CARDIOVASCULAR RISK FACTOR PROFILES OF BLACK AFRICANS UNDERGOING CORONARY ANGIOGRAPHY AT THE NAIROBI HOSPITAL

A DISSERTATION SUBMITTED

IN PART FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF

THE DEGREE OF MASTER OF MEDICINE IN INTERNAL MEDICINE BY:

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DECLARATION

I certify that this dissertation is my original work and has not been presented for a degree at any other university.

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To Joseph, Eunice, Jimmy, Maryanne and David.

TABLE OF CONTENTS

LIST OF ILLUSTRATIONS

FIGURES: **Page**

TABLES:

LIST OF ABBREVIATIONS

BMI	Body Mass Index
CA	Coronary Angiogram
CAD	Coronary Artery Disease
CATH LAB	Cardiac Catheterization Laboratory
CHD	Coronary Heart Disease
DBP	Diastolic Blood Pressure
DM	Diabetes Mellitus
DOB	Date of Birth
ECG	Electrocardiogram
EF	Ejection Fraction
EST	Exercise Stress Test
HDL	High Density Lipoprotein
IGT	Impaired Glucose Tolerance
IVS	Interventricular Septum
KNH	Kenyatta National Hospital
LAD	Left Anterior Descending Artery
LCx	Left Circumflex Coronary Artery
LDL	Low Density Lipoprotein
LMCA	Left Main Coronary Artery
MMed	Masters Degree in Medicine
OHA	Oral Hypoglycaemic Agents
OMB	Obtuse Marginal Branch
PAI	Plasminogen Activator Inhibitor
PCAD	Premature Coronary Artery Disease
PCI	Percutaneous Coronary Intervention
PDA	Posterior Descending Artery
PTCA	Percutaneous Transluminal Coronary Angioplasty
RCA	Right Coronary Artery
SBP	Systolic Blood Pressure
TG	Triglycerides
WC	Waist Circumference
WHO	World Health Organization
WHR	Waist to Hip Ratio

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1.0 ABSTRACT

1.1 BACKGROUND

Coronary artery disease is a growing epidemic on the African Continent. Indeed, over the last thirty years morbidity and mortality due to cardiovascular disease have increased rapidly in developing countries.[1] The risk factors that have been shown to influence the development of CAD in white populations are hypertension, hypercholesterolemia, low levels of high-density lipoprotein (HDL) cholesterol, cigarette smoking, diabetes mellitus, age, and male gender. Moreover, the large variation in the average extent of coronary atherosclerosis among black populations, as well as among white population, suggests that interplay between genetic factors and environmental factors might determine the severity and extent of atherosclerotic lesions within both groups.[2] It remains uncertain whether the risk factors identified as contributing to CAD in white populations contribute to a similar extent to CAD incidence in black populations.[3] No data of the local population exists that is based on the Coronary Angiogram (CA), the current "Gold Standard" diagnostic test for Coronary Artery Disease.

1.2 OBJECTIVES

The aim of the study was to analyze the relationship of conventional cardiovascular risk factors with presence of Coronary Artery Disease (CAD) in Black Africans.

Specifically the Study sought:

i) To describe the prevalence of conventional cardiovascular risk factors in Black Africans with CAD as documented on coronary angiography at the Nairobi Hospital Cath Lab.

ii) To describe the prevalence of the same risk factors in Black Africans with normal coronary arteries as documented on CA at the Cath Lab.

iii) To compare the prevalence of the said risk factors between the two groups.

1.3 DESIGN / METHODS

Dual-armed study, consisting of a retrospective, comparative arm; and a prospective, comparative one, involving questionnaires, and anthropometric measurements.

1.4 SETTING

The Cardiac Catheterization Laboratory (Cath Lab) of the Nairobi Hospital.

The retrospective arm was based on the analysis of data obtained from inception of the Cath Lab in April 1996 to Dec 2001; the prospective one was based on the collection and analysis of data obtained over a six-month study period, from October 2002 to March 2003.

1.5 SUBJECTS

All Black Africans who underwent coronary angiography at the Cath Lab of the Nairobi Hospital.

1.6 OUTCOME MEASURES

The conventional risk factors analyzed were: age, male gender, hypertension, obesity, smoking, diabetes mellitus, dyslipidemia, alcohol use and IVS hypertrophy, as a marker of LVH.

1.7 RESULTS

In total 169 patients fulfilled the inclusion criteria: 144 in the retrospective arm and 25 in the prospective. The larger retrospective arm showed that the group with CAD, compared to the Normal group, was significantly older, with a higher mean age of 54.4 years compared to 49.8 years (P=0.005); had significantly more males, with a male to female ratio of 5.5:1 compared to 2.3:1 (P=0.045); had a very significantly larger proportion of diabetics (38.5% compared to 12%, P=0.0002), and also had a significantly larger proportion of patients with dyslipidemia (67.3% compared to 35.9%, P=0.0003). The percentage of hypertensives was high in both groups, with 65.4% in the CAD group and 62% in the Normal group being hypertensive (P=0.68). The percentage of smokers was small in both groups, being 15.4% and 13% respectively. Smoking, increased BMI, alcohol use, and increased IVS were found each found to be distributed equally in both groups. In addition, the WHR and WC each did not differ significantly between the two groups studied.

1.8 CONCLUSIONS

The risk factors found to be most strongly associated with presence of angiographically-detected CAD in the population studied were Diabetes Mellitus, Dyslipidemia, Age and Male Gender. There was a high prevalence of hypertension, with equal distribution in both groups under study; hence this risk factor was not discriminatory for CAD. There was a low prevalence of cigarette smoking in this particular study; it was not predictive of CAD.

2.0 LITERATURE REVIEW

2.1 Coronary Risk Factors: Varying Scenarios

While Coronary Artery Disease is the leading cause of death among United States Blacks,[4] it has traditionally been known to be a much less significant cause of morbidity and mortality in developing countries, with a low prevalence in Black Africa[5].

In Black Africa in the years 1950 to 1980, the incidence of CAD was mostly reported as being less than 0.5% of all cardiovascular disease.[6] In Kenya there was one case of autopsy-confirmed myocardial infarction among 2000 adult admissions to a secondary referral hospital in 1960.[7]

Some data suggest that the incidence of CAD may be increasing in some black populations in developing countries as socioeconomic change occurs. While the 1990 estimate for the mortality in men and women due to ischemic heart disease in Sub-Sahara Africa was 1,900,000 and 1,200,000 respectively, the projected increase in the mortality to the year 2020 is 144% and 116% respectively.[1]

It remains uncertain whether the risk factors identified as contributing to CAD in white populations contribute to a similar extent.to its incidence in black populations.[3]

The risk factors that have been shown to influence the development of CAD in white populations are hypertension, hypercholesterolemia, low levels of high-density lipoprotein (HDL) cholesterol, cigarette smoking, diabetes mellitus, age, and male gender.

Moreover, the large variation in the average extent of coronary atherosclerosis among black populations, as well as among white population, suggests that interplay between genetic factors and environmental factors might determine the severity and extent of atherosclerotic lesions within both groups.[2]

Earlier evaluations of the consequences of culture change have suggested that among rural residents in developed countries, urbanization[8] and access to higher social status[9] might result in increased CAD mortality. Some of the life-style changes that accompany certain patterns of modernization can contribute to an increase in cardiovascular risk factors. In black underdeveloped populations, this may contribute to increased CAD risk.[4] This is illustrated by a recent study in an urban Nigerian population, which suggested that the absolute cardiovascular risk remains low. This could possibly be due to an aversion to smoking and heavy alcohol consumption, as well as consumption of a high-fiber low calorie diet, and generalized high physical activity. There appears, however, to be a growing trend towards the diets of the Western world and ischemic heart disease may become a problem.[1] Indeed, in developing countries there is a looming epidemic of CHD,[10 11] which requires proactive analysis and prevention.

2.2 Conventional Risk Factors

Age and Male Gender: Though there is a lack of reliable data from blacks in underdeveloped countries, CAD incidence, prevalence and mortality have been found to increase with age in black US populations,[4] and data from South Africa suggests a gradual increase in CAD with age.[12]

Data from the Caribbean suggests a higher mortality in males than females.[13] But the International Atherosclerosis Project found little sex difference in advanced coronary lesions in any black group.[6]

Hypertension: This is a significant, strong and independent risk factor for CAD. With regard to the prevalence of hypertension in developing black populations, there is an emerging picture with studies revealing significantly higher blood pressures in urban subjects of both sexes than rural subjects,[14] and in other conditions of psychosocial stress such as low income and poor conditions of employment.[15]

Dyslipidemia: Elevated total and low-density cholesterol are powerful risk factors for CAD in white Caucasians. A strong inverse relationship between HDL-C and the risk of CAD exists. Some populations in transition tend to develop increased triglycerides levels and low HDL-C patterns, while others (i.e. rural-urban migration) have elevated LDL and total serum cholesterol. [16]

Tobacco: There is currently strong data to suggest a causal relationship between tobacco use and development of coronary artery disease.[17] Cigarette smoking doubles the risk of developing CAD, and approximately 30 percent of CAD deaths are attributable in a dose-related manner to smoking. 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.[18, 19] Moreover, smoking rates in "transitional" countries are increasing in contrast to the decreasing rates in most industrialized countries.[20]

Diabetes Mellitus (DM) and Impaired Glucose Tolerance (IGT): In two clinical series of East African diabetics (one of which was in Kenya, the other in Tanzania)[21, 22] ECG abnormalities suggestive of ischemia were found in 15.6% of 198 subjects and 21.6% of 139 subjects; in the same groups the prevalence of chest pain was 4.3% and 15.2%, respectively. Obesity is commonly associated with diabetes.

Also IGT is another strong and independent risk factor for CAD. Insulin is released in response to elevated glucose levels and insulin resistance is a characteristic feature of abdominal obesity, IGT and DM Type II, as part of the metabolic syndrome. Insulin resistance is associated with high triglycerides and low HDL-C, and with increased levels of plasminogen activator inhibitor-1 (PAI-1) which links it to impaired fibrinolysis.[23]

Obesity: Currently estimated at about 26% among urban South African Blacks, obesity is associated with increased prevalence of cardiovascular risk factors (hypertension, dyslipidemia, and DM), and increased morbidity and mortality from CAD.[24]

Physical inactivity is an independent risk factor for CAD and is an example of adverse lifestyle changes that accompany industrialization and urbanization. It predisposes to obesity, hypertension, glucose intolerance, hypertriglyceridemia and low HDL-C levels.[9]

2.3 Emerging Risk Factors and Associations

Other risk factors are being identified as definite or possible contributors to CAD risk in whites. These include:

Left Ventricular Hypertrophy (LVH): Data, primarily from the Framingham Heart Study, have identified electrocardiographic left ventricular hypertrophy as a blood pressure-independent risk for sudden cardiac death,[25 26] acute myocardial infarction,[27] and other cardiovascular morbidity and mortality.[28] LVH is a common finding in patients with hypertension and can be diagnosed either by ECG or by echocardiography.[29 30] The latter is the procedure of choice, since the sensitivity of the different ECG criteria may be as low as 7 to 35 percent with mild LVH and only 10 to 50 percent with moderate to severe disease.[31] Nevertheless, if echocardiography is unavailable or too expensive, appropriate ECG criteria can be used to detect increased LV mass.[32]

Lipoprotein (a) (Lp(a)): a genetically determined, plasminogen-like apolipoprotein; probably related to both atherogenesis and thrombogenesis.[33 34]

Homocysteine: Moderate hyperhomocysteinemia is associated with development of premature atherosclerosis, and with increased risk for thrombosis.[35] A significant inverse association has been reported between homocysteine levels and plasma folate levels.[36]

Coagulation Markers: some (fibrinogen, Factor V Leiden, Factor VII, von Willebrand factor), and fibrinolytic markers (TPA, PAI-1) are associated with CAD. [37 38]

Dietary factors: Aspects of the *nutrition transition* are the increased availability of cheap, hardened vegetable oils and fats; increased consumption of energy-dense foods poor in dietary fiber and several micronutrients; [39 40]a shift from plant to animal protein; and shifts towards refined carbohydrates. The former have adverse effects on serum cholesterol while the excessive intake of total energy as refined sugars predisposes to IGT.

