Cape Peninsula University of Technology

ECHOCARDIOGRAPHY FOR EARLY DETECTION OF HEART DISEASE IN HIGH RISK DIABETIC PATIENTS

BY

MARIA DIANA HARTNICK

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Internal Supervisor:	Prof Penelope Engel-Hills
Co-supervisor:	Ms. Ferial Isaacs
External Supervisor:	Dr. Bert Posen

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DECLARATION

I, Maria Diana Hartnick, declare that the content of this dissertation represent my own unaided work, and that the dissertation has not previously been submitted for academic examination towards any qualification. Furthermore, it represents my own opinions and not necessarily those of the Cape Peninsula University of Technology.

M.D. Hartnick (192055836)   December 2014
Signed   **Date**

DEDICATION

To my husband, Marlon and our children, Mark and Rebekah -

Thank you very much, your love is priceless

"The greatest commonality between successful people is that most of them had huge obstacles to overcome."

- John C. Maxwell

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ABSTRACT

Introduction: Diabetes mellitus is a chronic disease with a significant impact on personal lifestyle and wellbeing. It is associated with a high prevalence of myocardial disease, the early detection of which is important for prevention of disease progression. Although echocardiography is recognised as a leading cardiovascular imaging modality, there has been limited work on its role in the early detection of diabetes-related myocardial dysfunction. The aim of this study was therefore to evaluate the role of echocardiography in the early detection of diabetes-related myocardial disease, in a population with a high prevalence of type 2 diabetes mellitus. **Methodology:** A single sonographer, blinded to individual biochemical markers conducted detailed echocardiographic examinations on 407 participants from a Cape Town community with a high prevalence of diabetes mellitus. Participants were subsequently stratified by biochemical status, as normoglyceamia or hyperglycaemia. The echocardiographic features of the two groups were compared using the Pearson chi-squared and Mann-Whitney U tests. **Findings:** Hyperglycaemia was associated with left atrium (LA) enlargement **(p < 0.0014),** aortic enlargement **(p < 0.0067)** and inter-ventricular septal (IVS) thickening **(p < 0.0001). Conclusion:** The findings suggest that echocardiography can be a useful screening tool for myocardial dysfunction in Type 2 diabetes mellitus.

KEY WORDS

Left ventricle dysfunction, left ventricular hypertrophy, echocardiography, cardiovascular heart disease, myocardial Infarction, type 2 diabetes mellitus, hypertension

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GLOSSARY

The following terms and definitions are relevant to this study

Dyslipidemia: a condition marked by abnormal concentrations of lipids or lipo proteins in the blood

Ejection fraction: the ratio of the volume of blood the heart empties during systole to the volume of blood in the heart at the end of diastole expressed as a percentage usually between 50 and 80 percent

Glucagenesis: The formation of glycogen from fatty acids and proteins, instead of from carbohydrates

Glycogenesis: The conversion of excess glucose into glycogen storage in the liver for later use as needed

Insulin shock: A state of shock due to extremely low blood sugar levels, caused by an over dose of insulin, a decrease food intake or excessive exercise by a diabetic patient

Micro-albuminuria: Albuminuria characterised by a relatively low rate of urinary excretion of albumin typically between 30 and 300 milligrams per 24-hour period

Left ventricular hypertrophy: Thickening of the myocardium of the left ventricle of the heart

LIST OF ABBREVIATIONS

AO:	Aorta
AV:	Aortic valve
BP:	Blood pressure
CAD:	Coronary artery disease
CVD:	Cardiovascular disease
Hba1C:	Glycated haemoglobin
HDL:	High density lipoprotein
HPT:	Hypertension
HsCRP:	High sensitive C-reactive protein
IGT:	Impaired Glucose Tolerance
IFG:	Impaired Fasting Glucose
LA:	Left atrium
LDL:	Low density lipoprotein
LV:	Left ventricle
LVEDD:	Left ventricular end-diastolic diameter
LVESD:	Left ventricular end systolic diameter
LVH:	Left ventricular Hypertrophy
MI:	Myocardial Infarction
M-Mode :	Motion mode (Ultrasound)
MV:	Mitral valve
TV:	Tricuspid valve
2D Image:	Two-dimensional image (Ultrasound)

CHAPTER ONE: AN OVERVIEW OF THE STUDY

A total of 407 participants (n=407) in this study underwent an echocardiograph and biochemical marker testing. This research study focussed on myocardial dysfunction due to cardiovascular disease. A complication of diabetes is cardiovascular disease (CVD), which worsens the prognosis of survival for many diabetic patients, if there is a delay in recognizing cardiovascular disease (Grundy, Connely, Kelly, Pollock, Krum, 1999). It is within this context that the need arises for patients with DM to receive quality treatment to prevent premature death.

1.1   Background information

This study on echocardiography was conducted in Bellville South, Western Cape in the Republic of South Africa. This is the first research study of its kind in this community, with the focus on echocardiography and DM.

CVD in South Africa is the second leading cause of death after Human immunodeficiency virus infection / acquired immunodeficiency syndrome (HIV/AIDS) (Maredza, Hofman, Tollman, 2011). Most studies related to the role of echocardiography in the early detection of diabetic-related myocardial disease have been done outside of South Africa (Galderisi, Anderson, Wilson, Levy, 1991; Galderisi, 2006; Liu et al., 2001; Kral, Becker, Vaidya, Yanek, Becker, 2011; Palmieri et al., 2003; Poulsen et al., 2010). Diabetic women had increased left ventricular (LV) wall thickness (18.7 versus 17.1 mm, $p < 0.001$), and relative wall thickness (0.403 versus 0.377, $p = 0.008$) compare to non-diabetic women. According to the study, diabetes remained an independent contributor to LV mass ($p = 0.004$) and wall thickness ($p = 0.008$) in women.

A Study done by Poulsen et al., (2010) examined the prevalence of myocardial ischemia in type 2 diabetes patients in order to establish an algorithm to identify patients with a high risk of ischemic heart disease. Patients were screened using myocardial perfusion scintigraphy as well as echocardiography. According to their study the uni-variate predictors of myocardial ischemia were as follow; atypical or typical angina pectoris, two or more risk factors for CVD, BMI > 32kg/m², systolic

blood pressure > 140mmHg, HbA1c > 8.5%, high sensitivity C-reactive protein > 4.0mg/l, left atrial volume index > 32ml/m², left ventricular ejection fraction < 50%, and carotid and peripheral arterial disease. The algorithm identified low (n=115), intermediate (n=65) and high risk groups (n=115), in which the prevalence of myocardial ischemia was 15% in low risk and 23% in intermediate group and 43% in the high risk group.

Shapiro et al. (1981) noted that the left ventricular function is often abnormal in diabetic patients which can be due to scarring of the tissue from a silent myocardial infarction, which may be painless in patients with DM. Another concern for diabetic patients is heart failure, and according to Gilbert, Connely, Kelly, Pollock, Krum (2006) that is termed the forgotten disease and often is a fatal complication of diabetes. According to Lo & Thomas (2009) the following are indicators of heart failure; poor ejection fraction, ischaemic mitral regurgitation which is due to an infarction, dysynchrony, which is uncoordinated ventricular motion and is often present with LV dysfunction. Furthermore Grundy et al. (1999), stated that individuals with DM are at higher risk of developing CVD. American College of Cardiology/American Heart Association (ACC/AHA) (2003), indicated that two-dimensional (2D) echocardiography is the method of choice to assess the systolic function of the heart because it is non-invasive and cost-effective.

1.2   Rationale

Type 2 DM is associated with an increased risk of cardiovascular mortality, therefore detection of early cardiovascular changes in DM individuals plays an important role in prevention and treatment (Zapolski and Wysokiński, 2013). According Boras, Brkljačić, Ljubičić, Ljubić (2010) more than half of all diabetic patients die from CAD insufficiency, because CAD is usually more advanced at the time of diagnosis and has unfavourable prognosis in diabetic patients. Echocardiography according to Schmailzl & Ormerod (1994) is a powerful and safe technique to assess the diabetic heart. According to the ACC/AHA Guidelines for the Clinical Application of Echocardiography (2003) echocardiography has a 95% accuracy rate for confirming an event of myocardial infarction.

1.3   Research question

Can echocardiography be used in the early detection of diabetes-related myocardial disease?

1.4   Research objectives

The objective of the research study was to evaluate the role of echocardiography in the early detection of diabetes-related myocardial disease by correlating the echocardiographic features of early myocardial disease with biochemical markers of type 2 diabetes.

1.5   Conclusion

Since there is no known cure for diabetes mellitus, whether Type 1 or Type 2, the next best option would be to prevent the disease from causing those who suffering from the disease to suffer adverse effects, such as death. The first and foremost prevention method would be to stop the development of Type 2 diabetes mellitus, by leading a healthy lifestyle through exercising and following a healthy diet. Another preventative method would be to do diagnostic testing's, such as Echocardiography to assess the diabetic heart. According to Watkins, (2003) patients with longstanding diabetes mellitus, both Type 1 and Type 2, may develop various complications affecting the heart, eyes, kidneys and the major arteries.

CHAPTER TWO: Literature review

2.1   Introduction

A Medline search of English language articles in the period of June 2010 until December 2012 was conducted using the terms "echocardiography", "type 2 diabetes mellitus" and myocardial infarction. The abstracts of all articles were reviewed and the full manuscript of the relevant articles retrieved. Detailed discussions within a South African context will highlight issues related to echocardiography as a sonographic technique, to assess the diabetic heart. Arguments are presented, from the literature, on the need for strategy and intervention in communities in South Africa to provide a solution for the early detection of cardiovascular disease in diabetic patients.

2.2   Global impact of diabetes mellitus

In 2004 it was reported that about 200 million people worldwide suffered from DM and this number was expected to increase by more than 20 million every year (Walker & Rodgers, 2004). According to the Serious and Continuous Illnesses Policy and Practice Study (SCIPPS) (2012), diabetes mellitus caused 3.8 million deaths among adults who are 20 years of age and older in 2007, which is 6% of the total world population. Diabetes mellitus has a great impact on the day to day living of individuals that suffer from it, but more so it can have long term effects on the health, such as damage to the eyes, kidneys, ligaments and very importantly for this study the disease has an impact on the heart (Walker & Rodgers, 2004). The morbidity and mortality rate for individuals with diabetes mellitus is very high because of micro and macro-vascular disease that can cause death if left untreated. Patients with diabetes are two to five times more likely to develop heart failure than those individuals without diabetes. This could be due to a myocardial infarction, hypertension and left ventricular hypertrophy (LVH) which results in poor left ventricular function (Nesto, 2008). Diabetes therefore is a well known risk factor for CVD, especially congestive heart failure (CHF) (Liu et al., 2001). Patients with CHF together with diabetes have a poor prognosis and quality of life compared to patients with CHF and no diabetes (Grundy et al., 1999). Individuals with CHF and DM have

an increased prevalence of atherosclerosis and coronary artery disease (CAD) and the mortality and morbidity rate after a myocardial infarction (MI) due to the atherosclerotic plaque are much higher (Nesto, 2008). It is also reported that patients with DM have lipid-rich atherosclerotic plaque that is more vulnerable to rupture than plaque found in patients without DM and the rupturing of plaque can be a contributor to MI (Voors & Van der Horst, 2011). According to Burke (2013) an acute myocardial infarction indicates irreversible injury to the myocardium, which results in necrosis of generally more than 1cm. The term acute refers to myocardial injury less than 3-5 days.

The world is experiencing a global epidemic of diabetes and heart disease. In 2005 CVD was responsible for 17.5 million deaths and diabetes mellitus for 1.1 million deaths in Africa (The Diabetes Declaration and Strategy for Africa, 2006). With diabetes being an underlying cause of CVD, it is expected that by 2030, CVD will account for 41% of deaths in the 35 to 64 year age group (*The Diabetes Declaration and strategy for Africa,* 2006).

A study done by Erasmus et al. (2001) amongst a group of black factory workers from Umtata, South African found that the prevalence of diabetes mellitus was similar in males and females, and that the highest incidence of the disease was found in the age group 40 to 59 years. According to Norman et al. (2007) DM in South Africa has a higher prevalence in individuals older than 40 years of age. This confirms that diabetes mellitus is most prevalent in individuals older than 40 years of age. According to the Department of Health (2003), the prevalence of DM in South Africa varies from province to province and the prevalence is higher in females than in males. In 2003 in the Western Cape of South Africa, 3,2% of men were affected by diabetes mellitus against 4.9% of females, which suggest a higher prevalence of the disease among females.

2.3   Type 2 Diabetes mellitus

This research specifically focused on Type 2 diabetes mellitus which is the most common form of diabetes. Since there is no cure for Type 2 diabetes mellitus,

lifelong management is presently seen as the only option. Type 2 diabetes mellitus (T2DM) is a disease of mainly the overweight individual, where the hormone insulin is usually present in the plasma (Vander et al., 1990). It is a risk factor of coronary artery disease which is the leading cause of mortality (Tsujimoto et al., 2011). Excessive food intake leads to obesity, which in turn leads to an increased amount of plasma glucose that will increase the secretion of insulin by the Islet B cells, and ultimately cause an increase in plasma insulin (Vander et al., 1990). It is therefore important that a healthy diet and exercise are used as part of the management plan to reduce complications due to diabetes mellitus. According to the Juvenile Diabetic Research Foundation (2012), a person with diabetes mellitus requires treatment to lower cholesterol as well as their blood pressure. Watkins (2003) stated that individuals over 40 years of age, who are obese, have a family history of diabetes and a birth weight that exceeds 4kg, may have an increased risk of developing Type 2 diabetes mellitus later in life. Table 2.1 summarizes the World Health Organization's diagnostic criteria for the diagnosis of diabetes and intermediate hyperglycaemia (WHO, 2006).

