An assessment of coronary artery calcification, using the
calcium scoring technique, in an asymptomatic Indian
population in Durban, KwaZulu-Natal

By

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A Thesis submitted in fulfilment of the requirements
for the Master's Degree in Technology

To the

Department of Radiography: Faculty of Health Sciences
Durban University of Technology
2008

DECLARATION:

Except for quotations specifically indicated in the text and such help as I have
acknowledged, this thesis is wholly my own work, and has not been submitted for
any qualification at any other institution.

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Date

29-5-08
DEDICATION

THIS THESIS IS DEDICATED TO

MY DIVINE MASTER

AND FAMILY

‘THE END OF EDUCATION IS CHARACTER’
(Sri Sathya Sai Baba)
ACKNOWLEDGEMENTS

My sincere thanks and gratitude to the following individuals and Institutions:

The Durban University of Technology and Department of Radiography for the bursary to engage in this study.

Drs Jackpersad and Partners for their encouragement, support and use of their premises and equipment for the study.

Mrs S Naidoo for her support, knowledge and guidance as my supervisor.

Dr J.M Kalideen for his tremendous support and help as my clinical supervisor.

The staff at Drs Jackpersad and Partners for their support, words of wisdom and humour during my more difficult times.

The research participants for making my recruitment and data capture process smooth and stressless.

The application specialists at GE Medical systems for dealing with my queries during my study.
My family and friends for their love, support and faith in me during the two years of my study. My nephews and nieces for always making me see the lighter and brighter side of life.

My parents for always being there for me.

Finally my most sincere thanks and gratitude to my Lord and Supreme Guru Bhagwan Sri Sathya Sai Baba for providing me with spiritual guidance and peace in every step of my life.
ABSTRACT

Aim of the study

The main aim of this study, was to assess the prevalence of coronary artery calcification in asymptomatic risk and non risk individuals in the South African Indian population, within the age group of 20-70 years.

Research questions

1. Is there a significant difference in the calcium scores of risk and non-risk participants in the Indian ethnicity?
2. Is there a significant difference between calcium scores in male and female participants?
3. What percentage of individuals in each risk category present with calcium in the coronary arteries?
4. What is the percentage of individuals in each category presenting with calcium in the coronary arteries? The 5 categories of calcium scores according to Klodas (2005), in Hounsfield unit (HU) are: 0 / 1-10 / 11-100 / 101-400 / 400+.
5. What is the adjusted risk of calcification for demographic and risk factors in asymptomatic individuals in the Indian population in Durban, KwaZulu-Natal?

Motivation for the study
Motivation for the screening of asymptomatic risk and non-risk individuals for the prevalence of coronary artery calcification, is to triage such populations for risk of adverse coronary events.

**Methodology**

A convenience sample method of selection was used to recruit research participants who fitted the inclusion criteria. The inclusion criteria was that the research participants had to be asymptomatic (with risk or non-risk factors) for CAD, of Indian ethnicity, in the age group of 20-70 years. Informed consent was obtained from the research participants in the presence of the researcher. The research participants were prepared for the calcium score study and scanned according to routine technique. The calcium score was calculated using the General Electric (GE) Advantage windows workstation version 4.3. Data analysis was done on the 103 participants using the SPSS package version 13.

**Results and conclusion**

The final results of the study reported that being male, increasing age and the presence of diabetes were all independent risk factors for coronary artery calcification in the asymptomatic Indian population in Durban KwaZulu-Natal. The largest risk was due to being diabetic (odds ratio 12.1) followed by being male (odds ratio 9.7).

**Recommendations**
Hyperlipidemia as a risk factor for CAD should be further researched, as exclusion of the outlier has lowered the study's power marginally and this has resulted in the finding of a non significant effect of hyperlipidemia after exclusion of the outlier, whereas it was significant before.

**Future research**

- Calcium scoring studies on all ethnic groups in SA.
- 2 yr follow up on current study to assess disease status.
- The impact of level of education on the South African population with regards to CAD prevalence.
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LIST OF ABBREVIATIONS

ACC American College of Cardiology
AHA American Heart Association
AIT Adaptive intimal thickening
ASA Acetylsalicylic acid
BMI Body mass index
BPM Beats per minute
CAD Coronary artery disease
CHD Coronary heart disease
CSANZ Cardiac Society of Australia and New Zealand
CT Computerized Tomography
CVD Coronary vascular disease
CVS Calcium volume scan
DNA Deoxyribonucleic acid
DUT Durban University of Technology
EBCT Electron beam computerized tomography
ECG Echocardiography
FRS Framingham risk score
GE  General Electric
HDL  High density lipoprotein
HRT  Hormone replacement therapy
HU   Hounsfield unit
ICRP International Commission on Radiological Protection
ID   Identity
IHD  Ischaemic heart disease
IVUS Intravenous ultrasound
Kv   Kilovoltage
LAD  Left anterior descending
LCA  Left coronary artery
LCX  Left circumflex
LDL  Low density lipoprotein
LMA  Left main artery
mA   Milliampere
MDCT Multidetector Computerized Tomography
MI   Myocardial infarction
MRA  Magnetic resonance angiography
MRC Medical Research Council
MRI  Magnetic resonance imaging
mSv  Millisierverts
PDA  Posterior descending artery
PIT  Pathologic intimal thickening
PLB  Posterolateral branch
RCA Right coronary artery
1. **Agatston calcium score** - This is a reconstruction algorithm used to quantify the amount of calcium in the coronary arteries. It was developed for Electron Beam scanners. It is calculated by the area of calcified plaque, multiplied by a scaling cofactor with a peak attenuation of 130 HU (Online Medical Dictionary, 2006).

2. **Angina** - This refers to a pain in the chest due to over exertion when the heart is diseased (The Pocket Oxford Dictionary, 1978).

3. **Angiotensin** - This is an oligopeptide in blood that causes vasoconstriction and increase in blood pressure and release of aldosterone from the adrenal cortex (Online Medical Dictionary, 2006).

4. **Anticoagulant** – This is an agent used to prevent the clotting of
platelets in the blood plasma (Online Medical Dictionary, 2006).

5. **Atherosclerosis** - This is a disease of the arterial wall in which the layer thickens, causing narrowing of the channel and thus, impairing blood flow. It can occur in any area of the body, but is most important when it occurs in the heart, brain or blood vessels leading to the brain (Health Encyclopedia, 2006).

6. **Body mass index (BMI)** - This is a measure of body fat based on height and weight, in both males and females. BMI is calculated by the weight of an individual in kilograms divided by the height in metres squared (Department of Health and Human Services, 2006).

7. **Dyslipidemia** - This is an elevated concentration of lipids, such as cholesterol, triglycerides and lipoproteins, in the blood plasma (Online Medical Dictionary, 2006).

8. **DNA** - This is a substance in chromosomes storing genetic information (The Pocket Oxford Dictionary, 1978).

9. **Echocardiography** - This a diagnostic test which uses ultrasound waves to make images of the heart chambers, valves and surrounding structures (Online Medical Dictionary, 2006).

10. **High density lipoproteins (HDL)** - Refers to cholesterol which is contained
in or bound to high density lipoproteins. HDL transports cholesterol from peripheral tissues to liver thus acting as a scavenger to prevent excess accumulation and deposition of cholesterol in the blood vessels (Online Medical Dictionary, 2006).

11. **Hounsfield unit (HU)** - This is an x-ray attenuation unit used in CT scan interpretation- i.e. it is the calculation of the relative density of a substance e.g. calcium in the coronary arteries (Family Practice Notebook, 2000).

12. **Hyperlipidemia** - This is another word for dyslipidemia i.e. it is an excess of lipids in the blood (Online Medical Dictionary, 2006).

13. **Hyperuricaemia** - Refers to an elevated uric acid level in the bloodstream (Online Medical Dictionary, 2006).

14. **Millisieverts** - Refers to one thousandth of a sievert (Online Medical Dictionary, 2006).

15. **Myocardial infarction** - A term used to describe irreversible injury or damage to the heart muscle. Common symptoms include substernal, crushing chest pain that may radiate to the jaw or arms (Online Medical Journal, 2006).
16. **Obesity** – Refers to a BMI greater than or equal to 30 (Assman et al., 1999).

17. **Pathognomic** - Refers to a term often used in Medicine, which means diagnostic for a particular disease (Online Medical Dictionary, 2006).

18. **Percentile ranking** – Refers to the percentage of score in its frequency distribution which is lower e.g. a test score which is greater than 85% of the scores of people taking the test is said to the 85th percentile (Online Medical Dictionary, 2006).

19. **Scintigraphy** - Refers to a process of obtaining a photographic recording of the distribution of internally administered radiopharmaceuticals with the use of a gamma camera (Online Medical Dictionary, 2006).

20. **Sedentary lifestyle** - This is characterized by much sitting and little physical exercise (The Pocket Oxford Dictionary, 1978).

21. **Sieverts** - This is a unit of ionising radiation absorbed dose equivalent obtained as a product of the absorbed dose measure in grays and a dimensional factor stipulated by the International Commission on Radiological Protection (ICRP) and indicating the biological effectiveness of the radiation (Online Medical Journal, 2006).
22. **Spatial resolution** - Refers to the accuracy or detail of graphic display expressed as dots per inch, pixels per line or line per millimetre (Techencyclopedia, 2006).

23. **Statin therapy** - This is any of a class of lipid lowering drugs that reduces serum cholesterol levels inhibiting a key enzyme involved in the biosynthesis of cholesterol (Medical Encyclopedia, 2006).

24. **Surrogate marker/surrogate end point** - This is a term used in medical research for a change to the human body that is believed to be necessary to an eventual outcome or end point (Medical Encyclopedia, 2006).

25. **Volumetric Calcium Score** - This is a measurement used in Multislice Scanners with a volume and mass based algorithm (Online Medical Dictionary, 2006).

26. **Temporal resolution** - Refers to the accuracy of a particular measurement with respect to time. It is often in contest with spatial resolution (Online Medical Dictionary, 2006).

27. **Triage** - Refers to the process of screening patients to determine the nature and urgency of their medical condition (The Pocket Oxford Dictionary, 1978).
CHAPTER ONE

BACKGROUND TO THE STUDY

1.1 Introduction

The burden of cardiovascular disease has reached immense proportions. It is estimated to claim approximately 16.7 million lives per annum world-wide (Greenland et al., 2001). In the United State of America (USA) alone, it is commonly held that coronary artery disease (CAD) and coronary heart disease (CHD) are the leading causes of death (Greenland et al., 2001). CHD and CAD are by definition the narrowing of the coronary arteries that supply oxygenated blood to the myocardium (Medical Encyclopedia, 2007). This narrowing is caused by atherosclerosis, where there is accumulation of plaque in the vessel wall. As the coronary arteries narrow it can stop the blood flow to the myocardium thus causing an angina or a myocardial attack (Medical Encyclopedia, 2007). It has emerged that opportunity for prevention of these coronary events, is being missed as 25% of patients have had sudden death or non-fatal myocardial infarction without prior symptoms (Greenland et al., 2001).

There is paucity of data regarding CAD and its prevalence in developing countries. However it is projected that the mortality rate from CAD will double from 1990 to 2020 (Okrainec et al., 2004). Furthermore, it is predicted that by
2020 non-communicable diseases will account for three quarters of the deaths in developing countries with CAD as a major contributor (Yeolekar, 1998). Rapid socioeconomic growth in developing countries is increasing the risk of diabetes, genetic factors, hypercholesterolemia, hypertension and smoking. Therefore, prevention and targeted control of risk factors could potentially reduce the impact of CAD (Okrainec et al., 2004).

In order to engage in control and preventative risk measures one needs to be aware of the prevalence and status of a disease. This leads to the idea of utilising a screening tool to diagnose and measure the extent of the disease. Such a screening tool is the computerized tomography (CT) calcium scoring technique which holds promise as a non-invasive procedure, for obtaining valuable information on the extent and location of calcified plaque in the coronary arteries (Greenland et al., 2001). Calcified plaque is a surrogate marker for atherosclerosis i.e. the presence of coronary artery calcification is an indication of the presence of atherosclerosis (Carr et al., 2000).

The calcium score technique is currently being underutilized in South Africa (SA) and there appears to be no known publications cited on research done on South African populations on calcium scoring. Naidoo et al., (2005), in the Cardiovascular journal of SA stated that CHD has reached epidemic proportions in White and Indian population groups compared to the Black population group (it is noted that the authors have referred to the African population group in SA as Black). Although the Indian population group falls under the Black population subset in SA, the authors have made a distinction between the Black and Indian population groups for the
purpose of their research. The authors also suggest that South African Indians, descending from the Indian subcontinent, are more at risk for CHD than the other population subsets. The Indian subcontinent as defined by Kotha (2003) includes India, Sri Lanka, Pakistan and Bangladesh.

Yeolekar (1998), significantly states that religion, culture, climate and language confer particular characteristics in Indians that influence their dietary habits that predispose them to CAD risk. In agreement Kotha (2003) adds that Indians worldwide have a very high incidence of metabolic syndrome and diabetes which predispose them to heart disease. Sedentary life styles, unhealthy cooking practices and nutrition are the environmental factors that trigger the genes responsible for heart disease, heart attacks and premature death in Indians (Kotha, 2003). This current study has therefore targeted asymptomatic risk and non-risk individuals for CAD in the Indian ethnic group in Durban, KwaZulu-Natal, SA, in order to determine if this population presents with risk for CAD.

Greenland et al., (2001) contend that 25 % of all coronary patients in the USA who have suffered from non-fatal myocardial infarction or sudden death were asymptomatic. On the contrary Girshman and Wolff (2003), state that to their knowledge the incidence rate of CAD in an asymptomatic population with and without risk is unknown. It was therefore a worthwhile exercise to screen asymptomatic individuals, for coronary artery calcification in the Durban, KwaZulu-Natal Indian population, to ascertain if this population is at risk for adverse coronary events.
Interestingly, most studies in the USA and New Zealand on asymptomatic individuals were done on subjects with one or more risk factors (Greenland et al., 2001 and Lewis, 2003). There are no cited studies on individuals without risk factors. As CAD onset can be sudden it is important to know the status of one's coronary arteries even though symptoms and risk factors are not present (Greenland et al., 2001).

With the above consideration, this study was undertaken at Drs Jackpersad and Partners at Westridge Medical Centre, Durban on a General Electric (GE), 64 slice Multidetector Volume CT (VCT) scanner. The participants were recruited from Durban, KwaZulu-Natal and had to meet the inclusion criteria. The inclusion criteria were that participants had to:

1) be asymptomatic (have no symptoms of CAD i.e. chest pain or angina).
2) be between the age of 20 -70 years and of Indian ethnicity. The minimum age of 20 years was adhered to, in order to avoid the need for parental consent for participation.
3) fall under a risk or non-risk category for a coronary event. Smoking, diabetes, hypertension, high cholesterol, obesity and strong family history of cardiac events were considered to be risk factors for the study. An individual was considered obese if their body mass index (BMI) was greater than or equal to 30.

The calcium scoring technique is an ECG gated CT examination. The participants were connected to an ECG monitor and scanned during diastole to reduce cardiac motion artefacts on the CT scans. The data acquired from the CT scans was analysed to
produce the calcium score results, according to the data-base provided by the GE 64 slice VCT. The calcium scores were further analysed using the Statistical Package for Social Sciences (SPSS) version 13 in view of the research questions.

The primary aim of this study, was to assess the prevalence of coronary artery calcification in asymptomatic risk and non risk individuals in the South African Indian population, within the age group of 20-70 years. Any percent of calcification in an asymptomatic population should be considered as statistically significant as it indicates the presence of disease and the probability of future coronary events. The results of the study would therefore determine whether the calcium scoring technique would be a useful screening tool in preventative medicine in SA.

1.2 Motivation and significance

The motivation for screening of asymptomatic risk and non-risk individuals for the prevalence of coronary artery calcification, is to triage such populations for the risk of adverse coronary events. Early detection of atherosclerotic risk can lead to improved prognosis (Sadovsky, 2005). Furthermore, as stated by Greenland et al., (2001), CAD is the leading cause of death per annum in the USA (25%). There are no known statistics in SA on the mortality rate from CAD. However, the incidence of CHD has been reported to be higher in the Indian ethnic group than in the other population groups in SA (Naidoo et al., 2005).

Firstly, the motivation for this study has arisen from an indepth literature review (Chapter Two) which has shown CAD and the calcium scoring technique as an area that is
understudied in SA. Secondly, research questions have been devised based on this information and are as follows:

1. Is there a significant difference in the calcium scores between risk and non-risk participants in the Indian ethnicity?
2. Is there a significant difference between calcium scores between male and female participants?
3. What percentage of individuals in each risk category present with calcium in the coronary arteries?
4. What is the percentage of individuals in each category presenting with calcium in the coronary arteries? The 5 categories of calcium scores according to Klodas (2005), in Hounsfield unit (HU) are: 0 / 1-10 / 11-100 / 101-400 / 400+.
5. What is the adjusted risk of calcification for demographic and risk factors in asymptomatic individuals in the Indian population in Durban, KwaZulu-Natal for the 103 and 102 research participants respectively?

Chapter Three has served as a framework for the methodology and research design of this study. Chapter Four reports the results of the study according to the research questions and hypotheses. Discussion on these results and comparison to studies conducted elsewhere is presented in Chapter Five. Finally Chapter Six covers the conclusions and recommendations for this study.
CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Through research and case studies, medical practitioners have become increasingly aware that by waiting for a disease to manifest itself, the window of prevention can easily be missed (Klodas, 2007). It is widely recognized that medicine has to alter its short-sighted view of merely diagnosing a disease to enable proper treatment via drugs or surgery, to a more far-sighted view of lifestyle alteration so that the disease never manifests itself (Klodas, 2007). A challenge therefore, for medicine and public health, is to allocate available resources to effectively reduce major causes of disease burden globally (Michaud et al., 2001). In time, it is expected that by checking one’s deoxyribonucleic acid (DNA) at birth, one will be able to eliminate later-age related degenerative diseases. But, until then, it is necessary to develop techniques that detect diseases like CAD before symptoms appear (Klodas, 2007).

In 2002 the World Health Organization (WHO), stated that at least 16. 7 million people around the globe die of cardiovascular disease (CVD) each year. CAD and CHD has currently been established as the leading cause of death in the USA and is predicted to be the leading cause of death worldwide by the year 2020 (WHO, 2002). Although documented information on CAD prevalence in developing countries is sparse, there is sufficient data to suggest an impending epidemic (Okrainec et al., 2004). Statistics in SA
also documents that CVD is a major contributor of death and a large percentage of these deaths are as a result of CAD (WHO, 2002). It is estimated that by 2030, mortalities from CVD will be 28% higher in SA than the USA (WHO, 2002). The South African National Burden of Disease study for the year 2000 estimated that 17% of all deaths were due to cardiovascular diseases (Derman, 2007). On a positive note, the death rate world-wide from CAD has declined in the past few decades, through greater understanding of risk factors as well as through better treatment, which includes the creation of specialized coronary care units (Virmani et al., 2005).

The initial presentation of CAD in up to 50% of patients is either an acute myocardial infarction (MI) or sudden death (Arad et al., 1996). Therefore, of major economic and clinical importance is the identification of asymptomatic persons with sub clinical disease, who are at high risk of developing a future coronary event and could benefit from preventative efforts (Schermund et al., 2001). However many myocardial events are not accounted for by risk factors alone (Schermund et al., 2001).

Current risk prediction of CAD is based on the patient’s age and sex as well as on the presence and extent of established, modifiable coronary risk factors such as hypertension, hyperlipidemia, diabetes mellitus and cigarette smoking (Schermund et al., 2001). Kondos et al., (2003) state that asymptomatic middle and intermediate risk individuals, are 'the worried well'. They also maintain that knowledge of the presence and extent of calcium in the coronary arteries, on these individuals, provides incremental information for risk stratification of CAD (Kondos et al., 2003). However Schermund et al., (2001), adds that currently the available tools for the prediction of CAD onset are imperfect. There is therefore a need for new methods of screening apparently healthy individuals to
identify those at increased risk (Schermund, 2001). The Framingham Risk Score only explains 70% of the overall risk for CAD and is more sensitive than specific (discussed in detail in section 2.11). In addition Kondos et al., (2003) support that conventional CAD risk factors fail to explain nearly 50% of CAD events. Consequently, there is a definite need to develop new strategies to identify patients at high risk (Schermund et al., 2001). A relatively new screening technique is the CT calcium score, which provides an opportunity to accurately and non-invasively determine the presence, extent and severity of CAD (Klodas, 2007).

