Spectrum of sub-clinical Cardiovascular Diseases and relationship to the CD4 count among clinically healthy HIV infected patients at the University Teaching Hospital in Lusaka

DR. LORRITA KABWE (MBCHB)

A dissertation submitted to the University of Zambia in partial fulfilment of the requirements of the degree in

Master of Medicine in Internal Medicine

University of Zambia

DECLARATION

I declare that this dissertation is my own work. It is being submitted for the Masters degree in Internal Medicine at the University of Zambia, Lusaka. It has not been submitted before for any degree or examination at this or any other University.

Signed.....
Student: Dr Lorrita Kabwe

Signed.....
Supervisor: Dr S. Lakhi (Consultant Physician)

Signed.....
Co-supervisor: Dr S. Kalinichenko (Consultant Cardiologist)

COPYRIGHT

Dr. Lorrita Kabwe
2015

DEDICATION

To Yande…

You are the reason I strive to be better each day...

ACKNOWLEDGEMENTS

The execution and successful completion of this study would not have been possible without the contribution of the following people;

- My supervisors: Dr S. Lakhi, and Dr S. Kalinichenko for being constant guides and mentors throughout this project;
- Dr. Lloyd Mulenga and Dr. Ben Andrews for helping formulate the research protocol;
- The staff in the Echo/ECG lab at the University Teaching Hospital for their expertise;
- Sr. Mwila and all the staff at AIDC for their relentless work in recruiting my study participants;
- University Teaching Hospital and AIDC labs for their support;
- My research assistants for being dedicated to this research and seeing it through to its completion;
- My husband Marlon Nkomesha Nsofu and my family for their patience and being great pillars of support;

Finally, I would like to thank all the participants of this study without whom this research would not have been possible, I'm truly grateful.

TABLE OF CONTENTS

LIST OF FIGURES AND GRAPHS

TABLE OF ACRONYMS AND ABREVIATIONS

ABI	**Ankle Brachial Index**
AIDC	**Adult Infectious Diseases Centre**
AIDS	**Acquired Immunodeficiency Syndrome**
AV/AoV	**Aortic Valve**
ART	**Antiretroviral therapy**
ATT	**Antituberculous Therapy**
BMI	**Body Mass Index**
CD4	**Cluster of differentiation 4**
CVD	**Cardiovascular Disease**
DALY	**Disability Adjusted Life Years**
DRC	**Democratic Republic of Congo**
DT	**Deceleration time**
E/A	**E-early diastolic mitral flow velocity, A-late diastolic mitral flow velocity**
ECG	**Electrocardiography**
ECHO	**Echocardiography**
EDTA	**Ethylenediaminetetraacetic acid**
EDV	**End Diastolic Volume**
EF	**Ejection Fraction**
HAART	**Highly active antiretroviral therapy**
IQR	**Interquartile range**
IVC	**Inferior vena cava**
IVSd	**Intraventricular septum in diastole**
IVSs	**Intraventricular septum in systole**
HDL	**High density lipoprotein**
HIV	**Human immunodeficiency virus**

LA	**Left atrium**
LDL	**Low density lipoprotein**
LVH	**Left ventricular hypertrophy**
LV	**Left ventricle**
LVIDd	**Left ventricular internal wall diameter in diastole**
LVIDs	**Left ventricular internal wall diameter in systole**
LVOT	**Left ventricular outflow tract**
LVPwd	**Left ventricular posterior wall diameter**
MACS	**Multicentre AIDS cohort study**
MN	**Minnesota code**
MV	**Mitral valve**
MVOA	**Mitral valve orifice area**
NYHA	**New York heart association**
PAD	**Peripheral artery disease**
PHT	**Pressure half time**
PV	**Pulmonic valve**
PVAT	**Pulmonary valve acceleration time**
RA	**Right atrium**
RV	**Right ventricle**
SD	**Standard deviation**
SMART	**Strategies for Management of Antiretroviral Therapy**
TAPSE	**Tricuspid Annular Plane Systolic Excursion**
TR	**Tricuspid regurgitation**
TV	**Tricuspid valve**
UTH	**University teaching hospital**
WHO	**World Health Organisation**
WIHS	**Women interagency HIV study**

ABSTRACT

Background: - Cardiovascular diseases are among the leading cause of morbidity and mortality worldwide. The association between HIV and CVD has been established in many studies. However, information is still lacking on subclinical disease as well as its associated risk factors in this population. This study aimed at establishing the prevalence of subclinical CVD among clinically healthy HIV people attending their regular out- patient visits. It also looked at risk factors (traditional and non traditional) as well as the association of CVD to the CD4 count.