Table 2.1: The World Health Organization's diagnostic criteria for the diagnosis of diabetes mellitus and intermediate hyperglycaemia

	Normal individuals	Diabetes mellitus	Impaired glucose tolerance	Impaired fasting glucose
Fasting glucose	< 6.1mmol/l	≥ 7.0mmol/l	< 7.0mmol/l	≥6.1mmol/l and < 7.0mmol/l
2h glucose	< 7.8mmol/l	≥11.1mmol/l	≥7.8mmol/l and <11.1mmol/l	< 7.8mmol/l

[Figure 2.1 presented values are a representation of venous plasma glucose]

2.4   Oral glucose tolerance test

The oral glucose tolerance test which occurs over a period of 2 hours was one of the tests performed on participants to determine how quickly glucose was removed from the blood. Subjects were asked to refrain from drinking any fluid or eating food for 10-14 hours, after which they received 75 grams of glucose orally. In the WHO report of 1999 this was indicated as the test of choice for determining the source of diabetes. A statement was made in the 2006 report of the WHO where it was recommended that the oral glucose tolerance test should be retained as a diagnostic test for diabetes, for the following reasons;

- ➢ fasting plasma glucose alone fails to diagnose approximately 30% of cases of previously undiagnosed diabetes.
- ➢ oral glucose tolerance test is the only means of identifying people with IGT.
- ➢ oral glucose tolerance testing is needed to confirm or exclude an abnormality of glucose tolerance in asymptomatic people.

The WHO (2006) suggested that the amount of glucose in the blood is still the main test for the glucose tolerance status. The glucose should be measured immediately after collection, or if a blood sample is collected, the plasma should be separated immediately, or it should be collected into a container with glycolytic inhibitor and placed on ice until separated prior to the analysis (WHO, 2006). According to Hajat and co-workers (2011) one third of all patients with diabetes remain undiagnosed, which results in major complications because of late diagnosis.

2.5   Echocardiography

In this research study echocardiography was performed using a light weight portable ultrasound machine GE Logiq e, equipped with cardiovascular software and a 2.0 – 3.5 MHz linear transducer. Two dimensional (2D) echocardiography studies were performed with the participant lying in the partial left lateral decubitis position. The data that was collected and used in this study includes M-mode measurements of the left ventricle; left ventricle end diastole dimensions, left ventricle end systole dimensions, inter-ventricular septum thickness, posterior wall thickness, aorta size

and left atrium size. The term echocardiography covers a few techniques namely: Two-dimensional (B-Mode) echocardiography, Motion mode (M-Mode) echocardiography, and Doppler analysis. Two-dimensional (2D) echocardiography is an excellent imaging modality and a useful tool to assess the heart. According to Poulsen et al., (2010) the systolic function is a major concern in Type 2 diabetic patients. Echocardiography according to Schmailzl & Ormerod (1994) also plays an important role in the diagnosis of CVD and is a powerful and safe technique to assess the diabetic heart. It is therefore important that the appropriate diagnostic procedure is used to correctly identify and diagnose the effect of diabetes on the heart. According to Salamon (2011) ultrasound of the heart can assist doctors to better predict a patient at risk of suffering a heart attack or other cardiac event. Trans-thoracic echocardiography allows for a complete assessment of the LV function, since it makes visualisation of the septum, lateral wall, anterior and inferior wall possible (Smock, Larson, Brown, Conti, 2001). According to ACC/AHA (2003), when the clinical findings of a patient with possible cardiac disease are ambiguous, echocardiography is the test of choice since it can provide definitive diagnostic information.

All measurements were done according to recommendations of the American Society of Echocardiography (2011), who suggested that measurements should be made from the leading edge of one wall to the leading edge of another wall. The wall motion was assessed in para-sternal long axis, para-sternal short axis, apical 4 chambers and apical 2 chamber viewing. The base, mid – left ventricle and apex were assessed. The left ventricle wall motion was scored based on visual assessment of left ventricle motion in 3 or more views to establish each segments contribution to the systolic reduction of the left ventricle volume. The ejection fraction was determined by direct visual estimation of the left ventricle in multiple views. The ejection fraction may be reported quantitatively or qualitatively as increased; normal; mildly, moderately, or severely reduced. The LV was assessed qualitatively, using different views to assess myocardial kinesis (motion). The following wall motion actions were used to describe the heart; a decreased systolic inward motion of the wall in the left ventricle were defined as hypokinesis, a complete absence of systolic wall motion and ventricular wall thickening were defined as akinesis and systolic

outward motion, with systolic ventricular wall thinning was defined as dyskinesis. Parasternal long-axis M-mode dimensions were done to measure the left atrium at end ventricular systole.

2.5.1 The usefulness of echocardiography in diabetes-related cardiovascular disease

It is a well established fact that CAD is a major complication of diabetes mellitus and the cause of death in more than half of all diabetic patients according to Chiariello and Indolfi (1996). Tsujimoto et al. (2011) revealed that many patients with Type 2 DM with vascular complications have asymptomatic coronary artery disease, with severe multi-vessel stenosis as well as myocardial ischemia on stress single-photon emission computed tomography. Their study found that asymptomatic coronary artery disease was more common among men, than in women. In Australia, cardiovascular disease is the primary cause of death in diabetic patients with 65% of all CVD deaths occurring in people with diabetes and pre-diabetes (JDRF, 2012). People with diabetes have a fivefold higher risk for a first MI and a two-fold greater risk for a recurrent infarction than those who had a MI, but do not suffer from DM (Stratmann & Tschoepe, 2011). Coronary artery disease (CAD) is caused by an obstruction of the coronary arteries by arteriosclerotic plaque and diabetic patients have a two-to-four times greater risk for developing CAD (Morrow & Gersh, 2008). Their study also revealed that patients with DM may have asymptomatic CAD. CAD usually occurs earlier in life in patients with diabetes compared to patients without diabetes and is most often the main cause of death in patients with DM (Voors & Van der Horst, 2011). This information correlates well with research that was done in Australia which suggested that the risk of DM has a big impact on the management of patients who suffer from CAD (JDRF, 2012). According to Watkins (2003) diabetic patients who are hypertensive, smoke, are obese, are of Asian origin and have micro-albuminuria, suffer from nephropathy, have poor glycaemic control and have hyperlipidemia, and a high risk of developing CAD. Diabetic cardiomyopathy due to CAD is known to be associated with left ventricular dysfunction due to vascular dysfunction of the coronary arteries (Stratmann & Tschoepe, 2011). According to Ornato & Hand (2001) 1.1 million Americans experience a MI every year, of which

460 000 die and 230 000 have a sudden MI. Diabetic patients are prone to silent heart attacks. Boras, Brkljačić, Ljubičić, Ljubić (2010) define a silent myocardial infarction as the presence of objective evidence of myocardial ischeamia in the absence of chest discomfort. According to Kral et al. (2011), a silent myocardial infarction may occur very early, with mild stenosis. Chiariello and Indolfi (1996) confirm this fact by stating that asymptomatic myocardial infarctions occur more frequently in diabetic individual and the incidence of painless myocardial infarctions are higher in diabetics than in non-diabtetics. The atherosclerotic plaque within this stenosis may be vulnerable to rupture. The American Society of Nuclear Cardiology (2009) indicates that stress myocardial perfusion imaging detects silent myocardial ischemia in high risk primary prevention populations, which includes persons with a family history of premature CVD. According to Palmieri et al. (2003), segmental wall motion abnormality on echocardiography is an indication of CVD. In a study they conducted, the prevalence of clinical CVD was almost twice as high among patients with segmental wall motion compare to those with a normal systolic function. Echocardiography has a 95% accuracy rate in confirming an event of myocardial infarction. In the case of an acute myocardial infarction echocardiography can successfully make a diagnosis of the patient's condition (ACC/AHA, 2003). Individuals with diabetes have a poor long term prognosis after having a MI, because it increases their risk for congestive heart failure which can lead to death (Stratmann & Tschoepe, 2011).

2.5.2 The usefulness of echocardiography hypertensive heart disease

Hypertension is estimated to cause 7.5 million deaths, about 12.8% of all deaths. It is a major risk factor for cardiovascular disease and contributes to diabetic nephropathy (Grundy et al., 1999). A raise in blood pressure (BP) is defined as a BP of 140/90 mmHg or higher and it affects approximately 1 billion people worldwide. The incident is rising and is projected to affect 1.5 billion people by the year 2025. To date hypertension remains one of the leading causes of death and a major health problem worldwide (Victor & Kaplan, 2008). Individuals diagnosed with diabetes and concurrent hypertension have a higher risk of developing CVD compared to those with diabetes only (Watkins, 2003). According to Gerdts, Oikarinen, Palmieri, Okkerstad, Wachtell, Boman, Dahlöf and Devereux (2002) the LA enlargement

diagnosed with ECG or echocardiography is a common finding in hypertensive patients. According to their study from a total of 963 hypertensive patients, 512 (54%) had normal LA size and 429 (46%) had enlargement of the LA. The patients with LA enlargement were older, obese, women, and patients with DM. Stratmann & Tschoepe (2011) emphasised the idea for BP control in diabetic patients and continue by saying that 70% of all patients with DM have been treated or are on medication for hypertension. A BP of 160/100 mmHg and more, should be treated in any individual whether diabetic or not, and if there is a risk factor for CVD, the treatment to control the blood pressure should be more aggressive (Watkins, 2003). According to Palmieri et al. (2003), eccentric LV hypertrophy is often present in hypertensive individuals. Their study also revealed that the prevalence of eccentric LV hypertrophy on echocardiography was higher in the groups with wall motion abnormalities. The above statements stress the importance that all diabetic individuals should have their blood pressure checked frequently. A study done by Poulsen et al. (2010) confirmed the association of Type 2 DM, diastolic dysfunction and LV dysfunction. According to their study moderate or severe LV diastolic dysfunction and a dilated LA in the early phase of Type 2 DM is closely associated with intrinsic LV dysfunction. Left ventricular hypertrophy (LVH) with a dilated left atrium (LA) can be responsible for MI's and sudden death (Pearson et al., 1991). The above information are confirmed by Palmieri et al. (2003), who found that the left atrial diameter was greater in the group with global LV dysfunction and hypertension, than in the group with normal wall motion activities. Echocardiography makes it possible to assess the heart of the hypertensive individual to determine whether left ventricular hypertrophy and / or a dilated left atrium are present which most often lead to CHF (ACC/AHA, 2003). A study done by Zapolski and Wysokiński (2013) assessed LA volume index in T2DM found a strong correlation between HbA1C and LA volume index. Their study involved two-dimensional guided M-mode echocardiographic recordings of the heart, measuring the IVS in diastole and systole, as well as the PW, LA and Aorta diameter. According to their study most of the two-dimensional guided M-mode echocardiography parameters were significantly greater in T2DM patients compare to the control normoglycaemic group. The LA parameters were in particular greater in the T2DM group, than in the control group. In this specific study patients with T2DM exhibited greater aortic stiffness.

2.6.   Biochemical markers

Glycated haemoglobin (HbA1c) is a non fasting blood test, which can predict CVD. In a Middle-Eastern population, HbA1c has been the most suitable test for the diagnoses of diabetes (Hajat et al., 2011). HbA1c reflects in a single measurement, the average plasma glucose over the previous 2-3 months. It can be performed any time of the day and does not require any fasting (WHO, 2006). Because of the above qualities of HbA1c, it is said to be the gold standard for testing the glycaemic control in people with diabetes (WHO, 2006). Diabetic patients with elevated body mass index (BMI) or visceral fat and renal dysfunction, have a higher risk of developing CVD and have high HbA1c levels (Stratmann & Tschoepe, 2011). According to Hajat et al. (2011), the monitoring of the glycaemic status is considered to be a cornerstone of diabetic care and the results of such monitoring are used to evaluate the efficacy of the treatment. Blood and urine glucose testing as well as urine ketone testing provide useful information for the day to day management of diabetes mellitus. A single test can quantify the average glycaemia over weeks and months, which can compliment day to day testing for diabetes mellitus (Hajat et al., 2011). Another biochemical marker that played a role in this study was triglycerides. According to Miller et al. (2011) elevated triglyceride levels is a strong indicator of cardiovascular disease. According to Parmar, Sakariya, Vidja, Mehta, Kakaiya (2012), dyslipidemia an important cardiovascular risk factor in type 2 DM is characterise by low HDL, high triglycerides and elevation in LDL-cholesterol.

2.6.1   Normal biochemical marker levels

Table 2.2 shows the normal biochemical marker levels as indicators for cardiovascular disease (WHO, 2013).

Table 2.2: Normal biochemical marker levels according to the WHO (2013)

	Triglycerides	High density Lipoprotein	Low density Lipoprotein	Glycated haemoglobin
Men	40 – 160 mg/dl	30 – 70 mg/dl	80 – 140 mg/dl	200mg/dl
Women	30 – 85 mg/dl	30 – 85 mg/dl	80 – 140 mg/dl	200mg/dl

[mg= milligrams; dl= decilitre]

2.7 Conclusion

In this chapter echocardiography as an assessment tool for CVD was discussed, with the main focus being the role of echocardiography in making a diagnosis of myocardial dysfunction in individuals with type 2 DM. A delayed recognition of CVD worsens the prognosis for survival for many diabetic patients (Grundy et al., 1999). According to The Diabetic Declaration and Strategy for Africa Report (2006), the number of people with diabetes in the African region is expected to reach 15 million by the year 2025. There is therefore a need to not only prevent diabetes, but to make a diagnosis as early as possible and to start treatment as soon as possible.

CHAPTER THREE: METHODOLOGY

This chapter describes the research process and presents the strategy of the design and implementation of the research project.

