blood flow[64].
Sublingual nitroglycerin is used for acute anginal episodes and prophylactically for activities known to provoke angina. Chronic nitrate therapy, in the form of an oral or transdermal preparation, reduces the frequency of anginal episodes and improves exercise tolerance [65]

Beta blockers – Beta blockers relieve anginal symptoms by inhibiting sympathetic stimulation of the heart, reducing both heart rate and contractility .The cardioselective beta blockers (such as atenolol and metoprolol) have, in lower doses, the advantage of blocking beta-1-receptor mediated stimulation of the heart with lesser inhibition of the peripheral vasodilatation and bronchodilatation induced by the beta-2 receptors.

Beta blockers are proven to prevent reinfarction and to improve survival in patients who have sustained a myocardial infarction [66].

Calcium channel blockers – Calcium channel blockers cause coronary and peripheral vasodilatation, decreased atrioventricular (AV) conduction, and reduced contractility [67] .

They reduce anginal symptoms and increase exercise tolerance, especially when used in conjunction with other antianginal agents

- Verapamil is a negative inotrope that also decreases AV conduction. Potential side effects include heart block, worsening congestive heart failure, and constipation.
- Diltiazem has intermediate effects, being a modest negative inotropic agent and vasodilator with a low incidence of side effects.
- The dihydropyridines, such as nifedipine and amlodipine, are potent vasodilators with less effect on contractility and AV conduction.

CORONARY REVASCULARIZATION

Percutaneous transluminal coronary angioplasty

This is used to dilate coronary arteries by inflating a balloon with or without stenting.

It is indicated in patients with single vessel disease, especially if symptoms are refractory to medical therapy or if there is a large amount of ischemic myocardium as indicated by stress test or perfusion imaging.

In patients with two or three vessel disease and normal left ventricular (LV) function, either PTCA or CABG can be performed; they have similar rates of complications[68] . CABG offers the advantages of more complete revascularization, better relief of angina, and lower rate of reintervention, although the initial duration of hospitalization is longer .

There are three major contraindications to PTCA [69] .

- More than 50 percent stenosis in the left main coronary artery,
- Diffuse severe multivessel disease,
- Lack of surgical backup.

Complications are abrupt occlusion and restenosis; both are reduced by stenting.

Stents

The use of intracoronary stents in PTCA has resulted in significant reductions in acute vessel closure and restenosis.

Different stents are available and differ in composition (e.g., stainless steel, tantalum), design (slotted tube versus coiled wire), and mode of implantation (balloon expandable versus self-expanding).

Newer Drug-eluting stents (DES) consist of a metallic stent backbone, a biostable covering, and an anti-restenotic drug that is contained within the polymer and is released over a period of 14 to 30 days after implantation to modify the local healing response. Clinical trials of sirolimus-eluting stents and paclitaxel-eluting stents have demonstrated a marked reduction in the incidence of restenosis.

CORONARY ARTERY BYPASS SURGERY

The **main indications** for this procedure are:

- More than 50 percent stenosis of the left main coronary artery.
- Angina that is refractory to maximal medical therapy and not amenable to percutaneous revascularization.
- Severe ischemia in patients with LV dysfunction in whom complete revascularization is better achieved with CABG.
- Abrupt closure complicating PTCA in which there is a moderate to large amount of myocardium at risk.
- Three vessel disease and LV dysfunction .

Patients with three vessel disease, normal LV function, and moderate to severe ischemia by noninvasive testing would probably also benefit from surgery, although the outcome is not clearly better than multivessel angioplasty.

- Two vessel disease involving the proximal left anterior descending with a moderate size of myocardium at risk, unless angioplasty can be done safely [70] .

In the procedure the obstruction is bypassed by internal mammary artery or a reversed saphenous vein graft (long term patency is less).

Minimal invasive coronary bypass (MIDCAB) is being developed, ith no need for extracorporal circulatory support.

RATIONALE

Coronary Artery Disease is a serious condition and nowadays is increasingly recognized in Sudanese patients with the improved health care system and diagnostic tools. This is especially so in patients with recognized risk factors for ischaemia e.g. diabetes, which is an increasing problem in the country.

The recent availability of Catheter labs enables fast and accurate diagnosis of CAD, and delineates the exact coronary anatomy allowing proper intervention and thus decreasing morbidity and probably improving survival.

The aim of this study is to explore whether a specific presentation in patients with CAD correlates with a more severe form of coronary involvement, in which case prompt action would be needed.

OBJECTIVES

- **To identify lesion morphology in patients with coronary artery disease undergoing coronary angiography.**
- **To correlate angiographic findings with the different clinical presentations:**
  - **Stable against unstable Angina.**
  - **Diabetics against non-diabetics.**

CHAPTER TWO

METHODOLOGY

Study Design:

This study, a Prospective one, was conducted in Ahmed Qasim Hospital, from 1st of January to 30th of June 2005.

Study Population:

This included all patients with coronary artery disease who underwent coronary angiography.

Exclusion criteria:

Patients with CAD who underwent the procedure, and had no clinical data regarding mode of presentation.

Methods:

Information was collected using data sheet to show:

Demographic data, risk factors, complaints, physical examination, ECG changes at time of presentation and echocardiography findings.
The recordings of the actual angiographies were revised and morphology of coronary artery lesions was assessed. Each obstruction reducing the

luminal diameter of the vessel by **50%** or more was categorized using **Ambrose's modified criteria**.

Reduced Ejection Fraction was defined as ejection fraction <45% [11].

CHAPTER THREE

RESULTS

- **Total number** of patients studied 105; men (n=59), women (n=46). [Fig 1]
- **Age** ranged between 30-85 years. Mean age 59 years. [Fig 2]
- Regarding **Risk Factors**: 54% were hypertensive, 34% smokers, 29% diabetics and 15% had family history of ischaemic heart disease. [Fig 3]
- 53% of patient(n=56) presented with chest pain together with other symptoms, 31(30%)with chest pain alone,15(14%)with symptoms other than chest pain and 3(3%) were asymptomatic. [Fig 4]
- Out of 87 patients presenting with chest pain, only 73 could be classified into stable 60% and unstable angina 40%.[Fig 5]

Angiographic Findings:

- 46 patients had normal coronaries while 58 had significant disease. According to Ambrose modified criteria, the coronary lesions were simple in 20(34%) and complex in 38 (66%).[Fig 6]

- 41 patients had both angina and established CAD: 22 stable and 19 unstable.

In patients with **stable angina** 36.4% had simple lesions, 63.6% had complex lesions. In those with **unstable angina** 36.8% of the lesions were simple and 63.2% were complex (p= 0.96) [table 1]

- The number of vessels involved were as follows:

In **stable angina**, 31.8% single vessel , 22.7% two vessels, and 45.5% three vessels.
In **unstable angina**; 31.6%, 21.1% and 47.4% respectively.(p=0.98) [table2]

Comparing findings between **diabetics** and **non diabetics**:

- Patient **without diabetes** 36.8% had simple lesions while 63.2% had complex lesions. In **diabetics** the values were 30% and 70% respectively. (p=0.60) [table3]
- The number of vessels involved were as follows:

In **non diabetics**: 16.2% single vessel, 13.5% two vessels and 21.6% three vessels.
In **diabetics**: 16.7%, 6.7% and 43.3% respectively.(p=0.13) [Fig7]
Prevalence of three vessel disease among diabetics was tested against single, and two vessel disease; this was not statistically significant (p=0.4, and 0.2 respectively). [table: 4,5]

- Correlating number of vessels involved to ejection fraction:

Normal EF was found in 13 patients: 4(31%) had single vessel disease, 3(23%) two vessel disease, and 6(46%) three vessel disease.
Reduced EF was found in 12 patients : 1(8%) had single vessel disease, 2(17%) two vessel disease, and 9(75%) three vessel disease.(p=0.27) [Fig:8]

Three vessel disease [more prevalent among patients with low EF (75% against 46%)] was tested against prevalence of single vessel, and two vessel disease; this was not statistically significant (p=0.3, and 0.7 respectively).[table:6,7]

- In 16 patients with past history of MI, 13(81%) had complex lesions and 3(19%) had simple lesions [Fig10]. In those without history of MI(n=40), 18(45%) had simple lesions and 22(55%) complex lesions.(p=0.13)

- For patients with MI 2(13%) had single vessel disease, 2(13%) had two vessel disease and 12(74%) three vessel disease[Fig 11].In those without MI 14 (35%) had single vessel disease, 11(28%) had two vessel disease and 15(37%) three vessel disease. **(p=0.015) significant.**

- **ECG**: showed changes suggestive of ischaemia in 57% of patients with established CAD.(p=0.58)