Methods: we enrolled a total of 243 asymptomatic HIV-infected patients from the HIV outpatient clinic at the University Teaching Hospital. Data collected included demographic characteristics, duration of HIV infection, drug history including HAART regimen and cardiovascular risk factors (hypertension, diabetes and smoking). Clinical data included blood pressure, weight and height. Laboratory data included CD4 counts, serum creatinine, total cholesterol and triglycerides. We tested for subclinical CVD using 3 tools: Ankle Brachial Index (ABI) to measure for the presence of peripheral artery disease, 12 lead Electrocardiogram (ECG) for electrical abnormalities and transthoracic Echocardiography (ECHO), to measure abnormalities in cardiac structure and function. At analysis, patients where dichotomised into those with CD4≤350 and those with CD4>350.

Results: participants characteristics were as follows: the mean age, 42 years (SD±10); 143 (58.5%) females; CD4≤ 350cells/ml was found in 140 (57.6%); 112(86.2%) were receiving HAART with 86.2% being on 1st line regimen. Systolic hypertension was present in 84(34.6%), diastolic hypertension in 89(36.6%) and 39.5% had creatinine clearance<90. Diabetes and current smoking were not very common (3.3% and 2.9% respectively). High total cholesterol was found in 19(7.82%) of the participants while 37(15.23%) had high triglycerides. On ECG, ECHO and ABI, abnormalities were found in 53.9%, 44.4% and 20.2% respectively). The commonest cardiac lesion on both ECG and ECHO was left ventricular hypertrophy (27.4% and 23.3% respectively). Participants with CD4≤350 had higher prevalence of abnormalities on ECG (P=0.022) and ABI (P=0.043). Clinical factors associated with increased risk of subclinical CVD on multivariate logistical regression included CD4≤350, systolic BP>140mmHg and diastolic BP >90mmHg.

Conclusions: prevalence of subclinical CVD in healthy HIV infected patients is high and those with CD4≤350 have a higher risk. Hypertension is the most important traditional CVD risk factor in this population. There is need to screen HIV patients attending their routine clinic visits for hypertension and subclinical CVD. ABI and ECG are readily available in most institutions and can be used with minimal expertise.

CHAPTER 1

1.0 BACKGROUND

Africa bears a disproportionately large burden of the HIV/AIDS pandemic. Although only 14.4% of the world's population lives in Africa, approximately 69% of those living with HIV/AIDS are in Africa and 72% of all AIDS deaths are in this region.[1] Sub-Saharan Africa is the worst affected region, carrying a disproportionate two-thirds of the world's HIV/AIDS burden, and accounting for nearly three-quarters of AIDS-related deaths in 2008.[2] Zambia has an adult HIV prevalence estimated at 14.3%[3], with AIDS and AIDS-related illnesses contributing to the high mortality among patients.[4] The burden of cardiovascular diseases (CVDs) in the world is enormous and growing, and the majority of those affected are in developing countries.[5] In 2002 it was estimated that 29% of deaths worldwide (16.7 million deaths) were due to CVD and that 43% of global morbidity and mortality, measured in disability-adjusted life years (DALYs), was caused by CVD.[6]

Africa has not been spared with this global tide. In most African countries CVD is now the second most common cause of death after infectious disease, accounting for 11% of total deaths.[7] Projections from the Global Burden of Disease Project suggest that from 1990 to 2020, the burden of CVD faced by African countries will double. A large proportion of the victims of CVD will be middle-aged people. The poor will suffer disproportionately as a consequence of their higher disease risk and limited access to health care.[8]

The association of HIV infection and cardiac pathology was recognised in the early stages of the epidemic. Most studies were carried out in Europe and North America; these studies indicate that HIV infection is commonly associated with cardiac abnormalities.[9,10,11] Studies published over the past 3 years have tracked the incidence and course of HIV infection in relation to cardiac illness in both children and adults.[12] These studies show that sub-clinical echocardiographic abnormalities independently predict adverse outcomes in terms of morbidity and mortality and identify high-risk groups to target for early intervention and therapy.[12]