Alcohol: The inverse association between moderate consumption of ethanol and CAD has been well established.[41 42 43] Ethanol increases HDL-C levels and inhibits postprandial hyperlipidemia.[44]

Although ethanol in low doses causes a mild acute drop in blood pressure (by decreasing myocardial contractility and causing peripheral vasodilation), the consumption of three or more drinks per day results in a dose-dependent increase in blood pressure. As a result, heavy drinking is an important contributor to hypertension.[45]

Socio-Economic Factors: This refers to factors related to social and cultural conditions and economic development. CAD appears to be strongly related to these conditions, as is manifested in the West by the declines in the rates of CAD in parallel to economic development.[46] In Africa, however, given the lifestyle changes associated with affluence, CAD could still have a direct positive relationship with socio-economic status.[47]

Psychosocial Factors: Mental stress has been associated with an increased risk of subsequent CAD events.[48]

Sleep: The quality, rhythms and patterns may influence the epidemiology of myocardial infarction, perhaps by influencing stress levels.[49]

Genetic Markers: Various genes are associated with elevated blood pressure, diabetes, abnormalities in coagulation, lipids, and homocysteine.[50]

Infection, Inflammation and Atherosclerosis: There is an association between CAD and serological markers of infection by Chlamydia pneumonia, Helicobacter pylori, cytomegalovirus and periodontal disease.[51]

2.4 Some Recent Previous Studies

In a local, hospital-based study on hypertensive patients, the most prevalent cardiovascular risk factors other than hypertension were electrocardiographic left ventricular hypertrophy (31.7%), obesity (28.3%) and hypercholesterolemia (28.3%).[52]

A more recently-published population-based study in Nigeria revealed the following prevalence of risk factors in the random sample population in males and females respectively: cigarettes (>10 sticks/day) 0%; alcohol intake 5.4% in males, 2.8% in females; self reported diabetes 1.8%, 2.8%; obesity 21%, 28%; hypertension 16.4%, 25% and cholesterol >200mg/dl 6.4%, 13.9%. Multiple risk factors occurred infrequently in individual subjects. Only five men (4.5%) exhibited two risk factors and only one (0.9%) exhibited three risk factors apart from the gender.[53]

A local study in 2001 on the cardiovascular risk factors among diabetics at the Kenyatta National Hospital (KNH) showed that there is a high prevalence of vascular risk factors, frequently multiple, in patients with type 2 diabetes seen at KNH.[54]

3.0 RATIONALE AND JUSTIFICATION

Coronary artery disease is a growing epidemic on the African Continent. Indeed, over the last thirty years morbidity and mortality due to cardiovascular disease have increased rapidly in developing countries.[1] This phenomenon has raised concern in the African medical fraternity.

Since the setting up of the Cardiac Catheterization Lab (Cath Lab) at the Nairobi Hospital in 1996, hundreds of patients have been subjected to numerous interventions, [55] including cardiac catheterization, coronary angiography, and other percutaneous coronary interventions (PCIs). A wealth of data has been acquired from these procedures, which had previously not been analyzed as thoroughly as this paper has. This data, and its analysis, is valuable in elucidating peculiarities in cardiovascular risk in the local population.

This is the first study of its kind, in the region of East and Central Africa, which is based on the Coronary Angiogram (CA), the current "Gold Standard" diagnostic test for CAD. It sought to identify those cardiovascular risk factors that are particularly associated with the presence of Coronary Artery Disease (CAD) in Black Africans in Kenya. There is no such data for the local population.

The study was dual armed: While the retrospective study provided important information on the prevalence of cardiovascular risk factors in patients with and without CAD, there remained the real possibilities of missing information and inaccuracy of data concerning the studied patients, especially on issues such as detailed history of smoking habits.

The prospective arm, in a similar format of comparisons, but complete with questionnaire and a more thorough anthropometric examination, strengthened the retrospective one by overcoming the lack of data. Moreover, the results of the prospective arm served to corroborate or not, the results of the retrospective one, thus adding value to, or caution in the interpretation of the results.

Although not representative of the entire Black population in Kenya, the sample under study served as a surrogate marker. The results of the study gave useful insights into a population with angiographically-assessed CAD. Development of health policy will benefit from studies such as this, and others that may arise from it, to further examine and estimate prevalence of particular risk factors.

4.0 OBJECTIVES

4.1 Principal Objective

To analyze the relationship of conventional cardiovascular risk factors with Coronary Artery Disease (CAD) in Black Africans.

4.2 Specific Objectives

i) To describe the prevalence of conventional cardiovascular risk factors in Black Africans *with CAD* as documented on coronary angiography at the Nairobi Hospital Cath Lab.

ii) To describe the prevalence of the same risk factors in Black Africans with *normal coronary arteries* as documented on coronary angiography at the Cath Lab.[56]

iii) To *compare* the prevalence of the said risk factors between the two groups.

The conventional risk factors analyzed were: *age, male gender, hypertension, obesity, smoking, diabetes mellitus, dyslipidemia*, *alcohol use* and *LVH.*

5.0 STUDY DESIGN AND METHODOLOGY

5.1 Study Design

This was a comparative study consisting of a retrospective and a prospective arm.

The ***retrospective arm*** was based on the analysis of data obtained from all Black African patients who underwent coronary angiography at the Cath Lab of the Nairobi Hospital between April 1996 and December 2001; ***the prospective*** one was based on the collection and analysis of data obtained from all Black African patients who underwent a CA over a six-month study period, from October 2002 to March 2003.

5.2 Inclusion / Exclusion Criteria

i) Inclusion Criteria

- To have undergone a coronary angiogram at the Nairobi Hospital Cath Lab.
- Black Race.
- Consent - by the cardiologist to review patients' files.
  - informed consent by the patient for the interview (prospective arm).

ii) Exclusion Criteria

- Non-Black race.
- Age less than 18 years of age.
- Refusal to give consent.

5.3 Data Collection

The conventional risk factors analyzed in the retrospective and the prospective arms of the study were: *age, male gender, hypertension, obesity, smoking, diabetes mellitus and dyslipidemia.* Also, *alcohol use* and *IVS thickness* - as a surrogate of *LVH* - were studied.

a) Retrospective Arm

Case histories were studied from the files, and patient data obtained, including the findings on physical examination and laboratory tests.

The following data, as determined by the referring doctor, were obtained from the files and a **Pro Forma (see Appendix 11.2)** filled in:

i) Name of the patient

ii) Age

iii) Sex

iv) Tobacco use

v) Use of alcohol

vi) Hypertensive status

vii) Body mass index (BMI)

viii) Diabetic status

ix) Dyslipidemic status

x) ECG evidence of LVH

xi) Echocardiographic findings

xii) Results of Coronary Angiogram

b) Prospective Arm

Every morning the list of names of patients who had been booked for a coronary angiogram were obtained from the Cath Lab of the Nairobi Hospital, together with the name of the referring cardiologist or clinic. The patients were interviewed before or after the procedure, either at their respective clinics or at the Nairobi Hospital, and were invited to take part in the study. After informed consent, an investigator-administered questionnaire was filled in. Measurements of Waist Hip Ratio as well as BMI were taken, while ensuring at least six hours had elapsed after the angiogram, during which time the patient was to be in the supine position. The investigator carried out ECG and Echo monitoring of the patients, and participated in the coronary angiograms. Diagnoses and other data were obtained from the hospital and clinic notes.

See Appendix 11.4 for the **questionnaire** used in the prospective arm.

5.4 Anthropometric and Laboratory Methods

(See Appendix 11.1 for the Defining Criteria of the Variables)

5.4.1 Body Mass Index (BMI)

For the *retrospective* study the readings immediately prior to the CA, or the highest reading in the previous six months, were used.

For the *prospective* the measurement was done as follows:

Standing height was measured with the subject in bare feet, back square against the wall and eyes looking straight ahead. A setsquare resting on the scalp and a tape measurement from the wall was used to measure the height to the nearest 0.5 cm.

Weight was measured without shoes, in light vestments, using a platform scale, to the nearest 200 grams. The scale was standardized to 0 before each use.[57]

5.4.2 Measurement of Waist Hip Circumference Ratio (WHR)

This is considered to be a better marker for the metabolic hazards of obesity, including lipid levels and insulin resistance[58] but not all patients in the *retrospective study* had the required measurements.

In the *prospective study* it was measured as follows:

The waist circumference in centimeters was taken as the narrowest circumference between the lowest rib and the top of the pelvis, measured in the horizontal plane at the end of a gentle expiration, with the subject standing. The hip circumference in centimeters was taken as the maximum circumference in the horizontal plane, measured at the level of the greater trochanters of the femurs.[59]

The WHR was calculated as the ratio of the former to the latter. The waist circumference and the WHR were classified as per the Dietary Guidelines for Americans.[60 61]

5.5 Assessment of the other Study Variables

(See Appendix 11.1 for the Defining Criteria of the Variables)

5.5.1 Tobacco Use

The following classification was used:

Never smoked, quit smoking (last smoked more than one year ago), *current smoker* (last smoked within the last year).[18]

For the *prospective arm* the detailed questionnaire provided sufficient data to calculate the number of pack years.

5.5.2 Use of Alcohol

A distinction was made by the referring doctors between *abstinence* from alcohol, *mild, moderate*, and *heavy drinking* or *alcohol abuse*. (See Appendix.) Moderate drinking has been quantified as 3 to 9 drinks per week.[62] In this study the definitions of the National Institute of Alcohol Abuse and Alcoholism (NIAAA) were adopted. This distinction was adopted for the *retrospective* study, while a more accurate quantification was used for the *prospective* study, by interviewing on the type(s), quantity and frequency of alcoholic drink(s) used.

5.5.3 Hypertensive Status

The patients were already classified by their physicians as hypertensive or not, and, if hypertensive, were on medication. *This applied for both arms.*

WHO criteria were followed for a diagnosis of hypertension: Systolic Blood Pressure (SBP) >/=140 mmHg and Diastolic Blood Pressure (DBP) >/=90 mmHg, or the current use of antihypertensive therapy.[63]

5.5.4 Diabetic Status

The investigator followed the diagnosis made by the referring doctor as to the diabetic or non-diabetic condition of the patient. *This applied for both arms.*

The current criteria were used in defining diabetes mellitus (see Appendix 11.1 and discussion).

5.5.5 Dyslipidemia

The established status of the patient (dyslipidemic or not), and pre-treatment serum lipid values was used where available. (See Appendix 11.1) *This applied for both arms.*

5.5.6 Echocardiography

The investigator (under guidance) participated in the echocardiogram studies in the prospective arm, and, for the retrospective arm, evaluated the reports. Important features and pathological changes on Echocardiography immediately prior to the CA were noted. They included:

1. The dimensions of the Interventricular Septum during diastole (IVS): The normal range is 0.6-1.1 cm with a mean of 0.9 cm. [64]
2. Ejection fraction.
3. Diastolic dysfunction: Inversion of the ratio (from normal positive to a negative) of the mitral valve inflow rates during early and late filling of the left ventricle measured by Doppler ultasound.
4. Others, e.g. LV wall hypo- or akinesis; LV wall aneurysm, etc.

NB the IVS was used as a marker of LVH, a CAD risk factor.

5.5.7 Results of the Coronary Angiogram

In the *prospective arm* the investigator participated in the CA procedures by the cardiologists.

The results of the CA (normal / abnormal, diseased vessels and degree of stenosis) were noted.

Abnormal was normally taken as >/=50% stenosis on one or more of the coronary arteries, judged by the standard method for interpreting the presence and severity of stenoses in the epicardial coronary arteries, which continues to be visual assessment or "eyeballing." Those arteries with less than 50 % are defined as *sub-critical.* [56]

During the analysis of the results, these patients with sub-critical stenosis were placed in the *Normal* group.

5.5.8 Pilot Studies

A pilot study was carried out for the retrospective arm, to assess availability of data, whereupon the need of a prospective arm was confirmed in order to elicit more complete data concerning given variables, e.g. smoking and alcohol use.

The questionnaire for the prospective arm was also subjected to a pilot study. This was to ensure the comprehensibility of the items, and to assess the time required to complete it.

5.6 Ethical Approval

Ethical approval was obtained from the Nairobi Hospital Education Committee.

5.7 Data Analysis

All data from the proforma documents and the questionnaires was initially processed using MS Access and MS Excel. It was analysed using SPSS 10.0 and EpiInfo 2002.

Continuous data was analyzed into means and categorical data into percentages, with the corresponding 95% confidence intervals. Comparisons of continuous data were made using the Student t Test, and those of categorical data using the Chi-square test or Fischer's exact test. Correlations between variables were tested using the Pearson correlation coefficient.

Prevalence rates of risk factors were calculated as percentages with 95% confidence intervals.