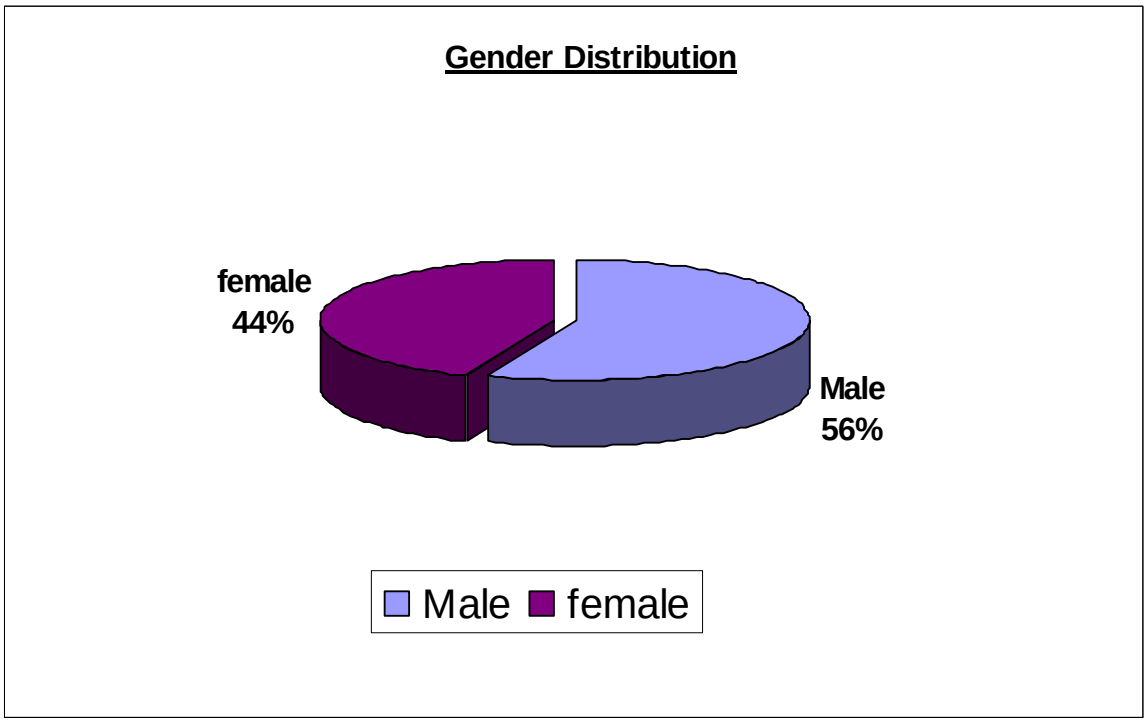


Fig:1

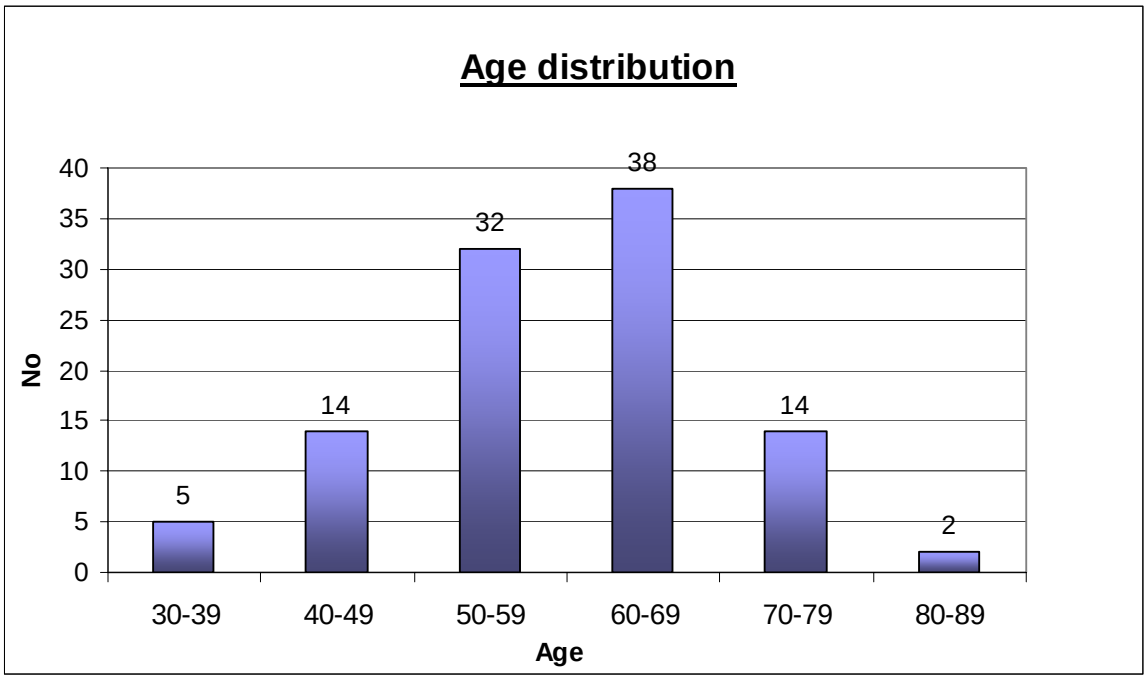

Age distribution
40
35
30
25
20
15
10
5
0
No
5
14
32
38
14
2
30-39
40-49
50-59
60-69
70-79
80-89
Age