The CT calcium score procedure has been in existence for a few years and has improved with time (Desjardin and Kazerooni, 2004). (Appendix K for an image of a CT scanner). The discussion on the different generations of CT scanners in section 2.17 demonstrate the improvements in this imaging modality that can now ensure a high degree of accuracy in the calcium scoring technique. The calcium scoring technique is however underutilized in SA and there are no known publications to date to indicate the contrary. This then brings one to the conclusion that there is a composite need for greater awareness of the benefits of calcium scoring as a screening tool for CAD, in SA.

Fishbach and Maintz (2005) state that direct demonstration of atherosclerotic vessel-wall involvement in asymptomatic populations with CHD risk is helpful to identify as well as to stratify individuals at risk. In evaluating the possible benefits of CT calcium screening, the purpose is to classify asymptomatic persons as likely or unlikely to have CAD (Fishbach and Maintz, 2005). Early diagnosis reduces morbidity and mortality from the specific disease in populations screened, because screening leads to effective preventative therapy.
with obvious benefit (Fischbach and Maintz, 2005).

It is apparent that only by preventing ischemic heart disease (IHD) can morbidity and mortality associated with CVD be substantially reduced (Schermund et al., 2001). Two main preventative strategies are:

(i) To focus on a community-wide population approach.

(ii) To focus on high risk individuals (high risk approach). The strengths and limits of both are complementary. With the community approach, it is recommended to promote an increase in physical activity and marginalize smoking (Schermund et al., 2001). In the current research study at Drs Jackpersad and Partners both approaches were utilized.

Hoffman et al., (2006) found that the CT calcium score effectively compliments the other currently available diagnostic tools, such as nuclear perfusion imaging and conventional angiograms in the imaging of the coronary arteries. Interestingly, the calcium score study costs approximately one fifth of a conventional angiogram (Schussler et al., 2005). Nonetheless, studies on the clinical utility, cost, and cost-effectiveness of the calcium scoring procedure are warranted to demonstrate whether and how this technique can change and improve the current management of patients with suspected or confirmed CAD (Hoffman et al., 2006).

2.2 Calcium scoring (Appendix L for a Calcium score image)

A calcium score, simply defined by Carr et al., (2000), is a non-invasive technique that quantifies the extent or severity of CAD. Furthermore, Carr et al,
(2000), maintain that it is a surrogate marker for atherosclerosis i.e. coronary artery calcification is not found in the absence of atherosclerosis. Coronary artery calcium scoring is also defined by Assey and Selby (2004), as calcification assessed by electron beam computerized tomography (EBCT), measuring calcified atherosclerotic plaque.

Calcium scoring can be used to assess individual risk for clinical coronary outcomes (Carr et al., 2000). The cumulative effect of risk factor exposure over time can be assessed by its impact on coronary plaque development (Schermund et al., 2001). There exists a relationship between the extent of calcified plaque burden and that of total plaque burden. Thus the primary aim is not to diagnose coronary stenosis but to detect and quantify coronary plaque burden (Schermund et al., 2001). Nissen (2007) supports that the presence of calcification in the coronary arteries invariably indicates the presence of CAD and the absence of calcification rules out significant plaque burden. Schermund et al., (2001) maintain that coronary calcium in many instances seems to indicate coronary disease activity. Calcium is the frequent feature of plaque rupture (found in 70-80 % of cases). Amongst all types of plaque that can be defined histological, the extent of calcium is greatest in healed plaque rupture, which is frequently observed in sudden coronary death (Schermund et al., 2001). All prospective studies in seemingly healthy older adults have found substantial increases in relative risk of CVD hard events in the presence of increased amounts of coronary calcium (Schermund et al., 2001). Similarly, Nissen (2007) states that the calcium score technique is a good predictor of coronary events on asymptomatic individuals with a high score. Therefore, the coronary calcium score is an excellent marker of CAD (Schermund et al., 2001).
2.3 Coronary atherosclerosis and CAD

Pathological studies have confirmed that coronary calcium is indicative of coronary atheroma, although the converse is not true. Atheroma can be present in the absence of detectable calcium (Wood et al., 1994). CAD is the atherosclerotic narrowing of arteries that supply blood to the heart (Wennberg and Wennberg, 2000). O’Rouke et al. (2000), adds that the presence of any calcification is indicative of CAD i.e. coronary artery calcification indicates the presence of atherosclerosis and is a potential indicator of significant coronary risks in the future. Similarly, Assey and Selby (2004), state that coronary artery calcium is part of the development of atherosclerosis. It occurs exclusively in atherosclerotic arteries and is absent in normal arteries. Calcification in the epicardial coronary arteries indicates that the patient has coronary atherosclerosis (Assey and Selby, 2004). The online Health Encyclopedia (2006), further describes atherosclerosis as a disease of the arterial wall, where it thickens, thus causing narrowing of the channel and impairing blood flow. This thickened wall can consist of low density lipoprotein (LDL), decaying muscle, fibrous tissue, clumps of blood platelets and calcium.

Importantly, Boyd (2005) states that in patients with stable CAD, the atherosclerotic process can induce a host of coronary functional and anatomic abnormalities that eventually affect myocardial performance. Atherosclerosis is a silent disease that develops slowly over decades of life until it manifests itself in clinical CAD with symptoms including angina, a heart attack and sudden death (Boyd, 2005). Atherosclerosis is also considered to be the only vascular disease associated with coronary calcification i.e. coronary calcification is pathognomonic for atherosclerosis (Hecht, 2006).
Significantly Rumberger (1999) has stated that there is a linear relationship between the amount of calcium and the overall amount of atherosclerotic plaque. Schermund et al., (2001) add that asymptomatic patients with detected calcification can be said to have CAD not detectable by usual clinical tests (sub clinical atherosclerosis). However, contrary to what Rumberger (1995) has stated, Schermund et al., (2001) states that controversy does exist regarding the relationship of the calcium score, to the prevalence of CAD and the incidence of cardiac events such as unstable angina, myocardial infarction and sudden cardiac death. On the other hand, numerous studies have shown that high Agatston calcium scores are indicative of a number of obstructive coronary artery lesions (Schermund et al., 2001). The Agatston score is discussed in detail in section 2.25.

Importantly, coronary plaques which are usually not highly stenotic are underlying substrates of acute coronary syndromes (Schermund et al., 2001). The relationship between calcified plaque burden and total plaque burden is that the more calcium there is, the more plaque there is. This carries direct implications for an individual’s coronary risk (Schermund et al., 2001).

2.4 Anatomy of the coronary arteries

The heart is composed of cardiac muscle that continuously contracts and relaxes and therefore requires a constant supply of oxygen and nutrients (Futrell et al., 2006). The vessels that supply oxygenated blood to the myocardium are known as the coronary arteries (Kaimkhani and Ali, 2005). The two main coronary arteries are the left and right coronary arteries that arise at the origin of the aorta above the
heart (Futrell, 2006). There are a few variations and anomalies in the coronary artery vessels (Van Geuns and Cademartiri, 2005).

Generally the left coronary artery (LCA), arises from the left posterior aortic sinus. The left main artery (LMA) is usually 1-2 cms in length (Van Geuns and Cademartiri, 2005) and is the initial segment of the LCA (Futrell et al., 2006). Van Geuns and Cademartiri (2005), state that in 2/3 rds of subjects, the main LCA divides beneath left atrial appendix into left anterior descending (LAD) and left circumflex arteries (LCX). The LAD and LCX are normally smaller in width than the LMA (Futrell et al., 2006). The LAD runs anteriorly in the interventricular groove (Trivellato et al., 1980). The LAD provides two main groups of branches. The septal branches supply the anterior 2/3 rds of the septum and the second is the diagonals which lie on the lateral aspect of the ventricle (Van Geuns and Cademartiri, 2005). Septal branches arise at 90 degrees from the LAD. The LCX turns backwards and runs downwards in the left atrioventricular groove. In 1/3 rd of individuals the LCA trifurcates into the intermediate artery (Van Geuns and Cademartiri, 2005).

The right coronary artery (RCA) arises from the anterior aortic sinuse, inferior to the origin of the LAD (Van Geuns and Cademartiri, 2005). The course of the RCA follows the right atrioventricular groove (Trivellato et al., 1980). The conus artery is the first branch of the RCA and runs anterior to the surface of the right ventricular outflow tract (Van Geuns and Cademartiri, 2005). The second branch is the atrial nodal branch alternately supplied by the proximal branch of the LCX. According to (Trivellato et al., 1980), in 85 % of patients the RCA gives rise to the posterior descending artery (PDA). The RCA continues forward from the crux along the posterior interventricular groove to become the PDA, running to the apex of the heart (Van Geuns and Cademartiri, 2005).
Septal branches supply the posterior 1/3 rd of the septum and arise from the PDA and connect with the septal branches of the LAD to form the collateral circulation (Van Geuns and Cademartiri, 2005). In addition the PDA supplies the inferior ventricular wall and posteromedial papillary muscle of the heart (Trivellato et al., 1980). The postero-lateral branch (PLB) supplies the postero-inferior aspect of the left ventricle and also arises from the RCA close to the crux. The PLB is also a continuation of the RCA and runs parallel to the PDA. Left coronary dominance exists when the PDA arises from the LCX (Van Geuns and Cademartiri, 2005). If the RCA supplies the PDA and PLB then right dominance exists. If the RCA supplies the PDA and the LCX supplies the PLB the circulation is co-dominant. The general population have 60% right dominance, 25% co-dominance and 15% left dominance. A very rare variation in 4% of the general population is the presence of a third posterior coronary artery (Van Geuns and Cademartiri, 2005). Another variation is where double coronary arteries exist, that run parallel to each other (Kaimkhani and Ali, 2005).

Diagram 1. below shows the 3 main coronary arteries in relation to the aorta
Diagram 1. showing the coronary arteries


2.5 Pathophysiology of coronary artery calcification

According to Libby (2001), atherosclerotic plaque accumulation in the coronary arterial wall begins long before the development of angiographic stenosis. Therefore coronary atherosclerosis is as a result of a sequence of changes over time in the arterial wall (Fishbach and Maintz, 2005). Although calcification is normally found in advanced lesions, it may occur in small quantities early in life (Wexler et al., 1996). Histologically, different types of atherosclerotic lesions can be distinguished which has led to a classification system by the American Heart Association (AHA), which follows (Fischbach and Maintz, 2005).

2.6 Classification of atherosclerosis
The histological classification of human atherosclerotic lesions are designated Roman numerals according to the sequence of lesion progression (Stary et al., 1995). Initial and intermediate lesions are types I, II and III (Virmani et al., 2005).

Type I and II lesions are composed of fatty streaks with lipid laden macrophages. Type III lesions have extra cellular lipid droplets and cell degeneration is evident (Ongen and Yilmaz, 2006). The advanced atherosclerotic lesions are subdivided into types IV, V and VI. The type IV lesion (atheroma) is characterized by extra cellular intimal lipid accumulation, the lipid core (Virmani et al., 2005). In type IV lesions the intimal layer is severely damaged (Ongen and Yilmaz, 2006). The type V lesion contains fibrous connective tissue formation (Virmani et al., 2006).

The Va lesion has a thin fibrous cap over the lipid core and can result in thrombus formation (Ongen and Yilmaz, 2006). If parts of the lesion are calcified, it becomes a Vb lesion. If the lipid core is absent and there is reorganization and repair to the lesion, the type Va or Vb lesion is classified as type Vc. Type IV and V lesions may develop fissures, haematomas and/or thrombi. The lesion that has progressed into a hematoma or thrombi is classified as a type VI lesion (Virmani et al., 2005).

2.7 Components of atherosclerotic plaque detected by CT, MRI, and pathological tests

The different components of plaque can be investigated with CT, Magnetic Resonance Imaging (MRI) and pathological tests. With CT application the different types of plaque can be quantified into three categories (Schroeder, 2003). Soft plaque generally has a density of < 50 hounsfield units (HU). Intermediate plaque has a density between 50 -120 HU. Calcified plaque has a density of > 120 HU (Schroeder, 2003). MRI is useful to discriminate between lipid cores, fibrous caps, calcium, normal media and adventitia in atheromatous
plaque. Intraplaque haemorrhage and acute thrombi can also be detected on MRI (Toussaint et al., 1996). Cellular components of atherosclerosis investigated by pathological tests include smooth muscle cells, endothelial cells, macrophages, T and B lymphocytes, red cells, platelets, neutrophils and basophils (Virmani et al., 2005). Non-cellular components include lipid proteoglycans, collagen, elastic fibres, calcium, iron and blood components. The lipid core is formed by macrophages that migrate into the intima to ingest lipids (Grech, 2003). The various components of the atherosclerotic process are adaptive intimal thickening (AIT), intimal xanthomas, pathologic intimal thickening (PIT), fibroatheroma, thin cap fibroatheroma, plaque rupture, calcified nodules, fibrocalcified plaque (either from healed plaque erosion or propagated thrombus) and plaque erosion (Virmani et al., 2005).

The least frequent lesion that results in a coronary luminal thrombus is a calcified nodule, which contains calcified plates at the site of luminal disruption (Virmani et al., 2005). This plaque formation can also be referred to as atheroma (Stary et al., 1995). There may or may not be a necrotic core within the plaque (Virmani et al., 2005). Occasionally bone formation with osteoblasts and osteoclasts are present.

In 50% of the cases lesions are located in the middle of the coronary artery, in a heavy calcified segment and are more common in older men than women (Virmani et al., 2005).

2.8 Statistics of death from CAD/CVD

At least 16.7 million people around the globe die of CVD each year and CAD is a major contributor of these deaths (WHO, 2000). Further statistics published by the WHO (2000),
reports that CVD is the leading cause of death in Europe, with over 4 million deaths per annum. Fifty percent of these deaths are from CHD (WHO, 2000). Kondos et al., (2003), add that coronary artery calcification is a primary cause of death in the USA and is most likely to remain the leading cause of death well into the 21st century. In agreement, with Kondos et al., (2003), Assey and Selby (2004) maintain that CAD is the number one cause of death in the USA and will remain so for the next 50 years. Fischbach and Maintz (2005) lend agreement to the other authors by stating that CVD has been the leading cause of death in the USA ever since the 1900’s, with the exception of the influenza epidemic in 1918.

CAD worldwide predominantly manifests in middle age and older men (Fischbach and Maintz, 2005). The average age of individuals with a myocardial event is 65-70 years in women. The first manifestation of the disease in 50% of CHD victims is a non-fatal myocardial attack or sudden death (Fischbach and Maintz, 2005). Contrary to Fishbach and Maintz’s (2005) statement that CVD manifests predominantly in men, Meires et al., (2005) state that cardiovascular disease has been found to be the leading cause of mortality in women in the USA. Men have experienced a decline in deaths from CAD. The number of deaths in women from CAD is approximately 240 000 annually and women have a far worse prognosis than men. Up to 40% of initial cardiac events in women are fatal, with coronary artery calcification being low in premenopausal women (Meires et al., 2005).

The South African National Burden of Disease study for 2000, estimated that 17% of all deaths in SA were due to CVD (Derman, 2007). Furthermore, Naidoo et al., (2005), add that CHD has been reported to be higher in the Indian population of SA, compared to the other population groups. Indian migrants from the Indian subcontinent suffer between 1.5 to 4 times higher mortality compared to other
The study conducted by Naidoo et al., (2005), on South African Indians examined risk factors and clinical features of individuals in different age subsets, with acute coronary syndromes. Participants less than and equal to 45 years were considered to be “young.” Individuals greater than 45 years and less than or 65 years of age were considered to be “middle age.” Individuals greater than 65 years were considered to be “old.” The outcome of the study was that myocardial infarction is more frequent (20%), in the young South African age group compared to myocardial infarction world-wide, which is between 4-10% in the same age group (Naidoo et al., 2005). In addition, smoking, low high density lipoproteins (HDL) levels, obesity and strong family history of CHD were common in young patients. Diabetes mellitus, hypertension and past history of CAD was greater in older patients. Also noted were significant differences in the risk factor status between gender types. Smoking and low HDL was noted in men, while hypertension, diabetes mellitus and obesity was more common in women (Naidoo et al., 2005).

An observation by Klodas (2005), is that most studies have evaluated patients in the age group of 40-70 years, although younger individuals may be appropriate candidates for evaluation of coronary artery calcification depending on their risk profile. On the other hand, Weissman et al., (2006) state that although younger patients with acute coronary events rarely exhibit coronary calcifications, calcium is a frequent feature of coronary arteries i.e. it is found in 70-80% of the population.

The current research includes the age group of 20-70 years.

2.9 Ethnic differences in coronary atherosclerosis
Budoff et al., (2002) conducted research on 782 participants in the Harbour-UCLA Medical Centre to determine if there exist any ethnic differences in the prevalence of coronary artery calcification with coronary obstruction. After controlling for age, gender and cardiac risks, the results of the study were as follows: differences do exist in coronary artery calcification and angiographic stenosis in the different ethnic groups. In the white population group (n=453), prevalence of coronary artery calcification (score>0), was 84% with 71% obstruction on angiography. In the Asian population group (n=44), coronary artery calcium percentage was 73% with 64% angiographic stenosis. In the Hispanic population (n=177), there was lower prevalence of coronary artery calcification and 58% angiographic stenosis. The Black population group (n=108), showed an even lower prevalence of coronary artery calcification i.e 62% and 49% angiographic stenosis (Budoff et al., 2002). The authors concluded from this data that there exists a difference in prevalence of coronary atherosclerosis in the different ethnicities. The White population subset has shown the greatest incidence of coronary artery calcification in this study population in the USA. In contrast in SA, the Indian population has the highest incidence of CAD/CHD (Naidoo et al., 2005).

2.10 Signs and symptoms of CAD and atherosclerosis

Greenland et al., (2001), contend that 25% of patients with CAD have sudden death or non-fatal MI without prior symptoms. Therefore, strategies for high risk primary prevention, address ways to identify more patients who are asymptomatic and clinically free of CHD, but are at high risk for future coronary events, to justify more intensive risk reduction efforts (Greenland et al., 2001). Similarly Budoff et al., (2002), state that the first indication of atherosclerosis is MI or sudden coronary heart death. In addition, Boxt et al.,
(2003), state that atherosclerotic plaque accumulation in the vessel wall begins long before the development of angiographic stenosis. Most acute coronary events are initiated by rupture or erosion of mildly stenotic but vulnerable (high risk) lesions (Boxt, et al., 2003). Sadovisky (2005) adds that symptomatic patients for CAD have chest pains, unexplained exertional dyspnoea or congestive heart failure. However, the essence of an article in the online Health Encyclopedia (2006) is that atherosclerosis can produce no symptoms until damage to the arteries is severe enough to restrict blood flow.

For the above reasons, the study conducted at Drs Jackpersad and Partners, targeted asymptomatic risk and non-risk individuals over a wide age span of 20-70 years.

2.11 The Framingham risk score (FRS) and risk factors for CAD

The Framingham Risk Score (FRS), is a scoring system for CAD risk derived from the White population of Framingham, Mass, in the USA (Grundy, 1999). Population patterns of CAD incidence in Framingham, Mass, were found to be similar although not identical among people of American White, Black and Hispanic origin. However, Framingham risk projections were found to be unreliable in other ethnic groups i.e. they underestimate risk in Asians living in the USA (Grundy, 1999). The risk factors as stipulated by the FRS are; elevated blood pressure, elevated cholesterol levels, smoking, diabetes and advancing age (Greenland et al., 2004). Lewis (2003) advises that atherosclerosis and CAD commences in early adult life. Therefore people with known cardiac risks should consider having a CT calcium score scan at the age of 40-50 years. Similarly, Greenland et al., (2004) advise that all adults undergo CAD risk assessment to guide preventative treatment. Although the FRS is often recommended for this, it is
suggested that risk assessment may be improved by additional tests such as coronary artery
calcium scoring (Greenland et al., 2004). Furthermore Lewis (2003), states that the risk
factors based on the Framingham equation reasonably accurately predicts the proportion of
people who will have a coronary event. Therefore, the reliability of the FRS, in assessing
individuals in the SA population for CAD is questionable and the calcium scoring technique
may be more desirable.