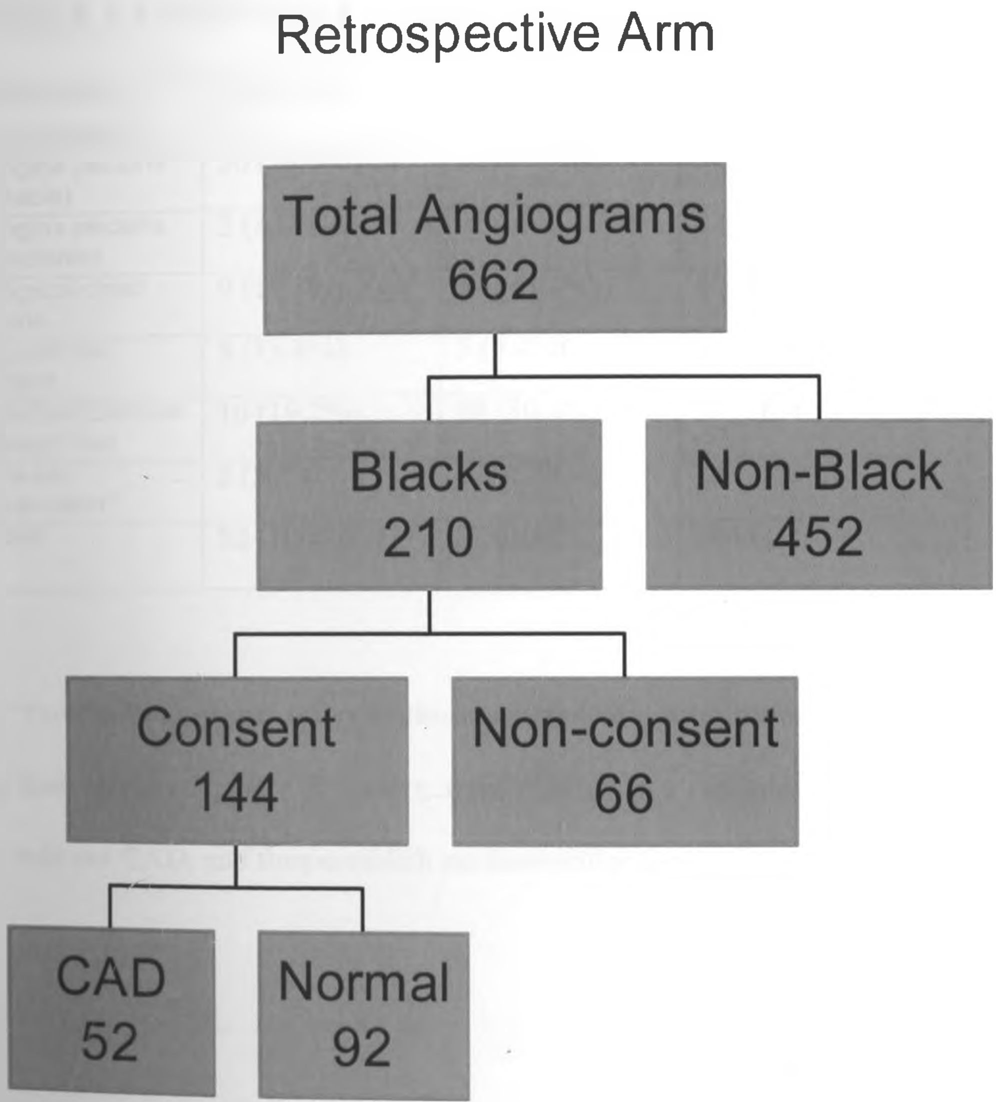
Statistical significance was defined as a two-tailed p value of less than or equal to 0.05 .

6.0 RESULTS

In total, 662 angiograms were carried out between 1996 and 2001 both inclusive. Four hundred and fifty-two were non-Black. Of the 210 Black patients, consent to review the files of patients was given by six out of the seven Consultants involved. Finally, therefore, 144 patients fulfilled the inclusion criteria and were included in the retrospective arm of the study. Of these, 52 had abnormal angiograms, 86 had normal studies, and 6 had sub-critical lesions. (See **Figure 1** on page 34 below.)

6.1 RESULTS OF THE RETROSPECTIVE ARM:

FIGURE 1: DISTRIBUTION OF CA PATIENTS IN RETROSPECTIVE ARM



An analysis of the presenting complaints and clinical events that prompted an investigative pathway culminating in a coronary angiogram study on the patients revealed the following for the retrospective arm:

TABLE 1: INDICATIONS FOR CA IN THE RETROSPECTIVE ARM

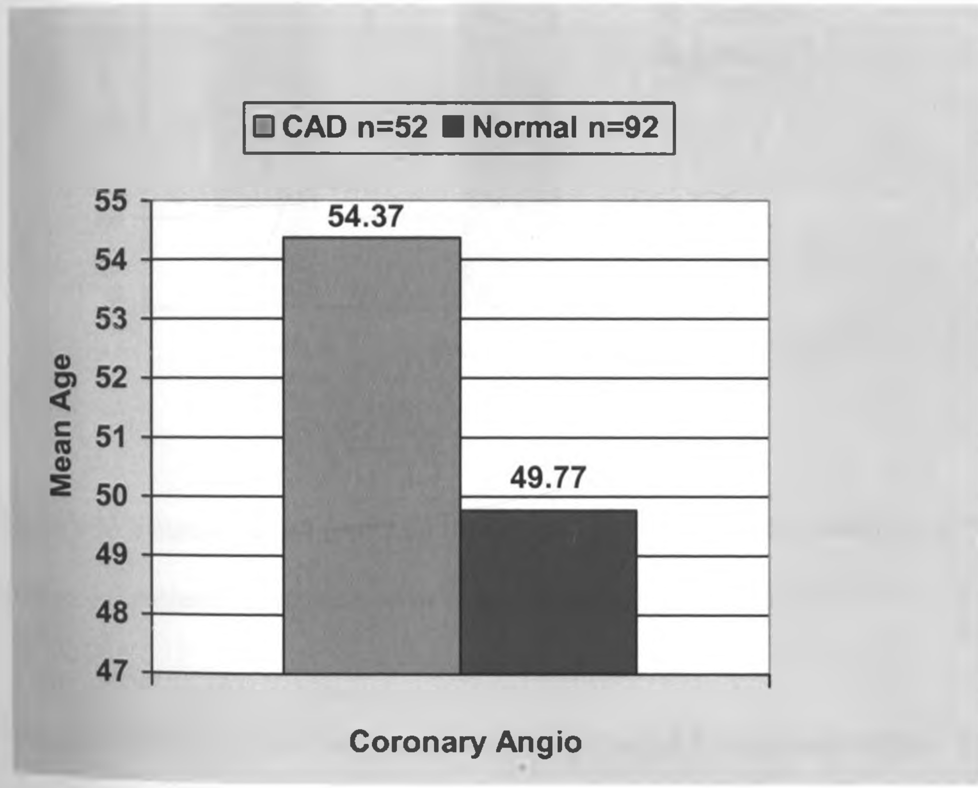
Presenting Complaints	Abnormal CA	Normal CA	Total
Angina pectoris (stable)	20 (38.5%)	12 (13.0%)	32 (22.2%)
Angina pectoris (unstable)	2 (3.8%)	(0%)	2 (1.4%)
Atypical chest pains	9 (17.3%)	31 (33.7%)	40 (27.8%)
Myocardial infarct	8 (15.4%)	5 (5.4%)	13 (9.0%)
Positive Exercise Stress Test	10 (19.2%)	28 (30.4%)	38 (26.4%)
Pre-Op Evaluation*	3 (5.8%)	16 (17.4%)	19 (13.2%)
Total	52 (100%)	92 (100%)	144 (100%)

* "Pre-Op Evaluation" refers to those patients who were scheduled for surgery and, due to their cardiovascular risk factors, were referred to a cardiologist and subjected to a CA to rule out CAD, and thus establish cardiovascular fitness for surgery.

AGE:

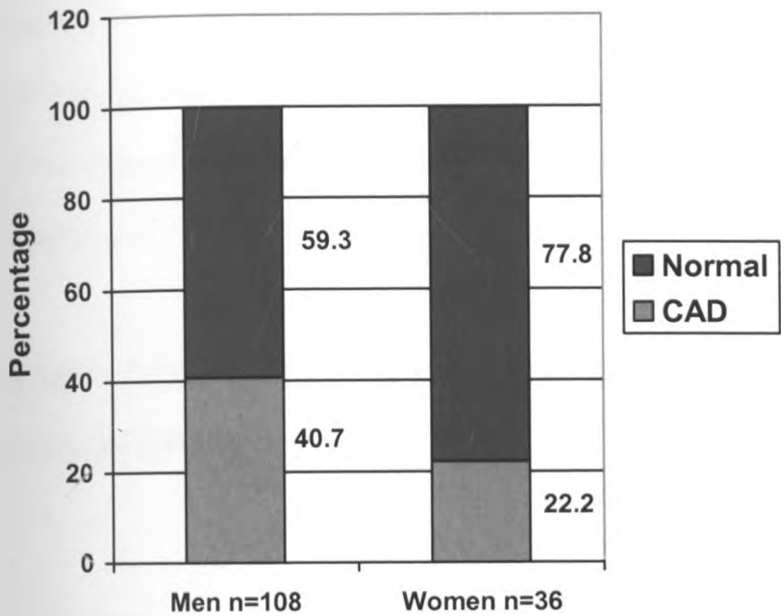
The mean age of those with diseased coronary arteries was 54.37 years, while that of those with normal coronaries was 49.77 years. This difference was statistically significant with a P = 0.05.

FIGURE 2: MEAN AGES OF CAD GROUP AND NORMAL GROUP (RETROSPECTIVE)



GENDER:

FIGURE 3: DISTRIBUTION OF CA RESULTS BY GENDER (RETROSPECTIVE)

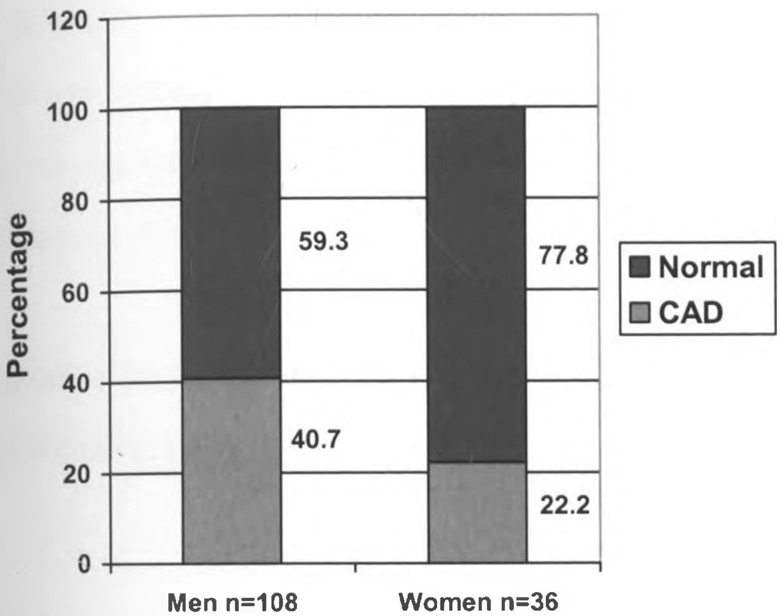


There was a statistically significant difference (P = 0.045) in the distribution of the sexes among the patients with diseased or non-stenosed coronary arteries:

More than 40% of all men who underwent a CA had abnormal coronaries as compared to some 22% of women who had an abnormal angiogram.

GENDER:

FIGURE 3: DISTRIBUTION OF CA RESULTS BY GENDER (RETROSPECTIVE)



There was a statistically significant difference (P = 0.045) in the distribution of the sexes among the patients with diseased or non-stenosed coronary arteries:

More than 40% of all men who underwent a CA had abnormal coronaries as compared to some 22% of women who had an abnormal angiogram.

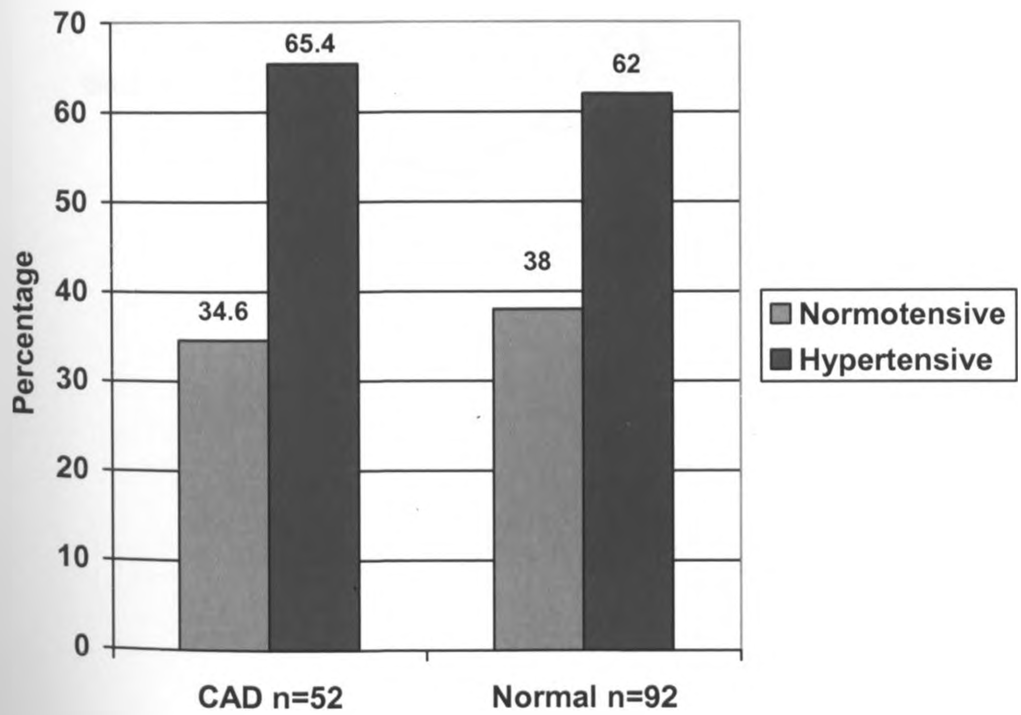
HYPERTENSION:

Hypertension was noted to be highly prevalent in both groups, and there was no statistical significance in the difference between the two groups. P = 0.68.