Fig:2

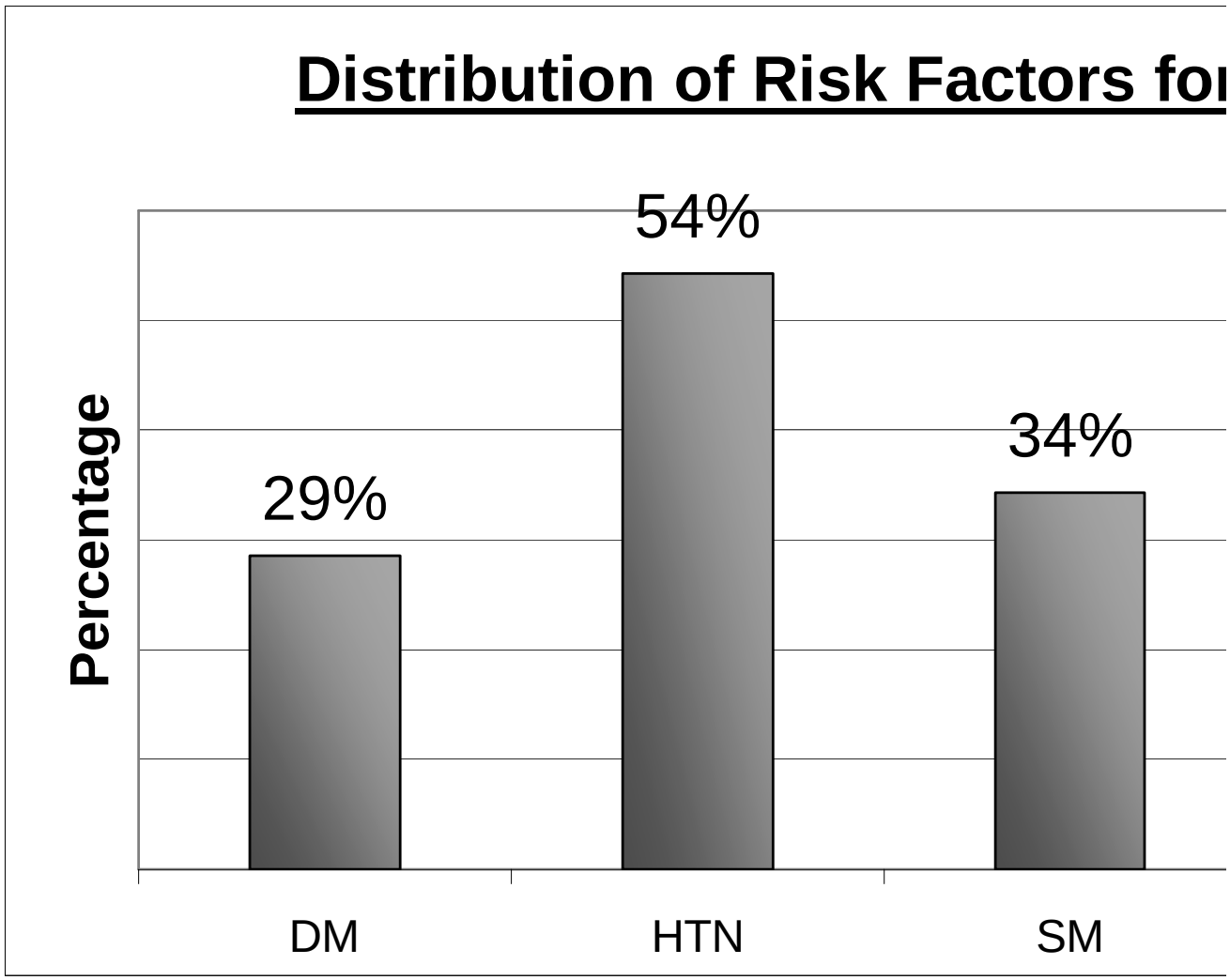

Distribution of Risk Factors fo
Percentage
54%
34%
29%
DM
HTN
SM

Fig:3

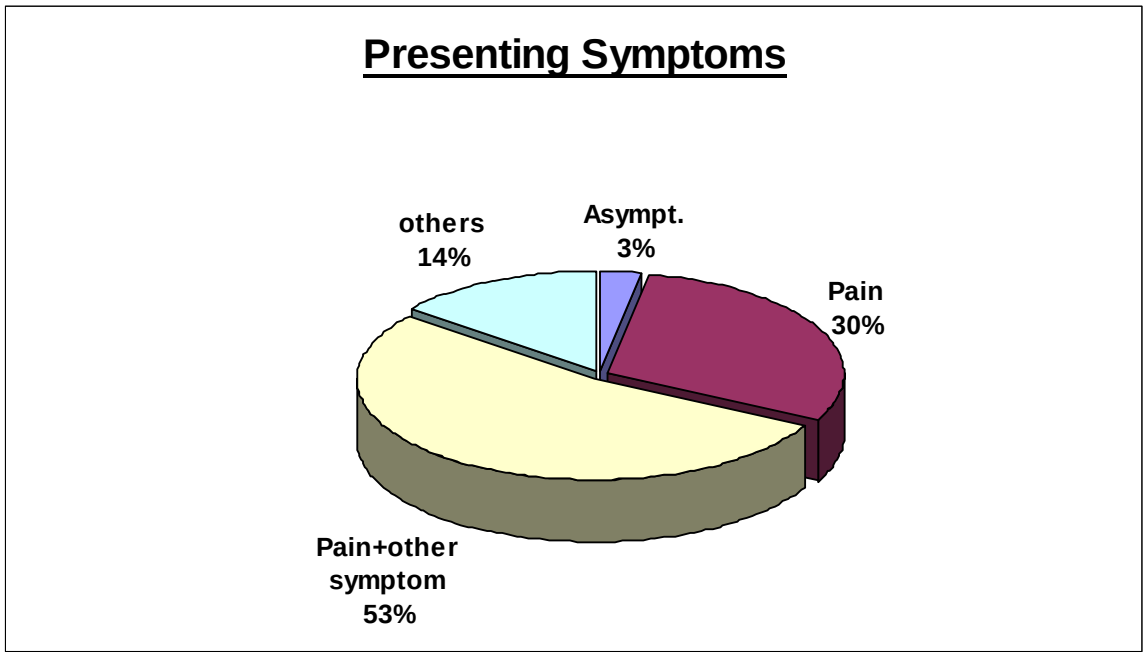

Presenting Symptoms
others
14%
Asympt.
3%
Pain
30%
Pain+other
symptom
53%

Fig:4

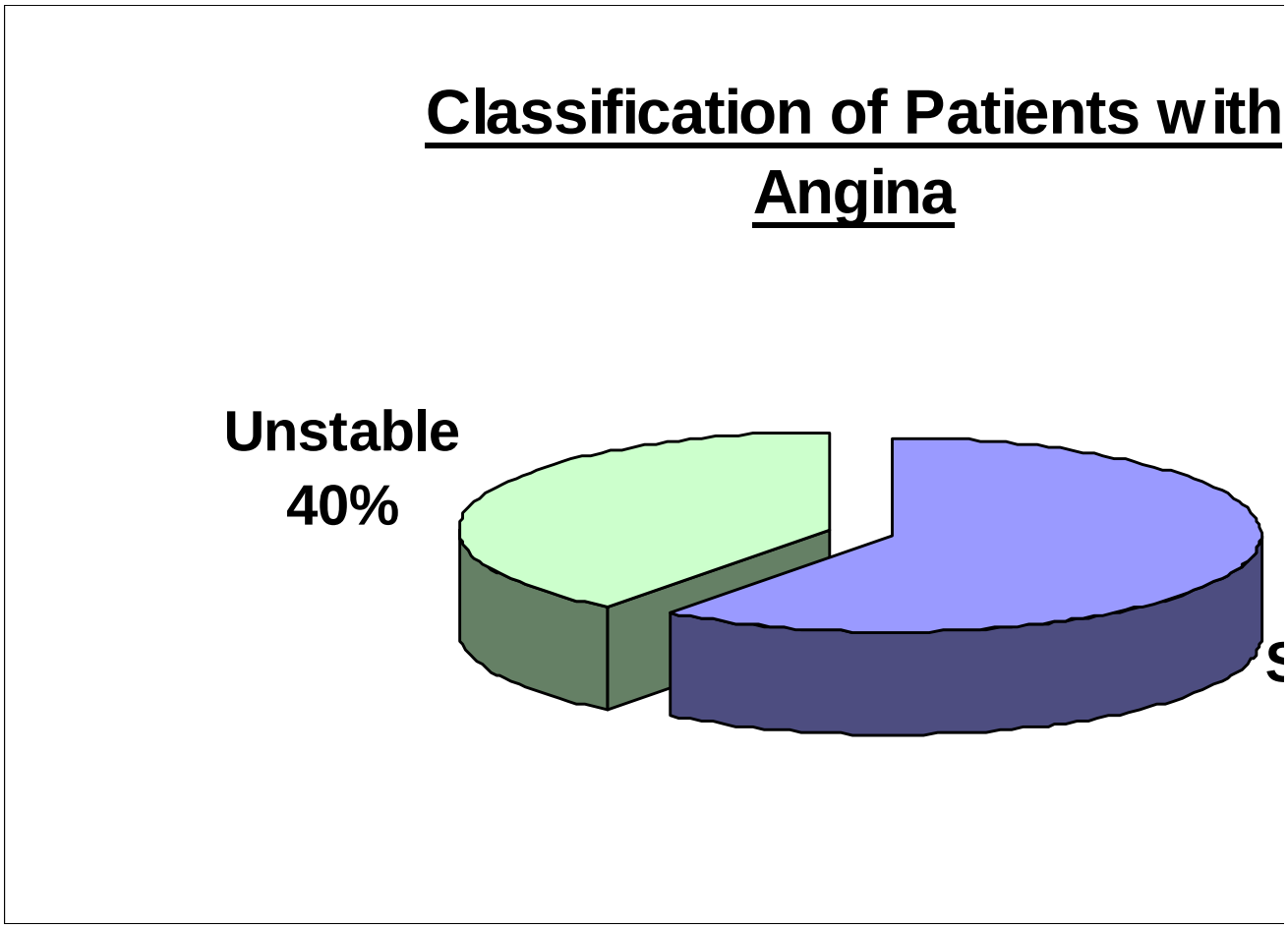


Fig:5

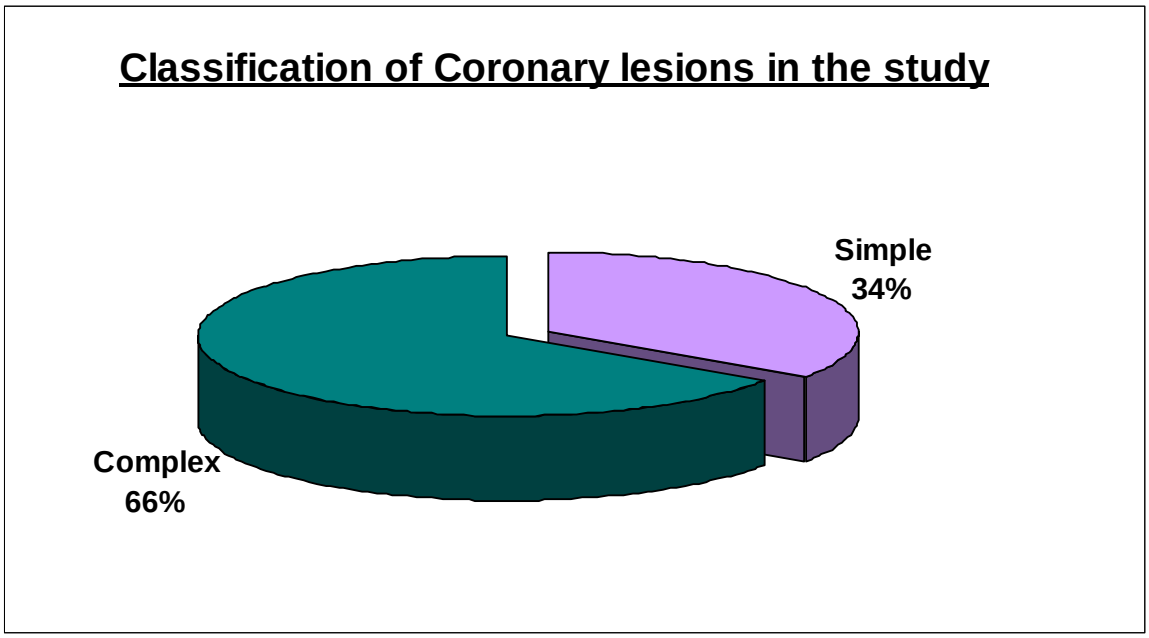

Classification of Coronary lesions in the study
Simple
34%
Complex
66%

Fig:6

Correlation between Type of Angina and Lesion Morphology

	Simple	Complex	Total
Stable	8(36.4%)	14(63.6%)	22(100%)
Unstable	7(36.8%)	12(63.2%)	19(100%)

(p= 0.96)

[Table1]

Correlation between Angina and Number of Vessels Involved

	svd	2vd	3vd	Total
Stable Angina	7(31.8%)	5(22.7%)	10(45.5%)	22(100%)
Unstable Angina	6(31.6%)	4(21.1%)	9(47.4%)	19(100%)