3.1   Ethical consideration

This research study was approved by the Research Ethics Committee of the Faculty of Health and Wellness Sciences at the Cape Peninsula University of Technology in September 2009 **(Appendix A)**. Permission was granted from the already existing diabetic study (Study A), from where patients for this study were drawn**.** All participants in this study did so voluntarily and each participant was informed that they can withdraw at any given time without prejudice or negative impact on their management. Prior to the collection of the data all procedures were explained to the participants by the researcher and only those who signed the informed consent were included in the study.

The echocardiograph was done in a secure and private area, and except for the researcher and the participant the only other persons that were allowed to be present while the echocardiography examination was conducted were the qualified nurse and the medical doctor. They were called to assist in cases such as a disabled participant or to offer medical support as necessary. At the end of each day the echocardiography records were taken to a secure place, where they were stored in a locked and secured cabinet. The participants' identity was kept confidential and records were kept according to a unique reference number (e.g. P123). The names of the participants were available to the researcher for quality assurance purposes and to allow for referral for clinical management in cases where the echocardiography results were abnormal.

The data obtained from this research study will only be used for the purpose of this research and related publications. Permission was granted to the researcher to publish the participant's images in this document. Medical research is subjected to ethical standards that promote respect for all human beings and protect their health and rights. The World Medical Association has developed the declaration of Helsinki

as an ethical protocol to follow when medical research involves human subjects. According to the World Medical Association Declaration of Helsinki, (2001), the health of any patient must be the first consideration when research is done. Any physician or person involved shall act only in the patient's interest.

3.2   Purpose of the study

Diabetes mellitus being a metabolic disease can influence the myocardium at a very early stage, even before there is any clinical manifestation (Rajput, Siwach, Rattan, 2002). Echocardiography also makes it possible to assess the heart of the hypertensive individual to determine whether left ventricular hypertrophy and / or a dilated left atrium are present which most often lead to CHF (ACC/AHA, 2003). To contribute to the management of diabetes and CVD, the research study sought to evaluate the role of echocardiography in the early detection of diabetes-related myocardial disease in Type 2 diabetic participants

3.3   Overview of the study

This research study contributes to a larger research study (Study A) that was conducted amongst the Bellville South population and involved collaboration between the Pathology Department of Tygerberg Hospital, the University of Stellenbosch, the University of Western Cape and the Cape Peninsula University of Technology. Permission was granted from the project leaders of Study A to the researcher, to make use of the sample population **(Appendix B)**. The dependent data for each participant consists of personal demographic information that was obtained through a structured questionnaire. The modified Rose Angina questionnaire **(Appendix C)** was designed by the project leaders of Study A and was used to recruit individuals for Study A. The information applicable to Study B is highlighted in the questionnaire **(Appendix C)**. Ten millilitre of blood was taken from each participant, by a phlebotomist and sent to a registered pathology laboratory to determine the diabetic status according to their standard operational procedures. The echocardiograph was done by the researcher, who is a sonographer trained to do echocardiography. B-Mode, M-Mode, and Doppler real time ultrasound imaging was used to assess each participant's heart.

3.4   Study population

In 2009 a research study (Study A) was conducted in the Bellville South community focussing on the prevalence of diabetes mellitus and metabolic syndrome. Echocardiography was not a component of Study A, but after the potential benefit of echocardiography as a tool to detect diabetic-related myocardial disease in the same community of Bellville South were discussed, Study B was conceptualized. Four hundred and seven participants were randomly drawn from the population group of Study A to form part of Study B. The 407 subjects participated in a screening program for diabetes mellitus in the Bellville South area in the northern suburbs of Cape Town, South Africa. Before 1963, Bellville South was a mixed-race area, but after the Group Areas Act of 1963, the white population were removed from the area and a mixed-ancestry population were brought into the area (City of Cape Town, 2001). According to the City of Cape Town Census (2001), Bellville South has a population of approximately 24 000 people, of which 11 000 are males and 13 000 are females. According to the information obtained from the 2001 Municipality census, a high proportion of the residents are older than 60 years. The predominant language spoken in the Bellville South community is Afrikaans, with a small percentage speaking English and Xhosa (City of Cape Town, 2001).

3.5   Study design

This research study was a cross-sectional observational study. All the participants were randomly selected from the larger population of Study A, with the aim to obtain a sample that will be a representative of the larger population who lives in Bellville South. Trained research assistant, visited potential participants at home to inform them about the potential research study and also to inform them about instructions that they need to follow should they want to take part in the study.

The instructions were as follow: refrain from eating 10 – 14 hours prior to the taking of the blood samples, to refrain from smoking, and using any alcohol as these may interfere with the serological measurements (Blackhurst & Marais, 2005). For each participant to take part in this research study they had to complete a consent form **(Appendix D)**, which was explained in detail in the language of their choice, by a

qualified research assistant. The consent form contained detailed information regarding the research study, which was explained by the research assistant. Echocardiography procedures were explained in detail to each participant by the researcher and informed consent was obtained **(Appendix E)**. The echocardiography studies were done by the researcher who was blinded to the diabetic status of each participant at the time the echocardiogram was done.

3.6   Sampling

The sample size of 384 was calculated for Study B, using the following formula (n= [z²p (1- p) / e²]. The following criteria were used to include and exclude participants for this study. Both male and female participants between 40-80 years who has signed informed consent were included in this study. Participants with a history of atrial fibrillation and left bundle branch block were excluded from this study because these disorders can affect the echocardiographic measurements and the display of the true left ventricular function.

3.7   Laboratory Analysis and Echocardiography

After informed consent was obtained and the questionnaire was completed, fasting blood sample of each participant was obtained by a qualified, registered nursing sister. The blood tests included: high sensitivity C-reactive protein (Hs-CRP), Glycated haemoglobin (HbA1c), Triglycerines (TG), total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL) and serum cotinine.

All participants who were not diabetic had to undergo an oral glucose tolerance test (OGTT). This was done by a qualified research assistant.

After the OGTT was completed, the echocardiogram was done. The echocardiography procedure was explained in detail to each participant before it was performed. The ACC/AHA Guidelines for the Clinical Application of echocardiography were used to perform the echocardiogram (ACC/AHA, 2003). Echocardiography data was recorded on a data sheet, **(Appendix F)** and placed in the information file of each participant that was coded with a unique file number.

3.8   Ultrasound equipment

A GE Logic e digital ultrasound system was used that complies with the regulatory requirements of the following European Directive, 93/42/EEC concerning medical devices. The machine consists of the following features:

- 2D black and white imaging of the heart and surrounding tissue.
- M-Mode imaging of the heart demonstrating measurement of the heart chambers as well of the wall thickness.
- 2-3.5 Multi-frequency cardiac probe so that the operator can select the best probe depending on the size of the participant.
- Cardiac software that enables optimum imaging and measurements of the heart.
- Dynamic range (DR) that controls how echocardiography intensities are converted to shades of gray, thereby increasing the adjustable range of contrast.
- Power output that optimizes image quality and allow reducing the beam intensity, to prevent bio-effects.
- Edge enhancement to bring out subtle tissue differences and boundaries by enhancing the grey scale differences corresponding to the edges of the heart.
- Line density allows for optimizing B-mode frame rate or spatial resolution for the best possible image.
- Zoom that can magnify the region of interest approximately the size of a full-sized image.
- Gray map determines how the echocardiography intensity levels received are presented as shades of grey.
- Color flow / Doppler imaging to obtain blood flow patterns and velocities to do spectral analysis.

3.9   Scanning Protocol

According to the American Heart Association two-dimensional echocardiography is the method of choice to assess the systolic function of the heart since it is non-invasive and cost-effective (ACC/AHA, 2003).

In this research study the echocardiography studies were performed using a light weight portable ultrasound machine GE Logiq e, equipped with cardiovascular

software and a 2.0 – 3.5 MHz linear transducer. Two-dimensional echocardiography studies were performed, using a 2-3.5 MHz transducer with the participant lying in the partial left lateral decubitis position.

The data collected and analysed in this study includes M-mode measurements of the left ventricle (LV), which include left ventricle end diastole diameter (LVEDD), left ventricle end systole diameter (LVESD), inter ventricular septum (IVS) thickness, posterior wall (PW) thickness, aorta (AO) size and left atrium (LA) size. All measurements were done according to recommendations of the American Society of Echocardiography, who suggested that measurements should be made from leading edge of one wall to the leading edge of another wall (American Society of Echocardiology, 2011).

3.9.1 Two-dimensional Echocardiography

In a private environment, each participant was asked to undress and put on a hospital gown for the duration of the examination.

Ultrasound gel was placed on the transducer to remove air between the transducer and the skin. Two dimensional imaging was used to obtain the desirable image of the heart structures. The transducer was placed between the left third and fourth intercostal space to obtain a longitudinal image of the LV, right ventricle (RV), AO and the LA), as well as the mitral valve (MV) and aortic valve (AV).
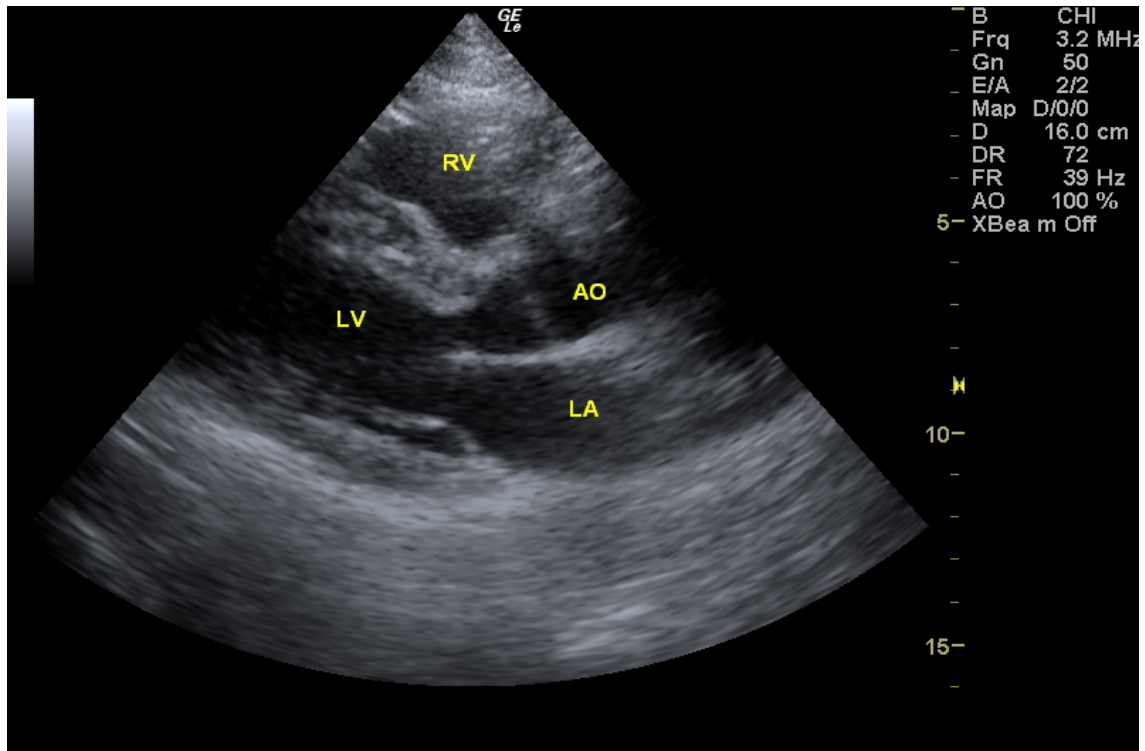
Figure 3.1: Two-Dimensional parasternal long axis image of a normal heart (permission obtained from research participant).
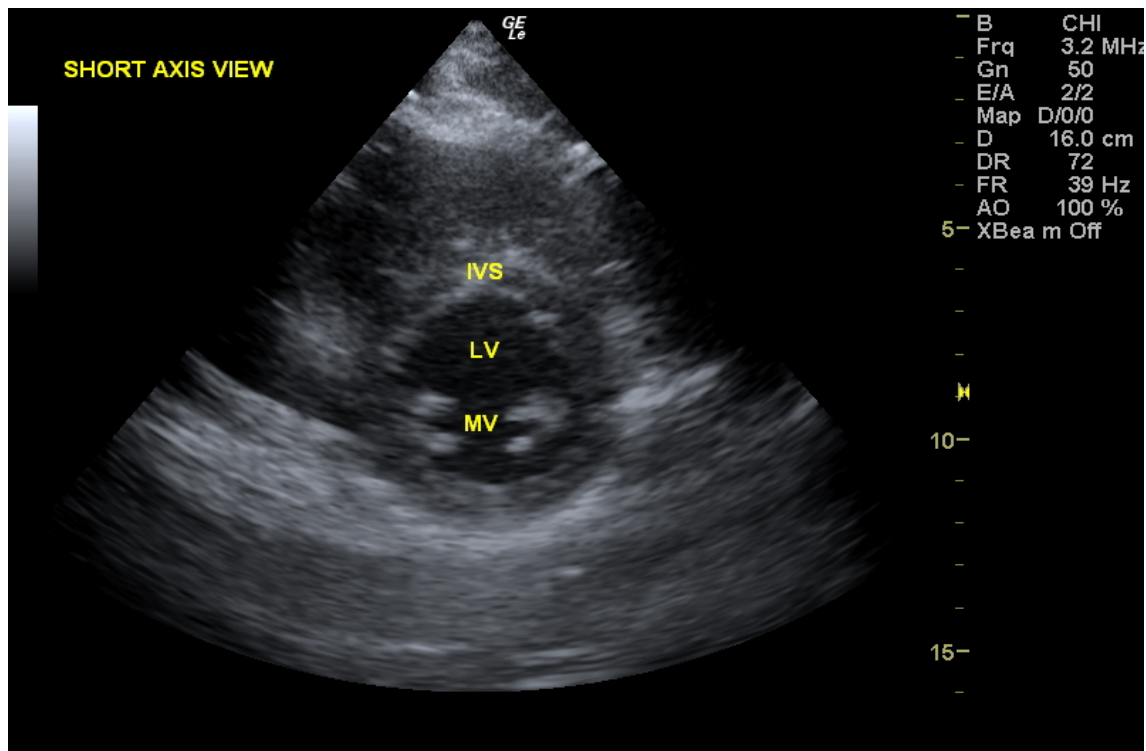
Figure 3.2: Two Dimensional Para-sternal short axis view of the LV (permission obtained from research participant).