In total 36.8% of the patients were normotensive, 16% were in Stage I hypertension, 26.4% were in Stage II, and 20.8% were classified as Stage III hypertensives.

Also, the percentage of those with CAD did not differ statistically with the stage of the Hypertension (P = 0.75).

FIGURE 4: DISTRIBUTION OF HYPERTENSIVES IN CA GROUPS (RETROSPECTIVE)

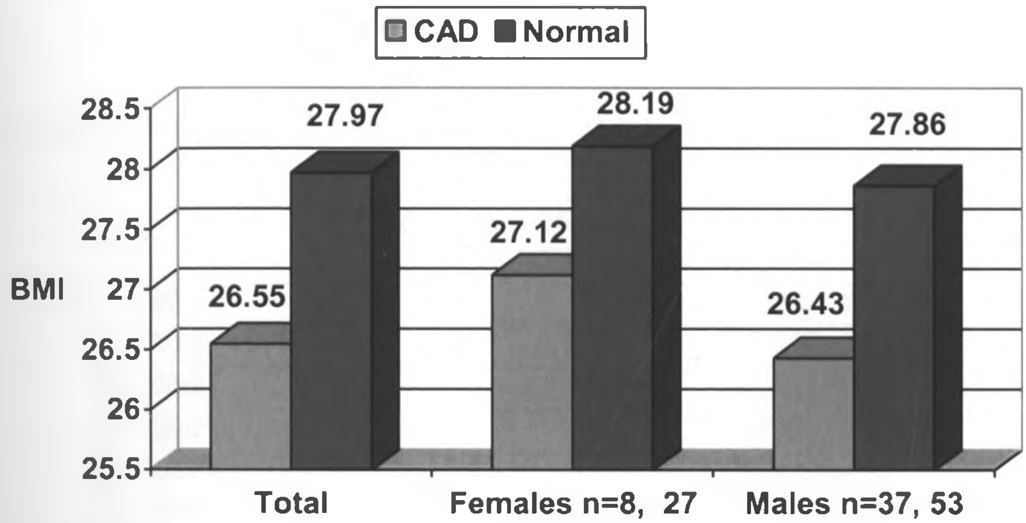


BMI:

There was no significant difference between the mean BMI of the two groups. P = 0.259

Sub-analysis by sex showed no significant difference, with P = 0.922.

FIGURE 5: BMI DISTRIBUTION OF CA PATIENTS (RETROSPECTIVE)

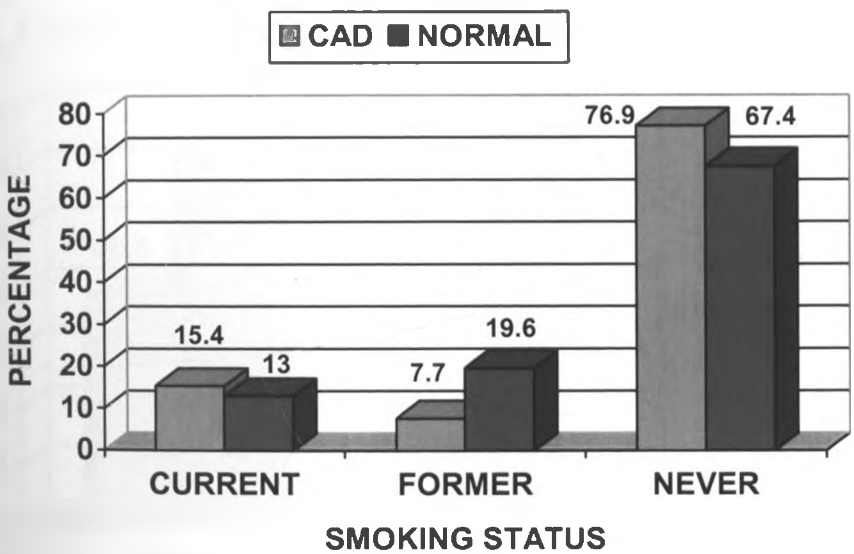


SMOKING:

There was no significant difference in the numbers of smokers and non-smokers between the two groups analyzed. P = 0.227.

Sub-analysis for women smokers and non-smokers did not reveal any statistically significant difference either. P = 0.739.

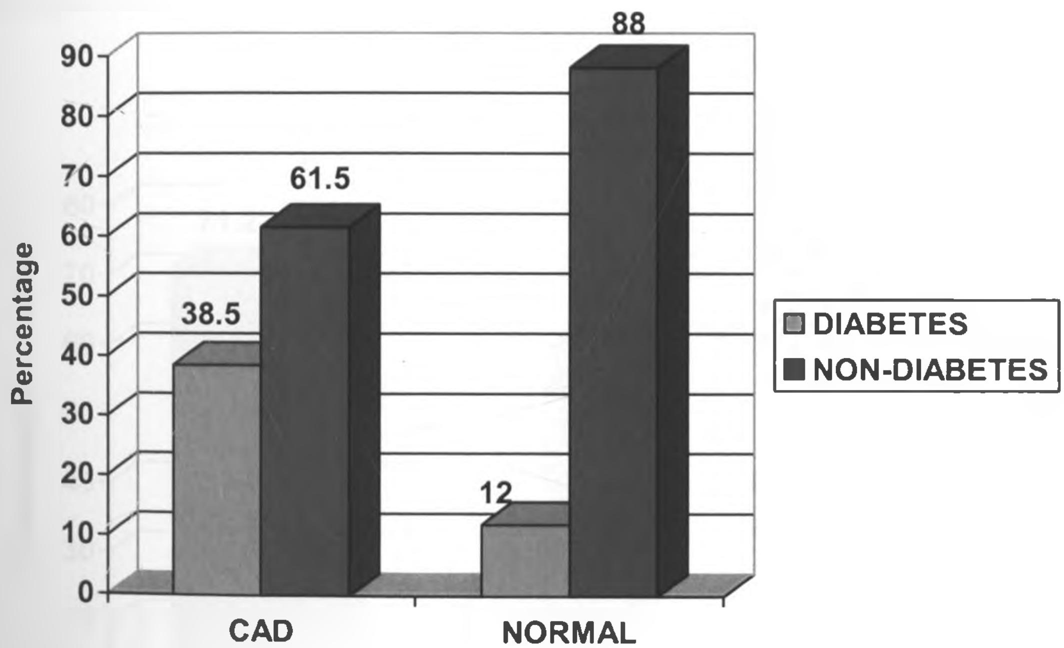
FIGURE 6: SMOKING STATUS OF CA PATIENTS (RETROSPECTIVE)



DIABETES:

A strong positive relationship was found between the presence of Diabetes Mellitus and the presence of Coronary Artery Disease. (All the diabetics except one suffered from Type II DM.) **P = 0.0002.**

FIGURE 7: DISTRIBUTION OF DIABETICS IN CA GROUPS (RETROSPECTIVE)

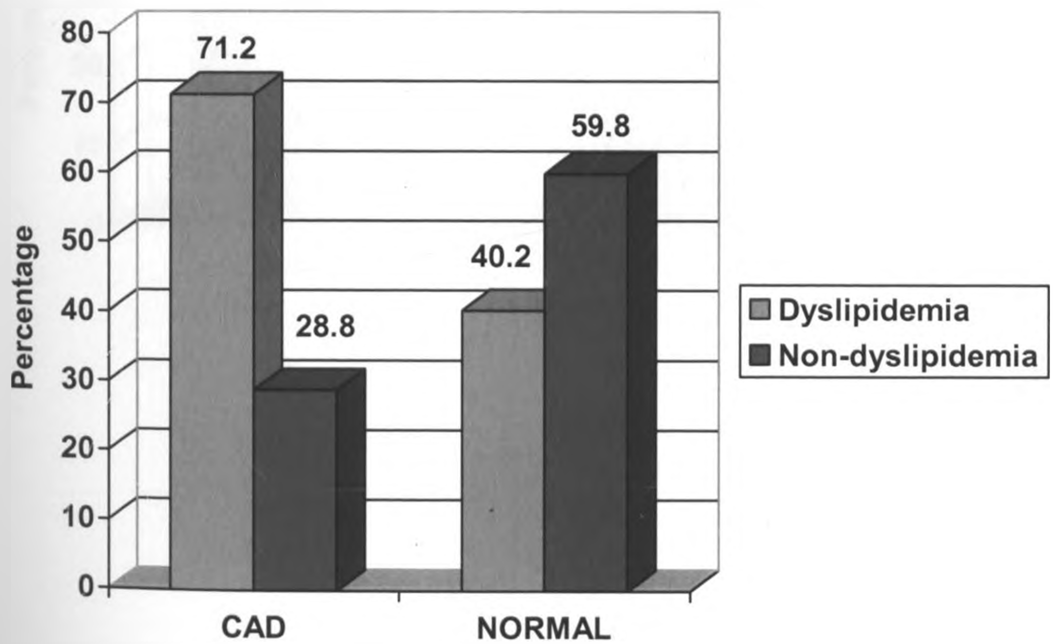


DYSLIPIDEMIA:

A very strong positive relationship was also found between the presence of dyslipidemia and coronary artery disease. **P = 0.0003.**

The various dyslipidemias are described below:

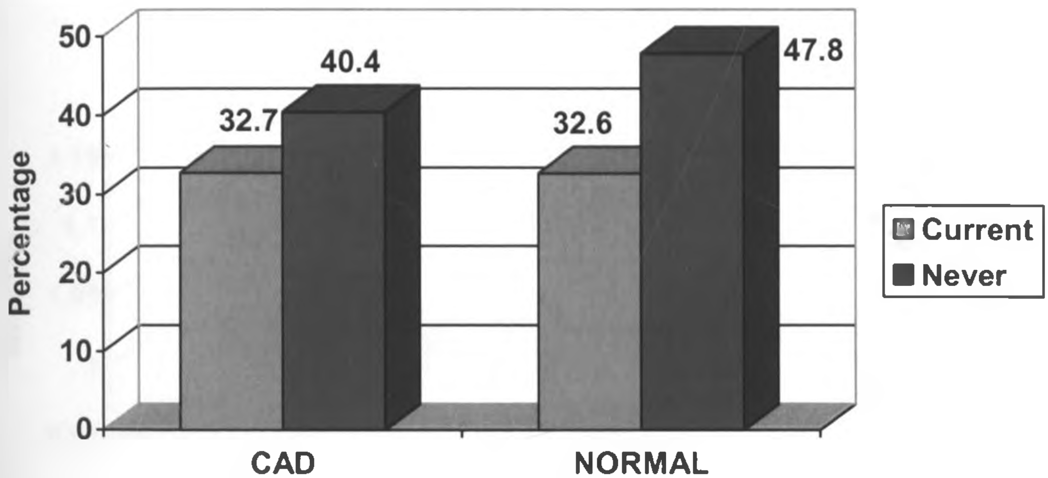
FIGURE 8: DISTRIBUTION OF PATIENTS WITH DYSLIPIDEMIA BY CA (RETROSPECTIVE)



ALCOHOL USE

The was no statistically significant difference in the status of alcohol consumption among the two groups. P = 0.67.

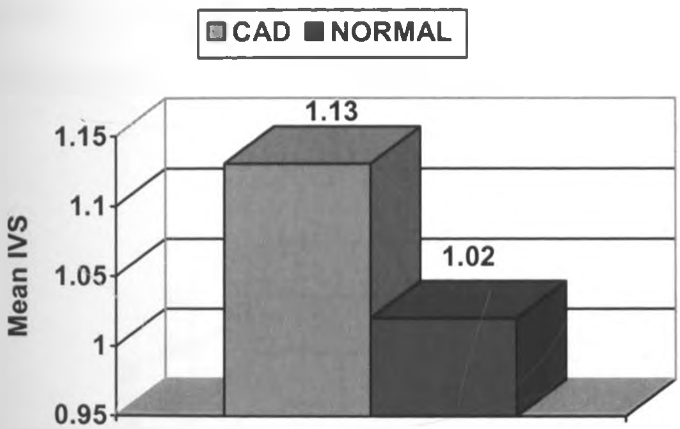
FIGURE 9: ALCOHOL STATUS OF CA PATIENTS (RETROSPECTIVE)



IVS:

There was a difference between the mean IVS value of the two groups that tended toward statistical significance, with a P value of 0.075.

FIGURE 10: MEAN IVS VALUES OF CAD AND NORMAL GROUPS (RETROSPECTIVE)



EJECTION FRACTION:

The mean ejection fraction of those patients with Coronary Artery Disease was found to be marginally – but not statistically significantly - lower than that of those with normal coronaries. P = 0.328.