(p=0.98)

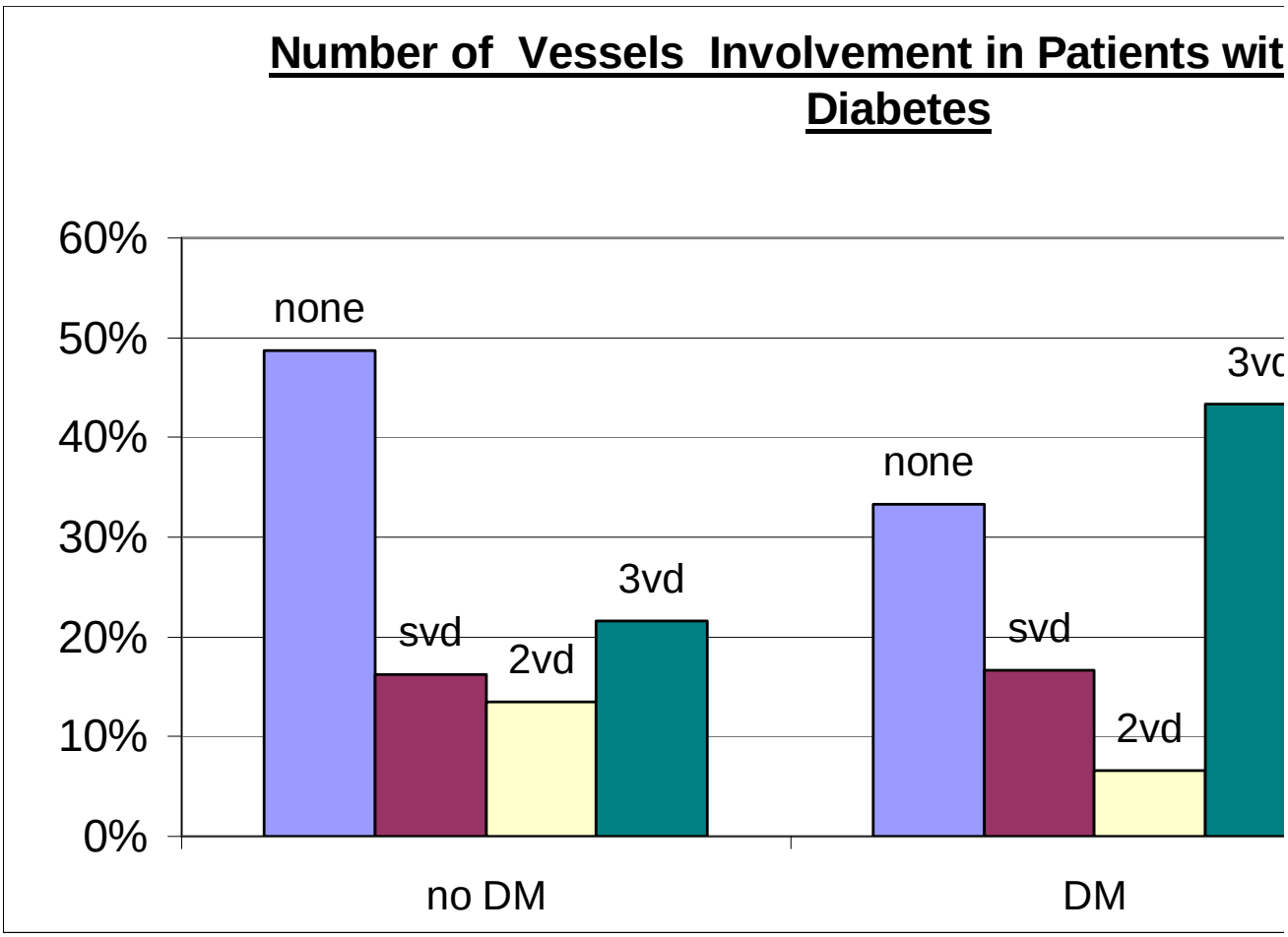
[Table2]

Lesion morphology in Patients with and without Diabetes

	Simple	Complex	Total
No DM	14(36.8%)	24(63.3%)	38(100%)
DM	6(30.0%)	14(70.0%)	20(100%)

(p=0.60)

[Table3]


Number of Vessels Involvement in Patients wit
Diabetes
60%
50%
40%
30%
20%
10%
0%
none
svd
2vd
3vd
none
svd
2vd
3vc
no DM
DM

(p =0.13)

Fig:7

Comparing Single and Three vessel disease in patients with and without DM

	svd	3vd	Total
No DM	12(42.9%)	16(57.1%)	28(100.0%)
DM	5(27.8%)	13(72.2%)	18(100.0%)

(p=0.471)

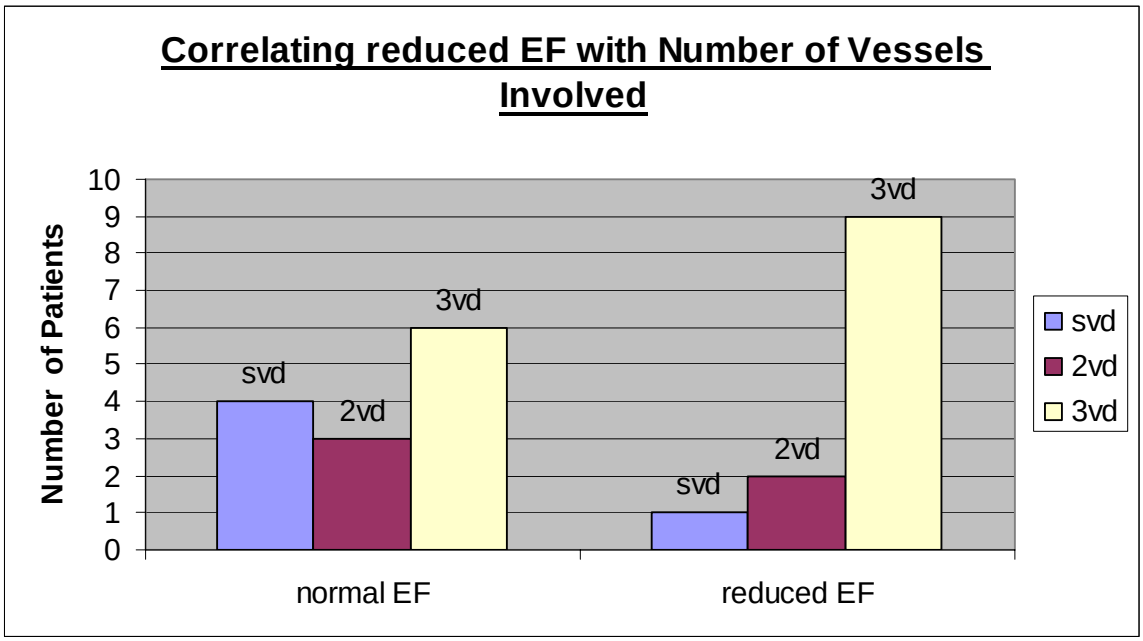
[Table:4]

Comparing Two and Three vessel disease in patients with and without DM

	2vd	3v	Total
No DM	10(38.5%)	16(61.5%)	26(100.0%)
DM	2(13.3%)	13(86.7%)	15(100.0%)

(p=0.178)

[Table:5]


Correlating reduced EF with Number of Vessels Involved
Number of Patients
10
9
8
7
6
5
4
3
2
1
0
svd
2vd
3vd
svd
2vd
3vd
normal EF
reduced EF
svd
2vd
3vd

(p =0.277)

Fig:8

Comparing Single and Three vessel disease in patients with Normal and Reduced EF:

	svd	3vd	Total
Normal EF	4(40%)	6(60%)	10(100%)
Reduced EF	1(10%)	9(90%)	10(100%)

(p=0.30)

[Table:6]

Comparing Two and Three vessel disease in patients with Normal and Reduced EF:

	2vd	3vd	Total
Normal EF	3(33%)	6(67%)	9(100%)
Reduced EF	2(18%)	9(82%)	11(100%)

(p=0.79)

[Table:7]