The Framingham technique works by grading the major risks, then sums
these gradations to obtain an aggregate risk (Grundy, 1999). Risk points are assigned
according to the severity of the risk factors. Different points are assigned to male and female
as is demonstrated in Table 2.1. The FRS projection in Table 2.2 derived from risk points in
Table 2.1 denotes the 10 year likelihood of developing hard CHD.
Table 2.1 Global Risk factors for CAD (Grundy, 1999).

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>HDL cholesterol mg/dL</th>
<th>Male</th>
<th>Female</th>
</tr>
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<tbody>
<tr>
<td>&lt; 34</td>
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<td>-9</td>
<td>&lt;35</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>35-39</td>
<td>0</td>
<td>-4</td>
<td>35-44</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>40-44</td>
<td>1</td>
<td>0</td>
<td>45-49</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>45-49</td>
<td>2</td>
<td>3</td>
<td>50-59</td>
<td>-1</td>
<td>0</td>
</tr>
<tr>
<td>50-54</td>
<td>3</td>
<td>6</td>
<td>&gt;60</td>
<td>-2</td>
<td>-3</td>
</tr>
<tr>
<td>55-59</td>
<td>4</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>60-64</td>
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<td></td>
</tr>
<tr>
<td>65-69</td>
<td>6</td>
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</tr>
<tr>
<td>70-74</td>
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</table>

<table>
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<tr>
<th>Total cholesterol mg/dL</th>
<th>Male</th>
<th>Female</th>
<th>Plasma glucose mg/dL</th>
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<tr>
<td>&lt; 160</td>
<td>-3</td>
<td>-2</td>
<td>&lt;110</td>
</tr>
<tr>
<td>169-199</td>
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<td>0</td>
<td>110-126</td>
</tr>
<tr>
<td>200-239</td>
<td>1</td>
<td>1</td>
<td>&gt;126</td>
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<td>240-279</td>
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</tr>
<tr>
<td>&gt;280</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

The risk points for each category i.e. male/female, total cholesterol, diabetes (plasma cholesterol, diabetes (plasma glucose).
glucose), HDL cholesterol and smoking, is totalled. The absolute risk (hard CHD) percentage is then calculated for male and female according to the risk points as demonstrated in Table 2.2. For example a risk point of 2 indicates that the total sum from the above global risk points for an individual is 2. Hence, according to Table 2.2 a male with a risk point of 2, and a female with a risk point of 2, have a 3% and 2% probability of having an absolute risk for CHD respectively (Grundy, 1999).

Table 2.2 Absolute risk (hard CHD) %

<table>
<thead>
<tr>
<th>Risk points</th>
<th>Male</th>
<th>Female</th>
<th>Risk points</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>11</td>
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<td>7</td>
<td>9</td>
<td>3</td>
<td>14</td>
<td>45</td>
<td>13</td>
</tr>
</tbody>
</table>

The FRS addresses ways to identify more patients who are asymptomatic and clinically free of CAD/CHD, but are of high risk for future coronary events (Greenland et al., 2001). Risk assessment begins in the physician’s office on examination of the patient. In addition to the FRS a recently investigated risk factor is the metabolic syndrome which is a cluster of metabolic disorders that predisposes one to the development and progression of atherosclerosis (Assman et al., 1999). Elevation of homocysteine levels (sulphur amino
acid), in the blood plasma is also a recently discovered risk factor for atherosclerosis, and is also part of the metabolic syndrome (Assman et al., 1999).

The FRS was endorsed by AHA and the American College of Cardiology (ACC) in the determination of global risk for CAD/CHD (Greenland et al., 2001). AHA classifies and calculates the percentage of risk as low, intermediate and high risk.

**Low Risk**: A 30 year old non-smoker with low cholesterol and blood pressure is at < 10 % risk i.e. the individual has < 10 % risk of having a heart attack in the next 10 years.

According to AHA, a heart scan is not recommended in these individuals.

**Intermediate Risk**: These individuals have a 10-20 % risk of having a heart attack in the next 10 years. Treatment can be guided by the calcium score result.

**High Risk**: Over 65 year old individuals, who smoke, have high cholesterol and high blood pressure have > 20 % risk of having a heart attack in the next 10 years. These individuals are not recommended for a heart scan, as it has already been established that they are at risk (Grogan, 2006).

### 2.12 Level of education and CAD

Hardson et al., (2001) and Yan (2006), conducted research to establish the relationship between an individual’s level of education and their prevalence of CAD.

The study conducted by Hardson et al., (2001) was on 18912 participants in Reykjavík Iceland over a 30 year period. When controlling for risk factors, the study showed that there was a 14% reduction in CAD in men with high school education relative to elementary school, and a 17% reduction in CAD mortality for college students compared to the 38% for University students. For women a 34% reduction in CAD
mortality in high school graduates was reported, a 55% in college graduates and too few women had university education for reliable results. The authors therefore established that education can be considered to be a strong protector for all cause and CAD mortality (Hardson et al., 2001).

Similarly Yan (2006), an assistant research professor from the North West University, Beijing, had studied the level of education and its association with CAD on 2913 individuals. The results documented that education is inversely associated with a wide array of clinical outcomes and death. After 15 years into the study, 9% of the individuals had coronary artery calcification. The result of the study reported that the prevalence of coronary artery calcification was four times higher in participants with less than a school education, compared to those with a college education (Yan, 2006). These findings were partially explained by an increase in risk factors over the 15 year period of the study. The risk factors were high blood pressure, elevated cholesterol levels, an increase in waist circumference, smoking and a decrease in physical activity. The standpoint of the study was that integrated prevention and intervention in strategies should be considered for less educated persons (Yan, 2006). Statistics according to Aitchison et al., (2005) have shown that 1.5 million people in SA have not received any formal education. How the level of education will and has impacted on this population’s health is an area that is understudied and should be considered in the future.

2.13 Accuracy of the calcium score technique

According to Sadovsky (2005) calcium scoring has accuracy similar to exercise/stress scintigraphy and echocardiography. On the other hand, Weissman et al., (2006) state that
calcium scoring is still experimental, but safe and reliable. Its high predictive value makes it a fast, reliable way of evaluating chest pains or suspected false positive results in patients with low/intermediate likelihood of CAD (Weissman et al., 2006).

2.14 Reliability and benefits of the calcium score technique

Calcium scoring is a useful index in CAD progression and a factor in prognostic estimation (Wood et al., 1994). The authors further state that calcium scoring can be used to exclude CAD in individuals with atypical chest pains or in high risk individuals like aviation professionals. Similarly Carr et al., (2000), state that calcium scoring can potentially be used to estimate individual risk for clinical coronary outcomes. Calcium can also be non-invasively measured for epidemiological studies (Carr et al., 2000). The search for coronary patients with sub clinical disease is critically important to potentially benefit from intensive primary prevention efforts (Greenland et al., 2001). Primary prevention efforts can be implemented once there is knowledge of the amount of calcium in the coronary arteries (Greenland et al., 2001). The need therefore arises for research to be conducted to evaluate the calcium score in asymptomatic, risk and non risk individuals.

The benefit of the calcium scoring technique as stated by Schermund et al., (2001) is that it allows for direct visualization and detection of coronary atherosclerotic plaque and estimation of the extent of disease and its distribution in the coronary tree. In addition CT high speed scanning is the only technique that has proven to be simple and reliable in demonstrating atheroma in an individual (Lewis, 2003). The research conducted at Drs Jackpersad and Partners was on such a scanner i.e. a Multidetector, General Electric (GE) Lightspeed 64 slice VCT scanner. As apposed to other methods of direct vessel wall
diagnostics such as B-mode ultrasound analysis of the carotid artery, coronary atherosclerosis can be directly assessed. As apposed to non invasive exercise tests such as exercise stress testing or stress echocardiography, actual coronary plaques are detected. Coronary calcium scanning adds previously unachievable prognostic power to the information derived from risk factor analysis (Schermund et al., 2001). Therefore, calcium scoring is the key to predicting cardiovascular risk (Lewis, 2003). In addition Weissman et al., (2006), state that the calcium scoring technique is safe and reliable in predicting risk of death from CAD.

A further benefit is that calcium scoring will eventually be used to decrease frequency of invasive interventional procedures (Sadovsky, 2005). In a recent publication by AHA (2007), it is stated that the coronary calcium score is known to predict occurrence of cardiac events and determines the need for coronary bypass surgery or coronary (balloon) angioplasty over the next one to two years. In contrast, a recent news report revealed that former US President Bill Clinton had passed stress tests only a few years before his need for coronary bypass surgery (Schussler, 2006). The question raised was if he had normal tests, why was there a complete lack of awareness of his coronary atherosclerosis? President Clinton believed he was healthy and had even stopped his statin therapy, resulting in the need for him to have bypass surgery. On the other hand, President George Bush had recently undergone a CT calcium score scan to be informed that he had minor plaque. He was immediately placed on statin therapy and it is conceived that by early non-invasive evaluation, the physicians may have altered the course of his disease process (Schussler, 2006).
2.15 Effectiveness of the calcium score technique

The advent of the electron beam computerized tomography (EBCT) as stated by Modic and Obuchowski (2003) has made it possible to scan small areas such as the heart, with high spatial and temporal resolution in a short period of time in the diastole mode. The authors further suggest that using such scanners, enables accurate scoring and detection of small plaque. Desjardin and Kazerooni (2004), state that the load of calcium increases by 15-25% per year without treatment, but slows or stops during statin therapy. Therefore the need arises for individuals to be aware of the disease status of their coronary arteries.

The efficacy of any screening study can be gauged by the fulfilment of certain criteria. This is well expounded by Modic and Obuchowski (2003) and Redberg et al., (2003). Modic and Obuchowski (2003), provide nine criteria for evaluating the effectiveness of screening for a risk factor. In addition, Redberg et al., (2003) provide three vital criteria for screening. These criteria have been utilized in the current research. The rationale for screening asymptomatic individuals for a risk factor like atherosclerosis is that early detection can lead to disease prevention.

The criteria for screening individuals for risks of CAD according to Modic and Obuchowski (2003) are:

- The disease has serious consequences.
- The population has a high incidence of the disease. Calcium scoring does not detect clinical CAD, but is a risk factor for subsequent development of clinical disease.
- The detection and quantification of coronary artery calcification is based on the
assumption that coronary artery calcification poses a risk of CAD and that primary prevention can lower the risk of disease. Calcium scoring is then used as a marker for CAD.

- There is high accuracy of detection for a risk factor. The EBCT technique is highly specific and sensitive for plaque detection.

- Very often, disease prevention is missed. Screening must detect disease or risk factor before it is critical for the patient.

- Radiation dose should be considered. The authors state that cancer inducing effects are not observed in radiation doses < 200 millisvert (mSv).

The radiation dose is automatically recorded on the General Electric (GE) 64 slice VCT and the smart mA option, allows for dose modulation according to thickness of area to be scanned.

- The test is affordable and available.

- Prevention characteristics should be considered before symptoms occur.

Prevention options are diet control, exercise, quitting of smoking, alcohol and drug cessation and surgical intervention. Prevention is cheaper than treatment after disease formation (Modic and Obuchowski, 2003).

Incidentally, the total cost in the United States to diagnose and treat CAD is nearly $115 billion annually (Desjard in and Kazerooni, 2004).

- Prevention measures are neither risky nor toxic.

In addition to the above criteria for screening, the US Preventative Services Task Force recommended in its 1996 report that any screening test utilized in assessment of CAD risk can be considered effective if :-
• It provides an accurate determination of the likelihood that an asymptomatic person has the condition.

• The results are stable when repeated i.e. reliable.

• Early intervention is likely to be beneficial (Redberg et al., 2003).

2.16 AHA and ACC consensus statements and the Cardiac Society of Australia and New Zealand (CSANZ) statement on coronary artery calcium studies

In an EBCT statement by AHA (2000), it was indicated that EBCT is not superior to alternative non-invasive imaging techniques at diagnosing CAD and is therefore not recommended. Published literature could not answer whether coronary artery calcium screening is additive to FRS. There was a degree of uncertainty around coronary artery calcium screening at that stage and the procedure was not advised to be made available to the general public without a physician’s request (Wood, 2006).

The publication by Loscalzo et al., (2004) state that the role of coronary artery calcium scoring in the primary prevention of cardiovascular disease has not been firmly established, and hence the AHA has not recommended their implementation on a population-wide basis. Furthermore AHA’s current position on CT scanning for calcium scoring is that calcium scoring may be appropriate when physicians are faced with patients with intermediate risk, if the results have the potential to alter the treatment of the patient (Loscalzo et al., 2004). Furthermore, it is not clearly defined whether long-term patient outcomes can be improved by modifying treatment based on coronary calcium scores (Loscalzo et al., 2004).
In 2005, CSANZ issued a statement, that the routine use of coronary artery calcium scanning using CT based modalities as a screening tool, cannot be advocated in unselected asymptomatic patients (Meires et al., 2005). Later in 2005, the ACC/AHA issued a joint statement advocating the use of coronary artery calcium testing for CAD risk in selected clinically referred individuals with intermediate risk (Meirs et al., 2005).

More recently a document that draws heavily on studies published in the past two years, reports a new statement by AHA. The statement is that majority of published studies have reported that the total amount of coronary calcification (referred to as the Agatston score) predicts CAD beyond standard risk factors. Coronary artery calcium screening is both independent and incremental to traditional risk factors in the prediction of cardiac events (Wood, 2006).

2.17 CT calcium scoring versus coronary angiograms

Broderick et al., (1996), in the American Journal of Roentgenology, compared CT calcium scoring to conventional coronary angiograms in 101 patients with suspected CAD. The studies were done within 24hrs of each other. In CT, a score greater than 0 defined disease. In conventional angiography lumen stenosis greater than 50% defined disease. Comparison was made with the results of CT and conventional angiography. The sensitivity, specificity and accuracy of CT scanning in predicting disease was 88%, 52% and 76% respectively. The conclusion from this study was that the quantity of calcium as measured by helical CT correlated positively with obstructive CAD measured by conventional angiography. The authors, Broderick et al., (1996), confidently state that the new scoring technique shows promise.
On the other hand Lewis (2003) and Weissman et al., (2006), state that conventional coronary angiography is currently the gold standard for CAD. However, it requires a high level of technical expertise and technology, making it relatively expensive and limited to a selected population. Although it demonstrates the lumen well, the information on coronary plaque is not extensive and is considered a drawback (Weissman et al., 2006).

2.18 Other modalities for calcified plaque detection

According to Schurjf et al., (2005), non-invasive cardiac imaging is of two fold, functional and anatomical imaging. Functional imaging by Nuclear Medicine, Stress Echocardiography and MRI is important for the haemodynamic assessment of CAD. On the other hand anatomical imaging by MRI and CT is for non-invasive visualization of the coronary artery tree (Schurjf et al., 2005).

Another anatomical imaging modality for the coronary arteries is with intravascular ultrasound (IVUS) where images of the coronary arteries are obtained by a catheter inserted into the coronary arteries and attached to a transducer (Weissman et al., 2006). Its advantages are that it provides cross sectional and 3 dimensional (3D) imaging of the coronary arteries. Its limitations are that it is operator dependent and is an expensive imaging modality (Grech, 2003). Multidetector CT(MDCT), an alternative to conventional angiography, shows coronary vessels and bypass grafts (Weissman et al., 2006). Cardiovascular MRI is a non-invasive procedure that requires no exposure to radiation. However Magnetic Resonance Angiography (MRA), is technically difficult to confidently determine the extent and severity of coronary stenosis due to breathing, cardiac motion and
small vessel tortuosity (Weissman et al., 2006). IVUS, CT and MRI are considered to provide more information on atherosclerotic lesions than conventional angiography.

2.19 The different generations of CT scanners for calcium score assessments

EBCT employs computer technology for the scanning procedure. In contra-distinction to conventional CT scanners no mechanical parts move (Schermund et al., 2001). The benefits of MDCT and EBCT as stated by the authors are that the scanner almost freezes the motion of the heart as a result of a very fast image acquisition and synchronization to ECG signals. A contribution by Buchgeister et al., (2003) is that ECG-pulsed tube current modulation can significantly reduce radiation dose in the calcium scoring technique by 46%. Another noteworthy development is the use of EBCT to monitor lipid lowering treatment. Achenbach et al., (2002) in a prospective study showed clinically significant progression of coronary calcification and hence atherosclerotic plaque disease in untreated patients with hyperlipidemia within 12 months. The authors further state that progression of the calcified plaque of the coronary arteries could be reduced by lipid lowering treatment after diagnosis by EBCT (Achenbach et al., 2002).

The evolution of CT scanners has had a positive impact on the speed and accuracy of the calcium scoring technique. The first generation of axial imaging CT was introduced in 1970. In the late 1970’s, the fast generation axial CT was introduced. Single slice CT was made for fast scanning and improved temporal resolution over non-helical scanners (Desjardin and Kazerooni, 2004). For the calcium scoring technique to be a success a high spatial resolution is required to view small structures and a high temporal resolution, is required for motion free imaging. Furthermore, respiratory motion must be
eliminated. Therefore the scan must ideally be performed in one breath-hold (Desjardin and Kazerooni, 2004). Thus, radiological enthusiasm for the vast capabilities of MDCT technology with an increase in the number of detector arrays has grown considerably (Rumberger and Ehrlich, 2004). Furthermore, the authors state that spatial resolution in new spiral scanners is truly extraordinary, producing strikingly clear images of stationary organs in the body (Rumberger and Erhlich, 2004). Such a scanner is the volume CT (VCT), the current generation of scanners. It has greater temporal and spatial resolution compared to other scanners (Desjardin and Kazerooni, 2004). A 64 slice VCT with cardiac gating facilities was utilized in the current research conducted at Westridge Medical Centre, Durban, KwaZulu-Natal.

2.20 Radiation dose from the calcium score study

Desjardin and Kazerooni (2004) state that the exposure received during a calcium score test is normally 1-2mSv per investigation. O’Donnell and Hoffman (2005), further state that the radiation exposure is minimal in the calcium score study i.e. between 0.7 to 3mSv and is equivalent to 25-100% of the natural background radiation exposure received by an individual in the USA. In addition Budoff (2006) states that ionizing radiation from natural sources is a part of our daily existence. Comparatively the radiation exposure from the calcium score study is less than that received during a cardiac catheterization procedure, which is approximately 4.5 mSv (O’Donnell and Hoffman, 2005). Although the radiation exposure in the calcium scoring test is low, for some individuals it is considered unacceptably high and incidental findings may result in anxiety and subject patients to further radiological investigations (O’Donnell and Hoffman, 2005). Therefore the role of healthcare professionals involved in medical imaging, should
be to understand the potential risks of a test and balance those against the benefits. (Budoff, 2006). This should particularly be adhered to in conducting diagnostic tests on healthy individuals as part of a disease screening or risk stratification programme. Clinical benefits should outweigh radiation risks (Budoff, 2006).

### 2.21 Limitations/pitfalls of the calcium scoring technique

According to Schroeder (2003), a major limitation of MDCT for its use as a screening test is the high radiation exposure i.e. 5-10 mSv (this MDCT study is a combination of the CT calcium score study and CT angiography). Radiation dose for a conventional angiogram is approximately 3mSv. However the radiation dose from conventional angiography and IVUS combined is much higher than that of MDCT for calcium screening (Schroeder, 2003).

Girshman and Wolff (2003), state that soft plaque and subsequent thrombi formation is the immediate precursor for coronary events. Although soft plaque is by definition devoid of calcium, the aggregate coronary artery calcification reflects underlying total plaque burden and therefore indirectly estimates the presence, but not necessarily the location of soft, vulnerable plaque (Girshman and Wolff, 2003). On the contrary Klodas (2005), states that early plaque formation is not calcified therefore minimal atherosclerotic changes may be missed by the technique.

Leber (2004) also states that lumen stenosis is difficult to assess on the calcium score study. Nonetheless, Girshman and Wolff (2003) maintain that coronary artery calcium scoring is a stronger predictor of future myocardial events than well known
traditional risk factors of hyperlipidemia, hypertension, smoking, diabetes and age.