The above view demonstrates a two-dimensional short axis view (Figure 3.2) that enables evaluation of the left ventricular walls, as well as the mitral valves in this view. The transducer is turned 90 degrees clock wise to obtain an image of the IVS, LV and MV.

3.9.2 M-Mode echocardiography

Recordings were made of M-mode echocardiogram measurements of the left ventricle. Two-dimensional M-mode echocardiography is important for measuring the size of the left ventricle. The curser must be placed in the middle of the left ventricle, to include the anterior septum, posterior septum as well as the left ventricle. By doing that it provides the most appropriate beam to accurately measure the inter-ventricular septum to exclude left ventricular hypertrophy as well as the left ventricle diameter in both systole and diastole, to exclude dilatation of the left ventricle. The assessment of the right ventricle, aorta root, left atrium as well as the mitral and aorta valve is made possible with M-mode echocardiography. The following

measurements were done; (LVEDD), (LVESD), (PW) thickness, (IVS) thickness, (RV), (AO) roots size and (LA) size.
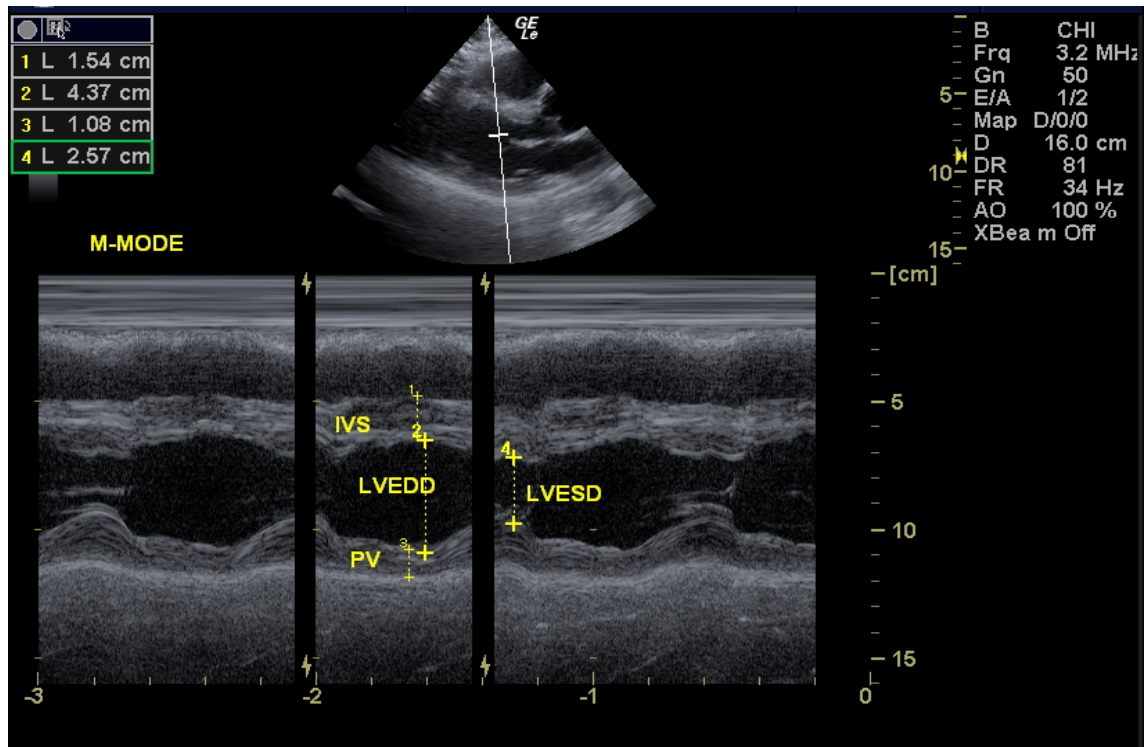
Figure 3.3: M-Mode recordings of the left ventricle to demonstrate the thickness of the IVS and PW as well as the LVEDD and the LVESD (Permission obtained from research participant).

3.9.3 Doppler echocardiography

The Doppler examinations were performed with the transducers held at the cardiac apex, so that an apical four chamber view could be obtained, as can be seen in figure 3.4. The Doppler beam was placed in the LV at the tip of the mitral valve to assess the mitral inflow pattern for diastolic function (figure 3.5). Measurement of the diastolic function is an important factor for individuals suffering from hypertensive heart disease.

From the mitral valve, the Doppler beam is shifted to the aortic valve (AV) to assess the outflow velocities of the heart. A complete evaluation of the mitral valve (MV), tricuspid valve (TV), and the pulmonary valve (PV) were done to exclude any significant valvular disease.
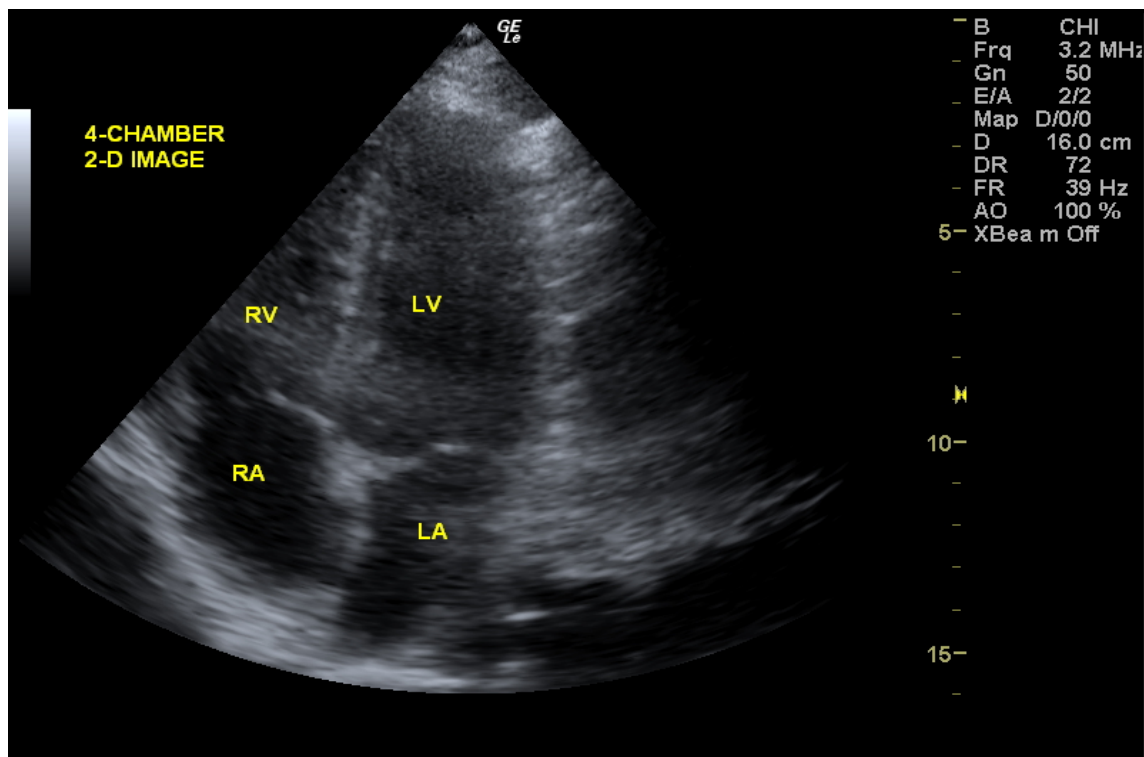
Figure 3.4: Two-dimensional four chamber view of the heart to demonstrate the RV, LV, RA and LA. (Permission obtained from research participant).
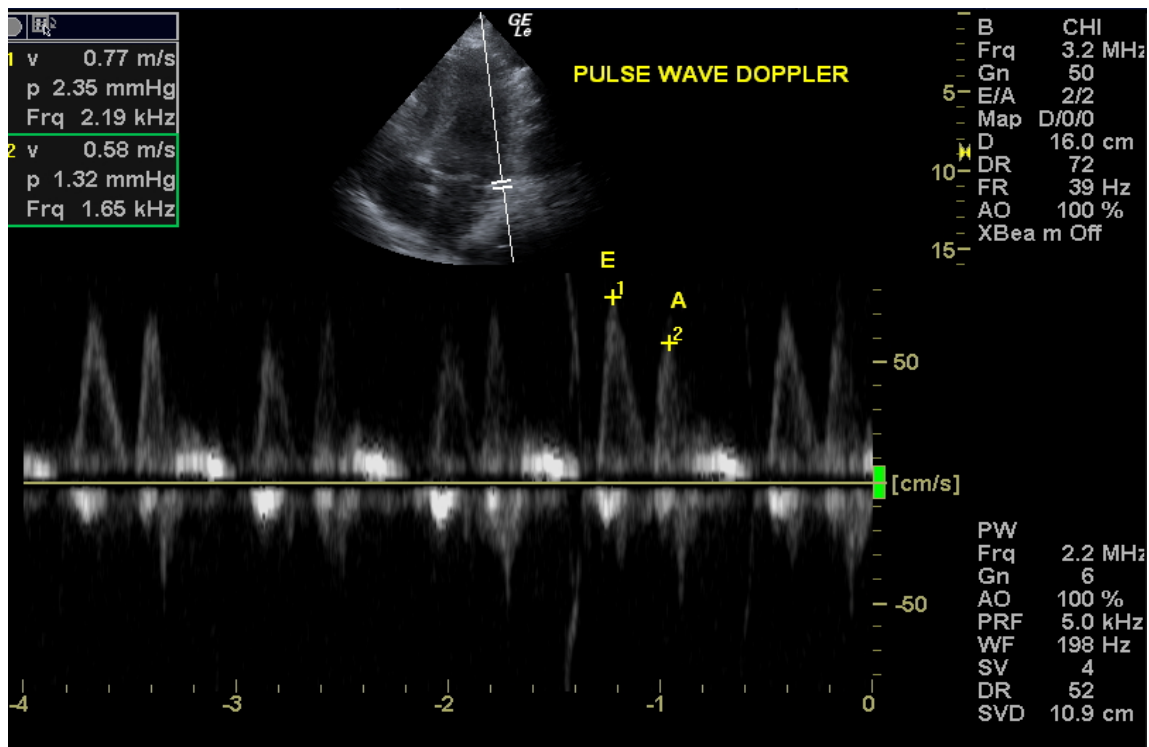
Figure 3.5: Pulse Doppler recordings of the mitral valve inflow (Permission obtained from research participant).

From the above Doppler recordings three to five consecutive cardiac cycles were chosen to analyse the Doppler results. From the mitral valve recordings the following variables were analysed: Peak early velocity (E) and the peak atrial velocity (A) (Figure 3.5). In cases where the echocardiograph results were abnormal the participants were referred to the on-site medical doctor.

3.10   Statistical analysis

The data was captured in a data spread sheet that was designed by the researcher. The data was quality controlled assured and analysed by a statistician using Microsoft excel statistical package for social science (SPSS) version 15. Each participant had a reference number, for example P123 and was sorted statistically into a hyperglycaemic group and normoglycaemic group. This was done after all the echocardiography test results were obtained.

The Pearson Chi Square and Mann-Whitney U test was used to compare the ultrasound findings of each participant with that of their laboratory results and to

determine the statistical significance. All tests were performed at a 5% level of significance, and the association was significant if the p-value was less than 0.05.

3.11   Conclusion

According to literature echocardiography plays a big role in diagnosing CVD and the effect the disease may have on the heart, because of the ability of echocardiography to provide a two-dimensional image of the heart. It is important to know that no single test is ideal in screening patients for CVD. According to Boras, Brkljačić, Ljubičić, Ljubić (2010), the predictive accuracy of any screening test is low and generally requires confirmation by further testing. They continue to recommend that baseline determination of cardiovascular function be performed upon diagnosis, followed by a yearly repeated test.

CHAPTER FOUR: RESULTS

4.1.   Introduction

A total of 407 patients were recruited for this research study. For statistical analysis the participants were categorized into two groups, 218 were normoglycaemic and 189 were hyperglycaemic. The latter group included 3 categories; impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and known diabetes mellitus (DM). This study focussed on the role of echocardiography in the detection of diabetes-related myocardial disease.