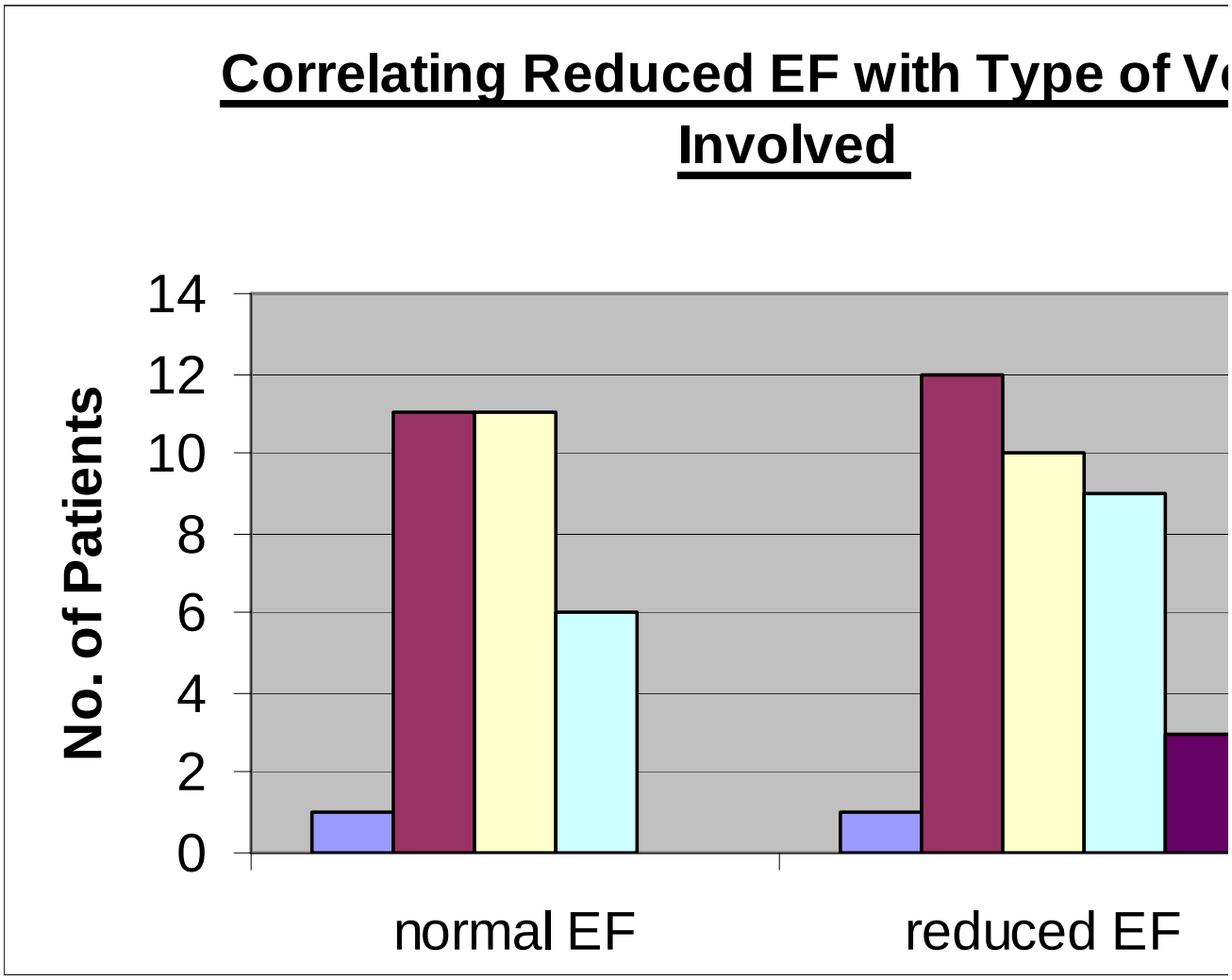

Correlating Reduced EF with Type of V
Involved
No. of Patients
14
12
10
8
6
4
2
0
normal EF
reduced EF

Fig: 9

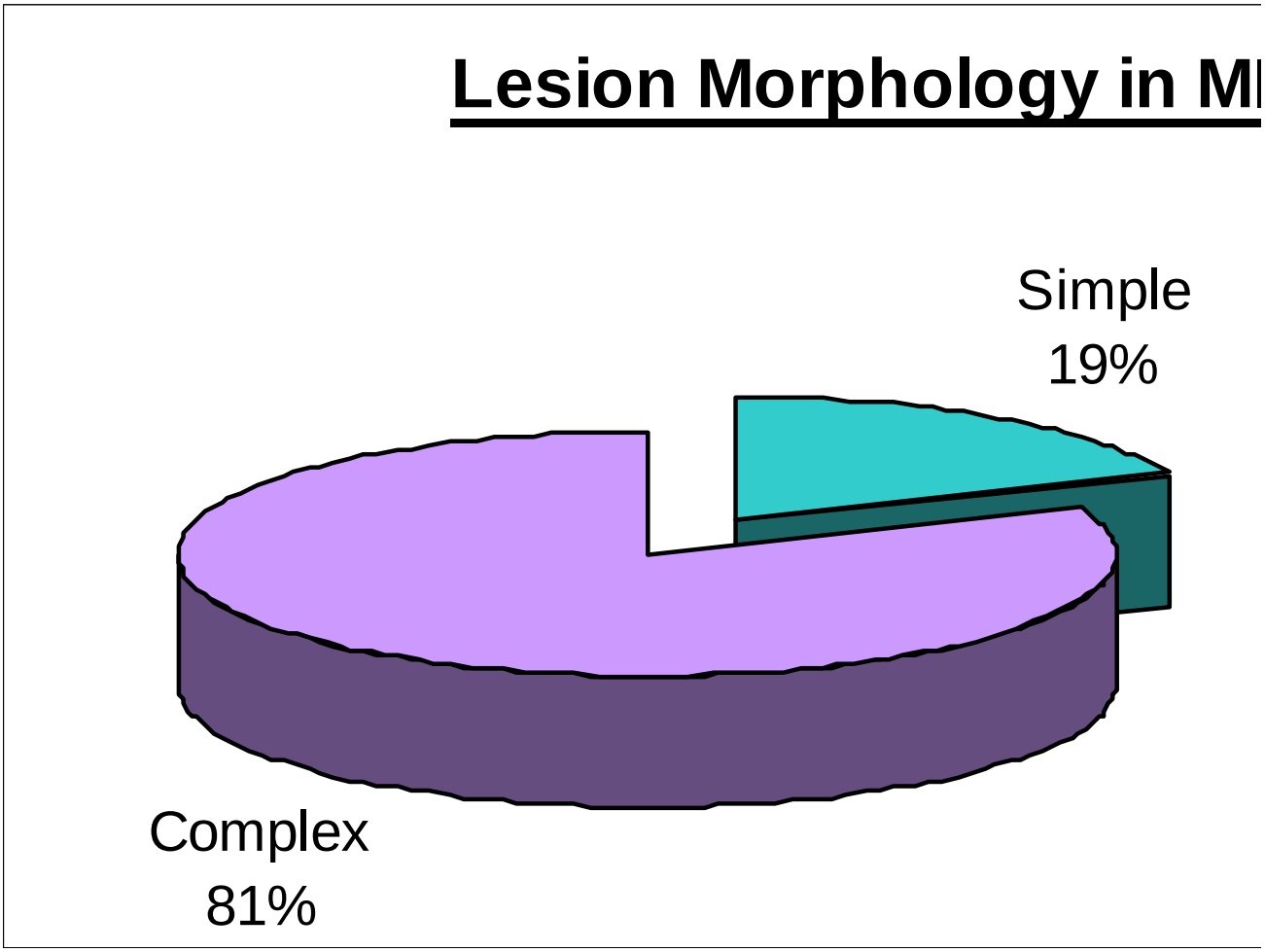


Fig:10

Type of Lesion
in patients with and without MI:

	Simple	Complex	Total
No MI	18(45%)	22(55%)	40(100%)
MI	3(19%)	13(81%)	16(100%)

(p=0.13)

[Table:8]