Ludema (2006) from the Michigan State department of Radiology, in agreement with Klodas (2005), state that the most problematic area of calcium scoring is respiratory and cardiac motion. Motion artefacts can cause false positive and false negatives due to areas of hyper-attenuation being scored or calcium being out of the plane of imaging. Fortunately, respiratory motion is less common in MDCT because the breath hold is between 20-25 seconds (Ludema, 2006). A 5-8 second breath hold was used in the current research, on the 64 slice VCT, which eradicated the problem of cardiac motion artefacts.

2.22 Contra-indications of the calcium score technique

According to Klodas (2005), patients with arrhythmias or resting tachycardia i.e. a heart rate greater than 90 beats per minute (bpm) are contraindicated for the calcium scoring technique, because the irregular and high heart rate causes cardiac motion artefacts. Pregnant patients are also contra-indicated for the calcium scoring procedure, because the procedure requires exposure to a minimal amount of radiation (Klodas, 2005). Further contra-indications are individuals who are at high risk or have had heart attacks. Individuals who have had bypass surgery or angioplasty and stenting are also contra-indicated for the calcium score studies, as these individuals are symptomatic and may require more aggressive treatment rather than preventative steps (Grogan, 2006).

2.23 The calcium score procedure

The calcium score procedure is outlined below. A more detailed explanation is provided in Chapter Three.
- No preparation is required for the patient (Assey and Selby, 2004).

- Risk assessment questionnaires should be completed to aid in the overall interpretation of the study. The risk factors based on the FRS are, advancing age, hypertension, dyslipidemia, diabetes, smoking and strong family history of CAD (Assey and Selby, 2004).

- A gown needs to be worn with the opening in front to allow ECG leads to be connected to the participants, whilst they lie supine on the table (Nissl, 2005). Assey and Selby (2004) and Nissl (2005), state that participants need to remove jewellery from the chest as it causes artefacts on images.

- ECG electrodes are placed appropriately on the chest and the electrical activity of the heart is noted (Nissl, 2005). Two or three ECG leads can be utilized to obtain an adequate ECG trace. A noise-free ECG signal is important to synchronize the ECG signal to the raw image data obtained (Hoffman et al., 2006). Furthermore Assey and Selby (2004), state that the scan may be done with prospective, retrospective gating or none.

- If the heart rate is greater than 90 bpm, a beta-blocker may be given to slow the heart rate (Nissl, 2005).

- Breath-hold for the scan is 15-30 seconds according to Assey and Selby (2004) and 20-30 seconds according to Nissl (2005).

- The scanning parameters are generally 165 Ma, 120Kv, 0.5 pitch, 0.25 mm. This is however manufacturer dependent (Assey and Selby, 2004). The scan parameters vary slightly between vendors of the same generation of CT scanners (Hoffman et al., 2006).

- The ‘voice prompt’ is used to reassure the participant during the procedure (Nissl, 2005).
2.24 Comparison of ECG – triggered CT calcium scoring and retrospective gated CT scans

According to Vembar et al., (2003), constant, rapid, cardiac motion can cause significant image artefacts. It is therefore necessary to synchronize data acquisition with the cardiac cycle. Lu et al., (2002), tested the hypothesis that scanning during ECG triggering can minimise image motion artefacts and reduce interexamination variation of calcium score in EBCT. Two hundred patients underwent EBCT once and their study was repeated after 5 minutes to evaluate the interexamination variability of calcium scoring. Group 1 participants had scans with ECG triggering. Group 2 participants underwent scanning with the use of conventional 80% of the R-R triggering. The results showed that 26% (27 of 104) participants in group 1 with ECG triggering had motion artefacts. In group 2, 80% (77 of 96) had cardiac motion artefacts. It is therefore evident that the ECG triggered calcium score tests as opposed to triggering set at a particular position in the R-R interval, was favourable as there were less motion artefacts in the former (Lu et al., 2002).

2.25 The Agatston, Volumetric and Hydroxypatite mass method of calcium quantification

Coronary calcium is defined as a hyper attenuating lesion above the threshold of a CT density of 130 HU, representing two or more pixels (Schermund et al., 2001). In comparison the density of air is approximately -1000 HU. The density of water is 0 HU and the density of dense cortical bone is 1000 HU (Hecht, 2006). Recently the quantification of calcium from contrast enhanced MDCT images has been proposed using a threshold of 350 HU (Hong, 2002).
Agatston in 1990 first developed a standard method of interpreting or quantifying calcium using results from EBCT (Girshman and Wolff, 2003). However this is the least reproducible method of quantification (Ulzheimer and Kalender, 2003). In this method of quantification, the calcium score is a product of the area of the calcium and a factor related from 1-4, dictated by the maximum CT density (Girshman and Wolff, 2003). The operator identifies areas of calcification to be analysed on axial images of the heart. The software thereafter calculates the area, mean density, and peak density of calcium for each segmental lesion in the coronary arteries (Girshman and Wolff, 2003). Schermund et al., (2001) state that the calcium score can be calculated for a given coronary segment, a specific coronary artery or entire coronary system. The area of each segment is 4 pixels or 1mm (Girshman and Wolff, 2003). However this is software dependent. The threshold used is 130 HU and over. A density weighting factor is then applied to each lesion. A factor of 1 is used for densities between 130-199 HU; 2 for 200-299; 3 for 300-399 and 4 for \( \geq 400 \) (Girshman and Wolff, 2003). The Agatston calcium score is derived from \((\text{area of lesion in } \text{mm}^2) \times (\text{weighting factor})\). The total calcium score is then derived for the LMA, LAD, LCX and RCA arteries (Girshman and Wolff, 2003). Smaller areas i.e. 2 pixels can now be detected with MDCT, hence low density lesions can be included in the analysis (Girshman and Wolff, 2003). Also, improving signal to noise, can lead to detection of calcification as low as 90 HU. A weighting factor of 1 is then applied for the range of 90-199 HU (Girshman and Wolff, 2003).

The risk stratification is then applied by tabling the score according to percentile ranking for gender and age for that particular population (Klodas, 2005). There is currently no reference data-base for calcium scores in the South African population, therefore
percentile ranking was not applied to calcium scores of participants in the research conducted at Drs Jackpersad and Partners.

Volumetric calcium scoring is another option of quantification and measures calcium by a volume method (Sadovsky, 2005). The calcium volume scan (CVS) for each lesion is calculated as the number of voxels x volume of one voxel (Fishbach and Maintz, 2005). Determination of calcified plaque volume is independent from the section thickness or image overlap used. The lack of density dependent weighting factor further reduces the influence of partial volume effects (Fishbach and Maintz, 2005). Therefore it is found to have better reproducibility than the Agatston method of quantification (Ulzheimer and Kalender, 2003). A drawback is that the measured volume of calcification depends on the attenuation and threshold used (Fishbach and Maintz, 2005). The CVS therefore does not represent the true volume of calcification i.e. traditional threshold of 130 HU used. Furthermore, CVS overstates the volume of very dense calcification and underestimates the volume of less dense calcification (Fishbach and Maintz, 2005).

A third method of quantification is the hydroxyapatite mass method. This is a physical quantitative measure used in EBCT (Ulzheimer and Kalender, 2003). The setup is cumbersome in that the patient lies supine with the chest area positioned within a chest phantom (Detrano et al., 1995). However Hong et al., (2003), state that the mass measurement is more accurate, less variable, and more reproducible in coronary calcium quantification than are measurements with other algorithms (Hong et al., 2003). Accurate quantification of calcium in each calcified plaque may require that the threshold be set individually, depending on the calcium density (Hong et al., 2003). Although the results
are most accurate with this method of quantification, it is not readily available (Ulzheimer and Kalender, 2003). The Agatston calcium scoring method was utilized for the current research at Drs Jackpersad and Partners.

2.26 Guidelines for interpretation of a calcium score result

AHA and ACC consensus document states that in the absence of coronary calcium i.e a negative calcium score test ;-

a. Atherosclerotic plaque, including unstable plaque, is very unlikely; although it is possible that significant atherosclerosis may not be detected i.e. soft plaque.

b. Significant luminal obstructive disease is highly unlikely.

c. Angiographically normal coronary arteries occur in majority of such patients.

d. The absence of calcium may be consistent with a low risk of CHD events over the next 2 to 5 yrs (O’Donnell and Hoffman, 2005).

For a test that is positive ;- 

a. The presence of calcium confirms the presence of coronary atherosclerotic plaque.

b. The greater the amount of calcium, the greater the likelihood of occlusive coronary artery disease, although there is no one-to-one relationship and findings may not be site specific.

c. The total amount of calcium correlates best with the total amount of atherosclerotic plaque, although true plaque burden is underestimated.

d. A high calcium score (e.g. Agatston > 400), may be consistent with a moderate-high risk of CHD events over the next 2-5 yrs (O’Donnell and
Coronary atherosclerosis underlies CHD and is influenced by the interaction of multiple risk factors over time in a susceptible host (O’Donnell and Hoffman, 2005). Furthermore, traditional risk prediction models such as the FRS are reasonable predictors of CHD risk. Therefore the intention of calcium score screening is aimed at improving prediction of risk for future clinical events (O’Donnell and Hoffman, 2005). Future studies will need to ascertain the incremental benefit of CAC measures over traditional risk factors and the cost effectiveness of incorporating such measures into global-risk assessment algorithms (O’Donnell and Hoffman, 2005).

### 2.27 Patient management

According to Klodas (2005), the presence of calcification alone can impact on secondary prevention and appropriate patient management. Discovery of any calcification may provide strong incentives for the patient to undertake healthy lifestyle changes (Klodas, 2005). Furthermore, the normal progression of coronary artery calcium is approximately 14–27% (average, 24%) increase per year and may be enhanced up to 33–48% in patients with advanced disease (Van Hoe et al., 2003).

Coronary calcium scoring is helpful, particularly in healthy subjects, with an undetermined cardiovascular risk whose management is unclear. In the case of a low or negative score, the physician can be guided on advising patients to maintain a healthy lifestyle (Schermund et al., 2001). Intermediate score ranges should be correlated with the patient’s age and clinical presentation (Klodas, 2005). An intermediate score is also helpful, as the physician has...
security in instituting treatment for the pathology (Schermund et al., 2001). In the case of a high score, guidance can be directed towards intensive treatment. In the absence of calcium no further testing is required (Klodas, 2005). Symptomatic patients with known CAD can also benefit when detailed information on the extent of atherosclerotic plaque disease is required for treatment and prognostication (Schermund et al., 2001). In addition, the calcium score should also determine whether further cardiac testing is required (Klodas, 2005). Table 2.3 by (Klodas, 2005), outlines salient points on plaque burden, implications for cardiovascular risk and recommendations.

Table 2.3 Implications for cardiovascular risk

<table>
<thead>
<tr>
<th>Calcium score</th>
<th>Plaque burden</th>
<th>Probability of significant CAD</th>
<th>Implications for cardiovascular risk</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>no identifiable plaque</td>
<td>very low, generally 5%</td>
<td>very low</td>
<td>reassure patient, general health guidelines</td>
</tr>
<tr>
<td>1-10</td>
<td>minimal identifiable plaque</td>
<td>very unlikely less than 10%</td>
<td>low</td>
<td>primary prevention, health guidelines</td>
</tr>
<tr>
<td>11-100</td>
<td>definite, mild atherosclerotic plaque burden</td>
<td>mild coronary stenosis</td>
<td>moderate</td>
<td>risk factor modification</td>
</tr>
</tbody>
</table>
Acetylsalicylic acid (ASA) is an anticoagulant used to control established modifiable risk factors like smoking, hypertension, diabetes, obesity, sedentary lifestyles and high cholesterol levels (Curnew, 2004). It is therapy therefore used for high cardiovascular risk individuals (Klodas, 2005).

Schermund et al., (2001) state that follow up coronary calcium scans are used to monitor the progression or regression of calcification. Coronary calcification can be lowered or stopped by lipid lowering or statin therapy (Schermund et al., 2001). In addition higher risk individuals may benefit from more aggressive pharmacological risk factor modification, like lipid lowering agents, anti-platelet therapies and angiotensin converting enzyme inhibitors (O’Donnell and Hoffman, 2005). Furthermore, new studies reported by Manson et al., (2007) advocate the use of oestrogen therapy in women between 50-59 years of age to reduce their coronary plaque burden. On the contrary Waters et al., (2002) state that hormone replacement therapy (HRT) and antioxidant vitamins are widely used in postmenopausal women for secondary prevention of CAD but no clinical trials have shown the benefit of its use. In addition long term use of HRT enhances breast cancer development (Manjer et al., 2004) and increases the risk of ovarian cancer (Auranen, 2005).

The economic and public health challenge is to adjudicate between the public’s desire for a...
new screening tool to assess their health, and on the other hand their inability to use the
diagnostic information to make necessary lifestyle changes (Wellberry, 2004). Even if
calcium scoring adds prognostic information, evidence of patient orientated impact is
lacking (Wellberry, 2004). Once again it has been re-iterated that greater awareness of the
calcium score study and its benefit is required in preventative medicine.

2.28 Treatment of CAD with lifestyle changes and surgery

Recent studies by the Medical Research Council (MRC) of South Africa have
shown that chronic lifestyle diseases such as lung cancer and heart disease account for 50-
60 % of deaths in SA (Steyn, 2007). Diagnosis of CAD by coronary angiography guides the
strategies for treatment (Michaels and Chatterjee, 2002). Treatment options are medical
therapy, angioplasty, stenting and bypass surgery depending on the disease status.

According to Steyn (2007) it is essential to assess and treat the risk factors for CAD. The
higher the individual’s blood pressure the higher is their risk of CAD (Steyn, 2007). One is
considered to have high blood pressure or hypertension when one’s systolic pressure is over
140 mm Hg and the diastolic pressure is over 90 mm Hg (Pauling, 2007). Significantly,
smokers have twice the risk of heart disease as compared to non-smokers. Smoking is also
the most preventable risk factor for CAD. The risk of heart disease also increases as one’s
cholesterol increases. In contrast, a diet low in cholesterol and saturated fat lowers
cholesterol and risk of CAD (Steyn, 2007). In addition ASA is medical therapy advocated
by Curnew (2004) as a blood thinning product used in the treatment of CAD. Significantly
nearly every second South African is overweight. This is also a contributor to CAD (Steyn,
2007). Poor control of stress is also a major contributor of CAD in SA. Diabetes, when not
controlled, can lead to significant heart damage and heart attacks. Hence, controlling the above risk factors is essential to reduce CAD risk (Steyn, 2007). Importantly Cooley et al., (2005), state that medical and surgical treatment does not cure CAD. Symptoms may be alleviated, but it is important to modify one’s lifestyle to prevent the disease from progressing or recurring.

Invasive treatment of CAD according to Youngman (1997) is surgery by means of angioplasty, stenting and bypass grafting. Another effective treatment of CHD is by transmyocardial laser revascularization (TMLR). The procedure entails the use of laser therapy to create blood perfusion channels in the heart muscle to supplement the function of the coronary arteries (Cooley et al., 2005).

2.29 Conclusion

This literature review has covered two main aspects of the study i.e CAD and the use of the calcium scoring technique in the diagnosis thereof. Symptoms, risk factors, treatment, management and statistics of CAD have been dealt with extensively in this chapter. Classification, types, level of education and ethnic differences in atherosclerosis was researched and presented. The calcium scoring technique has also been extensively studied and this review has included the procedure, reliability, benefits, limitations, pitfalls, contra-indications, radiation dose and technical aspects of this procedure. Furthermore other procedures for the detection of CAD as also been included.

From this review of related literature, it can be concluded that the calcium scoring technique is a highly effective and sensitive predictor (surrogate marker) in the diagnosis of
CAD. However, an in depth literature search has failed to reveal any peer reviewed publications on calcium scoring in SA. A composite need therefore exists for such a study to be conducted in the country. The intention of the study conducted was to evaluate the calcium scores on asymptomatic, risk and non-risk participants, between the ages of 20-70 years to ascertain whether this population is at risk for CAD and adverse coronary events. This would then determine whether the calcium scoring test is a useful screening tool for CAD onset and should be included in routine medical examinations in preventative medicine in SA.
CHAPTER 3

RESEARCH METHODS AND DESIGN

3.1 Introduction

This chapter describes the following issues relating to the research; the design, the location of the study, inclusion and exclusion criteria, recruitment method, sample size and selection, data output, ethical considerations, technique, preparation of participants, assumptions and statistical analyses. Information on the relevant letters of permission to perform the study and appropriate consent forms are also included.

3.2 Permission to perform study

On 9 July 2006 Drs Jackpersad and Partners had granted permission for the study to be conducted at their premises, at the Westridge Medical Centre, Mayville Durban (Appendix B). The research proposal was submitted to, and approved by the Faculty of Health Sciences Research Committee of the Durban University of Technology (DUT). Permission was granted to perform the study under the guidelines of this institution in October 2006 (Appendix C).

3.3 Invitation to participate

The population of Durban, KwaZulu-Natal was invited to participate in the study via word of mouth and pamphlets (Appendix G). The pamphlets briefly explained the aim of the research and the inclusion and exclusion criteria. Prior research has shown that the most densely populated area of Indians outside India is in Durban, KwaZulu-Natal (Naidoo et al., 2005). Secondly, the Indian population in SA presents with the highest incidence of
CAD compared to the other ethnicities (Naidoo et al., 2005). Considering this the study had targeted the Indian ethnic group in Durban, KwaZulu-Natal.

3.4 Sample size and selection

A convenience sample method of selection was used to draw research participants, who fitted the inclusion criteria, for the study. They had to be of Indian ethnicity, between 20-70 yrs of age, with no previous symptoms or history of CAD (common symptoms of CAD are chest pains, angina and MI). The intention was to scan the research participants as they came forward until a sample size of 100 was achieved. However, there was an overflow and the actual sample size was 103 as these extra participants were keen to be included in the study and given their risk profile, it was felt that they would provide valuable data for the study.

The sample size of 100, was also decided on after consultation with a statistician (Esterhuizen, 2006) and in keeping with feedback from the Faculty of Health Sciences Research Committee at DUT. When one engages in such a study there are various considerations employed to achieve a guideline for the appropriate sample size. One has to also consider the criteria that should be used to recruit participants for the study. In the case of this study, the participants had to be asymptomatic and had to fall under a risk or non-risk category for CAD. The risk factors were smoking, family history, obesity, diabetes, hypertension and hyperlipidemia. Firstly, when calculating the appropriate sample size an assumption had to be made as to whether the selected population would fall under the risk or non-risk category for CAD. Secondly, the sample
size depended on the percentage difference between risk and non-risk participants recruited. The greater the percentage difference between risk and non-risk participants recruited the smaller the sample size. With the use of formulae and calculations for unmatched cohort and cross-sectional studies, the statistician showed that, if the percentage difference between risk and non-risk participants was 40%, the sample size would be set at a minimum of 66. Furthermore, on assumption that the percentage difference between risk and non-risk participants was even higher i.e. 50%, the resultant sample size would be even lower, a minimum of 43 (Appendix M). The study included the research question of how each risk factor correlated with the calcium score and on the expectation of introducing more variables in the course of the study, the sample size was set at 100. Demographic factors such as age and gender and its effect on the calcium scores were variables included in the analysis. The recruitment method did not introduce any bias in the selection of male and female research participants and research participants were engaged in the study as they came forward. However, it was considered that a closer number of male and female research participants would allow for greater parity in the study.

3.4.1 Inclusion criteria

The criteria that were required for the research participants to be included in the study are listed below:

- Indian ethnicity in the age group of 20-70 years in order to include young, middle and old age groups.
- Asymptomatic, with no past or present history of CAD.
- Risk or non-risk for CAD. Risk factors were defined as obesity, hyperlipidemia, hypertension, smoking, family history and diabetes.
3.4.2 Exclusion criteria

The exclusion criteria were as follows.