4.2. Echocardiography results and biochemical marker results according to the glycaemic status

The results are presented as median ± 95% confidence interval. The Mann-Whitney U test was used to determine the statistical significant differences between groups. IVS measurement was shown to be significantly larger in the hyperglycaemic group (1.33 ± 0.38) than the normal group (1.23 ± 0.24) p = **< 0.0001.** Left atrium measurement was shown to be significantly larger in the hyperglycaemic group (3.86 ± 0.62) than the normal group (3.66 ± 0.62) p = **0.0014.** Aorta measurement is significantly larger in hyperglycaemic group (3.28 ± 0.42) than the normal group (3.17 ± 0.40) p = **0.0067.** Hs-CRP was shown to be significantly higher in the hyperglycaemic group (8.63 ± 10.85) than the normal: 6.61 ± 8.09; p = **0.0323.** HbA1c was shown to be significantly higher in the hyperglycaemic group (7.62 ± 2.15) than the normal group (6.09 ± 3.75) p = **< 0.0001.** TG was significantly higher in the hyperglycaemic group (1.71 ± 0.94) than the normal group (1.35 ± 0.85) p = **< 0.0001.** HDL was significantly higher in the normal group (1.41 ± 0.42) than the hyperglycaemic group (1.29 ± 0.40) p = **0.0030.** TC/HDL is significantly higher in hyperglycaemic group (4.61 ± 1.61) than the normal group (4.12 ± 1.38) p = **0.0010.** Serum cotinine was significantly higher in the normal group (139.7 ± 180.8) than the hyperglycaemic group (86.7 ± 148.3) p = **0.0015.**

Table 4.1: Echocardiography results and biochemical marker results according to the glycaemic status

	Normal, n=218	Hyperglycaemia, n=189	p-value
IVS (cm)	1.23 ± 0.24	1.33 ± 0.38	**< 0.0001**
Left atrium (cm)	3.66 ± 0.62	3.86 ± 0.62	**0.0014**
Aorta (cm)	3.17 ± 0.40	3.28 ± 0.42	**0.0067**
LVEDD (cm)	4.82 ± 0.57	4.93 ± 0.60	0.0557
LVESD (cm)	2.90 ± 0.56	3.01 ± 0.65	0.0655
PW (cm)	0.97 ± 0.21	1.01 ± 0.25	0.0769
HsCRP (mg/L)	6.61 ± 8.09	8.63 ± 10.85	**0.0323**
HbA1c (%)	6.09 ± 3.75	7.62 ± 2.15	**< 0.0001**
TG (mmol/L)	1.35 ± 0.85	1.71 ± 0.94	**< 0.0001**
HDL (mmol/L)	1.41 ± 0.42	1.29 ± 0.40	**0.0030**
LDL (mmol/L)	3.38 ± 0.95	3.40 ± 1.01	0.8108
TC/HDL	4.12 ± 1.38	4.61 ± 1.61	**0.0010**
Serum cotinine (ng/mL)	139.7 ± 180.8	86.7 ± 148.3	**0.0015**

Key:
IVS: Inter ventricular septum, LVEDD: left ventricle end diastolic diameter, LVESD: left ventricle end systolic diameter, PW: Posterior wall, Hs-CRP: High sensitive C-reactive protein, HbA1c: Glycated hemoglobin, TG: Triglycerides, TC: Total cholesterol, HDL: High density lipoprotein, LDL: Low density lipoprotein

4.3   Echocardiography results, according to the glycaemic status
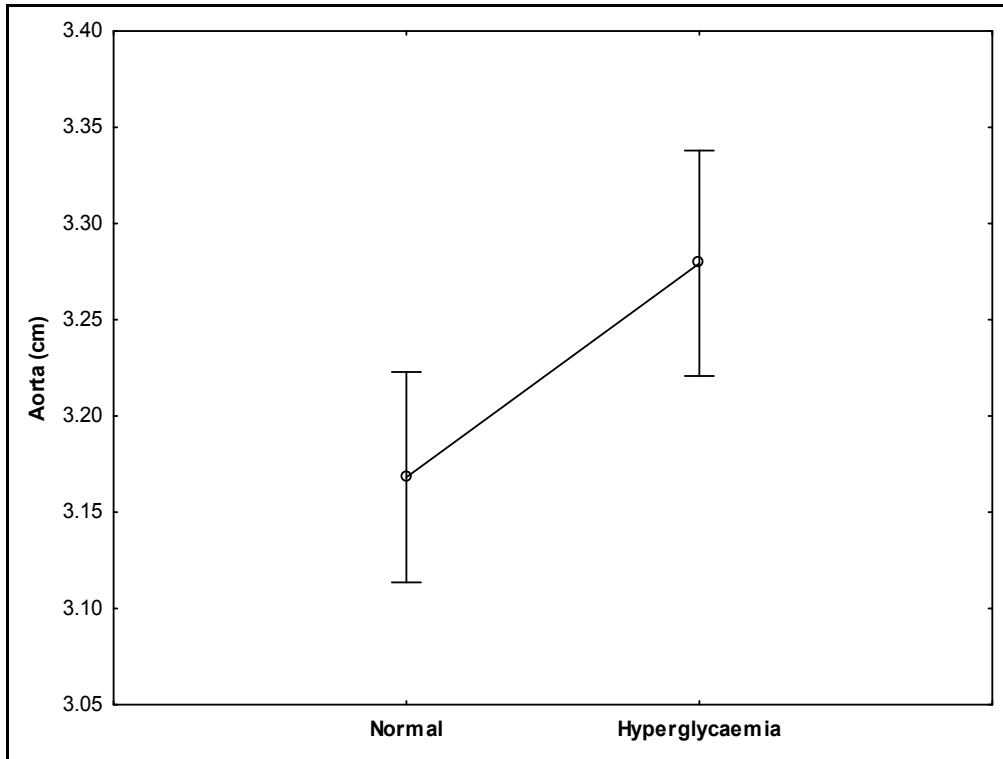
Figure 4.1: Aorta size according to glycaemic status

The size of the aorta was significantly increased in subjects with hyperglycaemia compared to those with normoglycaemia **(p = 0.0067).**
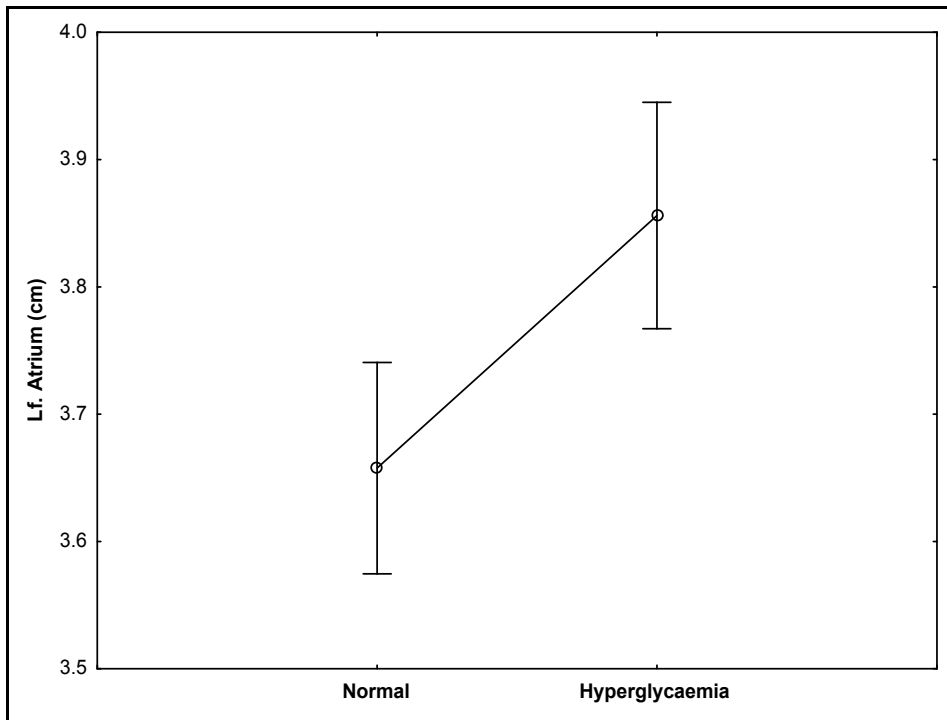
Figure 4.2: Left atrium size according to the glycaemic status

Left atrium was significantly increased in size in the subjects with hyperglycaemia, **(p = 0.00145)**
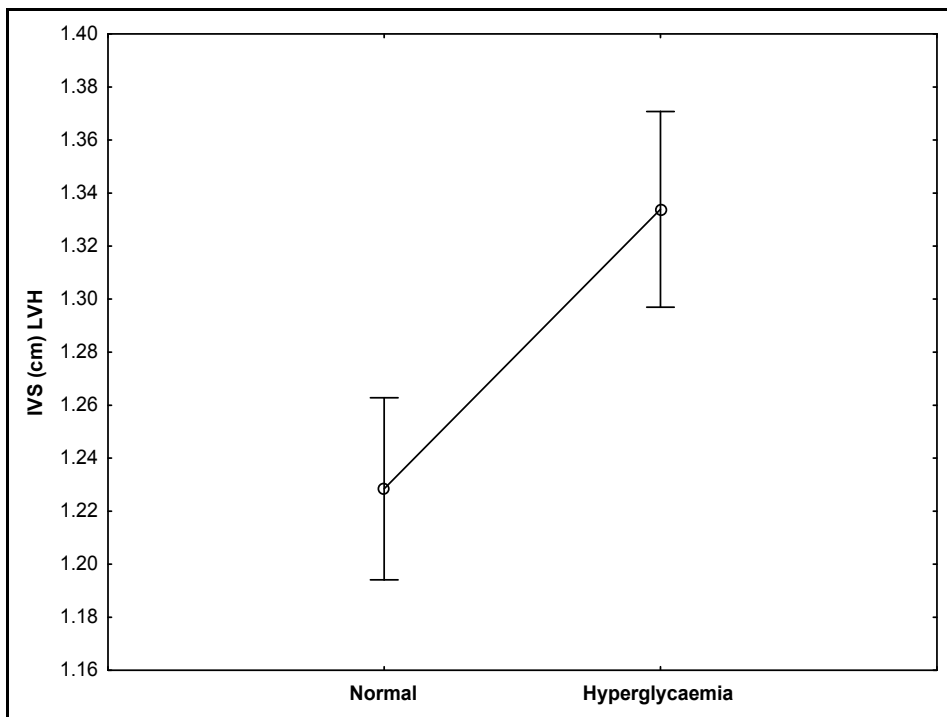
Figure 4.3: Inter-ventricular septum (IVS) dimension according to the glycaemic status

In individuals with hyperglycaemia the IVS was significantly thicker, which is an indication of hypertrophy **(p < 0.0001)**.

4.4   Conclusion

The analysis and the presentation of the results in this chapter can be used to answer the research question in this document. It is a well established fact that individuals diagnosed with T2DM, have a greater morbidity and mortality from CVD compare to non-diabetic individuals.   The main theme in this chapter was to determine whether echocardiography can be used to identify diabetic-related cardiac disease. In chapter 5 the results of this chapter will be discussed within the study context and the appropriate reviewed literature. The conclusions that were drawn from the findings will be discussed and the limitations and recommendations for further studies will be presented.

CHAPTER FIVE: DISCUSSION AND CONCLUSION

5.1   Introduction

Most studies on diabetes mellitus in South Africa was done in selected urban communities, and these studies indicate a higher prevalence of DM. The highest prevalence of diabetes mellitus was among the Indian population, followed by the coloured population and lastly the black population (Norman et al., 2007). According to the WHO (2006), it is estimated that diabetes mellitus will affect 366 million individuals worldwide by 2030, therefore becoming a major health epidemic. Considering all the complications to the human body due to the disease, diabetes mellitus is a disease of great concern world-wide. Drawing on the findings of this research study, this chapter presents a discussion on the role of echocardiography in Type 2 diabetes mellitus. This research study provides evidence that diabetes mellitus has adverse effects on the heart of individuals suffering from the disease. Following is a discussion of the echocardiography findings as well as the biochemical marker findings in normal as well as hyperglycaemic individuals.

5.2.   Echocardiography findings

The objective of this research study was to investigate early myocardial changes in individuals with diabetes, using echocardiography as well as to compare the echocardiographic findings with that of the biochemical markers. The key echocardiographic findings to be discussed are the left ventricular function, the left atrial size, the inter-ventricular septum size and the aorta. Despite there being a potential for error using echocardiography, the visual interpretation of echocardiography remains the clinical method of choice to assess the LV function (Smock et al. 2001). Echocardiography is an established tool for diagnosing CVD and the severity thereof and has a 95% accuracy rate in confirming an event of myocardial infarction (ACC/AHA, 2003). In this study, evidence is provided that CVD was indeed more prevalent in subjects with hyperglycaemia, than those in the normoglycaemic group. A study that was done by Tsujimoto et al. (2011) revealed that CVD with myocardial perfusion abnormalities were detected in more than 50% of patients with type 2 DM. They are confident that their study has revealed a

relationship between CVD and sudden death. A study done by Smock et al. (2001) noted that deaths occurred in 15.2% of individuals with an anterior MI, 7.3% of individuals with an inferior MI and in 23% with a MI in other locations. Their study suggests that echocardiography was also able to identify high risk patients within the first 24 hours of hospitalisation. From the four hundred and seven (407) participants that took part in study B, sixty four (64) presented with a myocardial infarction, as was seen on Echocardiography. The following echocardiography parameters according to study B seemed to be the best markers of poor diabetic control.

5.2.1 Myocardial disease

From a total of one hundred and forty eight (148) hyperglycaemic individuals, forty one (41), presented with a myocardial infarction (table 4.3). This indicated that 21.7% of hyperglycaemic individuals had a myocardial infarction. This finding is different to the study of Tsujimoto et al. (2011), which revealed 50% myocardial perfusion abnormalities, but it supports the suggestion that CVD is more prevalent in diabetic participants (Matsha et al., 2012). From the one hundred ninety four (194) normoglycaemic participants, twenty four (24) presented with an infarct which is (11%).

5.2.2 Left atrial size

According to Abhayaratna et al., (2006) a dilated LA size can cause death in high risk cardiovascular patients this makes an enlarged left atrium (LA) another predictor of cardiovascular disease that carries important clinical and prognostic implications for diabetic individuals. In this study the LA size of participants with hyperglycaemia was significantly larger than those participants with normoglycaemia, **(p = 0.0014)** (figure 4.2).