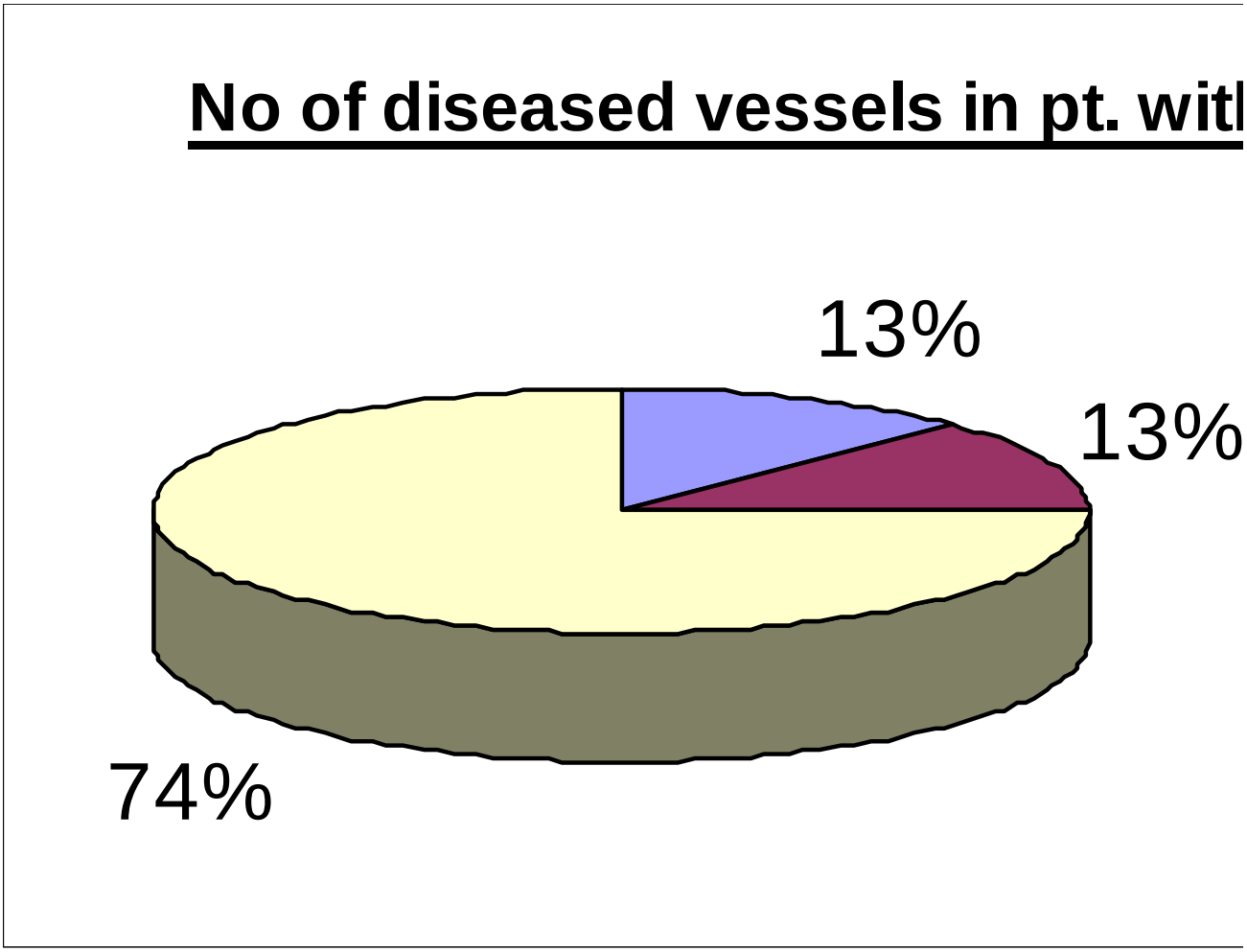


Fig:11

Number of Vessels Involved in Patients with and without MI:

	svd	2vd	3vd	Total
No MI	14(35%)	11(27.5%)	15(37.5%)	40(100%)
MI	2(12.5%)	2(12.5%)	12(75%)	16(100%)

(p=0.018) significant.

[Table:9]

CHAPTER FOUR

DISCUSSION

In our study most patients were found to have complex lesions 66%, while only 34% had simple lesions.

- **Complex lesions were more common in both stable (63.6%), and unstable angina (63.2%) patients. There was no statistical difference when associating lesion type to angina class.**

This result is in contrast to **Ambrose et al**.[2] who studied 110 patients with either stable or unstable angina, the morphology of coronary artery lesions was qualitatively assessed at angiography. Each obstruction reducing the luminal diameter of the vessel by 50% or greater was categorized according to Ambrose modified criteria.

In patients with unstable angina or non-Q myocardial infarction, the culprit lesion morphology was eccentric type II in 65-70%and concentric in 30%while in patients with stable angina the percentages were 16%and 80%respectively.

For the entire group, type II eccentric lesions were significantly more frequent patients with unstable angina ($p < 0.001$), whereas concentric and type I eccentric lesions were seen more frequently in patients with stable angina ($p < 0.05$).

- Still the percentage of complex lesions in patients with unstable angina is similar to that in Ambrose study: 64% and 65% respectively.

A similar value 67% was obtained in the study done by **Ben-Hamda et al** [71] which compared the clinical presentation and angiographic morphology of patients with unstable angina pectoris.

In 321 patients the morphology of coronary artery lesions was classified according to Ambrose's classification, 100 patients had simple lesions (type I or IIA), and 204 patients had complex lesions (type IIB, III, intracoronary thrombus or total occlusion). P value

Here again, high class unstable angina, i.e. thoracic rest pain (class III) or post infarction angina (class C), were associated with the presence of complex lesions.

- On the other hand two further studies concluded that morphology of lesions in coronary angiography did not differ significantly in different clinical classes of angina.

The first by **Calton R. et al** [72] studied 100 patient with unstable angina trying to correlate Braunwald's clinical classification of unstable angina pectoris with angiographic extent of disease, lesion morphology and intra-luminal thrombus.

Morphology of coronary artery lesions was classified according to Ambrose's classification. Concentric lesions were found to be higher in class C as compared to class B (40% vs. 19.8%; p = 0.014). Statistically significant difference was not present in the distribution of other morphological type of lesions among different clinical classes. In the whole study group, intra-luminal thrombus was found to be present in 17 (17%) of patients. Distribution of intra-luminal thrombus according to Braunwald's classification showed that none of the patients in class I had intra-luminal

thrombus, while 13 (19.1%) patients in class II and 4(26.7%) in class III had intra-luminal thrombus. There was significant difference in the presence of intra-luminal thrombus between class I and class II (p = 0.004) and class I and class III (p = 0 .03 was found to be significant). Intra-luminal thrombus was more frequently encountered with acute rest angina. However, the distribution of different morphological type of lesions on coronary angiography did not differ significantly in different clinical classes of unstable angina pectoris divided according to Braunwald's classification.

The second study by **Pim J. de Feyter et al**[73] assessed coronary lesions in patients with stable and unstable angina using coronary angiography, intracoronary angioscopy and determined their compositions with intracoronary ultrasound.

In 44 patients with unstable and 23 patients with stable angina, the angiographic images were classified as noncomplex (smooth borders) or complex (irregular borders, multiple lesions, and thrombus). Angioscopic images were classified as either stable (smooth surface) or thrombotic (red thrombus). The ultrasound characteristics of the lesion were classified as poorly echo-reflective, highly echo-reflective with shadowing, or highly echo-reflective without shadowing. There was a poor correlation between clinical status and angiographic findings. An angiographic complex lesion (n=33) was concordant with unstable angina in 55% (24 of 44); a non complex lesion (n=34) was concordant with stable angina in 61% (14 of 23). There was a good correlation between clinical status and angioscopic findings. An angioscopic thrombotic lesion (n=34) was concordant with unstable angina in 68% (30 of 44); a stable lesion (n=33) was concordant with stable angina in 83% (19 of 23). The ultrasound-obtained composition of the plaque was similar in patients with unstable and stable angina.

So the conclusion was that angiography discriminates poorly between lesions in stable and unstable angina. Angioscopy demonstrated that plaque rupture and thrombosis were present in 17% of stable angina and 68% of unstable angina patients. Currently available ultrasound technology does not discriminate stable from unstable plaques.

- In our study the percentage of patients with stable angina who were found to have complex lesion was high in comparison with all the other studies, those which found a correlation with clinical presentation and those which did not.

A possibility is that definition of stable angina cases here depended on the description of pain developing on exertion which may still include lower classes of unstable angina e.g., new onset angina and worsening angina. So there may be some cases included in the 'stable angina' category that rather be included in the 'unstable' category. **Great difficulty was encounterd in collecting the history data from the notes**.

Another possibility is the behaviour of atherosclerosis in our patients which may be different genetically; however this has not been studied.

- **Three vessel disease was the commonest in the two groups of angina with similar pattern of vessel involvement**.
- **There was no correlation between angina class and number of vessels involved.**

The study by **Calton et al**[72] , mentioned above, has also compared the extent of vessel involvement in different angina classes.

On coronary angiography, 26 (26%) patients had single vessel disease, 30 (30%) double vessel disease and 39 (39%) patients had triple vessel

disease. Five (5%) patients were found to have normal coronaries. Classification of patients according to Braunwald's clinical classification showed single vessel disease to be higher in class I as compared to class II (47% vs. 22%; p = 0.04) and classes III (47% vs. 20%; p<0.01). Single vessel disease was found to be higher in class C as compared to class B (41.7% vs. 16.4; p = 0.01). Two vessel disease was higher in class B as compared to class A (40.8% vs. 18.5%, p = 0.04). Triple vessel disease incidence was not found to be significantly different among different clinical classes.

Ben-Hamda et al studied 321 patients with unstable angina found that 148 (46%) patients had single vessel disease, double-vessel in 92(29%) and triple-vessel in 64(20%). No correlation with angina class was made.

Stylianos A. et al[74] studied the potential correlation between the angiographic lesion morphology and the early and one year clinical outcome in patients with unstable angina, found one-vessel disease in 46 (37%)patients, two-vessel disease in 40 (32%)patients, three-vessel disease in 36 (29%)and left main stem disease in 3 (2%).

In all these studies there was no specific pattern of vessel involvement in patients with unstable angina and no correlation with angina class was made.

- **Comparing diabetics and non diabetics complex lesions were more in diabetics: 70% and 63%.** The difference was not statistically

significant. However there was marked prevalence of complex lesions among diabetics.

- **Pattern of vessel involvement showed three vessel disease to be more common among diabetics**, **43% against 21%.**The prevalence of three vessel disease was compared to that of single vessel and two vessel disease but these were not significant.
- The results of our study were similar to that by **Pajunen P et al** [75] which compared the angiograms of 55 patients with noninsulin-dependent diabetes with 55 nondiabetic patients of similar age and with similar symptoms. No difference in the severity and extent of CHD was observed between the two groups.

However, many studies found that the extent of the disease in the coronary arteries is greater among diabetic patients[76]. Autopsy studies have reported that diabetic patients, compared to nondiabetics, have a higher incidence of two and three-vessel disease (83 versus 17 percent in one report) and a lower incidence of one vessel disease [62].