The Joint United Nations Program on HIV/AIDS estimated that 34.0 million [31.4 million–35.9 million] people were living with HIV at the end of 2011; if 8% to 10% of patients develop symptomatic heart failure over a 2- to 5-year period, then 3 million cases of HIV-related heart failure will present during that period.[13,37]

In Africa, the incidence of AIDS-related cardiac disease is very high compared to that seen in western developed countries. For instance, in the period from 1993 to 1999 in Burkina Faso, 79% of the AIDS patients exhibited heart involvement, Zimbabwe found a prevalence of 50% among acutely ill hospitalised patients, in DRC the prevalence was 55%,[38] whereas in an Italian study in the period from 1992 to 1995, the incidence of AIDS-related cardiac disease was 6.5%.[13,39] The trend remained similar in many other studies done in Africa.

However, to date, the prevalence of cardiovascular disease among Zambian HIV infected patients remains unknown despite several cases of end stage cardiac disease being

encountered on a daily basis.[14] At the moment, HIV programs are focused primarily on support of active campaigns to get universal access to combinational ART. As a result, most forms of sub-clinical cardiovascular diseases are missed in their early stages resulting in patients presenting with advanced disease, which has very high morbidity and mortality.[15] Studies show that the incidence of heart failure in patients with subclinical cardiac dysfunction may be as high as 30%.[15]

CHAPTER 2

2.0 LITERATURE REVIEW

The introduction of HAART has seen reductions in the overall morbidity and mortality due to HIV-related illnesses. As a result, people are now living longer leading to an increased risk of development of CVD risk factors, such as hypertension, metabolic abnormalities (hyperglycemia, hyperlipidemia, lipodystrophy), and accelerated atherosclerosis, including coronary artery disease. Left untreated, these conditions are associated with development of various forms of cardiac disease.[13]

2.1 Electrocardiographic (ECG) abnormalities

ECG abnormalities were found to be common among HIV-infected patients. A cohort of 4518 patients from the Strategies for Management of Antiretroviral Therapy (SMART) study found that more than half (51.1%) of their patients had either major or minor ECG abnormalities. Major abnormalities were associated with and increased risk of incident CVD with 3.4% developing incident heart failure after about 2 years of follow up.[47] These included arrhythmias such as complete bundle branch blocks, heart blocks, major ST-T segment abnormalities and Q waves.[47]

2.2 Echocardiographic (ECHO) abnormalities

Various other studies have been conducted worldwide and most across Africa found various abnormalities on echo among HIV infected patients. These are as follows:

2.2.1 Cardiomyopathies

The prevalence of cardiomyopathy was found to be 15.9 per 1 000 asymptomatic HIV-infected patients. This was associated with myocarditis in the majority of cases and the frequency increased as the disease progressed.[16,17] Cardiotropic viruses such as Coxsackie B virus, adenovirus, Epstein Barr virus and HIV itself were implicated as the cause of myocarditis.[18] Many other factors were found to cause cardiomyopathy such as nutritional deficiencies and drug toxicities.[19,20] HIV-associated cardiomyopathy is said to be associated with rapid progression to death within 100 days of diagnosis in patients who are not treated with antiretroviral drugs.[21]

2.2.2 Pericardial disease

The prevalence of pericardial effusion in asymptomatic HIV-infected persons was estimated at 22%.[22] Most often the cause was not found. However, clinically overt pericardial effusions were related to opportunistic infections or to malignancies.[23,24,25] Mycobacterium tuberculosis, atypical mycobacteria, fungi, Staphylococcus aureus, and Streptococcus pneumoniae were all described, as well as more unusual pathogens such as Nocardiaasteroides, Listeria monocytogenes, Rhodococcusequi, and Chlamydia trachomatis. Neoplasms, particularly lymphoma and Kaposi's sarcoma can also cause pericardial effusion.[27-31] Usually small clinically silent effusions tend to resolve spontaneously in up to

42% patients.[26] However, the finding of pericardial effusion in HIV-infected patients is associated with increased mortality even if the effusion resolves over time. The pericardial effusions rarely directly contribute to mortality but rather serve as a marker of advanced HIV infection.[26]