5.2.3 Inter-ventricular septum thickness

Systolic hypertension is another well-known complication of diabetes mellitus and a predictor of risk for cardiovascular disease in individuals diagnosed with diabetes mellitus. Individuals diagnosed with systolic hypertension develop left ventricular

hypertrophy (LVH), which is thickening of the inter-ventricular septum (Pearson et al., 1991). Individuals diagnosed with diabetes and concurrent hypertension have a higher risk of developing cardiovascular disease compared to those with diabetes only (Watkins, 2003). This study observed that the left ventricle septum of participants with hyperglycaemia was significantly hypertrophied compare to those in the normal group, **(p = < 0.0001)** (figure 4.3).

5.2.4   Aortic root

In their study Zapolski and Wysokiński (2013) found a strong correlation between poor glycaemic control and enlarged LA and AO stiffness. In this study the size of the aorta was significantly increased in subjects with hyperglycaemia compared to those with normoglycaemic **(p = 0.0067)** (figure 4.1).

5.3   Biochemical marker findings

Several biochemical markers are used to identify patients at high risk for developing cardiovascular disease (Ridker et al., 2000). According to Miller et al. (2011) elevated triglycerides levels are indicators of cardiovascular disease. This was confirmed in study B where the TG levels were higher in the glycaemic group than in the normal group. The evidence of the above mentioned information can be seen as **APPENDIX G.** Higher TG and lower HDL levels are further confirmed by Hajat et al. (2011) who states that both HbA1c and TG, when increased are indicators for cardiovascular disease. In a Middle-Eastern population, glycated hemoglobin (HbA1c) has been found to be the most suitable test for the diagnosis of diabetes (Hajat et al., 2011). A study done by Parmar et al (2012) found that HbA1c is not only a useful biochemical marker for long term glycaemic control, but it is also a good predictor of the lipid profile. They suggest that HbA1c can be a useful tool to monitor the glycaemic control, with the benefit of identifying diabetic patients who are at a greater risk of cardiovascular complications. In this study the HbA1c ratios were higher in the hyperglycaemic group. The findings of this study correlate well with other studies that show that biochemical markers can be used to identify patients at high risk for developing cardiovascular disease (Hajat et al., 2011). This study found that all biochemical markers were significantly higher in the hyperglycaemic group

and the ratios analysed were lower or normal in those with normoglycaemic. HDL was significantly lower in male participants than in female participants, **Appendix H.** According to Palmer et al. (2010) low levels of HDL is an indicator of dyslipidemia which is an important cardiovascular risk factor in type 2 DM. The FBG /Insulin and total cholesterol were significantly higher in the male participants.

5.4   Negative findings

The initial analysis found that there was no association between LVEDD, LVESD, PW and the glycaemic status, which suggests that the end diastolic and end systolic diameter of the left ventricle cannot be associated with the glycaemic status. The LVEDD, LVESD as well as PW however do have an association with the gender (Table 4.1). From the table it is noted that the LVEDD appears significantly larger in male individuals than in female individuals.

5.5   Limitation of the study

In most clinical practices an echocardiograph is done with the patient connected to an electrocardiogram machine. The echocardiograms for this study were performed without the electrocardiogram (ECG) connected to the chest, due to infrastructural financial constraints. According to ACC/AHA, (2003) scanning without electrodes has not been seen as a great limitation and these authors suggest that when an ECG is unavailable or unreliable, the echocardiography study without ECG can confirm or make a diagnosis of unstable angina. The ACC/AHA further suggests that even if the ECG is negative the echocardiograph is more helpful in making a diagnosis of myocardial infarction.

Another limitation was the fact that no information was available on the duration of one condition before another, for example whether a participant had long-standing hypertension or diabetes.

5.6   Conclusion

The researcher is aware of the fact that even though echocardiography is seen as the test of choice to assess the heart because of its non-invasive properties, no single diagnostic test is ideal for screening for CHD. The risk of CVD in people with Type 2 DM has increased significantly over the years (Parmar et al. 2012). Early detection and optimal quality care of diabetes individuals is very important. This is in line with the aim of this research study that focuses on early detection of diabetes-related myocardial disease amongst high-risk Type 2 DM individuals.

In conclusion, echocardiography demonstrated an important role in assessing the LV function of both Type 2 DM and normal individuals.

5.7   Recommendations

The researcher would like to recommend that more work should be done in the same community with a special focus on the time of diagnosis of hypertension. Another recommendation is that a follow-up study should be done; ECG leads should be made available. ECG leads can assist in making a diagnosis for myocardial infarction and it is a common procedure in cardiology practice. Left ventricular hypertrophy and coronary artery disease are much more common in diabetic hypertensive patients than in patients suffering from hypertension or diabetes alone (Grossman & Messeri, 2008). It was suggested by Boras, Brkljačić, Ljubičić, Ljubić (2010) that individuals diagnosed with DM should be sent for yearly assessment of the heart function and blood pressure to prevent silent myocardial infarctions which could cause death in diabetic individuals, as well as enlarged LA and AO size, which can lead to premature death.

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APPENDIX A

Cape Peninsula University of Technology

2 September 2009
CPUT/HW-REC 2009/H011

P.O. Box 1906 • Bellville 7535 South Africa •Tel: +27 21 442 6162 • Fax +27 21 447 2963
Symphony Road Bellville 7535

OFFICE OF THE CHAIRPERSON:
HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE (HW-REC)
Registration Number NHREC: REC- 230408-014

At the meeting of the Health and Wellness Sciences-REC on 7 August 2009 approval was granted
to Maria Diana Hartnick, pending minor amendments now received. This approval is for research
activities related to an M Tech: Radiography at this institution.

TITLE:
Echocardiography evaluation of the heart, for early detection of cardiac disease in high risk
diabetic patients.

INTERNAL SUPERVISOR: Prof P Engel-Hills

INTERNAL CO-SUPERVISOR: Ms F Isaacs

EXTERNAL CO-SUPERVISOR: Dr B Posen

Comment:
This ethics approval is supported by written permission from the research site where the study
will be conducted.

Research activities are restricted to those detailed in the proposal and application submitted in
August 2009.

Approval will not extend beyond 1 September 2010. An extension must be applied for should
data collection for this study continue beyond this date.

Prof PENELOPE ENGEL-HILLS
CHAIR: HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE

e-mail: *engelhillsp@cput.ac.za*

Consent from Study A

4 Halleria Cresent
Rouxville
Kuilsrivier
7580

The Team Leader
Bellville South Diabetic Research Study

RE: Permission to conduct research study

Dear Dr. T Matsha

This serves to confirm that I Maria D Hartnick is a registered MTech Radiography student at Cape Peninsula University of Technology.

The Topic of my research study is entitled: **Echocardiography evaluation of the heart for the early detection of cardiac disease in high risk diabetic patients.**

The aim of this study is to establish whether Echocardiography (Ultrasound of the heart) can be used for the early detection of cardiac disease in high risk diabetic patients.

This Research study would not require for any names of the participants to be recruited, and all the information will be treated confidential.

I would like to ask your permission if my participants for my research study can be recruited from your Diabetic Research study done at Kasselsvlei Primary School.

If you agree to this request can you please sign on the bottom line?

Signature: _____   Date: 4 | 01 | 2010

Thank you very much.

The Researcher
Maria Hartnick
Student no: 192055836

THE MODIFIED ROSE ANGINA QUESTIONNAIRE
FOR IDENTIFICATION OF CARDIOVASCULAR DISEASE IN BELLVILLE SOUTH

Overall project leaders: Prof. RT, Erasmus, Mr. MS, Hassan, Prof. T, Matsha

Principal investigators: Hartnick, M., Kisten, Y., Muiruri, M., Soita, D.J. & Zemlin, A.

Date of Interview:/…….../………..   New/Previous ref No ………………

To the respondent:
Thank you sincerely for your voluntary participation in this research study. The information obtained in this questionnaire will provide us with information on all the possible health, family, lifestyle and dietary risk factors within your household that might influence the development of cardiovascular disease. The questionnaire should not take long and we hope that you find it interesting and enjoyable. All answers provided will be treated as confidential and anonymous.

Note
No special knowledge is needed to complete this questionnaire. Please feel free to ask for clarification if needed.

Postal Address: ---

Residential address: ---

Telephone or

Cell phone Contacts: --

Name of Interviewer:…………………………………

Instructions:

Please complete the following general information about yourself by ticking in the appropriate box next to the appropriate answers. Please take your time and read through the questions carefully.

1. What is your date of birth?   ☐ ☐ ☐ ☐ ☐ ☐

2. What is your gender?

        Male   ☐   Female   ☐

3. What is your marital status?

    Married ☐   Single ☐   Widowed ☐

    Divorced ☐   Other ☐

4. How would you describe your ethnic background?

    Black ☐   White ☐

    Coloured ☐   Asian ☐

5. What is the highest level of education you have completed?

    (a) Primary School or less ☐
    (b)   High School (Not Completed) ☐
    (c) High School graduate ☐
    (d) College Or Technical College (Not Completed) ☐
    (e) College or Technical College Graduate ☐
    (f) University or Technikon (Not Completed) ☐
    (g) University or Technikon graduate ☐

6. What is your profession/occupation?

Please state……………………………………………………………..

7 How long have you been living in Bellville South?

Less than 6 months ☐   Less than 1 year ☐

1-5 years ☐   5 years and above ☐

Section B. Personal and family health history

Instructions:

The following questions will tell us about your family health history. Please complete all the questions by placing a tick in the appropriate box or writing in the answer.

8. (a) Are you currently on any medication?   Yes ☐   No ☐

   (b) Please list medication

....

....

....

....

9. Are you currently on treatment for high cholesterol?

Yes ☐   No ☐

If yes, please list medication

....

10. (a) Have you ever been told that you have diabetes?

Yes ☐   No ☐

   (b) If yes, when were you first told by a doctor that you have diabetes?

Please state ....

11. Are you currently on treatment for high blood pressure?

Yes ☐   No ☐

12. (a) Have you ever been treated for heart problems?

Yes ☐   No ☐

   (b) Have you ever had an operation for your heart?

Yes ☐   No ☐

13. Has either of your biological parents been diagnosed by a health professional that he/she is

(a) Overweight or obese

Yes ☐   No ☐

(b) Would you describe either of your biological parents as being or were overweight or obese?

Yes ☐   No ☐

14. Did either of your natural parents ever die of a heart attack?

(a) Before the age of 60?

Yes ☐   No ☐

(b) After the age of 60?

Yes ☐   No ☐

15. Have you recently been treated for infectious diseases such bronchitis, skin diseases, urinary tract infection?

If yes, mention…………………………………………………………………………………............................

Section C. Pain on activity

16. Have you ever had any pain, discomfort, pressure or heaviness in your chest?

Yes ☐   No ☐

17. Would any of these words describe the chest pain sensation?

(a) Heaviness   Yes ☐   No ☐

(b) Burning   Yes ☐   No ☐

(c) Tightness   Yes ☐   No ☐

(d) Stabbing   Yes ☐   No ☐

(e) Pressure   Yes ☐   No ☐

(If no, proceed to section D. If yes continue with the questions below)

18. Do you get the chest pain when you walk uphill or hurry?

☐   ☐

50

Yes   No

19. Do you get the chest pain when you walk at an ordinary pace on a flat level?

Yes ☐   No ☐

20. What do you do when you get the chest pain while you are walking?

Stop ☐   Slow down ☐   Carry on ☐

21. Please indicate if participant carries on after taking glyceryl trinitrate…………

22. What happens to the chest pain when you stand still?

                Relieved ☐   Not relieved ☐

23. If there is relief, how soon is it?

Ten (10) minutes or less ☐   More than Ten (10) minutes ☐
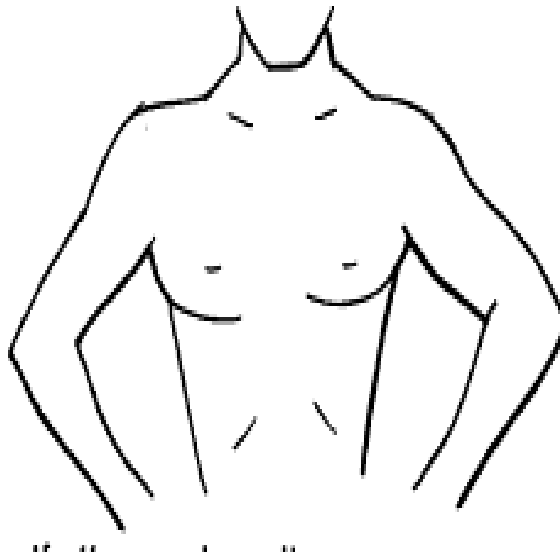
24. Will you show me where the chest pain was on this picture?

       (a)Breast bone (upper)   Yes ☐   No ☐

       (b)Breast bone (middle)   Yes ☐   No ☐

       (c) Breast bone (lower)   Yes ☐   No ☐

       (d)Left front chest   Yes ☐   No ☐

24 (e) Does the pain move to the left arm?

       Yes ☐   No ☐

25. <mark>Have you had this chest pain or discomfort more than once</mark>?

       Yes ☐   No ☐

26. Does any other kind of exertion bring it on?   Yes ☐   No ☐

27. Do any of these things tend to bring it on?

       (a) Excitement   Yes ☐   No ☐

       (b) Emotion such as stress   Yes ☐   No ☐

       (c) Stooping   Yes ☐   No ☐

       (d) Eating   Yes ☐   No ☐

       (e) Breathing   Yes ☐   No ☐

(f) Cold wind as may occur in winter

Yes ☐   No ☐

(g) Coughing   Yes ☐   No ☐

(h) Name any other kind of exertion which brings it on……………………….