Retrospective analyses of patients undergoing elective percutaneous transluminal coronary angioplasty (PTCA) support these data. One study, for example, retrospectively analyzed data on 1133 diabetic and 9300 nondiabetic patients undergoing PTCA [77] .The diabetic patients had more multivessel disease. Furthermore, the likelihood of remaining free of infarction or additional revascularization at five years was much lower in diabetics (36 versus 53 percent).

These findings are supported by two large-scale thrombolytic trials that have provided coronary angiographic data obtained during an acute myocardial infarction [78,79]. In the Thrombolysis and Angioplasty in

Myocardial Infarction (TAMI) trial included 148 diabetics and 923 nondiabetic patients in whom cardiac catheterization was performed at 90 minutes and 7 to 10 days after thrombolytic therapy [78]. Compared to the nondiabetics, the diabetic patients had a greater incidence of multivessel disease (66 versus 46 percent, p=0.0001) and a greater number of diseased vessels.

- **On correlating the number of vessels involved to ejection fraction (EF), three vessel disease was more common (75%) among patients with reduced EF compared to those with normal EF(46%).** No statistical significance as established. Main vessels involved were the same in both groups.

So in this study reduced ejection fraction is associated more with three vessel disease (thus extensive myocardial ischaemia).

- **In patients with past history of MI, complex lesions were the majority at 81%.**
- **Most patients with history of MI had three vessel disease (75%). This was highly significant when compared to single and two vessel disease(p=0.018)**

So patients who developed MI have both marked complexity of the lesions and more extensive involvement of the coronaries.

- **ECG: showed changes suggestive of ischaemia in only 57% of patients with established CAD.** (p=0.58)

This is in keeping with a study done by Weston MJ et al [80] that ECG is not a reliable method for detection of CAD.

In a retrospective series Norell M et al [81] studied 250 patients who presented to a cardiology clinic for evaluation of recent onset chest pain, 20 percent of those with normal ECGs were found to have unstable angina; one-third of patients diagnosed with unstable angina had a normal ECG.The false-negative rate was lower in a prospective series of emergency department patients presenting with chest pain; only 4 percent of those with a normal ECG were found to have unstable angina, but strict criteria were used to define the "normal" ECG [82] .

STUDY LIMITATIONS

Certain factors (e.g. cost) make coronary angiography not readily accessible to some patients. Possibly those with the more severe and persistant symptoms are the ones who eventually underwent the procedure, which may have introduced bias.

Assessement of the patients' clinical presentation in our study depended mainly on previously recorded data. This was deficient in many aspects and did not include the details necessary for classification of angina (e.g. duration of symptoms). This may explain the dominance of the complex lesions in this study.

CONCLUSIONS

- The commonest presenting symptom was chest pain.
- Most lesions in this study were complex lesions.
- Lesion morphology was similar in patients with stable and unstable angina. Number of vessel involvement was also similar.
- Diabetes is associated with more extensive coronary involvement i.e. more complex lesions and higher prevalence of three vessel disease.
- Myocardial infarction is more common in patients with three vessel disease.

RECOMMENDATIONS

- Data in the clinical records should be more detailed especially regarding the duration and severity of symptoms since this is crucial in risk stratification of cardiac cases .

- In studies where history-based information is needed, data is better collected through personal interviews.

REFERENCES

1. Levin DC, Fallon JT: Significance of the angiographic morphology of localized coronary stenosis. Histopathologic correlations. Circulation 1982; 66: 316-320.

2. Ambrose JA, Winters SL, Stern A, Eng A, Teichholz LE, Gorlin R, Fuster V: Angiographic morphology and the pathogenesis of unstable angina pectoris. J Am Coll Cardiol 1985; 5: 609-616.

3. Ambrose JA, Winters SL, Arora RR, Eng A, Riccio A, Gorlin R, Fuster V: Angiographic evolution of coronary artery morphology in unstable angina. J Am Coll Cardiol 1986; 7: 472-478.

4. Ambrose JA, Hjemdahl-Monsen CE, Borrico S, Gorlin R, Fuster V: Angiographic demonstration of a common link between unstable angina pectoris and non-Q wave acute myocardial infarction. Am J Cardiol 1988; 61: 244-247.

5. Ambrose JA: Plaque disruption and the acute coronary syndromes of unstable angina and myocardial infarction: if the substrate is similar, why is the clinical presentation different? J Am Coll Cardiol 1992; 19: 1653-1658.

6. Ahmed WH, Bittl JA, Braunwald E. Relation between clinical presentation and angiographic findings in unstable angina pectoris, and comparison with that in stable angina. *Am J Cardiol.* 1993;72:544–550.

7. Danges G, Mehran R, Wallenstein S, et al. Correlation of morphology and clinical presentation in unstable angina. *J Am Coll Cardiol.* 1997;29:519–525.

8. De Servi S, Arbustini E, Marsica F, et al. Correlation between clinical and morphologic findings in unstable angina. *Am J Cardiol.* 1996;77:128–132.

9. Depre C, Wijns W, Robert AM, et al. Pathology of unstable plaque: correlation with the clinical severity of acute coronary syndromes. *J Am Coll Cardiol.* 1997;30:694–702.

10. Rupprecht HJ, Sohn HY, Kearney P, et al. Clinical predictors of unstable coronary lesion morphology. *Eur Heart J.* 1995;16:1526–1534.

11. Kumar P, Clark M. Clinical Medicine, fifth edition, 2002, London:WB Saunders.

12. Thom, TJ, Kannel, WB, Silbershatz, H, D'Agostino, RB. Incidence, prevalence and mortality of cardiovascular disease in the United States. In: Hurst's "The Heart," 9th ed, Alexander, RW, Schlant, RC, Fuster, V, 1998, pp. 3-16.

13. Davies MJ, Woolf, N, Rowles, PM, Pepper, J. Morphology of the endothelium over atherosclerotic plaques in human coronary arteries. Br Heart J 1988; 60:459.

14. Kochx, MM, De Meyer, GRY, Muhring, J, et al. Apoptosis and related proteins in different stages of human atherosclerotic plaques. Circulation 1998; 97:2307.

15. Fuster, V, Badimon, L, Badimon, JJ, Chesebro, JH. The pathogenesis of coronary artery disease and the acute coronary syndromes. N Engl J Med 1992; 326:242.

16. Little, WC, Constantinescu, M, Applegate, RJ, et al. Can coronary angiography predict the site of a subsequent myocardial infarction in patients with mild to moderate coronary artery disease? Circulation 1988; 78:1157.

17. Ambrose, JA, Tannenbaum, MA, Alexopoulos, D, et al. Angiographic progression of coronary artery disease and the development of myocardial infarction. J Am Coll Cardiol 1988; 12:56.

18. Falk, E. Plaque rupture with severe pre-existing stenosis precipitating coronary thrombosis: Characteristics of coronary atherosclerotic plaques underlying fatal occlusive thrombi. Br Heart J 1983; 50:127.

19. Gotto, AM, Jr, LaRosa, JC, Hunninghake, D, et al. The cholesterol facts: A summary of the evidence relating dietary fats, serum cholesterol, and coronary heart disease: a joint statement by the American Heart Association and the National, Heart, Lung, and Blood Institute. Circulation 1990; 81:1721.

20. The Expert Panel. Second Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. NIH publication No. 93-3095. US Government Printing Office, Washington, DC, 1993.

21. Grundy, SM, Goodman, DS, Rifkind, BM, et al. The place of HDL in cholesterol management. A perspective from the National Cholesterol Education Program. Arch Intern Med 1989; 149:505.

22. Kinosian, B, Glick, H, Garland, G. Cholesterol and coronary heart disease: Predicting risks by levels and ratios. Ann Intern Med 1994; 121:641.

23. Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults. Summary of the second report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel II). JAMA 1993; 269:3015.

24. Shepherd, J, Cobbe, SM, Ford, I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Prevention Study Group. N Engl J Med 1995; 333:1301.

25. Downs, JR, Clearfield, M, Weis, S, et al for the AFCAPS/TexCAPS Research Group. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: Results of AFCAPS/TexCAPS. JAMA 1998; 279:1615.

26. Sacks, FM, Pfeffer, MA, Moye, LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. N Engl J Med 1996; 335:1001.

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.

28. Kannel, WB. Left ventricular hypertrophy as a risk factor: the Framingham experience. J Hypertens Suppl 1991; 9:S3.

29. Kannel, WB, Gordon ,T, Schwartz, MJ. Systolic versus diastolic blood pressure and risk of coronary heart disease: The Framingham Study. Am J Cardiol 1971; 27:335.

30. Wilking, SVB, Belanger, AJ, Kannel, WB, et al. Determinants of isolated systolic.

31. Hebert, PR, Moser, M, Mayer, J, et al. Recent evidence on drug therapy of mild to moderate hypertension and decreased incidence of coronary heart disease. Arch Intern Med 1993; 153:578.

32. Singer, DE, Nathan, DM, Anderson, KM, et al. Association of HbA1c with prevalent cardiovascular disease in the original cohort of the Framingham Heart Study. Diabetes 1992; 41:202.