2.2.3 Pulmonary hypertension

Pulmonary hypertension has also been described in HIV with prevalence ranging between 0.5 to 5%.[32,33] The aetiology is not very clear, but many of these patients have had multiple pulmonary infections or history of intravenous drug abuse.[34] Most idiopathic pulmonary hypertension in HIV is thought to be due to hyperplasia of vascular smooth muscles of the small pulmonary arteries, a cytokine-driven process.[35] The HIV-infected patient with pulmonary hypertension has a poor prognosis. Patients have the worst survival when they are in New York Heart Association (NYHA) Class III-IV.[36]

2.2.4 Valvular disease

Valvular heart disease was mainly manifested as infective endocarditis, non-bacterial thrombotic endocarditis and mitral valve prolapse. However, the incidence of these conditions has declined since the introduction of HAART.[37]

2.3 Effects of Antiretroviral drugs

Antiretroviral drugs have been associated with various metabolic abnormalities such as dyslipidemias, diabetes mellitus, insulin resistance, hepatic steatosis and lipodystrophies, and these may be associated with increased cardiovascular risk.[41] Other drugs such as Zidovudine are said to be directly cardiotoxic.

2.4 Peripheral Vascular disease

Peripheral vascular disease prevalence among HIV positive patients is high, with studies showing rates as high as 20.7% in relatively young populations of patients. In the general non-HIV population, the rates were only as high as 3% above 60 years of age.[42] Non-calcified atherosclerotic plaques were a common finding in HIV, and were usually associated with lipid abnormalities, smoking and use of protease inhibitors.[43,44] The presence of Peripheral Artery Disease (PAD) increases risk of premature coronary artery disease.[44]

2.6 Cardiac disease and CD4 count

A low CD4 count has been found to be an independent risk factor for development of incident CVD events in addition to the traditional risk factors for CVD. Evidence suggests that lower CD4 cell counts are associated with elevated levels of serum inflammatory markers and increased levels of activated CD4 T cells.[43] A CD4≤350 was associated with an increased risk of CVD events among HIV infected patients in an out-patient study.[54]

2.7 Traditional cardiovascular risk factors

Classic traditional cardiovascular risk factors of dyslipidemia, hypertension, diabetes, and smoking are common among HIV-infected populations. Two large cohorts (the Women's Interagency HIV Study [WIHS] and the Multicentre AIDS Cohort Study [MACS]) compared infected with HIV-uninfected controls. Compared to the uninfected, HIV-positive patients showed lower HDL and high LDL cholesterol and had higher predicted 10 year cardiovascular risk on the Framingham score. Protease inhibitors and BMI were independent predictors of CVD risk.[42]

2.8 Tools to predict CVD

Several tools have been used in various studies for assessing subclinical CVD risk which include clinical, laboratory and imaging techniques.

Ankle brachial index (ABI) has been shown to be an efficient tool for documenting the presence of peripheral artery disease in the lower extremities. It is simple, reproducible and a cost effective way of measuring lower extremity stenosis. An ABI of less than 0.9 is 90% sensitive and 98% specific for detecting arterial stenosis of greater than 50%. Presence of PAD on ABI is associated with systemic atherosclerosis.[42]

Electrocardiography (ECG) – has been described widely in medical literature as a valid and reproducible tool for detecting subclinical CVD. The development of the Minnesotta code and classification system has been the most important state in formalising and standardising the ECG reading across many studies. The finding of ECG abnormalities in an asymptomatic patient has been shown to be a major risk factor for the development of incident CVD.[43]

Echocardiography (ECHO) – the use of ECHO to detect abnormalities in cardiac structure and function among HIV infected patients has been extensively applied in many studies across Africa and other parts of the world. ECHO has been used to detect both subclinical and overt cardiac disease among in this population of patients.[12, 48]

CHAPTER 3

3.1 STATEMENT OF THE PROBLEM

Many HIV infected patients present to health care facilities with various forms of CVDs. Some present with advanced forms of disease while a large majority remain undetected. Most of these CVDs such as dilated cardiomyopathy and pericardial effusion are markers of advanced HIV disease and may have an impact on prognosis. In addition, with the advent of HAART, HIV infected patients are now living longer with the disease, implying that most traditional factors of CVD risk have become significant. Treatment of advanced forms of CVD is difficult and often associated with increased morbidity and mortality. As a result, early detection will determine which patients would require either immediate intervention and/or long term follow-up.