28. Does the chest pain get worse if you have a chest cold or bad cough?

Yes ☐   No ☐

29. Would you describe it as a pain or discomfort?

Pain ☐   Discomfort ☐

Section D. Pain due to possible infarction

30. Have you ever had a severe pain across the front of your chest lasting for half an hour or more?

Yes ☐   No ☐

31. If yes, how many of these attacks have you had?

(a) First attack:
Date……..………………
Duration………
Other information…………………………………………………………………………………………………

(b) Latest attack:
Date……….
Duration………..
Other information……………………………………………………………………………………………………

32. Have you ever had an electrical recording of your heart (ECG) performed?

Yes ☐   No ☐

33. If yes,   Where ………………………………. When……………

☐   ☐

53

34. Did you consult a doctor for this chest pain?   Yes   No

35. If yes,
      (a) What is the name of the doctor and hospital/clinic……………………
          ……………………………………………………………………………
      (b) What   did   he/she   say   was   the   cause   of   the   chest
          pain………………………………………………………………………

Section E. Intermittent claudication

36. Did you get pain in either leg on walking?   Yes ☐   No ☐

37. Does this pain ever begin when you are standing still or sitting?

                                                        Yes ☐   No ☐

38. In what part of your leg do you feel it?

Pain includes calf/calves ☐   Pain does not include calf/calves ☐

39. Where else in the leg do you feel the pain………………………………………

40. Do you get it when you walk uphill or hurry?

Yes ☐   No ☐   none of them ☐

41. Do you get it when you walk at an ordinary pace on a flat level?

Yes ☐   No ☐

42. Does the pain disappear while you are still walking?

Yes ☐   No ☐

43. What do you do when you get the pain while you are walking?

Stop or slacken pace ☐   Continue walking ☐

Section F. Lifestyle (tobacco use)

44. Do you currently smoke any cigarettes or other tobacco products (cigars or pipes)?

  (a)   Yes ☐   No ☐

  (b) If yes, how often do you smoke now?

Daily ☐   Occasionally ☐   Not at all ☐

  (c) If you smoke daily, on average, how many cigarettes, cigars or pipes do you smoke per day? Please state………….

  (d) For how long have you been smoking cigarette/other tobacco products? (Please circle answer)

  1 Year ☐   2-3 Years ☐   >5 Years ☐   >10 Years ☐

  (e) How old were you when you started smoking regularly at least 3-4 cigarettes per week? Please state age……….. ....

45. (a) If you have stopped smoking, did you ever smoke on a daily basis in the past?

    Yes ☐   No ☐

  (b) How old were you when you stopped smoking? Please state age…...............................

Section G. ==Ultrasound echocardiography findings== reported by……………….

46. Heart Rate? ……Beats per minute?

47. Is there evidence of infarction?..................................

48. Describe the classification of infarction

        (a) Mild   (b) Moderate   (c) Severe

49. Any evidence of plaque development?

50. Is there any valvular dysfunction, abnormalities, or ventricular or atria pathology?..

51. Is there evidence of any other cardiovascular disease?

……………………………………………………………………………………..

52. Other remarks………………………………………………...........................

………

…………………………………………

Section H
53. CAROTID ULTRASOUND DOPPLER STUDY: Ultrasound Report

CPUT **Faculty of Health & Wellness Sciences** **Bellville South Population** **Western Cape**	Please attach participant research no.

Ultrasound Carotid Assessment	Summary **RIGHT Carotid**

R   L

I   E   I   E
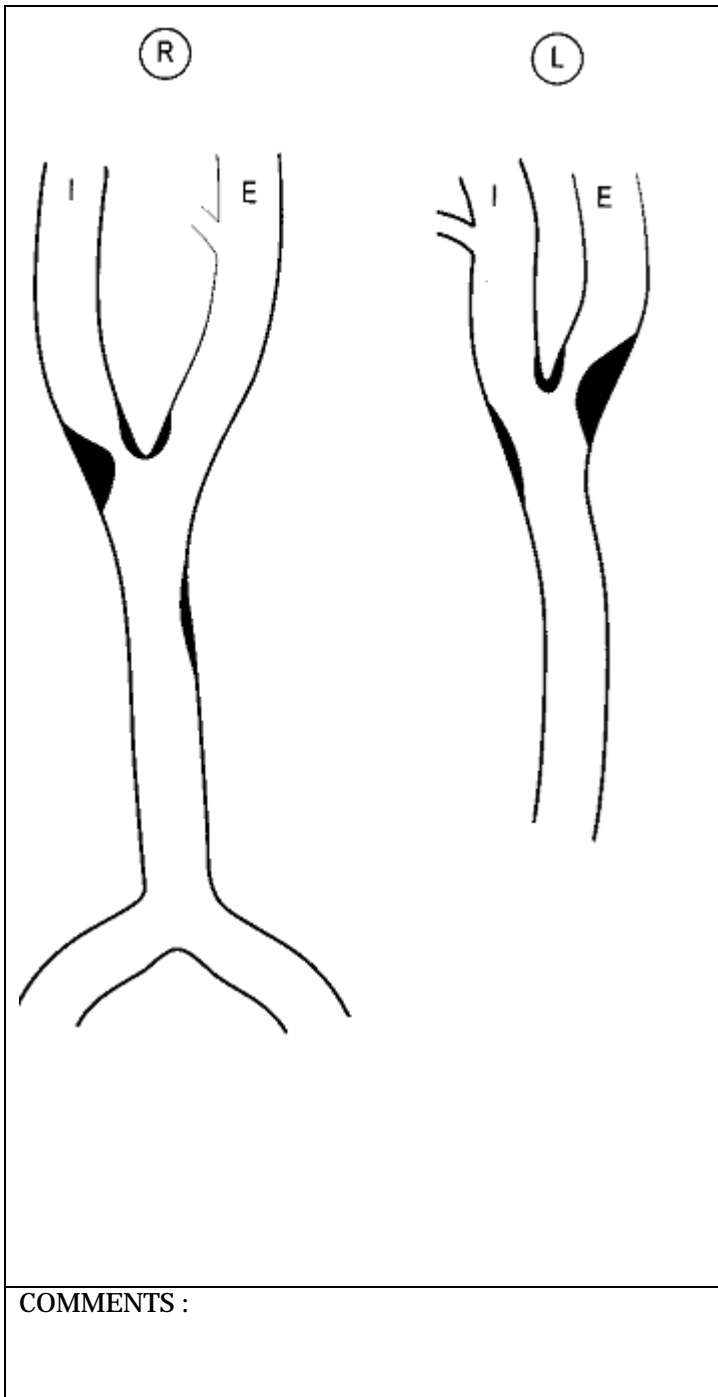
	CCA	ICA	ECA
PSV (m/s)			
EDV (m/s)			
ICA/CCA			
% Stenosis			
Plaque characteristics Echogenicity TPV			
IMT Measurement			
	Vertebral		
PSV (m/s)			
Direction			

LEFT Carotid

	CCA	ICA	ECA
PSV (m/s)			
EDV (m/s)			
ICA/CCA			
% Stenosis			
Plaque characteristics Echogenicity TVP			
IMT			
	Vertebral		
PSV (m/s)			
Direction			

COMMENTS :

SIGNATURE:
Print Name :
DATE:

Section I. Anthropometric measurements. Interviewers Name……………………

54. Weight and Height.

Body Weight (kg)			
Body height (cm)			
Body Mass Index			

55. CIRCUMFERENCE MEASUREMENTS

Waist Circumference 1 (cm)			
Waist Circumference 2 (cm)			
Waist Circumference 3 (cm)			
Total			

Hip Circumference (cm)			
Hip Circumference (cm)			
Hip Circumference (cm)			
Total			

56. BLOOD PRESSURE MEASUREMENTS. Interviewers Name………………………

Systolic Pressure 1 (mmHg)			
Systolic Pressure 2 (mmHg)			
Systolic Pressure 3 (mmHg)			

Diastolic Pressure 1 (mmHg)			
Diastolic Pressure 2 (mmHg)			
Diastolic Pressure 3 (mmHg)			

Pulse 1 (Beat per Minute)			
Pulse 2 (Beat per Minute)			
Pulse 3 (Beat per Minute)			

57. Oral glucose tolerance test (OGTT)   Interviewers Name…………………..

(i) Did subject eat this morning?........... If yes state time……………..

(ii) When did subject eat the last meal last evening?...........................

(iii) Please indicate the time when fasting blood taken……………….

(iv) Please indicate the time when Glucose was given…………………

(v) Please indicate when 2hour blood was taken……………………….

58. Section J: check list

1. Was fasting blood drawn? ☐

2. Was 2 hour blood drawn? ☐

3. Have all the participants' questions been answered? ☐

4. Were anthropometric measurements taken ☐

5. Have ultra sound findings been reported ☐

6. Has the consent form been signed and attached ☐

Checked by……………………………………

THE BELLVILLE, SOUTH AFRICA CARDIOVASCULAR STUDY CONSENT FORM

Project leaders:	**Mr. Shafick Hassan (CPUT)** **Prof Rajiv Erasmus (University of Stellenbosch)** **Prof. Tandi Matsha (CPUT)**
Principal Investigators:	**Hartnick, M., Kisten, Y., Muiruri, M., Soita, D.J. & Zemlin, A.E.**
Address:	**Faculty of Health and Wellness Sciences, Cape Peninsula University of Technology (CPUT), Bellville Campus** **Symphony Way, 7535** **Chemical Pathology Department, Faculty of Health Sciences, University of Stellenbosch (Tygerberg Campus), Tygerberg, 7505.**
Contact Numbers:	**Bianca—0219384643/Cell phone 0720465471** **Mr Hassan – 021 959 6274** **Prof Erasmus – 021 938 4107** **Prof. Matsha – 021 460 3209**

Dear Participant,

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied and that you clearly understand what this research entails and how you could be involved. Also, your participation is entirely voluntary and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do initially agree to take part.

This study has been approved by the Committee for Human Research at Cape University of Technology and The University of Stellenbosch and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

Worldwide new causes of certain diseases or conditions are continuously being discovered by research on the cells and molecules of the body. For research to be carried out on certain diseases it is necessary to first establish the incidence and prevalence of the disease. This project aims to determine the incidence, prevalence as well as factors which are predictive of cardiovascular disease. When a large group of patients with similar diseases has been collected, meaningful research into the disease processes may become possible.

Why have you been invited to participate?

The prevalence of cardiovascular disease in South Africa is not well documented and few studies have been conducted since 1994. Many subjects with cardiovascular disease are unknown to the health service, often because they are not yet diagnosed. In order to asses the magnitude of the problem, you have been approached to participate in this project to determine the incidence of cardiovascular disease amongst our adult population.

You have been selected since you previously participated in the diabetes study and that you were aged between 35-65 years at the time. You also meet other criteria used to select participants into this study.

What will your responsibilities be?

The participant will be requested to provide information about his/her medical history with specific emphasis on cardiovascular disease. Measurements such as weight, height, waist, hip and skin fold will be taken. You will also be asked to complete a questionnaire which will take no longer than 10 minutes. Fasting venous blood will be collected thereafter you will be asked to drink a glucose solution (glucose content 75g). After two hours another venous blood will be collected. The blood will be used to determine blood glucose level, cholesterol and heart muscle proteins. The remainder of the blood samples will be stored in special freezers at chemical pathology laboratories on 9th floor, Tygerberg Hospital and only accessed by Dr. Zemlin and Mr. Muiruri who are both principle investigators on the project. These samples will be stored for a maximum of ten years and will be used to study non genetic biochemical markers. Should we want to conduct any genetic studies in future, further ethical approval as well as participants consent will be sought in this regard.

A painless procedure known as ultra sound scan (Sonography) will there after be performed to check the health of your heart and neck arteries. No pharmaceutical agents (medication) will be tested in the study.

Will you benefit from taking part in this research?

You will be notified of your cardiovascular status by the medical nurse or doctor. Thereafter, you will be referred to your local health centre or general practitioner for further investigations and treatment.

In the unlikely event that the research may lead to the development of commercial applications, the participant or the participant's heirs will not receive any compensation, but

profits will be reinvested into supporting the cause of further research which may bring benefits to my/*the participant's family and to the community, such as health screening, medical treatment, educational promotions, etc.

Are there any risks involved in my taking part in this research?
A slight bruising might occur after blood has been drawn from the arm but this will heal quickly. You may also feel nauseous after drinking the glucose solution in which case you must notify the research staff. A nurse and doctor will be present on site at all times.

Who will have access to your medical records?
The participant's identity will be kept confidential throughout. Information will not be associated with the participant's name. The research staff will use only a coded number, access will be limited to authorized scientists and any scientific publications, lectures or reports resulting from the study will not identify me/*the participant.

Some insurance companies may mistakenly assume that taking part in research indicates a higher risk for disease. Thus no information about you or your family will be shared with such companies.

Will you or your child be paid to take part in this study and are there any costs involved?
You will not be paid to take part in the study, but your transport, if required will be covered for each study visit. There will be no costs involved for you if you take part in the project.

Is there any thing else that you should know or do?
You should inform your family practitioner or usual doctor that you are taking part in a research study.
You can contact *Prof Erasmus* **at Tel 938 4107 or rte@sun.ac.za** if you have any further queries or encounter any problems.
You can also contact the Committee for Human Research at **021 442 6162 or** engelhillssp@cput.ac.za
if you have any concerns or complaints that have not been adequately addressed by your study doctor.
You will receive a copy of this information and consent form for your own records if it is requested

DECLARATION BY PARTICIPANT:

I declare that:

I have read or had read to me this information and consent form and that it is written in a language with which I am fluent and comfortable.
I have had a chance to ask questions and all my questions have been adequately answered.
I understand that taking part in this study is voluntary and I have not been pressurized to take part.
I may choose to withdraw from the study at any time and will not be penalized or prejudiced in any way.