- Pregnant women or women in the process of family planning because the study required the participants to be subjected to a minimal amount of radiation which could be damaging to the foetus (Burnett and Munro, 2005).
- Participants below 20 yrs and above 70 years.
- Participants with a past or present history of CAD because the aim of the study was the assessment of CAD in asymptomatic individuals.
- Participants with heart rates greater than 80 bpm as these would provide undiagnostic studies due to too many cardiac motion artefacts in the coronary arteries.
- Participants over 150 kgs in weight as this exceeds equipment safety regulations. The GE 64 slice VCT specifications include a patient weight limit of 150 kgs.

3.5 Letters of permission

- A letter requesting permission to perform the study was addressed to Drs Jackpersad and Partners in June 2006 (Appendix A).
- A letter granting permission to perform study was received from Drs Jackpersad and Partners on 9 July 2006 (Appendix B).
- A letter of approval to perform the research was received from the Faculty of Health Sciences Research Committee at DUT on 16 October 2006 (Appendix C).
A second letter was addressed to Drs Jackpersad and Partners on 6 October 2006, to inform the partnership that the research would commence in due course as the research proposal had been approved by the Faculty of Health Sciences Research Committee of DUT (Appendix D).

### 3.6 Research participant’s information

This includes the research participant’s demographics, information sheets and informed consent forms.

The research participant demographics included the participant’s registered name, sex, age (date of birth) and weight. Each research participant received a subject number that was entered under their identity on the log sheet and CT scanner database in order to preserve participant anonymity for ethical reasons.

The participant’s information sheet (Appendix E) outlines the research topic, aim of the study, inclusion criteria, exclusion criteria, procedure, risks, benefits, confidentiality statement and ethics approval of the study. The researcher and the research participant signed this document.

The informed consent form explained the research participant’s role in the research (Appendix F). The research participants answered questions relating to their presentation of any risk factors for CAD. This was read and signed in the presence of a witness by both the researcher and the research participant.

### 3.7 Data collection sheets
This includes the research participants log sheets, data entry sheets and calcium score printouts. The log sheet was used to record the date of study, allocated ID, sex, age, risk factors, calcium score and radiation dose for each research participant (Appendix I). The data entry sheet contained the data which was submitted to the statistician for analysis (Appendix J). Each research participant’s study number, age, ethnicity, sex and calcium score was recorded. In addition, the participant’s risk stratification was recorded. The calcium score printout was acquired using the routine technique and protocol of the 64 slice VCT, and Advantage Windows workstation (version 4.3). A copy of the calcium score result was given to each research participant (Appendix H). The accumulated radiation dose was also recorded on the calcium score printout for each research participant. Table 3.1 by Klodas (2005) divides the calcium score into 5 categories. This was utilized to advise the research participants on their calcium score, their risk for CAD and the preventative measures.

**TABLE 3.1 THE 5 CATEGORIES OF CALCIUM**

<table>
<thead>
<tr>
<th>Calcium score</th>
<th>Plaque burden</th>
<th>Probability of significant CAD</th>
<th>Implications for cardiovascular risk</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>no identifiable plaque</td>
<td>very low, generally 5%</td>
<td>very low</td>
<td>reassure patient, general health guidelines</td>
</tr>
<tr>
<td>1-10</td>
<td>minimal identifiable plaque</td>
<td>very unlikely less than 10%</td>
<td>low</td>
<td>primary prevention, health guidelines</td>
</tr>
<tr>
<td>11-100</td>
<td>definite, mild atherosclerotic plaque burden</td>
<td>mild coronary stenosis</td>
<td>moderate</td>
<td>risk factor modification</td>
</tr>
<tr>
<td>101-400</td>
<td>definite plaque</td>
<td>non-obstructive plaque</td>
<td>moderate to high</td>
<td>secondary prevention, exercise testing, daily ASA</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------</td>
<td>------------------------</td>
<td>------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>400+</td>
<td>extensive atherosclerotic plaque burden</td>
<td>90 % and over risk of coronary stenosis</td>
<td>high</td>
<td>aggressive risk modification, daily ASA</td>
</tr>
</tbody>
</table>

### 3.8 Research participant’s preparation

- The procedure was explained in detail to the research participants before commencement of the scan.

- Research participants were asked to avoid smoking and drinking of caffeinated beverages, 3-4 hours prior to the procedure because a high caffeine content in the bloodstream raises the heart rate.

- Research participants were asked to remove their clothes and jewellery from the chest area, to avoid artefacts on the CT images. The research participants were asked to wear a gown with the opening in the front, in order to provide easy access for attachment of the ECG electrodes.

### 3.9 The calcium score scan technique

- The research participants were positioned supine, feet first, on the table. Three ECG electrodes were positioned on the research participant’s chest. Two were placed below the centre of each clavicle. The third electrode was positioned slightly above the lower costal margin on the left.

- The ECG monitor was connected to the back of the gantry via a cord. A valid signal from the ECG monitor was indicated on the gantry by a heart symbol.

The research participant’s heart rate which was displayed on the ECG.
monitor, was sent to the CT scan console via an ethernet connection where it could be monitored.

- The research participants were briefed on the scanner’s automatic voice instruction and inspiratory breath-hold was practised with the research participants prior to commencement of the scan.
- The research participant’s relevant data was entered into the patient entry platform. A subject identity (ID) was entered under patient name to guarantee anonymity for ethical reasons.
- The research participants were scanned according to a routine technique. The smartscore protocol was selected. A scout was acquired in the anteroposterior and lateral planes. The field for the axial scans was centred on the heart. The superior border i.e start location was 2cm below the carina and inferior border i.e end location was 1cm below the apex of the heart. The smart mA option was used to acquire a diagnostic scan (This option of mA modulation allows for the relevant mA to be calculated according to the participant’s body part thickness, hence reducing the radiation dose to the research participant). The exposure time utilized was approximately 0.5 seconds, but this was dependent on the scan length. The exposure factors for each study were approximately 120 Kv, 600 mA and 0.35 second rotation time.
- The radiation dose was recorded for each research participant as the scanner outputs an automatic dose report.
- The scan data was automatically transferred to the Advantage Windows workstation for post processing.
- The research participant’s clinical history and demographics were entered
into the Advantage Windows clinical history platform.

- Images that contained calcium in the coronary arteries were identified and selected. They were labelled as the RCA, LMA, LAD, LCX and the diagonal arteries.
- The calcification was scored according to the Agatston method of quantification. The calcium score was recorded in the participant’s log sheet. The participants received a copy of the calcium score. A minimum threshold of 130 HU was used in the Agatston scoring method i.e. plaque with a threshold of 130 HU and higher was detected by the software. Lesions below a threshold of 130 HU were considered to be soft plaque and were not included in the analysis.
- Finally, the participants were advised by the researcher and co-supervisor, Dr J.M Kalideen on their calcium score.

3.10 Assumptions

The various assumptions made during the course of the study are outlined below:

- It is assumed that the research participants have provided the correct clinical information.
- It is assumed that the participants have followed the correct preparation for the procedure.
- It is assumed that the equipment was functioning optimally. A daily calibration of the scanner is done for quality assurance purposes.

3.11 Ethical considerations
• A letter had been addressed to Drs Jackpersad and Partners requesting permission to utilize their premises and equipment for the study.

• A reply had been received in writing granting permission to perform the study.

• Confidentiality of participant information was maintained at all times.

• Referring clinicians and research participants were briefed on their role in the study. The referring clinicians helped in the recruitment process.

• Radiation dose due to the exposure from the scanner was automatically calculated by the GE 64 slice VCT, and was recorded on the participant’s calcium score printout and log sheet. Prior to conducting the study, the average radiation dose from a calcium score study was compared to the permissible radiation dose to the public and was found to be within normal limits (Chapter 2, Section 2.18).

• The research proposal for the study was approved by the Faculty of Health Sciences Research Committee at DUT (Appendix C).

3.12 Statistical analysis

The participant’s log sheet was used to record data output i.e. the research participant’s calcium score (Appendix I). A data entry sheet was then used to record data for analysis according to the calcium scores, risk/non-risk categories, sex and age of participants (Appendix J). The SPSS version 13 (SPSS Inc, Chicago, III, USA), was used to analyse the data. A p value of <0.05 was considered statistically significant. Non-parametric Mann Whitney tests were used to compare median calcium scores between two risk and demographic groups since the dependent variable i.e calcium score was not normally distributed. Pearson’s chi square tests and Fisher’s exact tests were used to compare the proportion of calcification in the different risk categories. Binary logistic regression analysis
was done to assess the adjusted risk of each of the risk factors and demographics whilst
controlling for confounders (detailed explanation in the Chapter 4, section 4.1). Odds ratio
and 95% confidence intervals were reported. Chapter Four reports the results obtained from
the statistical analyses.
CHAPTER FOUR

STATISTICAL RESULTS

4.1 Introduction

This chapter reports the results of the data analysis for the 103 participants of Indian ethnicity in Durban, KwaZulu-Natal. The SPSS version 13 (SPSS Inc., Chicago, 111, USA) was used for data analysis. A p value of <0.05 was considered as statistically significant. Non parametric statistics were found appropriate for the study because the results showed that the dependent variable, which in this study were the calcium scores were not normally distributed i.e. there were many individuals with calcium scores of 0 and a few very high calcium scores. All demographic and risk variables which were significant on Bivariate analysis were used as independent variables in the model.

The highest calcium score was 4937. Therefore the calcium scores ranged from 0 to 4937. In the light of the very high calcium score of 4937, a rescan of this research participant was considered in order to ensure that the value was not due to a technical error during data capture. However, daily calibration of the scanner ensures optimal performance and accuracy. The rescan was not possible due to the unavailability of the research participant. Nonetheless a full clinical history was obtained from this research participant which correlated with the calcium score findings (Chapter 5, section 5.4.1). Analysis with and without the outlier (high calcium score of 4937) is included to show any differences in the statistical results obtained. Hence the data analysis was done on 103 and 102 participants (minus the outlier) respectively. The same statistical methodology was used as with the full data set (103) to reanalyze the data with the outlier excluded (102). The calcium scores were
not normally distributed before and after the omission of the outlier. The direction of skewness was to the left (negatively skewed) because of the large number of zero values (Figure 4.1), with the outlier and (Figure 4.2) without the outlier. Table 4.1 shows that the skewness statistic was 8.477 before the exclusion of the outlier, which was much larger than twice the standard error skewness, justifying the use of non parametric statistical tests for this variable. Even after exclusion of the outlier, the skewness statistic was still more than twice the standard error of skewness (4.254) shown by Table 4.2. In both tables 4.1 and 4.2 the mean and the median differ as the mean is affected by the value of the high no zero calcium scores while the median is a better indicator of the midpoint of the data by reflecting a zero score before and after the exclusion of the outlier.

Table 4.1: Distributional tests on calcium score with the outlier included

<table>
<thead>
<tr>
<th></th>
<th>Valid</th>
<th>103</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Mean</td>
<td>102.01</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>.00</td>
<td></td>
</tr>
<tr>
<td>Skewness</td>
<td>8.477</td>
<td></td>
</tr>
<tr>
<td>Std. Error of Skewness</td>
<td>.238</td>
<td></td>
</tr>
</tbody>
</table>

Table 4.2: Distributional tests on calcium score with the outlier excluded

<table>
<thead>
<tr>
<th></th>
<th>Valid</th>
<th>102</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Mean</td>
<td>54.61</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>.00</td>
<td></td>
</tr>
<tr>
<td>Skewness</td>
<td>4.254</td>
<td></td>
</tr>
<tr>
<td>Std. Error of Skewness</td>
<td>.239</td>
<td></td>
</tr>
</tbody>
</table>

Figure 4.1 and Figure 4.2 below show the negative skewness of the calcium scores with and without the outlier respectively.
The different tests used:

- Mann Whitney tests were used to compare the median calcium scores between two risks.
or demographic groups since the dependent variable was not normally distributed.

- Pearson’s chi square tests or Fisher’s exact tests as appropriate were used to compare the proportion of individuals with calcification in the different risk groups.
- Binary logistic regression analysis was done to assess the adjusted risk of each of the risk factors and demographics whilst controlling for confounders. The dependent variable was the presence of calcification. All demographic and risk variables which were significant on bivariate analysis were used as independent variables in the model. A backward selection technique based on likelihood ratios was used with entry and exit probabilities set at 0.05. Odds ratio and adjusted risk with 95 % confidence intervals were reported.

The statistical analysis is formatted and reported in view of the five research questions which were devised according to the aim of the study i.e. the assessment of the prevalence of coronary artery calcification in asymptomatic risk and non-risk individuals in the SA Indian population, within the age group of 20-70 years.

4.2 Results

The research questions were stated as null hypotheses. The results are reported under each null hypothesis initially for the 103 research participants followed by analysis of the 102 research participants (excluding the outlier) to determine if there was any statistical difference in the results in both data sets.

**Null hypothesis one :**

There is no significant difference in calcium scores between risk and non-risk
asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal.

Of the 103 participants, 32 (31.1%) were classified as having no risk factors, whilst 71 (68.9%) had at least one risk factor. Thus the prevalence of any risk factors in the asymptomatic Indian population is approximately 69%. Of the 71 participants with risk factors, 14 (19.7%) presented with hypertension, 14 (19.7%) presented with obesity, 13 (18.3%) presented with smoking, 14 (19.7%) presented with hyperlipidemia, 54 (76.1%) presented with family history and 13 (18.3%) presented with diabetes. There is a significant difference between the two groups with regard to the calcium score (p=0.018), with the risk group having a higher calcium score than the non-risk group. This is shown in Table 4.3 below. Therefore the null hypothesis is rejected as there is a significant difference in calcium scores of risk and non-risk asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal.

### Table 4.3: Mann Whitney test to compare calcium score between risk groups (n=103)

<table>
<thead>
<tr>
<th>Calcium score</th>
<th>Risk group</th>
<th>N</th>
<th>Mean Rank</th>
<th>Sum of Ranks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no risk factors</td>
<td>32</td>
<td>43.41</td>
<td>1389.00</td>
</tr>
<tr>
<td></td>
<td>any risk factors</td>
<td>71</td>
<td>55.87</td>
<td>3967.00</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>103</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Test Statistics 4.3(a)

<table>
<thead>
<tr>
<th>Calcium score</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mann-Whitney U</td>
<td>861.00</td>
</tr>
<tr>
<td>Wilcoxon W</td>
<td>1389.00</td>
</tr>
<tr>
<td>Z</td>
<td>-2.366</td>
</tr>
<tr>
<td>Asymp. Sig. (2-tailed)</td>
<td>.018</td>
</tr>
</tbody>
</table>

*a Grouping Variable: Risk group*

Figure 4.3 shows that the median calcium scores of the two groups were both 0 but the distribution of the group with any risk was wider than that of the groups with no risks, and
included a calcium score close to 5000.

Figure 4.3: Box and Whisker plot of calcium score by risk group
Of the 102 participants, 32 (31.4%) were classified as having no risk factors, while 70 (68.6%) had at least one risk factor. Thus the prevalence of any risk factors in the asymptomatic Indian population is once again approximately 69%.

There was a significant difference between the two groups with regard to calcium score (p=0.023), with the risk group having a higher calcium score than the non risk group. This is shown in Table 4.4. Therefore the null hypothesis is rejected. There is a significant difference in calcium scores of risk and non risk asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal.

Figure 4.4 shows that the median calcium scores of the two groups were both 0 but the score distribution of the group with any risks was more likely to be higher than that of the group with no risks.

Table 4.4: Mann Whitney test to compare calcium score between risk groups (n=102)

<table>
<thead>
<tr>
<th>Calcium score</th>
<th>Risk group</th>
<th>N</th>
<th>Mean Rank</th>
<th>Sum of Ranks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no risk factors</td>
<td>32</td>
<td>43.41</td>
<td>1389.00</td>
</tr>
<tr>
<td></td>
<td>any risk factors</td>
<td>70</td>
<td>55.20</td>
<td>3864.00</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>102</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test Statistics 4.4(a)

<table>
<thead>
<tr>
<th></th>
<th>Calcium score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mann-Whitney U</td>
<td>861.000</td>
</tr>
<tr>
<td>Wilcoxon W</td>
<td>1389.000</td>
</tr>
<tr>
<td>Z</td>
<td>-2.270</td>
</tr>
<tr>
<td>Asymp. Sig. (2-tailed)</td>
<td>0.023</td>
</tr>
</tbody>
</table>

a Grouping Variable: Risk group
Figure 4.4: Box and Whisker plot of calcium score by risk group
Null hypothesis two:

There is no significant difference in the calcium scores between male and female asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal.

Of the sample of 103, 65 (63.1%) were males, and 38 (36.9%) were females. There was a significant difference in calcium scores between genders (p=0.007), with males having higher scores than females. This is shown in Table 4.5 below. Thus the second null hypothesis is rejected. There is a significant difference in the calcium scores of male and female asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal.

Table 4.5: Mann Whitney test to compare calcium score between genders (n=103)

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>Mean Rank</th>
<th>Sum of Ranks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium score</td>
<td>male</td>
<td>65</td>
<td>57.00</td>
</tr>
<tr>
<td></td>
<td>female</td>
<td>38</td>
<td>43.45</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>103</td>
<td></td>
</tr>
</tbody>
</table>

Test Statistics 4.5(a)

<table>
<thead>
<tr>
<th>Calcium score</th>
<th>Mann-Whitney U</th>
<th>Wilcoxon W</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>910.000</td>
<td>1651.000</td>
</tr>
<tr>
<td>Z</td>
<td>-2.682</td>
<td></td>
</tr>
<tr>
<td>Asymp. Sig. (2-tailed)</td>
<td>.007</td>
<td></td>
</tr>
</tbody>
</table>

a Grouping Variable: Gender

Figure 4.5 shows that while the median calcium scores of both gender groups were 0, the distribution of the males’ calcium scores was higher than that of the females’.
Of the sample of 102, 64 (62.7%) were males, and 38 (37.3%) were females. There was a
significant difference in calcium score between the genders (p=0.010), with males having higher scores than females. This is shown in Table 4.6. Thus the second null hypothesis is rejected. There is a significant difference in calcium scores of male and female asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal. Figure 4.6 shows that while the median calcium scores of both gender groups were 0, the distribution of the males’ calcium scores was higher than that of the females.

Table 4.6: Mann Whitney test to compare calcium score between genders (n=102)

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>Mean Rank</th>
<th>Sum of Ranks</th>
</tr>
</thead>
<tbody>
<tr>
<td>male</td>
<td>64</td>
<td>56.28</td>
<td>3602.00</td>
</tr>
<tr>
<td>female</td>
<td>38</td>
<td>43.45</td>
<td>1651.00</td>
</tr>
<tr>
<td>Total</td>
<td>102</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test Statistics 4.6(a)

<table>
<thead>
<tr>
<th>Calcium score</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mann-Whitney U</td>
<td>910.00</td>
</tr>
<tr>
<td>Wilcoxon W</td>
<td>1651.00</td>
</tr>
<tr>
<td>Z</td>
<td>-2.574</td>
</tr>
<tr>
<td>Asymp. Sig. (2-tailed)</td>
<td>0.010</td>
</tr>
</tbody>
</table>

a Grouping Variable: Gender
Null hypothesis three:

There is no association between any of the 6 risk categories and calcification in the
coronary arteries in asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal.

On bivariate analysis of 103 participants there was a significant association between calcification and hypertension (p=0.030), hyperlipidemia (p=0.030), and diabetes (p=<0.001). Of those with hypertension or hyperlipidemia 57.1 % presented with calcification. The percentage of calcification in diabetic individuals was 76.9 %. Of those with obesity 42.9 % presented with calcification and 30.8 % of smokers had calcification. Of those with family history 35.2 % had calcification. Diabetics therefore presented with the highest risk for coronary artery disease i.e. 76.9 % and smokers presenting with the lowest risk i.e 30.8 %. This is shown in Tables 4.7- 4.12 and Figures 4.7- 4.12. Thus the null hypothesis is rejected, since 3 of the 6 risk categories had a significant association with calcification.