FIGURE 11: MEAN EF VALUES OF CAD AND NORMAL GROUPS (RETROSPECTIVE)

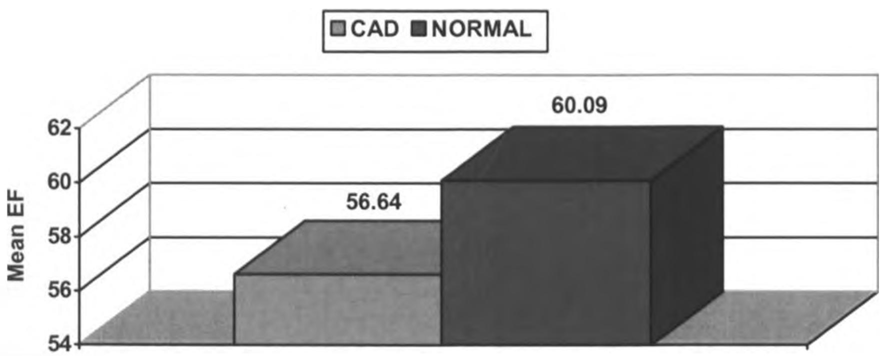


TABLE 2: SUMMARY OF RESULTS OF RETROSPECTIVE ARM

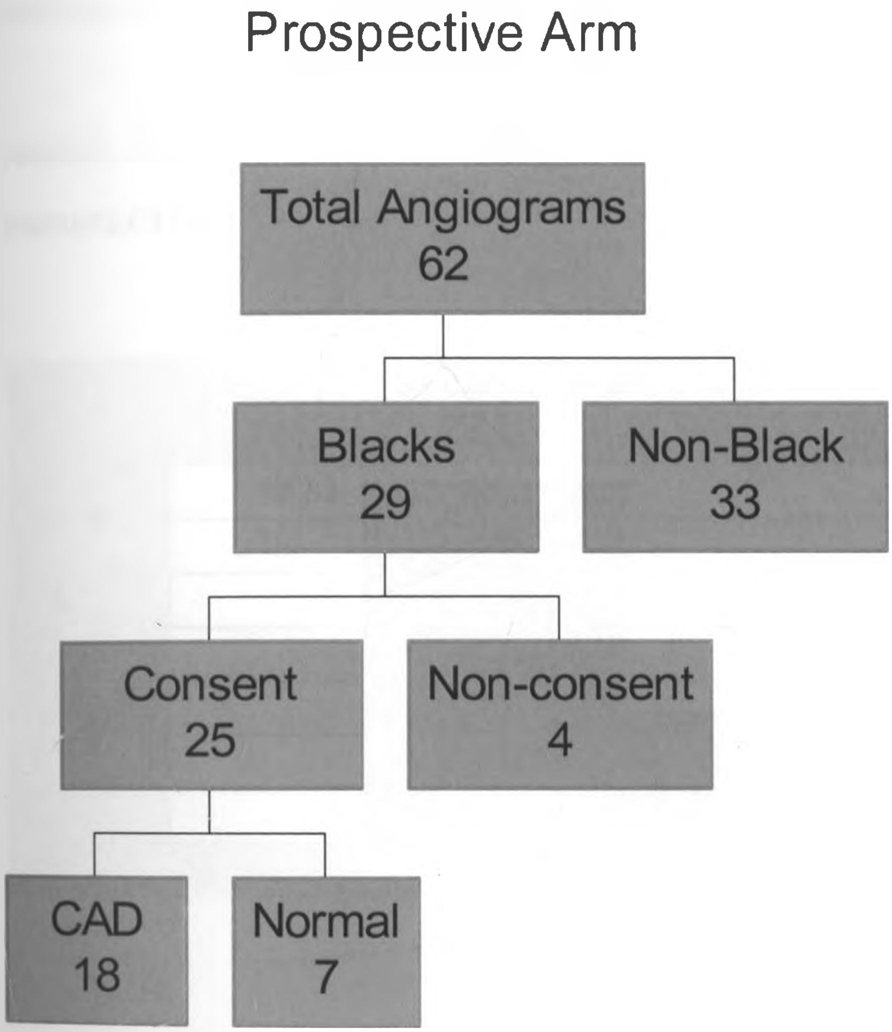
Coronary Angio: **Variable:**	*CAD* *(N = 52 ie 36.1%)*	*Normal* *(N = 92 ie 63.9%)*	*P value*
Prevalence of Diabetics: (%)	38.5	12.0	**0.0002**
Prevalence of Patients with Dyslipidemia: (%)	67.3	35.9	**0.0003**
Male to Female Ratio	5.5:1	2.3:1	**0.045**
Mean Age (years)	54.4	49.8	**0.005**
Percentage of Hypertensives (%)	65.4	62.0	0.68
Mean BMI	26.55	27.97	0.259
Prevalence of Smokers: (%) *Current*	15.4	13.0	0.227
Former	7.7	19.6	
Prevalence of Alcohol Users: (%)	32.7	36.9	0.67
Mean IVS: (cm)	1.13	1.02	0.075

6.2 RESULTS OF THE PROSPECTIVE ARM

In the six-month study period between October 2002 and March 2003, 62 patients underwent coronary angiograms at the Nairobi Hospital Cath Lab. Twenty-nine were Black, and four did not give consent. Data was thus eventually collected prospectively for 25 patients. Of these, 18 had CAD, 3 were normal, and 4 had sub-critical stenoses. (See **Figure 12** on page 48)

A similar trend in most of the variables was noted in this arm of the study as compared to the larger retrospective arm.

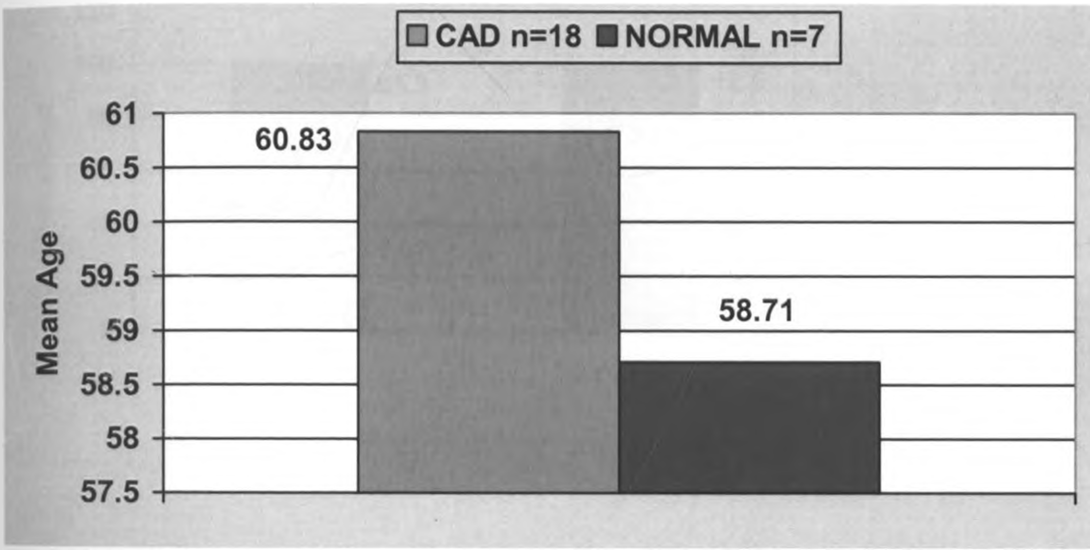
FIGURE 12: DISTRIBUTION OF CA PATIENTS IN PROSPECTIVE ARM



AGE:

The difference in ages was not statistically significant, with a P value of 0.623.

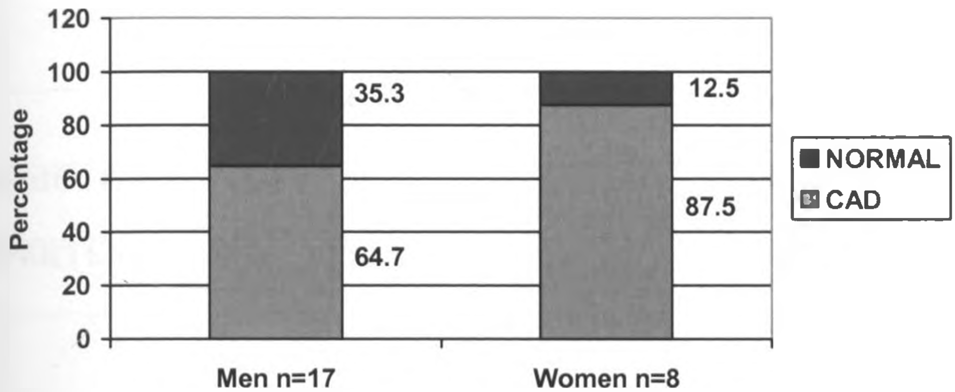
FIGURE 13: MEAN AGES OF CAD GROUP AND NORMAL GROUP (PROSPECTIVE)



GENDER:

There was no significant difference between the proportions of the different sexes among the two groups of patients. P=0.362

FIGURE 14: DISTRIBUTION OF CA RESULTS BY GENDER (PROSPECTIVE)



HYPERTENSION:

As seen in the retrospective arm there was a high prevalence of hypertension, but no significant difference in the distribution of hypertensives among the CAD group and the one with normal angiogram. P = 1.0

TABLE 3: DISTRIBUTION OF HYPERTENSIVES IN CA GROUPS (PROSPECTIVE)

	CAD	NORMAL
NORMOTENSIVE (%)	16.7	14.3
HYPERTENSIVE (%)	83.3	85.7

BMI:

There was no difference between the two groups on the values of mean BMI. The P value was 0.793.

TABLE 4: MEAN BMI FOR CAD AND NORMAL GROUPS (PROSPECTIVE)

	CAD	NORMAL
MEAN BMI	25.47	26.50

WHR:

No significant difference in WHR among the two groups. P = 0.737.

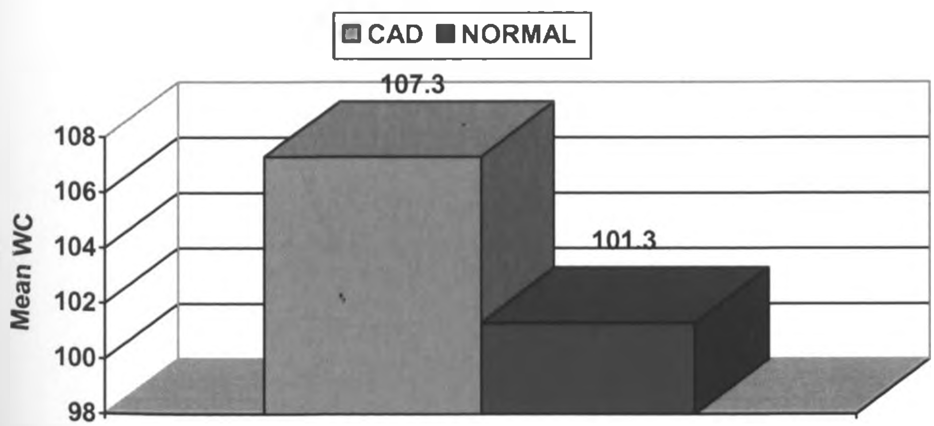
TABLE 5: MEAN WHR FOR CAD AND NORMAL GROUPS (PROSPECTIVE)

	CAD	NORMAL
MEAN WHR	0.94	0.95

WAIST CIRCUMFERENCE:

There was no statistical significance in the difference in Mean Waist Circumference of both groups under investigation. P = 0.143.

FIGURE 15: MEAN WHR'S FOR CAD AND NORMAL GROUPS (PROSPECTIVE)



SMOKING:

There were no current smokers among the patients in the prospective arm. An analysis of prevalence of CAD between former smokers and patients who had never smoked revealed a P value of 0.058.

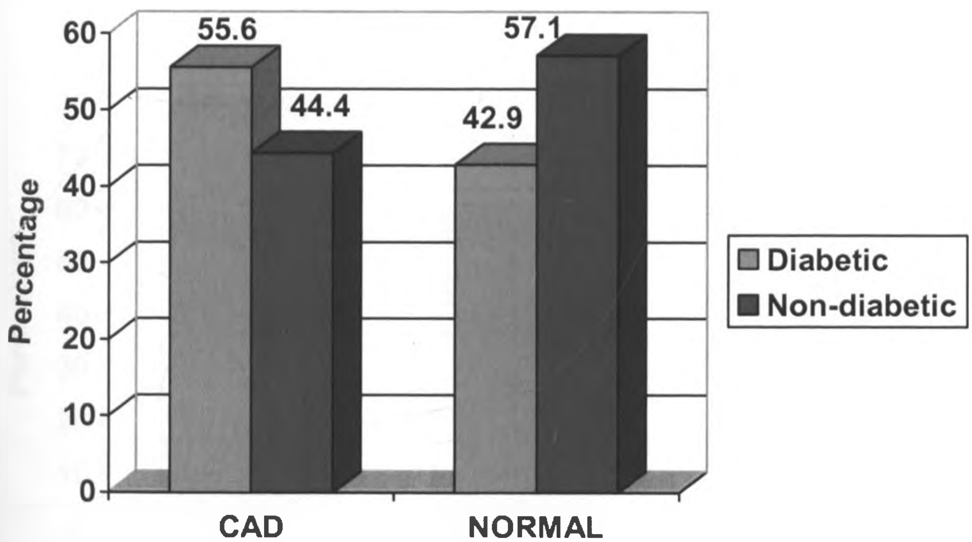
TABLE 6: SMOKING STATUS OF CA PATIENTS (PROSPECTIVE)

SMOKING STATUS	CAD	NORMAL
CURRENT (%)	0	0
FORMER (%)	22.2	71.4
NEVER (%)	77.8	28.6

DIABETES:

A similar trend to that noted in the retrospective arm was noted in the prospective, with a higher incidence of CAD among Diabetic patients. P = 0.673, i.e. no statistical significance.