33. The Writing Group for the PEPI Trial: Effects of estrogen or estrogen/progestin regimens on heart disease risk factors in postmenopausal women. The Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. JAMA 1995; 273:199.

34. Leon, AS, Connett, J, Jacobs, DR, et al. Leisure-time physical activity levels and risk of coronary heart disease and death. The Multiple Risk Factor Intervention Trial. JAMA 1987; 258:2388.

35. Prescott, E, Hippe, M, Schnohr, P, et al. Smoking and the risk of myocardial infarction in women and men: Longitudinal population study. BMJ 1998; 316:1043.

36. Willhemsson, C, Elmfeldt, D, Vedim, JA, Tibblin, G. Smoking and myocardial infarction. Lancet 1975; 1:415.

37. Rimm, EB, Ascherio, A, Giovannucci, E, et al. Vegetable, fruit, and cereal fiber intake and risk of coronary heart disease among men. JAMA 1996; 275:447.

38. Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. Lancet. 1993 Oct 23;342(8878):1007-11.

39. Krauss, RM, Winston, M. Obesity: Impact on cardiovascular disease. Circulation 1998; 98:1472.

40. Stec, JJ, Silbershatz, H, ofler, GH, et al. Association of fibrinogen with cardiovascular risk factors and cardiovascular disease in the Framingham offspring population. Circulation 2000; 102:1634.

41. Chauhan, A, Mullins, PA, Petch, MC, et al. Cardioesophageal reflex: A mechanism for "linked angina" in patients with angiographically proven coronary artery disease. J Am Coll Cardiol 1996; 27:1621.

42. Baliga, RR, Rosen, SD, Camici, PG, et al. Regional myocardial blood flow redistribution as a cause of postprandial angina pectoris. Circulation 1998; 97:1144.

43. Constant, J. The clinical diagnosis of nonanginal chest pain: the differentiation of angina from nonanginal chest pain by history. Clin Cardiol 1983; 6:11.

44. Cook, DG, Shaper, AG. Breathlessness, angina pectoris and coronary artery disease. Am J Cardiol 1989; 63:921.

45. Kumar P, Clark M. Clinical Medicine, fifth edition.

46. Braunwald E: Unstable angina: a classification. Circulation 1989; 80: 410-414.

47. Hamm C, Braunwald E: A classification of unstable anginarevisited. Circulation 2000; 102: 118-122.

48. Calvin JE, Klein LW, Vandenberg BJ, et al. Risk stratification in unstable angina: prospective validation of the Braunwald classification.*JAMA.*1995;273:136–141.

49. Miltenburg-van Zijl AJ, Simoons ML, Veerhoek RJ, et al. Incidence and follow-up of Braunwald subgroups in unstable angina pectoris. *J Am Coll Cardiol.* 1995;25:1286–1292.

50. van Domburg RT, van Miltenburg-van Zijl AJ, Veerhoek RJ, et al. Unstable angina: good long-term outcome after a complicated early course. *J Am Coll Cardiol.* 1998;31:1534–1539.

51. Rizik, DG, Healy, S, Margulis, A, et al. A new clinical classification for hospital prognosis of unstable angina pectoris. Am J Cardiol 1995; 75:993.

52. Goldberger, AL. Clinical Electrocardiography: A Simplified Approach, 6th ed, Mosby Year Book, St Louis, 1998.

53. Joel WH, James TN, Cardiology, ch:3, Exercise Stress Testing, Maryland: Williams& wilkins 1998 p:83-86

54. Hauser, A, Gangadharan, V, Ramos, R, et. al. Sequence of mechanical, electrocardiographic and clinical effects of repeated coronary occlusion in human beings: Echocardiographic observations during coronary angioplasty. J Am Coll Cardiol 1985; 5:193.

55. Iskandrian, AS, Verani, MS, Heo, J. Pharmacologic stress testing: Mechanism of action, hemodynamic responses, and results in detection of coronary artery disease. J Nucl Cardiol 1994; 1:94.

56. Beller, GA, Zaret, BL. Contributions of nuclear cardiology to diagnosis and prognosis of patients with coronary artery disease. Circulation 2000; 101:1465.

57. Iskandrian, AS, Verani, MS, Heo, J. Pharmacologic stress testing: Mechanism of action, hemodynamic responses, and results in detection of coronary artery disease. J Nucl Cardiol 1994; 1:94.

58. Scanlon, PJ, Faxon, DP, Audet, A-M, et al. ACC/AHA guidelines for coronary angiography: Executive summary and recommendations. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on coronary angiography. Circulation 1999; 99:2345.

59. Armstrong, PW, Fu, Y, Chang, W-C, et al, for the GUSTO-IIb Investigators. Acute coronary syndromes in the GUSTO-IIb trial: Prognostic insights and impact of recurrent ischemia. Circulation 1998; 98:1860.

60. Coronary Revascularisation in the management of stable angina pectoris, SIGN publication no.32,1998.**Intercolleg**

61. Owa M, Origasa H, Saito M. Predictive validity of the Braunwald classification of unstable angina for angiographic findings, short-term prognosis, and treatment selection. *Angiology.* 1997;48:663–670.

62. Waller, B, Palumbo, P, Roberts, W. Status of the coronary arteries at necropsy in diabetes mellitus with onset after age 30 years. Am J Med 1980; 69:498.

63. Pajunen, P, Nieminen, MS, Taskinen, MR, et al. Quantitative comparison of angiographic characteristics of coronary artery disease in patients with noninsulin-dependent diabetes mellitus compared with matched nondiabetic control subjects. Am J Cardiol 1997; 80:550.

64. Parker, JO. Nitrates and angina pectoris. Am J Cardiol 1993; 72:3C.

65. Abrams, J. Nitroglycerin and long-acting nitrates in clinical practice. Am J Med 1983; 74:85

66. Depelchin, P, Sobolski, J, Jottrand, M, Flament, C. Secondary prevention after myocardial infarction: Effects of beta blocking agents and calcium antagonists. Cardiovasc Drugs Ther 1988; 2:139

67. Braunwald, E. Mechanism of action of calcium-channel-blocking agents. N Engl J Med 1982; 307:1618

68. RITA Trial Participants. Coronary angioplasty versus coronary artery bypass surgery: The Randomised Intervention Treatment of Angina (RITA) trial. Lancet 1993; 341:573.

69. Ryan, TJ, Faxon, DP, Gunnar, RM, et al. Guidelines for percutaneous transluminal coronary angioplasty: A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Transluminal Angioplasty). Circulation 1988; 78:486.

70. Alderman, EL, Bourassa, MG, Cohen, LS, et al. Ten-year follow-up of survival and myocardial infarction in the randomized coronary artery surgery study. Circulation 1990; 82:1629.

71. Ben-Hamda K, Gharbi M, Hendiri T, et al. Correlation of clinical and angiographic morphology in unstable angina,Tunis Med. 2004 Jan;82 Suppl 1:164-75.

72. Calton R, Satija T, et al. Correlation of Braunwald's clinical classification of unstable angina pectoris with angiographic extent of disease, lesion morphology and intra-luminal thrombus. Indian Heart J. 1998 May-Jun;50(3):300-6.

73. Pim J. de Feyter, Yukio Ozaki, et al. Ischemia-Related Lesion Characteristics in Patients With Stable or Unstable Angina, A Study With Intracoronary Angioscopy and Ultrasound. American Heart Association, Circulation. 1995;92:1408-1413.

74. Stylianos A. Paraskevaidis, et al. Unstable Angina., Angiographic Morphology of the Atherosclerotic Lesion and Clinical Outcome. Hellenic J Cardiol 43:189-194,2002.

75. Pajunen, P, Nieminen, MS, Taskinen, MR, et al. Quantitative comparison of angiographic characteristics of coronary artery disease in patients with noninsulin-dependent diabetes mellitus compared with matched nondiabetic control subjects. Am J Cardiol 1997; 80:550.

76. Pajunen, P, Taskinen, MR, Nieminen, MS, Syvanne, M. Angiographic severity and extent of coronary artery disease in patients with type 1 diabetes mellitus. Am J Cardiol 2000; 86:1080.

77. 10. Stein, B, Weintraub, W, King, S. Influence of diabetes mellitus on early and late outcome after percutaneous transluminal coronary angioplasty. Circulation 1995; 91:979.

78. Granger, C, Califf, R, Young, S, et al. Outcome of patients with diabetes mellitus and acute myocardial infarction treated with thrombolytic agents. J Am Coll Cardiol 1993; 21:920.

79. Mueller, HS, Braunwald, E, and the TIMI Investigators Predictors of early morbidity and mortality after thrombolytic therapy of acute myocardial infarction. Analysis of patient subgroups in the Thrombolysis in Myocardial Infarction (TIMI) trial, phase II. Circulation 1992; 85:1254.

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

81. Norell, M, Lythall, D, Cheng, A, et al. Limited value of the resting electrocardiogram in assessing patients with recent onset chest pain: Lessons from a chest pain clinic. Br Heart J 1992; 67:53.

82. Lee, TH, Cook, F, Weisberg, M, et al. Acute chest pain in the emergency room. Identification and examination of low-risk patients. Arch Intern Med 1985; 145:65.