Table 4.7: Cross tabulation and Pearson’s chi square analysis of the association between Hypertension and calcification (n=103)

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Calcium score category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1-400+</td>
</tr>
<tr>
<td>No</td>
<td>Count</td>
<td></td>
</tr>
<tr>
<td></td>
<td>64</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
<td></td>
</tr>
<tr>
<td></td>
<td>71.9%</td>
<td>28.1%</td>
</tr>
<tr>
<td>Yes</td>
<td>Count</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
<td></td>
</tr>
<tr>
<td></td>
<td>42.9%</td>
<td>57.1%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td></td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
<td></td>
</tr>
<tr>
<td></td>
<td>68.0%</td>
<td>32.0%</td>
</tr>
</tbody>
</table>

Pearson’s chi square = 4.69, p=0.030
Figure 4.7: showing the association of Hypertension and calcification

Table 4.8: Cross tabulation and Pearson’s chi square analysis of the association between Obesity and calcification (n=103)
<table>
<thead>
<tr>
<th></th>
<th>Calcium score category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1-400+</td>
</tr>
<tr>
<td>Obesity no</td>
<td>Count</td>
<td>62</td>
</tr>
<tr>
<td>% within Obesity</td>
<td>69.7%</td>
<td>30.3%</td>
</tr>
<tr>
<td>yes</td>
<td>Count</td>
<td>8</td>
</tr>
<tr>
<td>% within Obesity</td>
<td>57.1%</td>
<td>42.9%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>70</td>
</tr>
<tr>
<td>% within Obesity</td>
<td>68.0%</td>
<td>32.0%</td>
</tr>
</tbody>
</table>

Pearson’s chi square = 0.87, p=0.351

Figure 4.8: showing the association of Obesity and calcification

Table 4.9: Cross tabulation and Pearson’s chi square analysis of the association between Smoking and calcification (n=103)
<table>
<thead>
<tr>
<th>Smoking</th>
<th>Calcium score category</th>
<th>Count</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>no</td>
<td>0</td>
<td>61</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>1- 400+</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>% within Smoking</td>
<td>67.8%</td>
<td>32.2%</td>
</tr>
<tr>
<td>yes</td>
<td>Count</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>% within Smoking</td>
<td>69.2%</td>
<td>30.8%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>70</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>% within Smoking</td>
<td>68.0%</td>
<td>32.0%</td>
</tr>
</tbody>
</table>

Pearson’s chi square = 0.011, p=0.916

**Figure 4.9:** showing the association of Smoking and calcification

**Table 4.10:** Cross tabulation and Pearson’s chi square analysis of the association between Hyperlipidemia and calcification (n=103)
Hyperlipidemia  | No  | Count  | 64  | 25  | 89  |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>% within Hyperlipidemia</td>
<td>71.9%</td>
<td>28.1%</td>
<td>100.0%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Yes  | Count  | 6  | 8  | 14  |
| % within Hyperlipidemia  | 42.9%  | 57.1%  | 100.0%  |

Total  | Count  | 70  | 33  | 103  |
| % within Hyperlipidemia  | 68.0%  | 32.0%  | 100.0%  |

Pearson’s chi square = 4.69, p=0.030

Figure 4.10: showing the association of Hyperlipidemia and calcification
Table 4.11: Cross tabulation and Pearson’s chi square analysis of the association between Family history and calcification (n=103)

<table>
<thead>
<tr>
<th>Calcium score category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Family history</td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>35</td>
</tr>
<tr>
<td>% within Family history</td>
<td>71.4%</td>
</tr>
<tr>
<td>yes</td>
<td>35</td>
</tr>
<tr>
<td>% within Family history</td>
<td>64.8%</td>
</tr>
<tr>
<td>Total</td>
<td>70</td>
</tr>
<tr>
<td>% within Family history</td>
<td>68.0%</td>
</tr>
</tbody>
</table>

Pearson’s chi square = 0.516, p=0.473

Figure 4.11: showing the association of Family history and calcification
Table 4.12: Cross tabulation and Pearson’s chi square analysis of the association between Diabetes and calcification (n=103)

<table>
<thead>
<tr>
<th>Calcium score category</th>
<th>0</th>
<th>1-400+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>Count</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>67</td>
<td>23</td>
<td>90</td>
</tr>
<tr>
<td>% within Diabetes</td>
<td>74.4%</td>
<td>25.6%</td>
<td>100.0%</td>
</tr>
<tr>
<td>yes</td>
<td>Count</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>% within Diabetes</td>
<td>23.1%</td>
<td>76.9%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>33</td>
<td>103</td>
</tr>
<tr>
<td>% within Diabetes</td>
<td>68.0%</td>
<td>32.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Pearson’s chi square = 13.76, p<0.001

Figure 4.12: showing the association of Diabetes with calcification

On bivariate analysis of the 102 participants there was also a significant association between
calcification and hypertension (p= 0.033) and diabetes (p<0.001). Of those with hypertension, 57.1% presented with calcification, and with hyperlipidemia, 53.8% had calcification. Of those with obesity 42.9% presented with calcification and smokers had 25% calcification. Of those with family history 35.2% had calcification, while the risk in diabetics was 76.9%. This is shown in Tables 4.13- 4.17. Thus the null hypothesis is rejected, since 2 of the 6 risk categories had a significant association with calcification.

Omission of the outlier has changed the significance of hyperlipidemia in the results i.e from 57.1 % risk to 53 % risk. Table 4.13 and 4.14 and Figures 4.13 and 4.14 demonstrate the omission of the outlier in the smoking and hyperlipidemia risk category, as these were the risk factors that the participant with the high calcium score of 4937 presented with. Tables 4.15- 4.18 demonstrate the association of hypertension, obesity, family history and diabetes with calcification. Figures demonstrating the calcium score category by hypertension, obesity, family history and diabetes are attached (Appendices N-Q).
Table 4.13: Cross tabulation and Fisher’s exact analysis of the association between Smoking and calcification (n=102)

<table>
<thead>
<tr>
<th>Smoking</th>
<th>Calcium score category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1- 400+</td>
</tr>
<tr>
<td>no</td>
<td>Count</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>% within Smoking</td>
<td>67.8%</td>
</tr>
<tr>
<td>yes</td>
<td>Count</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>% within Smoking</td>
<td>75.0%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>% within Smoking</td>
<td>68.6%</td>
</tr>
</tbody>
</table>

Fisher’s exact p=0.749

Figure 4.13: showing the association of Smoking and calcification
Table 4.14: Cross tabulation and Fisher’s exact analysis of the association between Hyperlipidemia and calcification (n=102)

<table>
<thead>
<tr>
<th>Hyperlipidemia</th>
<th>Calcium score category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1-400+</td>
</tr>
<tr>
<td>no</td>
<td>Count</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>64</td>
</tr>
<tr>
<td>% within Hyperlipidemia</td>
<td>71.9%</td>
<td>28.1%</td>
</tr>
<tr>
<td>yes</td>
<td>Count</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>% within Hyperlipidemia</td>
<td>46.2%</td>
<td>53.8%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>70</td>
</tr>
<tr>
<td>% within Hyperlipidemia</td>
<td>68.6%</td>
<td>31.4%</td>
</tr>
</tbody>
</table>

Fisher’s exact p=0.105

Figure 4.14: showing association of Hyperlipidemia and calcification

Table 4.15: Cross tabulation and Fisher’s exact analysis of the association between Hypertension and calcification (n=102)
### Table 4.16: Cross tabulation and Fisher’s exact analysis of the association between Obesity and calcification (n=102)

<table>
<thead>
<tr>
<th></th>
<th>Calcium score category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1-400+</td>
</tr>
<tr>
<td>Hypertension</td>
<td>no</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
<td>72.7%</td>
</tr>
<tr>
<td></td>
<td>yes</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
<td>42.9%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
<td>68.6%</td>
</tr>
</tbody>
</table>

Fisher’s exact p=0.033

### Table 4.17: Cross tabulation and Pearson’s chi square analysis of the association between Family history and calcification (n=102)

<table>
<thead>
<tr>
<th></th>
<th>Calcium score category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1-400+</td>
</tr>
<tr>
<td>Obesity</td>
<td>no</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>% within Obesity</td>
<td>70.5%</td>
</tr>
<tr>
<td></td>
<td>yes</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>% within Obesity</td>
<td>57.1%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>% within Obesity</td>
<td>68.6%</td>
</tr>
</tbody>
</table>

Pearson chi square =0.775, p=0.379

### Table 4.18: Cross tabulation and Fisher’s exact analysis of the association between Diabetes and calcification (n=102)

<table>
<thead>
<tr>
<th></th>
<th>Calcium score category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1-400+</td>
</tr>
<tr>
<td>Family history</td>
<td>no</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>% within Family history</td>
<td>72.9%</td>
</tr>
<tr>
<td></td>
<td>yes</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>% within Family history</td>
<td>64.8%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>% within Family history</td>
<td>68.6%</td>
</tr>
</tbody>
</table>

Fisher’s exact p=0.033
**Research question four:**

What percentage of individuals in each category of calcium scoring presents with calcium in the coronary arteries for 103 participants?

Table 4.18 shows that the majority of individuals presented with a score of 0 (68%). There were 8.7% with a score of 1-10; 11.7% with a score of 11-100; and 5.8% each with scores of 101-400 and above 400.

---

**Table 4.19: Frequency distribution of calcium score categories (n=103)**

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>68.0</td>
</tr>
<tr>
<td>1-10</td>
<td>8.7</td>
</tr>
<tr>
<td>11-100</td>
<td>11.7</td>
</tr>
<tr>
<td>101-400</td>
<td>5.8</td>
</tr>
<tr>
<td>400+</td>
<td>5.8</td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Table 4.19 shows that the majority of individuals in the 102 sample size presented with a score of 0 (68.6%). There were 8.8% with a score of 1-10; 11.8% with a score of 11-100; and 5.9% with scores of 101-400 and 4.9% above 400.

Table 4.20: Frequency distribution of calcium score categories (n=102)

<table>
<thead>
<tr>
<th>Category</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>70</td>
<td>68.6</td>
</tr>
<tr>
<td>1-10</td>
<td>9</td>
<td>8.8</td>
</tr>
<tr>
<td>11-100</td>
<td>12</td>
<td>11.8</td>
</tr>
<tr>
<td>101-400</td>
<td>6</td>
<td>5.9</td>
</tr>
<tr>
<td>400+</td>
<td>5</td>
<td>4.9</td>
</tr>
<tr>
<td>Total</td>
<td>102</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Research question five:

What is the adjusted risk of calcification for demographic and risk factors in asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal for the 103 participants?

Table 4.21 shows that age, gender, hyperlipidemia and diabetes were all independently associated with calcification. With every one year increase in age, the adjusted risk of calcification increased by 1.21 times (95% CI 1.1 to 1.3). Males had a 11.9 times higher adjusted risk of calcification than females (95% CI 2.5 to 58.0). Hyperlipidemia conferred a 5.4 times higher adjusted risk (95% CI 1.0 to 27.8). Diabetes increased the risk by 11.7 times (95% CI 2.0 to 69.6). In the gender and diabetes categories, the upper and lower
limits of the CI denote a very wide range, suggesting an imprecise estimate of risk in the population. The risk could be anywhere in the range of these values. The relatively small sample size for this multivariate study has affected the width of the confidence interval. If the sample size was larger more precise estimates would have been obtained.

Significantly tests for interactions between these variables showed that there was no effect modification present, thus these factors operated independently.

Table 4.2: Final step of logistic regression analysis showing variables significantly related to calcification (n=103)

<table>
<thead>
<tr>
<th></th>
<th>Wald</th>
<th>df</th>
<th>P value</th>
<th>OR</th>
<th>95.0% C.I. for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Upper</td>
</tr>
<tr>
<td>Step 5(a)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>15.547</td>
<td>1</td>
<td>&lt;0.001</td>
<td>1.208</td>
<td>1.100</td>
</tr>
<tr>
<td>Gender (males vs. females)</td>
<td>9.408</td>
<td>1</td>
<td>0.002</td>
<td>11.911</td>
<td>2.446</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>4.023</td>
<td>1</td>
<td>0.045</td>
<td>5.370</td>
<td>1.039</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7.311</td>
<td>1</td>
<td>0.007</td>
<td>11.697</td>
<td>1.967</td>
</tr>
<tr>
<td>Constant</td>
<td>19.772</td>
<td>1</td>
<td>&lt;0.001</td>
<td>1.000</td>
<td></td>
</tr>
</tbody>
</table>

a Variable(s) entered on step 1: Age, Gender, Hypertension, Obesity, Smoking, Hyperlipidemia, Family history, Diabetes.

Table 4.22 shows that age, gender and diabetes were all independently associated with calcification in the 102 data set. With every one year increase in age, the adjusted risk of calcification increased by 1.21 times (95% CI 1.1 to 1.3). Males had a 9.7 times higher adjusted risk of calcification than females (95% CI 2.2 to 42.9). Diabetes increased the risk by 12.1 times (95% CI 2.0 to 71.8). Once again these imprecise estimates are due to the relatively small sample size for this multivariate study. Also, tests for interactions between these variables showed that there was no effect modification present, thus these factors operated independently.
Table 4.2: Final step of logistic regression analysis showing variables significantly related to calcification (n=102)

<table>
<thead>
<tr>
<th>Step 6(a)</th>
<th>Wald</th>
<th>df</th>
<th>P value</th>
<th>Odds ratio</th>
<th>95.0% C.I. for Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td>Age</td>
<td>16.134</td>
<td>1</td>
<td>&lt;0.001</td>
<td>1.210</td>
<td>1.102</td>
</tr>
<tr>
<td>Gender (males vs. females)</td>
<td>8.959</td>
<td>1</td>
<td>0.003</td>
<td>9.697</td>
<td>2.191</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7.531</td>
<td>1</td>
<td>0.006</td>
<td>12.103</td>
<td>2.039</td>
</tr>
<tr>
<td>Constant</td>
<td>19.521</td>
<td>1</td>
<td>&lt;0.001</td>
<td>0.000</td>
<td>1.000</td>
</tr>
</tbody>
</table>

a Variable(s) entered on step 1: Age, Gender, Hypertension, Obesity, Smoking, Hyperlipidemia, Family history, Diabetes.

4.3 Conclusion

This chapter has reported the statistical results of the study. The research questions and null hypotheses were devised according to the aim of this study i.e the assessment of the prevalence of coronary artery calcification in asymptomatic risk and non-risk individuals in the SA Indian population, within the age group of 20-70 years.

Null hypothesis one states that there is no difference in the calcium scores of risk and non-risk asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal. In the sample of the 103 participants, 32 (31.1%) were classified as having no risk factors, whilst 71 (68.9%) had at least one risk factor. In the sample of 102 participants, 32 (31.4%) were classified as having no risk factors, while 70 (68.6%) had at least one risk factor. Thus the prevalence of any risk factors in the asymptomatic Indian population is approximately 69%.

Furthermore, there is a significant difference between the two groups with regard to the calcium scores (p=0.018), with the risk group having a higher calcium score than the non-risk group in the 103 sample size. In the 102 dataset there remains a significant difference cix
between the two groups with regard to the calcium scores (p=0.023), with the risk group having a higher calcium score than the non-risk group. The median calcium scores of the two groups were both 0 but the score distribution of the group with any risks was more likely to be higher than that of the group with no risks. Therefore null hypothesis one is rejected. There is a significant difference in the calcium scores of risk and non-risk asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal.

The second null hypothesis states that there is no difference in the calcium scores of male and female asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal. Of the sample of 103, 65 (63.1%) were males, and 38 (36.9%) were females. There was a significant difference in calcium scores between genders (p=0.007), with males having higher scores than females. Of the sample of 102, 64 (62.7%) were males, and 38 (37.3%) were females. There was a significant difference in calcium score between the genders (p=0.010), with males having higher scores than females. Therefore the second null hypothesis was rejected.

Null hypothesis three states that there is no association between any of the 6 risk categories and calcification in the coronary arteries in asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal. In the sample with 103 participants, of those with hypertension or hyperlipidemia 57.1% presented with calcification. Of those with obesity 42.9% presented with calcification and 30.8% of smokers had calcification. Of those with family history 35.2% had calcification. The percentage of calcification in diabetic individuals was 76.9%. Thus the null hypothesis is rejected, since 3 of the 6 risk categories had a significant association with calcification. Diabetics presented with the highest risk for CAD i.e. 76.9% and smokers presenting with the lowest risk i.e 30.8%.
The results changed slightly in the analysis of the 102 sample size. It was concluded that there was a significant association between calcification and hypertension (p= 0.033) and diabetes (p<0.001). Of those with hypertension, 57.1% presented with calcification, and with hyperlipidemia, 53.8% had calcification. Of those with obesity 42.9% presented with calcification and smokers had 25% calcification. Of those with family history 35.2% had calcification, while the risk in diabetics was 76.9%. Thus the null hypothesis is rejected, since 2 of the 6 risk categories had a significant association with calcification. Hyperlipidemia was statistically significant before removal of the outlier but was not as statistically significant after removal of the outlier. Since the number with hyperlipidemia was low and the p value was greater than 0.05, the statistical power as been reduced in this comparison.

From the above reports it can be concluded that being male, increasing age, the presence of hyperlipidemia and diabetes are all independent risk factors for coronary artery calcification in asymptomatic Indians in Durban, KwaZulu-Natal. The largest risk was due to being male, odds ratio 11.9 (95% CI 2.5 to 58.0) followed by being diabetic, odds ratio 11.7 (95% CI 2.0 to 69.6). However as stated under research question five, the relatively small sample size has affected the accuracy of the estimates for gender and diabetes.

After omission of the outlier, being male, increasing age and the presence of diabetes are all still independent risk factors for coronary artery calcification in asymptomatic Indians in Durban. The largest risk was due to being diabetic, odds ratio 12.1 (95% CI 2.0 to 71.8), followed by being male, odds ratio 9.7 (95% CI 2.2 to 42.9). However exclusion of the
outlier has lowered the study’s power marginally and this has resulted in the finding of a non significant effect of hyperlipidemia after exclusion of the outlier, whereas it was significant before. One needs to consider the clinical importance of the difference detected in risk between those with and without hyperlipidemia to decide whether a type II error has been made. Further larger studies are needed to confirm these findings.

Finally the statistical analysis showed that the majority of individuals in the 103 sample size presented with a score of 0 (68%). There were 8.7% with a score of 1-10; 11.7% with a score of 11-100; and 5.8% each with scores of 101-400 and above 400. Of the 102 participants 68.6% had a score of 0. There were 8.8% with a score of 1-10; 11.8% with a score of 11-100; and 5.9% with scores of 101-400 and 4.9% above 400.

In conclusion, the assessment of coronary artery calcification in the Indian ethnicity in Durban, KwaZulu-Natal has shown the prevalence of coronary artery calcification in approximately 32% of the population studied. This is considered significant because any percentage of a disease above 0 in an asymptomatic population signifies the prevalence of disease.
CHAPTER FIVE

DISCUSSION

5.1 Introduction

Atherosclerosis is a silent disease that develops slowly over decades of life until it manifests itself in coronary artery disease (CAD), with symptoms of angina, myocardial infarction or catastrophic death (Boyd, 2005). CAD is the leading cause of cardiovascular mortality worldwide, accounting for > 4.5 million deaths per annum (Okrainec et al., 2004). The treatment of CAD is by lifestyle modification and medical therapy. Histological studies have shown that approximately 20% of the volume of plaque in coronary atherosclerosis is marked by detectable levels of calcium. Furthermore, an increase in detectable levels of calcium increases the risk of CAD and future coronary events (Boyd, 2005). Lifestyle modification to abate this disease stems from knowledge of the presence and extent of calcium in the coronary arteries which the calcium scoring technique provides. Modification of lifestyle involves preventative and therapeutic steps such as exercise, following the correct diet, eliminating or controlling of risk factors and medical therapy. Relating to the current research, the screening of 103 asymptomatic risk and non-risk individuals for CAD has firstly created a greater awareness of the disease and its fatality. Secondly, knowledge of the presence and extent of calcium in the coronary arteries in the research population has prompted lifestyle changes and medical intervention where it was deemed necessary.