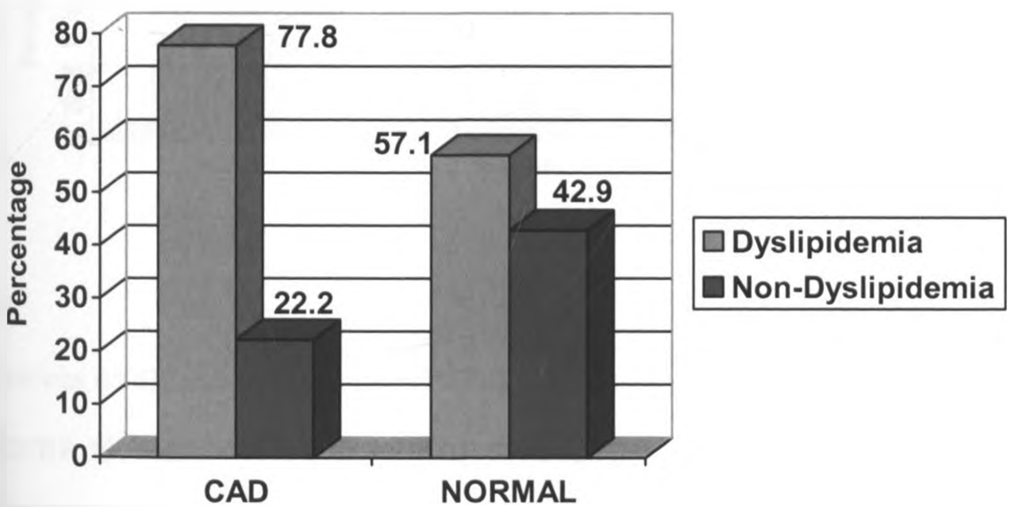
FIGURE 16: DISTRIBUTION OF DIABETICS IN CA GROUPS (PROSPECTIVE)



LIPIDS:

Similarly, conformity with the results of the retrospective arm was noted in the difference in prevalence of dyslipidemia among the group with diseased coronary arteries and that with normal coronary arteries on angiogram. But P = 0.355.

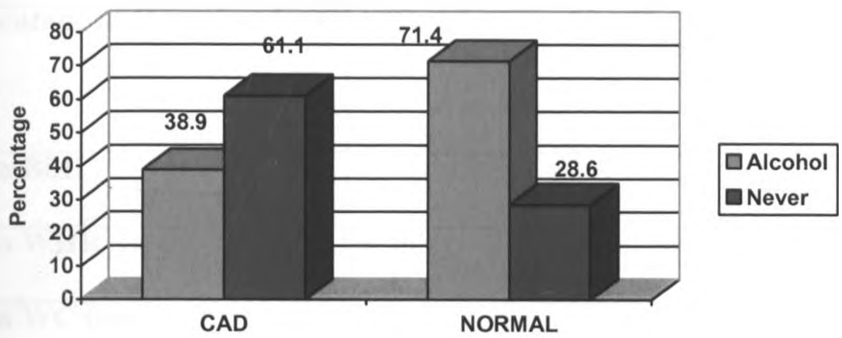
FIGURE 17: DISTRIBUTION OF PATIENTS WITH DYSLIPIDEMIA BY CA (PROSPECTIVE)



ALCOHOL:

There was a trend towards significance in the difference in incidence of Coronary Artery Disease, with those with no history of alcohol use developing more disease than those with a positive history of alcohol use. P = 0.202.

FIGURE 18: ALCOHOL STATUS OF CA PATIENTS (PROSPECTIVE)



IVS:

There was no difference in the mean IVS of both groups. P = 0.993.

FIGURE 19: MEAN IVS VALUES OF CAD AND NORMAL GROUPS (PROSPECTIVE)

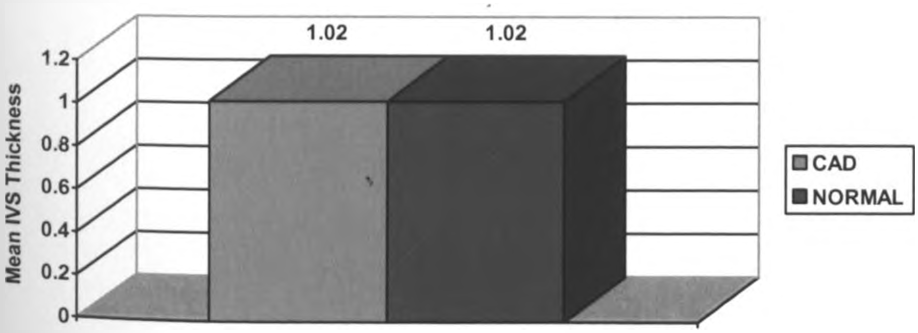


TABLE 7: SUMMARY OF RESULTS OF PROSPECTIVE ARM

Coronary Angio Variable	*CAD* *(N = 18 ie 72 %)*	*Normal* *(N = 7 ie 28%)*	*P Value*
Prevalence of Diabetics: (%)	55.6	42.9	0.673
Prevalence of Patients with Dyslipidemia: (%)	77.8	57.1	0.355
Male to Female Ratio	1.6:1	6:1	0.362
Mean Age (years)	60.8	58.7	0.623
Percentage of Hypertensives (%)	83.3	85.7	0.886
Mean BMI	25.5	26.5	0.793
Mean WHR	0.94	0.95	0.737
Mean WC (cm)	107.3	101.3	0.143
Prevalence of Smokers: (%) ***Current***	0	0	
Former	22.2	71.4	0.058
Prevalence of Alcohol Users: (%)	38.9	71.4	0.152
Mean IVS: (cm)	1.021	1.020	0.993

7.0 DISCUSSION

This study is the first of its kind in the region of East and Central Africa, being the prototype study to analyze the prevalence of cardiovascular risk factors among blacks who have undergone a coronary angiogram locally.

The established cardiovascular risk factors have been determined from several well-conducted landmark studies. However, these have centered mainly on populations from Western Europe and North America. Sub-Sahara Africa is lacking in such studies, which are pertinent, given the differences in genetic heritage and lifestyle from the typical Western populace.

Of the 662 patients in the retrospective arm, approximately one third were Blacks, the remainder being Asian and European. A similar distribution, but with a slightly higher proportion of Blacks, was noted in the prospective arm.

This could be due to a higher prevalence of symptoms and features of acute coronary syndromes in Asians and Europeans compared to the Africans (possible subject of another study). It may also be explained by availability of economic means for the procedure. In recent years, however, the proportion of Africans undergoing CA has continued to rise, again both due to the increased awareness and sensitization among medical person of the increasing incidence of coronary heart disease among Blacks, and to the greater involvement of Health Management Organizations in the financing of such important diagnostic tests as coronary angiograms.

A small number of patients (6 in the retrospective arm, 4 in the prospective) had *sub-critical stenosis* on CA. These numbers were small compared to the total of 144 in the retrospective and 25 in the prospective. Due to their relative numbers, it would not make statistical sense to analyze them as a separate group apart. Therefore they were grouped together with the Normal group for analysis. They would indeed not influence the results significantly even if they were excluded all together.

The analysis of the ***presenting complaints and clinical events*** that prompted an investigative pathway culminating in a coronary angiogram study (Table 1 pg 35) showed that the majority (63%) of patients who presented with stable angina pectoris had abnormal coronaries on CA. The two who presented with unstable angina both (100%) had an abnormal CA. Some 62% of patients presenting with an MI were documented to have obstructive CAD, while a relatively large percentage (38%) of those with a clinical diagnosis of MI were found to have normal coronaries.

The large percentage of patients with a clinical diagnosis of MI and yet found to have a normal CA (including subcritical CA) adds weight to the role of plaque instability, rupture and microembolism in the pathogenesis of acute coronary syndromes including MI.[65]

The majority of those who presented with chest pain that was atypical of angina (77%) was found not to have CAD on CA.

Meanwhile, the majority (38.5%) of the patients with abnormal angiograms presented with stable angina, and 17.3% presented with atypical chest pains.

Some of those with CAD and atypical chest pain were diabetics. Autonomic neuropathy involving cardiac afferent nerves in diabetes mellitus might account for the high incidence of atypical chest pains (and also silent ischemia) in diabetics.[66]

Age: The retrospective arm of the study found a statistically significant difference in age between the Coronary Artery Disease group and the Normal group. In the smaller prospective arm the difference was not statistically significant.

Of note is this study is the rather low age of the patients who had coronary artery disease with a mean age of 54 years in the retrospective arm, as compared to the ages mentioned in Western data.[67] Age is thus noted to be an important discriminatory factor in this study population.

With the availability of improved health services, the life expectancy in Africa is hoped to rise to similar ages as those in the West. Hence the importance for health-care workers to be increasingly aware of the possibility of coronary artery disease among the elderly.

Male Gender was also found to be associated with coronary artery disease, with a significant P value of 0.045 in the retrospective arm. This too was an expected result. The P value in the prospective arm was 0.362.

The percentage of men who had an abnormal angiogram was almost twice that of women.

In total, males who underwent coronary angiograms were three times the number of females. This may be a reflection of the skew in exposure to other cardiovascular risk factors that males have been subjected to. With an average age in the fifties and currently in the middle and upper sectors of society, these could be among those first few well-educated men who got jobs in the civil service soon after independence, and adopted early an urban lifestyle. Meanwhile, most women of the same ages tended to remain in the rural homes. With an increased presence of women in professional lives, an increase in coronary symptomatology and need for catheterization is expected in this group in the next few years.

Moreover, the mean age of the CAD group, 54 years, would include a large proportion of premenopausic women, who still enjoy hormonal cardiovascular protection. Hence fewer women in that age group would have coronary artery disease.

Studies have shown that at age 65, coronary artery disease (CAD) is more prevalent in men than it is in women; by age 80 the prevalence of symptomatic CAD is nearly equivalent in men and women.[68]

The sex gap in morbidity tends to diminish during the later years of the age range, mainly because of a surge in growth of female morbidity after age 45 years, while by that age, the growth in the male rate begins to taper off. An approximate 10-year difference between the sexes persists in mortality rates throughout the life span. The relative health advantage that is possessed by women, however, is buffered by a case fatality rate from coronary attacks that exceeds the male rate (32% vs 27%).[67]

Whereas ***hypertension*** is known to be a major coronary risk factor, there was no major difference noted in the prevalence of hypertension between the two groups under study. The P values were 0.68 in the retrospective arm and 1.0 in the prospective. A sub-analysis by Stage of Hypertension did not reveal any significant difference in either arm of the study.

This study did, however, reveal a high prevalence of hypertension among all the patients who underwent a coronary angiogram. Hypertension is a well-established risk factor for CAD, with a comparatively high prevalence also among Blacks in the US.[63]

The results show that hypertension was not a discriminatory risk factor for the presence of coronary heart disease in the population studied. Although hypertension is a major risk factor *per se* for stroke and heart failure, it is a significant *coronary* risk factor especially so when associated with target organ damage.[69] Probably the patients in question suffered little, if any, of this. Also, the large prevalence of hypertension would necessitate a larger study to show a (significant) difference between the two groups.

Obesity was assessed by the **Body Mass Index, Waist Hip Ratio** and the **Waist Circumference.** The results of the retrospective arm showed an unexpected trend in the first two measurements, with the Normal groups in both arms having a BMI or WHR that was marginally higher or equal to the values in the CAD group. The WC (prospective arm) on the other hand showed a positive correlation (albeit not statistically significant) with CAD.

Now, the unexpected trend in the first two parameters (BMI and WHR) could be explained by the higher proportion of women in the Normal group than in the CAD group. The low average age includes women who still enjoy hormonal cardiovascular protection, and, as shown by Vaghela et al[54], females were significantly more likely to have abnormal WHR's. Therefore this proportion increased the parameters in the Normal group.

As for the lack of statistical significance in the difference in mean WC between the two groups, this was probably due to the low numbers in the prospective arm, which thus lacked power to show the difference. A larger study would probably bring out the statistical significance better. The results, notwithstanding, were congruent with those from large population studies, such as the Framingham Study.

In both the retrospective and the prospective arms, the mean BMI in both groups under study, was found to be in the "overweight" group, marginally above 25.

From the perspective of data from the Framingham Heart Study and the Nurses' Health Study, this particular study would appear, therefore, to place these patients at a relatively lower risk of developing CAD, given the marginally elevated values of BMI.[70 71 72]

The analysis for ***smoking*** did not reveal any significant difference between the number of smokers and non-smokers. In total 29.2% of the patients in the retrospective arm and 36% in the prospective had a history of smoking. There were no current smokers in the prospective arm. A sub-analysis for women smokers did not reveal any statistical significant difference for presence of CAD or not.