I may be asked to leave the study before it has finished if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan as agreed to.

I also consent that my information may be:

♦   **Used and kept for future research studies** ☐

♦   **Used and discarded** ☐

Signed at (*place*) ....…......……………….. on (*date*) …………...……….. 20

Signature of participant-------------------------------- Signature of witness-------------------

DECLARATION BY THE INVESTIGATOR

I *(name)* ……………….……………………………..……… declare that:

I explained the information in this document to (*Names of*

Participant)…………………………………………………………….………

I encouraged him/her to ask questions and took adequate time to answer them.
I am satisfied that he/she adequately understand all aspects of the research, as discussed above

Signed at (*place*) ....…......……………….. on (*date*) …………...……….. 2010.

Signature of investigator------------------------------- Signature of witness-------------------

Echocardiography evaluation of the heart for early detection of cardiac disease in high risk diabetic patients

BELLVILLE SOUTH COMMUNITY, WESTERN CAPE, SOUTH AFRICA
INFORMED CONSENT

Participant's File no: **Date:**

I, MARIA HARTNICK, am currently a Masters student at Cape Peninsula University of Technology in Radiography. This involves doing: *"Echocardiography evaluation of the left ventricle of the heart for early detection of cardiac disease in high risk diabetic patients."* This study will need participants to have an ultrasound scan of the left the heart. If you are willing to participate I need you to give Permission, before I can commence with the examination. Confidentiality will be maintained and the data obtained from the examination will be used for this study only, will be available to you on your request. You can leave this study at any time, without you being questioned.

By signing below you give permission that an ultrasound scan can be performed on you, and that the data obtained through the examination may be used in this research study and in any publications or presentations about this study. I stress though that your identity will remain anonymous at all times.

What is an ultrasound scan of the heart?
It is when an ultrasound machine is used to look at the heart. It is a painless and harmless procedure to assess the heart's function and structures. You will be asked to undress, put on a hospital gown and to lie on your left side. A probe with special jelly that helps to make the image visible on the screen will be placed on your chest area. The study will take 20 to 30 minutes.

I ………………………….. declare that:
I understand what an ultrasound of the heart is.
The agreement to partake in this study is my own choice.
I have read and/or someone has read to me the information on this study.
The information is in a language with which I am fluent and comfortable.
I was given an opportunity to ask questions and all my questions have been adequately answered.
I understand that taking part in this study is voluntary.
I may choose to leave the study at any time.

_____   at Bellville Clinic   _____
      Signature of participant   on this day

_____   at Bellville Clinic   _____
      Signature of witness   on this day

Declaration by Investigator:
I (name) ……………………… …………………………declare that:-

I have explained the information in this document to the participant.
I encouraged him/her to ask questions and took adequate time to answer them.
I am satisfied that he/she adequately understands the information.
The information obtained from this study, will ONLY be used for the purpose of this study and academic publications/presentations emanating from it.
The information will be available to the participant when requested.
The participant will be able to leave the study at any time without him / her being victimized.

Signature of investigator   at Bellville Clinic   on this day
_____   _____

Cape Peninsula University of Technology

Title: Echocardiography evaluation of the heart for early detection of cardiac disease in high risk diabetic patients

Echocardiography Report

Patients ID:
Study Date:
Institution name
Sonographer:

Gender: **DOB:**   **Age:**

2D Mode Dimensions
LV (Left ventricle)

IVS (Intra-ventricular septum)
LVPW (Left ventricular posterior wall)
LVIDd (Left ventricle diameter in diastole)
LVIDs (Left ventricle diameter in systole)

EF (Ejection Fraction)

RV (Right ventricle) - Dimensions
RVAWd (Right ventricle anterior wall in diastole)
RVID (Right ventricle diameter in diastole)
LA (Left Atrium)

AO root (Aorta)

Doppler Mode – Velocity measurements
Mitral valve (MV)

MV E/A
MV Peak E
MV peak A

Aorta valve (AV)
AV V max
Max PG

Tricuspid valve (TV)
TV Peak E velocity
Vel
PG

Pulmonary Valve (PV)
Mean PG
Max PG

Echocardiography Findings

LV Size and shape

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………………………………………………………………………………………………

LV Function:

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………………………………………………………………………………………

LV Wall Motion:

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RV size / masses:

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………………………………………………………………………………………

RV wall:

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………………………………………………………………………………………

RV Function:

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Left Atrium:

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………………………………………………………………………………………
Right Atrium:

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………………………………………………………………………………………

Aortic Root:

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……………………………………………………………………………

Mitral valve:

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……………………………………………………………………………

Tricuspid valve:

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………………………………………………………………………………

Aortic valve:

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………………………………………………………………………………

Pulmonary valve:

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………………………………………………………………………………

Pleural effusion:

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<u>Comments:</u>

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………………………………………………………………………………………………………

Signature: Maria Hartnick

Biochemical marker result according to the glycaemic status
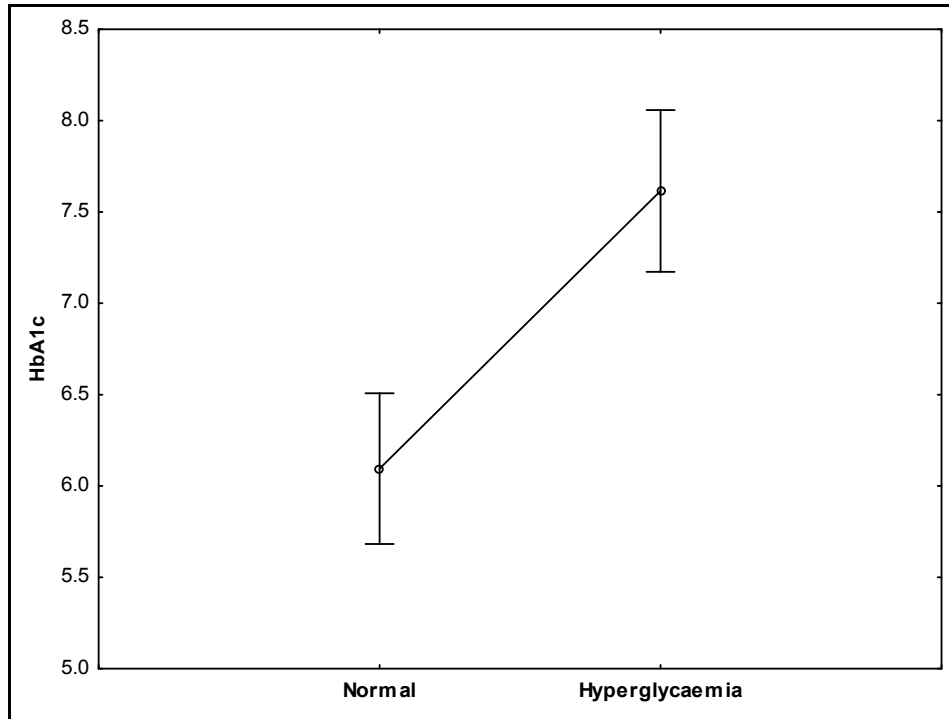

Figure 4.4: Glycated haemoglobin (HbA1c) according to the glycaemic status

HbA1c was significantly higher in individuals with hyperglycaemia than in those with normoglycaemia, **$p < 0.0001$.**
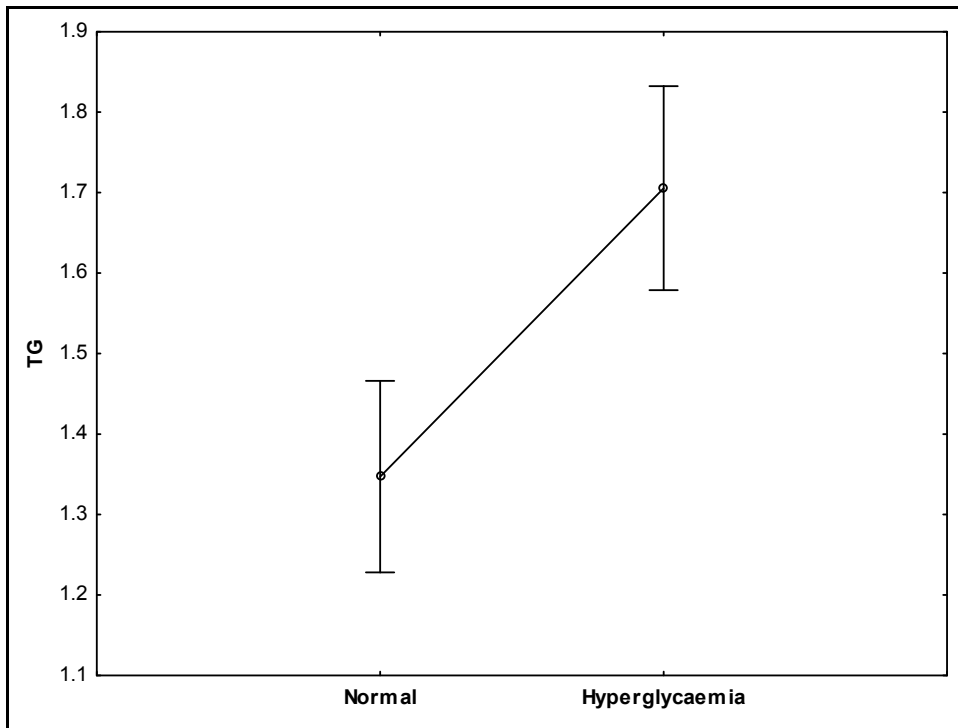
Figure 4.5: Triglycerides (TG) according to the glycaemic status

The TG was significantly increased in the hyperglycaemia group than in the normal group, **p < 0.0001.**

APPENDIX H

Biochemical marker and echocardiography results according to gender

The results are presented as the median ± 95% confidence interval. The Mann-Whitney U test was used to determine whether or not a statistically significant difference exists between males and females who are normoglycaemic and hyperglycemic. HDL was significantly higher in females (1.39 ± 0.40) than in males (1.24 ± 0.43) p = **0.0014.** FBG/Insulin was significantly higher in males (1.18 ± 1.99) than in females (0.71 ± 0.95) p = **0.0015.** TC/HDL was significantly higher in males (4.78 ± 1.70) than in females (4.20 ± 1.42) p = **0.0006.** GGT was significantly higher in males (49.10 ± 49.83) than in females (37.11 ± 43.07) p = **0.0192.** IVS measurement was significantly thicker in male (1.36 ± 0.30) than in females (1.26 ± 0.24) p = **0.0006.** Left atrium size was significantly larger in males (3.90 ± 0.65) than in females (3.71 ± 0.63) p = **0.0067.** Aorta size was significantly larger in males (3.41 ± 0.38) than in females (3.16 ± 0.41) p = **< 0.0001.** LVED diameter was significantly larger in males (5.15 ± 0.51) than in females (4.79 ± 0.57) p = **< 0.0001.** LVES diameter was significantly larger in males (3.16 ± 0.56) than in females (2.90 ± 0.62) p = **0.0001.** PW measurement was significantly thicker in males (1.05 ± 0.25) than in females (0.98 ± 0.22) p = **0.0031.**

Biochemical marker and echocardiography results according to gender

Variable (Unit)	Males, n = 105	Females, n = 306	p-value
Age (years)	54 ± 13	54 ± 13	0.9381
FBG (mmol/L)	6.70 ± 4.12	6.5 ± 3.1	0.5110
Post-BG (mmol/L)	6.3 ± 2.5	6.8 ± 2.6	0.1161
HbA1c (%)	6.6 ± 1.8	6.9 ± 3.6	0.3610
Insulin (uU/mL)	13.8 ± 13.8	16.1 ± 14.8	0.1499
FBG/Insulin	1.18 ± 1.99	0.71 ± 0.95	**0.0015**
TC (mmol/L)	5.4 ± 1.1	5.4 ± 1.1	0.7200
TG (mmol/L)	1.68 ± 1.05	1.46 ± 0.85	0.0352
HDL (mmol/L)	1.24 ± 0.43	1.39 ± 0.40	**0.0014**
LDL (mmol/L)	3.40 ± 1.00	3.39 ± 0.97	0.8957
TC/HDL	4.78 ± 1.70	4.20 ± 1.42	**0.0006**
Serum cotinine (ng/mL)	124 ± 175	110 ± 165	0.4845
GGT (IU/L)	49.10 ± 49.83	37.11 ± 43.07	**0.0192**
HsCRP (mg/L)	7.07 ± 11.27	7.62 ± 8.75	0.6053
IVS (cm)	1.36 ± 0.30	1.26 ± 0.24	**0.0006**
Left Atrium (cm)	3.90 ± 0.65	3.71 ± 0.63	**0.0067**
Aorta (cm)	3.41 ± 0.38	3.16 ± 0.41	**< 0.0001**
LVED (cm)	5.15 ± 0.51	4.79 ± 0.57	**< 0.0001**
LVES (cm)	3.16 ± 0.56	2.90 ± 0.62	**0.0001**
PW (cm)	1.05 ± 0.25	0.98 ± 0.22	**0.0031**

Key:

FBG: Fasting blood glucose, Post BG: Post blood glucose, HbA1c: Glycated hemoglobin, TC: Total cholesterol, TG: Triglycerides, HDL: High density lipoprotein, LDL: Low density lipoprotein, GGT: Gammaglutamyl transferase, Hs-CRP: High sensitive C-reactive protein, IVS: Inter ventricular septum, LVEDD: left ventricle end diastolic diameter, LVESD: left ventricle end systolic diameter, PW: Posterior wall