The subject of CAD in Indians (living in and out of India), has become a challenge for many research centres (Rissam et al., 2001). Religion, culture, climate, language and geographic habitation have conferred particular characteristics to people living in the Indian
subcontinent (India, Pakistan, Bangladesh and Sri Lanka) and to those who have migrated to other overseas countries. These factors in turn influence dietary habits to a great extent (Yeolekar, 1998). Furthermore, migration from rural to urban areas and migration from India to industrialized countries contributes to stress, a significant risk factor for CAD (Rissam et al., 2001). In addition, sedentary lifestyles associated with lack of exercise, a higher consumption of saturated fats, salt, tobacco and alcohol contribute to risk factors such as hyperlipidemia, obesity, hypertension, diabetes and hyperuricaemia. CAD in Indians is 3-4 times higher than White Americans, 6 times higher than Chinese and 20 times higher than Japanese in their respective countries (Rissam et al., 2001). Furthermore, Indians worldwide are more prone to CAD at a younger age. Statistics in South Africa verify that South African Indians also have a higher incidence of CAD, and at a much younger age than other ethnic groups (Naidoo et al., 2005). Therefore the current research has targeted the Indian ethnic group between the ages of 20-70 years in Durban KwaZulu-Natal, South Africa.

The data from the current research has been interpreted and reported in Chapter Four in the form of text, tables, figures and graphs. The results of the study derived from the statistical analyses are discussed in this chapter with reference to the aim, motivation, significance and research questions of the study. The significant patterns and trends in the results and comparison with other studies are also discussed.

**5.2 The aim of the study**

The primary aim of the study was to assess the prevalence of coronary artery calcification in asymptomatic risk and non-risk individuals of Indian ethnicity, in the age group of 20-70
years. This outcome was achieved by scanning a total of 103 participants, both with and without risk factors for CAD, in the age group of 20-70 years, in the Indian ethnic group in Durban, KwaZulu-Natal. The results are discussed according to the research questions, risk categories, age and gender of the participants.

5.3 Motivation and significance

The motivation for screening of asymptomatic risk and non-risk individuals for the prevalence of coronary artery calcification, is to triage such populations for the risk of adverse coronary events. This outcome was achieved by scanning a total of 103 participants both with and without risk factors for CAD in the age group of 20-70 years.

Seventeen percent of all deaths in SA in 2000 were due to cardiovascular disease (Derman, 2007) and CAD accounts for a major portion of these cardiovascular deaths. It is recognised that acute coronary events may occur in asymptomatic risk free populations. Therefore an ideal, non-invasive, highly specific test is desirable to preampt catastrophic coronary events. Furthermore, the presence of calcified plaque documents the presence of atherosclerosis and identifies patients at high risk for myocardial infarctions and cardiovascular death (Medical Encyclopedia, 2007).

Conventional angiograms are currently the gold standard for investigation of the coronary arteries (Weissman et al., 2006). However, it is invasive and costs approximately ten times more than the calcium scoring study. Therefore the calcium scoring technique was utilised in the current research to assess the prevalence of coronary artery calcification in the South African Indian population in Durban, KwaZulu-Natal.
5.4 The study population

Firstly, the study was performed on the Indian ethnic group in Durban, KwaZulu-Natal because a literature search showed that this population group presented with a higher incidence of CAD compared to the other ethnic groups in South Africa (Naidoo et al., 2005). Secondly Kotha (2003) suggests that Indians have a high incidence of metabolic syndrome and diabetes that predispose them to heart disease. The sedentary life styles, unhealthy cooking practices and nutrition are the environmental factors that trigger the genes responsible for heart disease, heart attacks and premature death in Indians (Kotha, 2003). The main aim of the study was therefore to assess if the Indian ethnic group in Durban, KwaZulu-Natal, given their risk profile presented with coronary artery calcification.

According to Carr (2005) calcified plaque is fundamental in the atherosclerotic process and small foci can develop as early as in teenagers and youth. The current study has therefore been conducted on research participants in the age group of 20-70 years, to include young, middle age and older individuals.

5.5 Radiation dose

The radiation dose was significantly reduced in the current study by employing the smart mA option. The thickness of the body part in the X, Y and Z planes detected on the scout image, determined the required mA for the axial scans. The average radiation dose per participant was approximately 2mSv. Individuals from the McMaster University (2006), published information in the Health and Safety Resource site, stating that the maximum
permissible dose limit in mSv/year, for any single organ is 50mSv. The radiation exposure for the calcium scoring technique in the current study is therefore within the annual permissible dose limits.

5.6 The research questions

5.6.1. Is there a significant difference in the calcium scores of risk and non-risk participants in the Indian ethnicity?

According to the Framingham model risk factors for CAD are hypertension, hyperlipidemia, smoking, diabetes and advancing age (Assey and Selby, 2004). For the current study hypertension, hyperlipidemia, smoking, diabetes, obesity and family history were utilized as risk factors for CAD because these risk factors were more relevant to the South African Indian population.

In the current research, of the 103 participants 32 (31.1%) were classified as having no risk factors, whilst 71 (68.9%) had at least one risk factor. Thus the prevalence of any risk factors in the asymptomatic Indian population was 69%. Furthermore, there is a significant difference between the two groups with regard to the calcium score (p=0.018), with the risk group having a higher calcium score than the non-risk group.

As discussed in Chapter Four the data was analysed with and without the outlier. The outlier fell under the risk category of research participants. The rationale for having analysis with and without the outlier was that the calcium score for the outlier was extremely high i.e. 4937 and there was need for comparison of the results with and without this high calcium score to establish if there was any significant change in the results. A
rescan of the research participant was considered in order to ensure that the high calcium score was not due to a technical error. This was not possible due to the unavailability of the research participant. However, the clinical history from the participant correlated with the calcium score findings. Following on from the calcium score test the participant was advised to consult a physician. The participant underwent a conventional angiogram that showed two areas of stenosis in the RCA (stated in the Mibi scan request form, Appendix R). However the participant had a Radionuclide myocardial perfusion study that showed no significant evidence of infarction or exercise induced ischemia (Appendix S).

Interestingly the second highest score obtained was 1063 and also fell under the risk category of participants. The score for the outlier was more than four times that of the second highest calcium score.

There remained a significant difference in the calcium scores of risk and non-risk participants for CAD with the removal of the outlier. Of the 102 participants, 32 (31.4%) were classified as having no risk factors, while 70 (68.6%) had at least one risk factor. Thus the prevalence of any risk factors in the asymptomatic Indian population is 69%. Furthermore there was a significant difference between the two groups with regard to the calcium score (p=0.023), with the risk group having a higher calcium score than the non risk group. Thus one can conclude that there is a significant difference in the calcium scores of risk and non risk asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal.

5.6.2 Is there a significant difference between calcium scores in male and female participants of both risk categories?
Firstly of the sample of 103, 65 (63.1%) were males, and 38 (36.9%) were females. While the median calcium scores of both gender groups were 0, the distribution of the males’ calcium scores was higher than that of the females’. There was a significant difference in calcium scores between genders (p=0.007), with males having higher scores than females. The mean calcium scores of the males were 57.00 and the mean calcium scores of the females were 43.45.

Secondly of the 102 sample, 64 (62.7%) were males, and 38 (37.3%) were females. There was a significant difference in calcium scores between the genders (p=0.010), with males having higher scores than females. The mean calcium scores of the males were 56 and that of the females were 43. The median calcium scores of both gender groups were 0, the distribution of the males’ calcium scores was higher than that of the females.

Comparatively, the correlation between calcified plaque burden and the calcium score were found to be equal in men and women in the USA, however CAD onset was found to be delayed in men compared to women (Klodas, 2007).

5.6.3 What percentage of individuals in each risk category present with calcium in the coronary arteries?

Interestingly Assman et al., (1999) state that age, sex and family history are non-modifiable risk factors for CAD. Hyperlipidemia, hypertension, cigarette smoking, obesity and diabetes are modifiable risk factors for CAD. In the current study, of the 71 participants with risk factors, 14 (19.7%) presented with hypertension, 14 (19.7%) presented with obesity, 13 (18.3%) presented with smoking, 14 (19.7%) presented with hyperlipidemia, 54 (76.1%) presented with family history and 13 (18.3%) presented with diabetes. A similar study was conducted by Shaw et al., (2003), on 10, 377 asymptomatic participants for CAD.
in New Orleans, Los Angeles (LA). 44% of the population presented with hypertension, 40% presented with smoking, 62% presented with hyperlipidemia, 69% presented with family history and 9% presented with diabetes. Family history has been found to be the most common risk factor in both study populations inferring a result of 69% in New Orleans, LA and 76.1% in Durban KwaZulu-Natal.

On bivariate analysis of the 103 participants, there was a significant association between calcification and hypertension (p=0.030), hyperlipidemia (p=0.030), and diabetes (p=<0.001). Of those individuals with hyperlipidemia 57.1 % presented with calcification. According to Assman et al., (1999), hyperlipidemia can be corrected by a lipid lowering diet and medical therapy. Achenbach et al., (2002) conducted a study showing the benefits of lipid-lowering therapy on coronary artery calcification on an asymptomatic population. The study population composed of 66 individuals with LDL cholesterol levels > 130mg/dL. An initial EBCT scan was performed on these individuals and repeated after 14 months without any treatment. A third EBCT scan followed after 12 months with cerivastatin treatment (0.3mg/d). The calcium scores using VCS quantification were: median volume of 155mm$^3$ on baseline scans; median volume of 203mm$^3$ on follow up scans without treatment; median volume of 201mm$^3$ on the third scan with treatment. The median annual absolute increase of calcium scores without treatment was 25mm$^3$ and the median annual absolute score increase with treatment was 11mm$^3$ (p= 0.01). The median annual percentage increase in calcium scores without treatment was 25% versus 8.8% with treatment. Therefore it was inferred by Achenbach at al., (2002) that cholesterol treatment significantly deterred the progression of calcium in the asymptomatic
high risk population studied. The calcium score study has played a significant role in the monitoring of this outcome. Significantly Grundy (1999) states that when LDL cholesterol levels are low atherogenesis proceeds slowly even when other risk factors are present. This is in keeping with the results of the study by Achenbach et al., (2002).

Of those individuals with hypertension 57.1% presented with calcification. Hypertension can be treated by reduction in salt intake and medical therapy (Assman et al., 1999). Meta-analysis studies confirm that lowering of blood pressure in an individual lowers the risk of an acute myocardial event (Grundy, 1999).

In the current study the percentage of calcification in diabetic individuals was 76.9 %. Detrano (2003) states that there is no clear and strong relationship between coronary calcium and future coronary events in diabetic individuals. In the study conducted by Detrano (2003) 269 diabetic participants underwent a CT calcium score scan. In a 6.3 year follow up there were 64 coronary events. The study could not however prove that there was any correlation between the calcium score and the incidence of cardiac events. Detrano (2003) maintains that the study of diabetes and atherosclerosis is embryonic and it is therefore a disservice to the public to promote the application of coronary calcium screening in diabetic individuals. On the other hand Shaw et al., (2003) advocates that diabetes is a predisposing risk factor for CAD. A study was performed on 10,377 asymptomatic individuals of whom 903 were diabetic and 9474 were non-diabetic. In a 5 year follow up there was 15.8% mortality in the diabetic population subset compared to 7.8% in the non-diabetic population subset (Shaw et al., 2003). There was therefore greater mortality of the diabetic individuals compared to the non-diabetic individuals. Diabetes is a modifiable risk factor that can be controlled by reduction in carbohydrate intake and by cxxi
Of those individuals with obesity 42.9 % presented with calcification. Obesity which can be due to truncal or intra-abdominal excess of fat is a major risk factor for CAD (Assman et al., 1999). It is also the most modifiable risk factor for CAD (Grundy, 1999). Obesity is calculated as a BMI greater than or equal to 30 (Assman et al., 1999). Obesity can be reduced with the correct diet and exercise programme.

The percentage of smokers with calcification was 30.8% in the current study. Assman et al., (1999) significantly state that 30% of all CVD deaths are due to smoking. Furthermore smoking increases the risk of CAD by 3-4 times. Grundy (1999) adds that cigarette smoking predisposes plaque rupture in atherosclerosis and cessation thereof significantly reduces the risk of plaque rupture.

Of those with family history 35.2 % had calcification. Family history as a risk factor for CAD is inherited. This risk factor cannot be modified except by controlling of the other risk factors (Grundy, 1999).

It can therefore be inferred, that three of the six risk categories had a significant association with calcification. Diabetics presented with the highest risk for CAD i.e.76.9 % and smokers presented with the lowest risk i.e 30.8 %. These findings correlate with the statement by Kotha (2003), that Indians suffer from diabetes and metabolic syndromes that predispose them to CAD.
On bivariate analysis of the 102 participants there remained a significant association between calcification and hypertension \((p= 0.033)\) as well as diabetes \((p<0.001)\). Of those with hypertension, 57.1% presented with calcification, and of those with diabetes 76.9% presented with calcification. Of those with obesity 42.9% presented with calcification and smokers had 25% calcification. Of those with family history 35.2% presented with calcification, while the percentage of hyperlipidemia individuals with calcification was 53.8%. Omission of the outlier has changed the significance of hyperlipidemia in the results. Hyperlipidemia was significant with the outlier included and has been rendered not as statistically significant as a risk factor for coronary artery disease when the outlier has been excluded. One needs to therefore consider the clinical importance of the difference detected in risk between those with and without the outlier to decide whether a type II error has been made (Chapter 6, section 6.6. for recommendations).

5.6.4 What is the percentage of individuals in each category presenting with calcium in the coronary arteries? The 5 categories of calcium scores according to Klodas (2005), in HU are:

- 0 / 1-10 / 11-100 / 101- 400 / 400 +.

A minimum threshold of 130 HU was used in the Agatston scoring method i.e. plaque with a threshold of 130 HU and higher was detected by the software. Lesions below a threshold of 130 HU were considered to be soft plaque and were not included in the analysis. The minimum area of each lesion analysed was 1mm and a weighting factor of 1 was used for densities of plaque between 130-199 HU (Girshman and Wolff, 2003). The calcium score for each lesion was
derived from (area of lesion in mm$^2$) x (weighting factor of 1). The total calcium score was then calculated for each segment of calcification in the LMA, LAD, LCX, RCA, and the diagonal arteries. Hence a score between 0-400+ was obtained for each research participant.

The majority of individuals in the 103 sample size presented with a score of 0 (68%). There were 8.7% with a score of 1-10; 11.7% with a score of 11-100; and 5.8% each with scores of 101-400 and above 400. According to Klodas (2007), a score of 0 indicates absence of detectable plaque i.e. a very low likelihood of CAD and good prognosis for the participant. A score of 1-10 also indicates a low likelihood of CAD, but there is identifiable plaque. A score of 11-400 indicates moderate plaque burden. A score of > 400 implies extensive plaque burden and a > 90% likelihood of at least one obstructive vessel with approximately 70% stenosis. Furthermore the calcium odds ratio of developing CVD is as follows:
calcium score > 50 = 7: 1.
calcium score > 100 = 20: 1.
calcium score > 160 = 35: 1.

Relating to the current research a 47 year old male research participant with no risk factors, presented with a high calcium score of over 1063. This suggests a very high risk for a coronary event. According to the odds ratio a 35:1 likelihood of a coronary event with 90% likelihood of one obstructive vessel, with 70% stenosis is expected (Klodas, 2007). On the contrary the research participant had a courtesy CT coronary angiogram which showed no significant atherosclerotic stenosis or soft plaque formation. On the other hand a study by Wayhs et al., (2002) has shown that a significant percent of a study population with calcium scores > 1000 presented with cardiac events in the study period. The population comprised
of 98 asymptomatic individuals with a mean age of 62 years. All participants had a calcium score of > 1000. No further testing in addition to the EBCT calcium score procedure was performed on these participants. In the observatory period of 28 months 36% i.e. 35 participants had a coronary event in the form of fatal or non-fatal MI (Wayhs et al., 2002). Despite these findings Wayhs et al., (2002) suggest that there exists controversy on the prognostic significance of calcium in the coronary arteries as it is believed to stabilise atherosclerotic plaque.

In the current research another research participant with a very high calcium score of 4937, and risk factors of smoking and hyperlipidemia underwent a conventional angiogram that detected two areas of stenosis in the RCA. Therefore this high calcium score correlated with the individual’s clinical outcome.

The majority of individuals in the 102 sample size presented with a score of 0 (68.6%). There were 8.8% with a score of 1-10; 11.8% with a score of 11-100; and 5.9% with scores of 101-400 and 4.9% with scores above 400.

It can therefore be concluded that majority of the population studied were devoid of calcium in the coronary arteries. However any percentage of calcification above 0 should be considered significant as it indicates prevalence of CAD. The screening of the Indian population in Durban, KwaZulu-Natal has definitely created greater health awareness and interest in the calcium score study, which is advocated by AHA as a useful screening test in CAD assessment (Wood, 2006).

**5.6.5. What is the adjusted risk of calcification for demographic and risk factors in**

*cxxv*
Asymptomatic individuals from the Indian population in Durban, KwaZulu-Natal?

As discussed in Chapter Four in the 103 data set, it was shown that age, gender, hyperlipidemia and diabetes were all independently associated with calcification. With every one year increase in age, the adjusted risk of calcification increased by 1.21 times. According to Grundy (1999) one weakness of the FRS is that age is an overriding risk factor in older individuals (Grundy, 1999). Therefore age is not necessarily a good indicator for severity of atherosclerosis. Males had an 11.9 times higher adjusted risk of calcification than females. Hyperlipidemia conferred a 5.4 times higher adjusted risk, and diabetes increased the risk by 11.7 times.

However on removal of the outlier, with every one year increase in age, the adjusted risk of calcification still increased by 1.21 times. Males had a 9.7 times higher adjusted risk of calcification than females. The risk in diabetes increased by 12.1 times. Importantly hyperlipidemia has shown a non-significant effect as a risk factor for coronary artery disease on removal of the outlier. Tests for interaction between these variables showed that there was no effect modification present, thus these factors operated independently.

Therefore being male, increasing age and the presence of diabetes are all independent risk factors for coronary artery calcification in asymptomatic Indians in Durban, KwaZulu-Natal. The largest risk was due to being diabetic (odds ratio 12.1) followed by being male (odds ratio 9.7). However, exclusion of the outlier has lowered the study’s power marginally but this has resulted in the finding of a non significant effect of hyperlipidemia after exclusion of the outlier, whereas it was significant before.
Klodas (2007), states that the significance of a particular score is influenced by a patient’s age and gender. A score of 150 may be average for a 70 year old man but would be considered abnormal for a 40 year old female. Interestingly calcium score and plaque burden correlation is identical in men and women, but the clinical manifestation of CAD is delayed in women (Klodas, 2007).

5.7 Percentile ranking

As defined by Lane (2007), percentile ranking is the proportion of scores in a distribution that a particular score is greater than or equal to. Percentile ranking is based on a study performed at the University of Illinois on greater than 19000 patients without symptoms or risk factors for CAD (Carr et al., 2000). The lower the percentile rank, the lower the cardiac risk. Percentile rank assumes the absence of symptoms and does not account for risk factors or for the number of calcified vessels in CAD (Carr et al., 2000). However, percentile ranking was not applied to the current study as there is currently no database for percentile ranking in the South African population. Larger studies across all age groups and ethnicities should be considered in the future in order to create a database as a reference for normal values of the calcium score for all age groups and ethnicities.

5.8 Ancillary findings

- A participant with a calcium score of 0, had calcification within the aorta, close to the LMA.

- A participant presented with the appearance of tuberculosis on the localizer scan. This participant was advised to have a chest x-ray and to consult with a chest physician.

- A hernia was diagnosed on the axial scans of one research participant.
5.9 Conclusion

The FRS has been the cornerstone of preventative cardiology for some time (Pearson, 2002). Risk factor assessment and reduction has been found to be pivotal in optimal patient management and treatment. The tide has turned and primary prevention of CAD is getting more attention than previously. The time is now to integrate high risk primary prevention into standard clinical practice (Grundy, 1999). The calcium scoring technique is a relatively new technique that accurately and non-invasively determines presence, extent and severity of CAD (Klodas, 2007). This effective screening tool had been utilized in the current research in assessing the prevalence of calcium in the coronary arteries in the research population.

Rissam et al., (2001) advises that to combat CAD onslaught it is important to have a high index of suspicion of CAD, particularly in a high risk asymptomatic population. The screening of asymptomatic risk and risk free individuals for CAD in the Indian ethnic group in Durban, KwaZulu-Natal has shown prevalence of the disease in 32% of the population. Any percentage of calcification above 0 is considered significant in an asymptomatic population because as discussed in the literature review and introductory chapters CAD, can have a sudden onset and most often the coronary events are fatal. Knowledge of the presence and degree of CAD is necessary in order to implement lifestyle changes and risk modification on these individuals.