This study manifests, therefore, the rather low prevalence of smokers in the population studied. This is in keeping with a Nigerian study of cardiovascular risk factors in middle-aged Nigerians, which illustrated, among the 146 persons studied, a 0% prevalence of smokers of more than 10 sticks per day. Cultural and religious reasons could have a role in maintaining the low prevalence. However, with the increased marketing in Africa by tobacco companies, and the rising numbers of women smokers, the epidemiology of smoking and the pattern of its deleterious effects could change within the next few years.

Thus while this study did not reveal cigarette smoking to be a discriminatory factor for CAD, cigarette smoking remains an important and reversible risk factor for CAD. Western data shows that 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.[18] The risk increases with tobacco consumption in both men and women and is higher in inhalers compared to non-inhalers. [19] One 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.[73]

A strong association was found between ***Diabetes Mellitus*** and Coronary Artery Disease. A significantly higher proportion of those with CAD were diabetic as compared to those with normal coronary arteries. The P value was 0.0002 (in the retrospective arm). In the prospective arm there was a trend in the same direction. The changes (1997) in case definition for DM, with fasting plasma glucose changing from 7.8 mMol/l to 7.0 mMol/L, had the effect of including more individuals as diabetic. This was taken to affect both CAD and Normal groups equally and thus was not expected to change the overall results.

These findings are in keeping with previous findings that insulin resistance, hyperinsulinemia and glucose intolerance appear to promote atherosclerosis.[74 75] In the Framingham Heart Study, for example, diabetes, impaired glucose tolerance, and high-normal levels of glycosylated hemoglobin were powerful contributors to atherosclerotic cardiovascular events, particularly in women.[76 77]

It is also known that 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.

A local study on diabetics described the prevalence of hypertension at 64.8%, dyslipidemia at 93.5%, and a clustering of at least two cardiovascular risk factors (excluding the diabetes itself) in all patients.[54]

The CHD risk in diabetics varies widely with the intensity of these cardiovascular risk factors. 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.[63 78] In addition, there is increasing evidence of the value to aggressive blood pressure control in diabetics. (On the other hand, strict glycemic control does not appear to reduce macrovascular disease despite its clear benefit in microvascular disease.[79])

Dyslipidemia was also noted to be much more prevalent among those with Coronary Artery Disease than among those with normal coronaries. The P value was highly significant at 0.0003. The prospective arm tended to show a higher percentage of patients with dyslipidemia among those with CAD but did not achieve statistical significance.

Conclusive results of a stratified analysis of the various types of dyslipidemia could not be drawn from this study. This is because most of the data was retrospective, and the prospective data was lacking in number. Also, some of the patients were on lipid-lowering therapy.

As mentioned above, the diagnosis of dyslipidemia was taken from the referral letters and medical reports of the primary physician. All the patients had a diagnosis about their lipid status. Most (80%) of the patients did undergo subsequent serum lipid level assays by the cardiologist prior to the angiogram. Hence the diagnoses of lipid status were more than the actual lipid assays. Moreover, some (10%) of the assays involved only a Total Cholesterol screen, while the rest included the various cholesterol subtypes. After the procedure all the patients with diseased coronary arteries were put on lipid-lowering therapy with a low-cholesterol diet and statins. For the prospective arm all values were pretreatment levels. Once again the low numbers in this arm could not allow a stratified analysis.

Alcohol: In the prospective arm, those who had used alcohol in the CAD group were slightly fewer than those in the Normal group. Conversely, those who never used alcohol in the CAD group were marginally more than those in the Normal group. The P value was not significant at 0.202. These findings were expected, due to the fact that moderate alcohol intake has a protective effect on coronary heart disease.[80 81]

However, in the retrospective arm, those who had not used alcohol in the CAD group were slightly fewer compared to the Normal group. The difference was not statistically significant, with a P value of 0.67. The trend found was unexpected, and could be because those who were current or former alcohol consumers did so to excessive levels, leading to other complications such as hypertension and dyslipidemia.

A prospective study of 490,000 men and women in the United States found that the relative risk of death from cardiovascular disease in moderate drinkers compared to nondrinkers was 0.7 for men and 0.6 for women.[82] Alcohol also appears to reduce the risk of peripheral arterial disease among apparently healthy men. In the Physician's Health study 22,071 male physicians were followed for 11 years; daily drinkers (> or =7 drinks per week) had a relative risk (RR) of peripheral artery disease of 0.92 compared with the reference group (<1 drink per week); after controlling for smoking, the RR was 0.68.[83] Most of the benefit of alcohol appears to be mediated by an elevation in serum HDL-cholesterol.[84]

The thickness of the interventricular septum was assessed by echocardiography. Increased thickness served as a surrogate maker of ***Left Ventricular Hypertrophy.*** The mean IVS values in the CAD group were slightly higher than those of the Normal group, with a P value tending towards significance.

Detection of increased IVS thickness by echocardiography is a valid surrogate indicator of increased left ventricular mass. It is indeed a preferred method compared to ECG diagnosis of LVH given the higher sensitivity of the echocardiographic method. Notwithstanding, limitations of using IVS measurements include the fact that there may be left ventricular dilatation with consequent increase in left ventricular mass while the IVS remains within normal limits.

In the Framingham study anatomical and electrocardiographic left ventricular hypertrophy (LVH), based upon the finding of an enlarged cardiac silhouette on a chest x-ray, each independently increased the risk of cardiovascular disease.[85] Echocardiographic evidence of LVH, which is more sensitive than the ECG, also is predictive of cardiovascular risk.[86 87]

The study therefore showed that there was a trend to higher IVS thickness in the diseased group. This is again in keeping with the fact that LVH is a blood pressure – independent risk factor for sudden cardiac death and acute MI.

Other findings made in this study included an analysis of ***Ejection Fraction*** on Echo for the two groups. It was found in the retrospective arm that the mean EF in the CAD group was marginally lower (56.64) than that of the Normal group (60.09), with a P value of 0.328. (The prospective arm did not show any difference.) This would suggest that a reduced ejection fraction should increase the index of suspicion for coronary heart disease. However, in this study, the mean value in the CAD group was still within normal limits.

8.0 LIMITATIONS

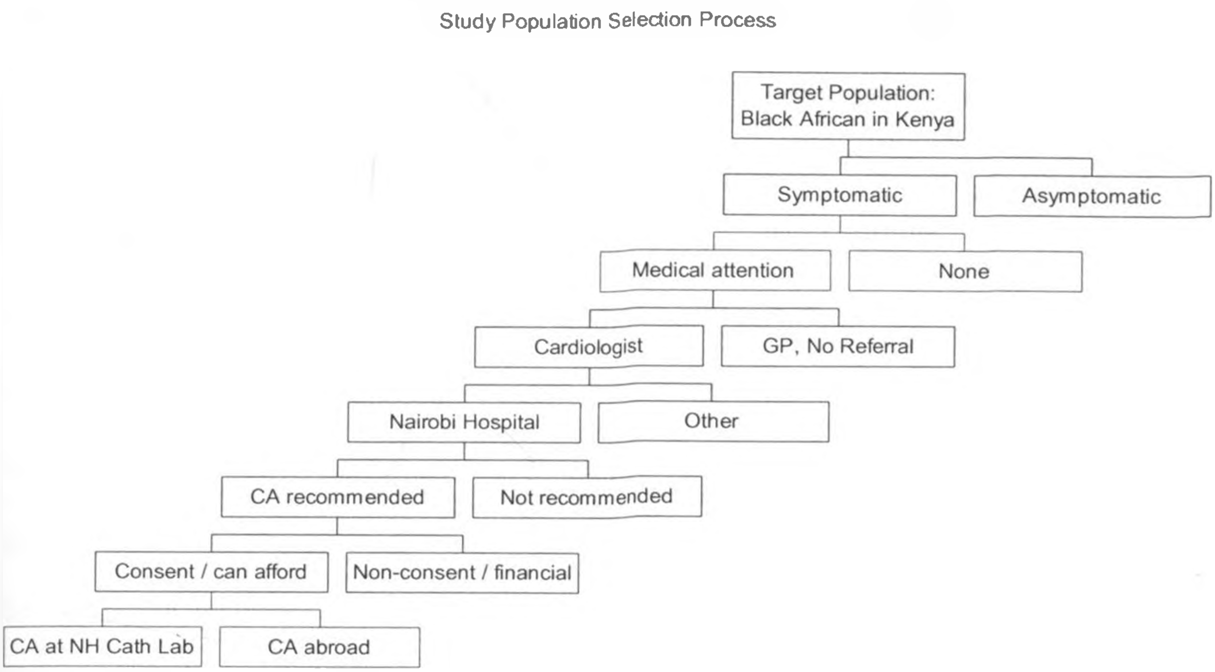
Several limitations were inherent in this study, by default or due to its very design.

Selection Bias: This was the principal limitation of this study. The selection of the patients was on the basis of a CA. Now, as shown in the results, all those patients referred for a CA, including those who eventually had Normal studies, were patients at high risk for coronary artery disease, either from their clinical presentation, or from their clinical analyses.

Again, referral patterns differed with different clinics. Hence the opportunity for introduction of bias on the persons undergoing the CA, with some physicians referring more than others.

These points and others are illustrated in the **Figure 20** below.

FIGURE 20: STUDY POPULATION SELECTION PROCESS



The figure above illustrates the selection process that the patients undergoing a CA at the Nairobi Hospital Cath Lab were subjected to. While the target population was the Black African population in Kenya, the sample studied was a highly select and non-randomized group, mainly from the middle and upper sectors of society. The potential for introduction of bias was also high and therefore generalization for the target population was restricted.

The results accruing from this study, however, - save for those to do with obesity – are consistent with established knowledge concerning the various risk factors, knowledge accrued from the study of large free-living populations, as discussed above.

Measurement bias: This applied in the evaluation of the actual coronary angiograms and the subsequent classification as Normal, Sub-critical or Abnormal. The coronary angiogram remains the gold standard diagnostic test for the evaluation of epicardial atherosclerotic coronary artery disease. The standard method of interpreting the severity of stenosis continues to be visual assessment or "eyeballing." The subjective measurement bias thus introduced would apply equally to both groups studied, such that it did not affect the comparison results. The high technical quality of the facility contributed to better and reproducible assessment of the CA. The investigator, who was present during the angiogram procedures, was able to observe an acceptable uniformity in interpretation by the various cardiologists.

Lack of data / lack of statistical significance: This applied, for example, to the stratified analysis of the various types of dyslipidemia. Conclusive results could not be drawn because most of the data was retrospective, and the prospective data was lacking in number.

Recall bias: This applied mainly in the prospective arm. On filling the questionnaire, the subject's recollection of lifestyle or historical factors was likely to be biased, depending on whether or not the coronary arteries were diseased. This led to over- or underestimation of some of the risk factors e.g. tobacco or alcohol use.

9.0 CONCLUSIONS

1) The risk factors most strongly associated with presence of Coronary Artery Disease in this population were Diabetes Mellitus and Dyslipidemia. These two conditions are thus strongly predictive of CAD demonstrated on CA.

2) Age and Male Gender were found to be strongly associated with CAD.

3) There was a high prevalence of hypertension in the population studied. There was, however, equal distribution of this risk factor in the two groups, and thus it was not found to be discriminately associated with CAD in this particular study.

4) Tobacco use and BMI were not found to be particularly associated with CAD compared to the Normal group in this study. There was a low prevalence of cigarette use in this study.

10.0 RECOMMENDATIONS

1) Blacks with Diabetes Mellitus and / or Dyslipidemia should undergo vigorous primary and secondary prevention of Coronary Artery Disease.

2) Despite not being found to be associated with CAD in this study, given its high overall prevalence, hypertension should be treated to lower overall cardiovascular risk.

3) More prospective studies should be carried out with a wider sample base and larger numbers, to further elucidate the significance of particular risk factors, such as smoking.

4) Ideal anthropometric parameters (BMI, WHR, and WC) should be attained and maintained to reduce cardiovascular risk.

11.0 APPENDICES

11.1 Diagnostic Criteria

11.1.1 Age and Sex

Age and sex as cardiovascular risk factors are defined as age >/= 45 years for males and >/= 55 years in females.[88]

11.1.2 Smoking

Never smoked; quit smoking (or *former smoker:* last smoked more than one year ago, smoked at least 100 cigarettes in lifetime); *current smoker* (last smoked within the last year, smoked at least 100 cigarettes in lifetime).[20, 89]

11.1.3 Use of Alcohol

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) defines *moderate drinking* as the average number of drinks consumed daily that places an adult at low-risk for alcohol problems[90]. This number was defined as less than three and less than two drinks per day for men and women, respectively, and less than two drinks per day for those over the age of 65. The criteria for *"at risk" (heavy) drinking* established by the NIAAA, which suggest that the person is at risk for adverse consequences, were greater than 14 drinks per week or 4 drinks per occasion for men, and greater than 7 drinks per week or 3 drinks per occasion for women[91]. A standard "drink" contains 12 g of alcohol, and is equivalent to 360 mL (12 oz) of beer, 150 mL (5 oz) of wine, or 45 mL (1.5 oz) of 80 proof distilled spirits[92, 93].

11.1.4 Blood Pressure

WHO criteria for a diagnosis of hypertension:

SBP (mmHg)	DBP (mmHg)	
<120	<80	Optimal BP
<130	<85	Normal BP
130-139	85-90	High Normal
140-159	90-99	Stage I Hypertension
160-179	100-109	Stage II Hypertension
>/=180	>/=110	Stage III Hypertension

11.1.5 Body Mass Index (BMI)

A measure of obesity is the BMI, defined as the ratio of the weight (kg) to the square of the height (m^2).

W.H.O. Classification:[94](kg/ m^2)

18.5 - 24.9	Normal
25.0 - 29.9	Overweight
30.0 – 34.9	Class I Obesity
35.0 – 39.9	Class II Obesity
>= 40.0	Class III Obesity

11.1.6 Waist Circumference

Central obesity is defined by a waist circumference of >/= 94.0 cm in males, and >/=80.0 cm in females.

11.1.7 WHR

Abnormal if >0.95 in males and > 0.80 in females.

11.1.8 Diabetes Mellitus

W.H.O. criteria for diagnosis:[95]

1. Random, or casual plasma glucose ≥ 200 mg/dL (11.1 mmol/L), associated with symptoms (polyuria, polydipsia, unexplained weight loss);
2. Fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L);
3. 2-h glucose ≥ 200 mg/dL (11.1 mmol/L) after a 75-g glucose load.

(Any of these criteria are sufficient for diagnosis, but each should be confirmed on a separate day.)

11.1.9 Dyslipidemia

Desirable cholesterol levels will be according to the second report of the National Cholesterol Education Programme:[96]

Total Plasma Cholesterol: <5.20 mmol/l (<200 mg/dl)

LDL Cholesterol: <3.36 mmol/l (<130 mg/dl)

HDL Cholesterol: >1.55 mmol/l (>60 mg/dl).

The following criteria are used for serum LDL cholesterol:

Desirable: Below <3.4 mmol/L (130 mg/dL)

Borderline high-risk: 3.4 to 4.1 mmol/L (130 to 159 mg/dL)

High-risk: Above >4.1 mmol/L (160 mg/dL)

11.1.10LVH by ECG

The Sokolow-Lyons QRS voltage criteria for LVH are used. They include $R_I + S_{III} >= 2.5$ mV, R in $aV_l > 1.2$ mV, R in $aV_f > 2.0$ mV, S in $V_1 >= 2.4$ mV, R in V_5 or $V_6 > 2.6$ mV, and R in V_5 or V_6 + S in $V_1 > 3.5$ mV.[97]

11.1.11Coronary Angiogram

Abnormal is normally taken as >/=50% stenosis on one or more of the coronary arteries, judged by the standard method for interpreting the presence and severity of stenoses in the epicardial coronary arteries, which continues to be visual assessment or "eyeballing."[56]

CAD is defined as a more than 50 percent diameter stenosis in one or more of the three major coronary arteries (LAD, LCx, and the RCA), although it is clear that stenoses of less than 50 percent have major prognostic implications because these lesions most commonly lead to plaque rupture and acute myocardial infarction. Subcritical stenoses of less than 50 percent are best characterized as nonobstructive CAD. CAD is classified as one-, two-, or three-vessel disease.[66]

11.2 Pro Forma Document (Retrospective arm)

<table>
<tr><td colspan="2"><u>PRO FORMA DOCUMENT</u></td></tr>
<tr><td colspan="2">SURNAME:

OTHER NAMES:</td></tr>
<tr><td>CLINIC:</td><td>FILE No:</td></tr>
<tr><td>AGE:

D.O.B.:</td><td>SEX:
MALE FEMALE</td></tr>
<tr><td>PRESENTING COMPLAINTS/BRIEF HX:</td><td>FAMILY HX:
SD
PCAD
HYPERCHOL.</td></tr>
<tr><td colspan="2">SMOKING: QUANTITY DURATION

NEVER:

CURRENT:

FORMER:
(PERIOD OFF)</td></tr>
<tr><td colspan="2">ALCOHOL: QUANTITY DURATION

NEVER:

CURRENT:

FORMER:
(PERIOD OFF)</td></tr>
<tr><td colspan="2">BLOOD PRESSSURE: SBP: JNC NORMAL

(mmHg) STAGE I
DBP: STAGE II
STAGE III</td></tr>
</table>

NAME:	FILE No:

BMI: WEIGHT (Kg): BMI: NORMAL HEIGHT (m): OVERWEIGHT OBESE
DIABETIC STATUS: DIABETIC NON-DIABETIC TYPE I TYPE II
LIPID PROFILE: TOTAL (mmol/L DYSLIPIDEMIA Or HDL mg/dl) LDL NON-DYSLIPIDEMIA TG
E.C.G.: LVH: YES NO ISCHEMIC CHANGES:
ECHO FINDINGS: IVS(cm): DIASTOLIC DYSFUNCTION YES NO EF: WALL HYPO-/AKINESIS: YES NO
EST: POSITIVE: ST DEPRESSION (cm) STAGE DURATION (min) NON-DIAGNOSTIC / NEGATIVE PRES. OF CHEST PAIN: YES NO
CA: ABNORMAL: VESSEL % STENOSIS LMCA LAD LCx RCA PDA NORMAL:

11.3 Consent Form

CARDIOVASCULAR RISK FACTOR PROFILES OF BLACK AFRICANS UNDERGOING CORONARY ANGIOGRAPHY AT THE NAIROBI HOSPITAL

CONSENT FORM

I ____,

having been explained to the nature of the project by Dr Charles Kamotho, do voluntarily agree to take part in this research on *Cardiovascular Risk Factor Profiles Of Black Africans Undergoing Coronary Angiography At The Nairobi Hospital.* I understand that I am free to participate or not in it, and failure to do so will not in any way affect the appropriate treatment I have been receiving, or will continue to receive.

Signed:

____

Witnessed:

____

Dated:

____

11.4 Questionnaire for the Prospective arm

CARDIOVASCULAR RISK FACTOR PROFILES OF BLACK AFRICANS UNDERGOING CORONARY ANGIOGRAPHY AT THE NAIROBI HOSPITAL

QUESTIONNAIRE

Dear Sir / Madam,

Welcome to this study, the first of its kind in the region of East and Central Africa.

You have been chosen to participate in this research because you have undergone a coronary angiogram, which was either diagnostic of heart disease or did not reveal any disease. We would like to compare your group data with that of the other group.

Following are a series of questions. Kindly fill in all answers to the best of your ability and return the questionnaire to me.

Thank you,

Dr Charles Kamotho

(Principle Investigator)

A. Personal data:

For Official Use
Clinic:
File Number:

1) Surname: ____________________

2) First Names: ____________________

3) Date of Birth: ____________________ Age: ____________

4) Sex: Male/Female

5) Marital Status: (specify by writing the appropriate number in the box)

1=Single 2=Married 3=Widowed 4=Separated 5= Cohabitation 6=Divorced ☐

6) Level of Formal Education: (specify the number)

1=None 2=Primary School 3=Secondary School ☐

*4=University 5=Other (specify)*____________

7) Usual Occupation: ____________________

8) Current status of formal employment: (specify the number) ☐

1=Self-employed 2=Employed 3=Unemployed 4=Never had formal employment
5=Retired 6=Student/Training

B) Past Medical History: (Tick the appropriate answer for each question below)

Do you suffer from, or have you ever had, any of the following?

	No	Yes	Unsure	Unknown
High blood pressure?				
High blood cholesterol?				
Diabetes mellitus?				
A heart attack before age 55?				
Heart bypass surgery before age 55				
A stroke before age 65?				

C) Family History: (Tick the appropriate answer for each question below)

Do any of your parents suffer from, or have they ever had, any of the following?

	Father				*Mother*			
Names (Optional):	______				______			
	No	Yes	Unsure	Unknown	No	Yes	Unsure	Unknown
High blood pressure?								
High blood cholesterol?								
Diabetes mellitus?								
A heart attack before age 55?								
Heart surgery before age 55?								
A stroke before age 65?								
Death due to heart disease?								

Do any of your relatives suffer from, or have they ever had, any of the following?

Tick the appropriate box:

	brother	sister	children	uncle/aunt
High blood pressure?				
High blood cholesterol?				
Diabetes mellitus?				
A heart attack before age 55?				
Heart bypass surgery before age 55?				
A stroke before age 65?				
Death due to heart disease?				

D) Physical Activity (Tick as appropriate)

1. Do you do any exercise on a regular basis? *Yes* ☐ *No* ☐ *In-the-past* ☐
2. What does it consist of?

Jogging ☐ *Walking* ☐ *Swimming* ☐ *Aerobics* ☐

*Other (specify)*________________

3. For how many minutes per session?

20 min ☐ *40min* ☐ *1 hour* ☐ *more than1hr* ☐

4. How many times a week?

Once ☐ *Twice* ☐ *Four times* ☐ *More than four* ☐

E) Smoking.

Do you normally smoke cigarettes? Yes ☐ No ☐

If yes,

How many cigarettes do you smoke per day? <5 ☐ 5-10 ☐ 10-20 ☐ 20-40 ☐ >40 ☐

For how many years have you been smoking? <1 yr ☐ 1-5 yrs ☐ 5-10yrs ☐ >10yrs ☐

Were you ever a cigarette smoker? Yes ☐ No ☐

If yes,

When did you stop? <1 yr ago ☐ 1-5 yrs ago ☐ >5 yrs ago ☐

How many cigarettes did you smoke per day? <5 ☐ 5-10 ☐ 10-20 ☐ 20-40 ☐ >40 ☐

For how many years had you been smoking? <1 yr ☐ 1-5 yrs ☐ 5-10yrs ☐ >10yrs ☐

Do you live with somebody who smokes cigarettes? Yes ☐ No ☐

If yes,

Who is this person? husband ☐ wife ☐ partner ☐ relative ☐ guardian ☐

How many cigarettes does he/she smoke per day? <1 packet ☐ >1packet ☐

For how long have you been living with this person? < 1 year ☐ >1 year ☐

F) Alcohol:

Do you currently take any alcoholic drinks or have you ever taken alcohol on a more or less regular basis? Yes ☐ No ☐

If *yes*, please quantify:

How many times per month? Once ☐ Twice ☐ Thrice ☐ Four or more ☐

	1-2	3-4	5-6	>6
How many bottles of beer in a session?				
How many glasses of wine in a session?				
How many glasses of sherry in a session?				
How many minipacks of vodka in a session?				
Other drinks (please specify) ____________				

For how long have you been taking alcohol?

1 yr ☐ *2-5 yrs* ☐ *6-10 yrs* ☐ *More than 10 yrs* ☐

If you have stopped, for how long **had** you been taking alcohol?

1 yr ☐ *2-5 yrs* ☐ *6-10 yrs* ☐ *More than 10 yrs* ☐

How many years ago did you stop?

1 yr ☐ *2-5 yrs* ☐ *6-10 yrs* ☐ *More than 10 yrs* ☐

Why did you stop?

Advised by doctor ☐ *Financial* ☐ *Social problems* ☐

*Other (please specify)*________________

G) Cardiovascular Risk Factors:

Which of the following do you think are considered as risk factors for the development of ischemic heart disease, i.e. factors that make it easier to have a heart attack? **(Specify by ticking in the box.)**

		Yes	No
i)	Old age	☐	☐
ii)	Being male	☐	☐
iii)	Women beyond menopause	☐	☐
iv)	Family history of heart disease (ischemic heart disease)	☐	☐
v)	Hypertension	☐	☐
vi)	Diabetes	☐	☐
vii)	Cigarette smoking	☐	☐
viii)	High cholesterol levels in the blood	☐	☐
ix)	Being overweight	☐	☐
x)	Depression	☐	☐
xi)	Lack of exercise	☐	☐
xii)	Being tall	☐	☐

And which of the following protect you from having heart attacks?

i)	Regular exercise	☐	☐
ii)	Eating chicken skin	☐	☐
iii)	Good control of diabetes	☐	☐
iv)	Dancing	☐	☐

The End

FOR OFFICIAL USE ONLY

A) Physical Examination:

Weight (kg) ______________________

Height (cm) ______________________

BMI (kg/m2) ______________________

Waist circumference (cm) ______________________

Hip circumference (cm) ______________________

WHR ______________________

B) Diabetes

Type I Yes / No

Type II Yes / No

C) Hypertension

Yes / No JNC VI Class: I II III

D) Dyslipidemia

Yes / No

E) Procedures Sheet

Electrocardiogram (ECG) Date:

Findings: LVH:

Ischemic changes:

Echocardiography: Date:

Findings: IVS (cm):

EF (%):

Diastolic Dysfunction: Yes / No

Wall Hypo-/Akinesis Yes / No

Exercise Stress Test (EST): Date:

Findings: Positive ST Depression (cm):

Stage:

Duration (min):

Non-Diagnostic / Negative

Presence of Chest Pain: Yes / No

Coronary Angiogram (CA): Date:

Findings: Abnormal: Vessel % Stenosis

LMCA
LAD
LCx
RCA
PDA

Normal

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