The statistical results of the current study have shown the highest risk factor was due to
being diabetic, followed by being male. Smokers presented with the lowest risk for CAD. Importantly, diabetes, hypertension, obesity, hyperlipidemia and smoking are modifiable risk factors for CAD. Advancing age, sex and family history are non modifiable risk factors. In conclusion, it is once again emphasized that risk modification by lifestyle changes and medical therapy could abate the onslaught of CAD in the South African Indian population, in Durban KwaZulu-Natal. Therefore knowledge of the presence and extent of disease in this population, assessed by the calcium score study added prognostic value in the screening of asymptomatic risk/non-risk individuals for CAD.
CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

6.1 Introduction

The current study represents the first documented research on the calcium score done in South Africa. One hundred and three volunteers in Durban, KwaZulu-Natal of Indian ethnicity, in the age group of 20-70 years, participated in the research. Firstly the study placed the participants into the risk and non-risk categories for CAD. Thereafter the calcium scores were obtained on these participants. Analysis and reporting of the data followed. Finally the study compared the findings of this study with other reported studies worldwide to compare the similarities and discrepancies with other work. The literature review served as a framework for this study as it provided incremental information on the calcium score study already documented in other countries.

6.2 Significance of the study

The calcium scoring technique has been advocated in many countries like America and New Zealand as an effective screening tool for CAD and atherosclerosis (Lewis, 2003 and Meires et al., 2005). In 2005 AHA and ACC, in a consensus statement advocated the use of the calcium scoring technique as a tool that predicts CAD beyond traditional risk factors (Meires et al., 2005). It is suggested that the calcium scoring technique is both independent and incremental to traditional risk factors in the prediction of cardiac events (Wood, 2006). The standard risk factors according to the Framingham risk model are hypertension,
hyperlipidemia, smoking, diabetes and advancing age (Assey and Selby, 2004). For the current research the risk factors utilised were hypertension, diabetes, hyperlipidemia, family history, obesity and smoking.

This study is beneficial to the South African population as it has created greater awareness of CAD and the calcium scoring technique. Furthermore, it would be beneficial worldwide, as it would add to the statistical data already existing globally on the calcium score technique.

6.3 Research findings

Similar to reports on calcium score studies done globally on the Indian ethnicity, there is definite prevalence of coronary artery calcification in the South African Indian population in Durban KwaZulu-Natal. Interestingly, not all participants in the risk category for CAD, presented with calcium in the coronary arteries. On the other hand there was a prevalence of coronary artery calcium in non-risk participants. The calcium scores ranged from 0 to 4937.

The final results of the study reported that being male, increasing age and the presence of diabetes were all independent risk factors for coronary artery calcification in the asymptomatic Indian population in Durban KwaZulu-Natal. The largest risk was due to being diabetic (odds ratio 12.1) followed by being male (odds ratio 9.7).

6.4 Limitations

• Firstly, the current study was limited to the Indian ethnicity and therefore did not represent other ethnic groups in Durban, KwaZulu Natal.
Secondly, the study did not represent the entire population of SA, as it was conducted in one province only i.e. Durban, KwaZulu-Natal.

6.5 Future research

- This research could serve as a framework for future research on calcium scoring, in other ethnic groups in SA. Larger studies can be considered on all ethnic groups, on non-risk asymptomatic individuals for CAD, in order to create a data-base for percentile ranking in South Africa.
- A 2 year follow up to reassess the disease status in the research population should be considered.
- Education is considered to be a strong protector for all cause and CAD mortality (Hardson et al., 2001). Significantly statistics according to Aitchison et al., (2005) has shown that 1.5 million people in SA have not received any formal education. How the level of education has impacted on the population’s health is an area that is understudied and should be considered in the future.

6.6 Recommendations

Hyperlipidemia as a risk factor for CAD should be further researched, as exclusion of the outlier has lowered the study’s power marginally and this has resulted in the finding of a non significant effect of hyperlipidemia after exclusion of the outlier, whereas it was significant before. The percentage of calcification changed from 57.1% with the outlier to 53.8% on exclusion of the outlier. Since the number with hyperlipidemia was low and the p value was greater than 0.05, the statistical power has been reduced in this comparison. Thus by removal of one data point, the power decreased.
significantly. With inclusion of the outlier, a sample of 88 in total was needed with 80 % power. In the second scenario with exclusion of the outlier, a sample of 112 was required to show statistical significance at 80 % power. As stated in 5.6.3 one needs to consider the clinical importance of the difference detected in risk between those with and without hyperlipidemia to decide whether a type II error has been made. Further larger studies are needed to confirm these findings.

6.7 Concluding statements

The screening of asymptomatic risk and non-risk individuals for CAD has shown that being diabetic is the highest risk, followed by being male. Calcium scores have also shown to increase with age. 32% of the research population in Durban, KwaZulu-Natal has presented with coronary artery calcification, which denotes 32% prevalence of CAD. 71% of the research population was devoid of coronary artery calcification and therefore were at low risk for CAD. However one needs to consider that any percentage of disease prevalence in an asymptomatic population poses risk for future coronary events. Therefore the study population was advised on medical treatment and lifestyle modification where it was deemed necessary to abate the onslaught of CAD.
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82. Stary, H.C., Chandler, A.B., Dinsmore, R.E., Fuster, V., Glasgov, S., Insull,

Circulation. Vol 92. pp. 1355-1374. A definition of advanced types of
atherosclerotic lesions and a histological classification of atherosclerosis.
2007.

Hospital Group. Ed. Jones,S.V.

on 23 July 2006.


Appendix A

Permission letter to perform study

P.O. BOX 339
UMKOMAAS
4170

Drs Jackpersad and Partners
603-604 Lorne Street
Durban
4000

Dear Sir/Madam

Re: Request for Permission to perform Research

I am currently registered as a Master’s Degree student at the Durban Institute of Technology. My proposed topic is:
A comparative assessment of the prevalence of coronary artery calcification in the age group of 30–50 years, in an asymptomatic risk and non-risk population, to triage such populations for risk of adverse coronary events.

My Research Proposal is attached for your perusal.

I hereby request permission (in writing) to perform this study, at the Westridge Medical Centre on the G.E. multislice scanner. I intend to scan approximately 100 participants at the Department’s convenience. It is my earnest belief that this study will benefit the Practice and the population in terms of creating an awareness of the value of the calcium scoring procedure in preventative medicine. The research has received the appropriate Ethics approval from the Durban Institute of Technology.

Your Support and permission to undertake this study will be greatly appreciated.

Yours Sincerely

________________________
K Moodley
APPENDIX B

Jackpersad, Rooknoodeen & Partners Inc
Diagnostic Radiologists
PR 3864917 Co.Reg. No. 97/1989321

9th July 2006,

TO WHOM IT MAY CONCERN,

RE: MS. K. MOODLEY

Ms. Moodley will be conducting research at the practice of Dr. Jackpersad & Partners INC. with full approval.

Yours sincerely,

DR. M. VAYEJ
Director
Appendix C

Technology studies be retained by you as the initiator of the project:
(b) should you make any profit from the results of your Master’s Degree in Technology studies, you will be required to repay pro rata, the R10 000.00 investment which the Institution Research Committee has made in approving your request for funding;
(c) If the Durban University of Technology provided the equipment/materials for the creation of artefacts, this cost would be refunded to the University if such artefacts were sold and
(d) Durban University of Technology be given first refusal in respect of any possible future sale by you of any patent that may be registered in respect of your said project.

May we remind you that in terms of Rule G24(2) (b), if a candidate fails to obtain the Master’s Diploma or Degree within four years, after first registering for the qualification, the Senate may refuse to renew the student’s registration or may impose any conditions it deems fit. A student may apply to the Faculty Board for an extension.

Furthermore, if you experience any problems relating to your research studies, your supervisor must be informed as soon as possible. If the difficulty persists, you must then approach your Head of Department and thereafter the Executive Dean of the faculty.

I attach:

(a) a duplicate of this letter which you are required to sign, where indicated, acknowledging your acceptance of the above conditions. Please return it urgently. Failure to comply will necessitate the Faculty of Health Sciences Research Committee reviewing their decisions set out herein;
(b) a copy of the 2006 General Rules governing the submission of your dissertation;

Please do not hesitate to contact me if I can be of any assistance.

Yours sincerely,

[Signature]

MR VIKESH SINGH
FACULTY OFFICER
FACULTY OF HEALTH SCIENCES

[Signature]

Student’s signature accepting the conditions.
27/10/06.
Date of accepting the conditions.
The Directors
Drs Jackpersad and Partners
6/10/06

Re: Research

I am pleased to inform you that my Research Proposal had been approved by the Durban University of Technology on the 2/10/06.

The title of the research is: An assessment of coronary artery calcification, using the calcium scoring technique, in an asymptomatic Indian population in Durban, KwaZulu Natal.
A copy of the research proposal will be handed to Dr Kalideen who will be acting as my Supervisor in the clinical environment. The next step in the research will be the recruitment process which will be done simultaneously with the scanning of participants. The Research committee has indicated that to validate the research, ideally 100 participants should be scanned. However, this will depend on the recruitment. The Faculty of Health Sciences will fund R10 000 towards the research.

My intention is to scan the participants on the Saturday mornings when I am off duty, so that it does not affect or disrupt my normal working hours. Due consideration will also be given to the departmental CT bookings and the logistics will be discussed with Dr Kalideen.

I would also like to express my gratitude to the Directors for their continued support in my research and Dr Kalideen for his tremendous contribution thus far. I am confident that I will receive this kind of support throughout my research.

Thanking You
K. Moodley (Linda)
Appendix E

Participant’s Information Sheet

TITLE OF RESEARCH: An assessment of coronary artery calcification, using the calcium scoring technique, in an asymptomatic Indian population in Durban, KwaZulu-Natal.

RESEARCHER: Karanigie Moodley

AIM OF STUDY: You are requested to volunteer for a study that will determine the incidence of coronary artery calcification in an asymptomatic risk and non-risk population. The risk factors for the study are: smoking, obesity, high cholesterol levels, diabetes, hypertension and strong family history. Approximately 100 participants from Durban, KwaZulu-Natal will be utilized in the study. You are required to fill in a questionnaire that will outline the criteria for inclusion in the study. If you cannot understand the information on this form it will be translated to you in your required language.

INCLUSION CRITERIA:
1. You must be between 20-70 years old.
2. You must be asymptomatic for a coronary event i.e. must not have angina, chest pain or prior history of a myocardial infarction.

EXCLUSION CRITERIA:
1. You must not be pregnant.
2. You must not have angina, chest pain or history of a myocardial infarction (heart attack).

PROCEDURE:
1. If you fit the inclusion criteria you will be given an appointment for your CT Smartscore scan (calcium score).
2. You are expected to avoid coffee and smoking for 3-4 hrs prior to the procedure.
3. You will be required to remove the clothes from your chest.
4. Before the actual Smartscore scan you will be connected to an ECG monitor and your heart rate will be checked. (Ideally it should be between 60-70 beats per minute or lower). If it is below 70 bpm you will continue as a participant for this study.
5. The scan time is approximately 5-8 seconds. You would therefore be required to hold your breathe for this duration of time.
6. Your calcium score will be calculated using the GE Advantage Window version 4.3 software package.
8. You will be given a copy of your report.
WHAT TO EXPECT: The procedure is painless. The Scanner generates a minimal amount of noise.

RISKS: Because of the radiation dose as a result of the procedure you are expected not to volunteer if you are pregnant.

BENEFITS: You will be made aware of the amount of calcification that exists within your coronary arteries so that you can adapt lifestyle changes accordingly.

CONFIDENTIALITY: All information concerning you will be kept private and confidential. Should there be a need to publish any information, it will be in a manner where you cannot be identified. However, some research records may be obtained by court order should the need arise.

CONTACT DETAILS: K. Moodley. ph H - 039 979445
ph W - 031 2731050
ph C - 0834595481

EMAIL: lindam@polka.co.za

VOLUNTARY PARTICIPATION/ WITHDRAWAL:
Your participation in this study is completely voluntary. You must not be forced into this study. You may withdraw from this study with no penalty. Any questions that you may have will be answered by the researcher at any stage of the study. (contact details above.)

ETHICS APPROVAL:
This study has been approved by the Durban University of Technology Ethics Committee.

A copy of this form will be given to you. Your signature below indicates that the researcher has answered all of your questions to your satisfaction, and that you consent to volunteer for this study.

PARTICIPANTS’ SIGNATURE __________________________DATE: ___________

PARTICIPANT’S ADDRESS ____________________________________________

PARTICIPANT’S TELEPHONE NO. ________________________________

RESEARCHER’S SIGNATURE ______________________DATE ___________
Appendix F

Participant’s Informed Consent Form

I, ……………………………………. date of birth ………., and weight of……..kgs consent to voluntarilly participate in the research on, ‘the incidence of coronary artery calcifications in an asymptomatic risk and non-risk population ‘.

Researcher : Miss K.Moodley - student B.Tech. Radiography
Supervisor : Mrs S.Naidoo - Master of Applied Science (MRT)
Co-supervisor: Dr J.M.Kalideen - F.R.C.R. (UK).

Please circle the appropriate answer

1. Is there any chance of you being pregnant?                                        YES/ NO
2. Have you read and understood the information sheet?                              YES/ NO
3. Have you had the opportunity to ask questions ?                                   YES/NO
4. Have you had an opportunity to discuss the study?                                 YES/ NO
5. Have you received satisfactory answers to your questions?                          YES/NO
6. Do you understand that you can withdraw from the study at any time, without a reason?    YES NO
7. Do you understand that should you withdraw from the study, there are no repercussions?  YES/ NO
8. Do you understand that there is no financial implication on you to participate in the study? YES/NO
9. Do you understand & voluntarily agree to participate in the study?                 YES/NO

If you have answered No to any of the above, please obtain any necessary information before signing.

Risk factors for CAD : answer Yes/No to the following questions

1. Are you hypertensive?…….. 5. Are you diabetic?............
2. Are you a smoker?……. ….  6. Are you overweight?.........
3. Do you have any family history of coronary artery disease?........
4. Do you have hyperlipidemia?.........

K.MOODLEY ( Miss)________                              _____________
Name of Researcher                          Date                          Signature

__________________
Name of Participant:                          Date                          Signature

__________________
Name of Witness                          Date                          Signature

clx
INVITATION TO INDIAN PARTICIPANTS BETWEEN 20 – 70 YRS

A study on CT calcium scoring i.e. a procedure to assess calcium in the Coronary arteries is currently being done. If you do not have history of heart disease, chest pain or angina you are invited to participate in the study.

BENEFITS: The study will show any calcium in your coronary arteries. Likewise the study will reveal whether Indian individuals living in Kwa-Zulu, Natal between 20-70 years, are at risk for coronary artery disease.

PROCEDURE: Is painless, however you will need to have a stable heart rate and will be subjected to a minimal amount of radiation. Pregnant individuals and individuals who are planning to fall pregnant should therefore not volunteer for the procedure.

ETHICS APPROVAL: The study has gained ethics approval from the Durban University of Technology.

IF YOU ARE INTERESTED IN PARTICIPATING IN THIS STUDY;

Please contact: Linda Moodley at Westridge Medical Centre, 95 Jan Smuts Highway,
Durban, 4001.
w) 031-2731050
h) 039-9794445
e.mail: lindam@polka.co.za

ps: please pass this pamphlet to whomever may be interested.
Appendix H (calcium score printout).

Westridge Medical Centre

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<th>103</th>
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<tbody>
<tr>
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<tr>
<td>Birth Date</td>
<td>6/21/63</td>
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<tr>
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<tr>
<td>Smoking</td>
<td>No</td>
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<td>Scored By</td>
<td>LM</td>
</tr>
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Cardiac History
DOSE: 160.10 DLP
Calcium Score
Greater than 0.1:

Score Summary
Your total calcium score is 0.

Ranking Guide
Your score of 0 places you in the 10 percentile rank. That means 90 percent of the male at the ages from 40 to 45 will have a higher calcium score than you.

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<td>Left Circumflex (LCX)</td>
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<td>Right Coronary Artery (RCA)</td>
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<td>Posterior Descending Artery (PDA)</td>
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APPENDIX I

Participants’ Log sheet

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<th>Sex</th>
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<th>Risk factors</th>
<th>Calcium scores</th>
<th>Radiation dose</th>
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Appendix J

Data entry sheet

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<th>Non-risk individuals</th>
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Appendix K

Image of a Multislice scanner

Appendix L

Calcium score images
Accessed from: http: www.healthscan.com
Appendix M
Tables to calculate sample size
(Supplied by statistician Tonya Esterhuizen on 23/8/06)

Unmatched Cohort and Cross-Sectional Studies (Exposed and Nonexposed)
Sample Sizes for $\text{Disease in Unexposed Group} = 5\%$

<table>
<thead>
<tr>
<th>Conf.:</th>
<th>Power</th>
<th>Unex:Exp.</th>
<th>Disease in Exposed</th>
<th>Risk</th>
<th>Odds</th>
<th>Sample Size</th>
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Formula: $n' = \frac{S(a/2)\sqrt{(r+1)*PQ - c(1-b)\sqrt{r*P1Q1+P2Q2}}}{(r*\sqrt{P2-P1})}$

Figure 4.15: showing the association of Hypertension and calcification (n=102)
Figure 4.16: showing the association of Obesity and calcification (n= 102)
Appendix P

Figure 4.17: showing association of Family history and calcification (n=102)
Appendix Q

Figure 4.18: showing association of Diabetes and calcification (n=102)
Appendix R

```
JACKPERSAD & PARTNERS INC.
SPECIALIST DIAGNOSTIC RADIOLOGISTS Practice No. 3834917
ADMINISTRATION ACCOUNTS
Floor Maxwell Centre, 7177 Lorne Street, Durban - Tel: 3661000 Fax: 3652199

X-RAY REQUEST FORM / MOTIVATION LETTER / CLINICAL DETAILS

PATIENT'S NAME: Dr. P. A. Govender
AGE: 10-0.0

CLINICAL DETAILS:

Hepi Scan 32945

MOTIVATION:

Catheterisation for coronary artery

2 areas of narrowing in angio.

DISTRIBUTION OF SPECIALISED EQUIPMENT:

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<th>CT</th>
<th>PET</th>
<th>ULTRASOUND</th>
<th>ENDOSCOPY</th>
<th>RADIOTHERAPY</th>
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<td>MRI</td>
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TOTAL P. 01
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Appendix S

MYOCARDIAL PERFUSION STUDY

BACKGROUND

Dr Govender is a 55-year-old gentleman in whom coronary artery calcification was found in a CT study, and 2 areas of narrowing in angiogram. Was referred to evaluate presence of ischaemia.

PROCEDURE

Physical stress test, Standard Bruce, 2 day Protocol was performed. 20 mCi Tc-99m Sestamibi was administered at peak exercise. Rest images were obtained after the administration of 20 mCi Tc-99m Sestamibi.

FINDINGS

Baseline ECG showed normal sinus rhythm 90 BPM, tracing within normal limits, and BP was 126/80. Peak heart rate 172 145 BPM was achieved at 8 minutes 15 seconds, being the target heart rate 155 BPM. Maximal BP was 140/92. Stress ECG is not clearly read showing an apparent ST segment depression of 1mm, horizontal in V4 not visualised at the end of the stress during recovery period. Patient had no complaints.

PERFUSION IMAGES

Right ventricle appears normal. Left ventricle appears normal with no evidence of post-stress dilatation. No evidence of fixed or reversible perfusion defects. Excellent LV function with no regional wall motion abnormalities. LVEF measures 65 % post-stress and 96% at rest.

COMMENT

The study was considered clinically negative and electrically equivocal. No evidence of infarction or exercise induced ischaemia. Excellent LV function with no evidence of stress induced dilatation.

CONCLUSION

Myocardial perfusion study shows no evidences of infarction or exercise induced ischaemia. Excellent LV function with no evidence of stress induced dilatation.

DR CARLOS D LIBHABER / DR K.D. DJI/ JR
Appendix R  (Request form for Mibi scan on research participant)
Appendix S (results of Mibi Scan)