3.2 STUDY JUSTIFICATION

HIV infection has been associated with a high incidence of overt CVD compared to the general population. However information regarding subclinical CVD in this patient population is scarce. It is these clinically quiescent conditions that result in devastating cardiovascular morbidity and mortality if not identified. To date, patients who are seen in various HIV out- patient clinics in Zambia do not undergo any form screening for subclinical CVD. As such, a good number of patients end up developing progressive disease which is often a challenge to treat and usually results in significant morbidity and mortality. Most of these conditions are preventable and reversible if appropriate screening methods are put in place.

To this effect, data obtained in this study will help identify the significance of subclinical CVD and risk factors among HIV infected patients in our setting. This will in turn help establish algorithms for prevention and/or treatment of these diseases at the very earliest possible stage. The study will also lay important ground work for future research in HIV-related CVDs.

3.3 RESEARCH QUESTION

What are the various forms of subclinical CVD and risk factors in asymptomatic HIV infected patients presenting to the HIV out- patient clinic?

HYPOTHESIS

A CD4 count of less than 350 is associated with a higher prevalence of subclinical CVD.

3.4 OBJECTIVES

3.4.1 General objective

To describe the prevalence of subclinical CVDs among clinically healthy HIV infected patients in relation to their CD4 count.

3.4.2 Specific objectives

1. To describe the presence of sub-clinical CVDs on ECG, ECHO and ABI measurements
2. To correlate various cardiovascular abnormalities found with the CD4 count
3. To determine risk factors (traditional and others) associated with the presence of subclinical CVDs in these patients.
4. To assess the significance of ECG, ECHO and ABI measurements in screening for subclinical CVD among clinically healthy HIV infected people.

CHAPTER 4

4.0 METHODOLOGY

We conducted a cross sectional study at the Adult infectious diseases Centre (AIDC), which is an out-patient HIV clinic located in UTH. The study population included all HIV infected patients without documented CVD, who came for their regular scheduled clinic visits.

4.1 Inclusion Criteria

1. HIV-infected patients of either sex 18 years of age and above
2. Willingness to undergo study procedures
3. Signed informed consent

4.2 Exclusion criteria

1. Known cardiac patients with documented lesions on file review.
2. Amputated limbs
3. Woody edema/Kaposi Sarcoma of limbs or gross limb ulcerations

4.3 Clinical procedure

Patients were recruited during working hours on a daily basis in AIDC. Screening was done in line with exclusion criteria. Informed signed consent was sought and enrolment was done. All patients in this study were able to give individual consent without requirement for a surrogate.

A detailed history was taken by research staff at recruitment. Information gathered included patient demographics, duration of illness from time of diagnosis, type of ART being taken and duration. Other drugs being taken were also documented. Participants were asked on the presence of any CVD risk factors namely; diabetes, hypertension and tobacco smoking history. A physical examination was conducted, including measurements of BP, pulse, weight and height.

4.3.1 Laboratory tests

Blood samples were collected from each patient for the measurement of random lipid profile (total cholesterol and triglycerides), CD4 counts and serum creatinine. Blood for lipid profile was collected in plain specimen bottles, that for CD4 count in EDTA specimen bottles and blood for creatinine in heparin containing specimen bottles. A Cobus 611 analyser was used for all the chemistry samples, while the PENTRA XD was used for CD4 samples.

4.3.1 Electrocardiographic (ECG) measurements

ECG measurements were conducted on each patient using the Schiller AT-10 PLUS ECG machine. The participant was placed in supine position with chest and all limbs exposed. ECG leads were placed on the standard limb and chest locations and a 12 lead ECG tracing was obtained. Limb lead II was used as the rhythm strip. The tracing was then attached to a standard reporting sheet. The Minnesota Code was used for interpretation of the ECG tracings.

4.3.2 Echocardiographic (ECHO) measurements

Echo studies were done using My Lab version 40 and Logic 500 ultrasound machines. The participant was placed in the left lateral position with the chest exposed and left arm tucked under the head. Left ventricular systolic function was measured from the left parasternal long axis or short axis views using the Teicholz method in M-Mode; any abnormal result was verified using the 2-dimensional Simpsons biplane method in the 4 chamber apical view. Chamber sizes and wall thicknesses were measured in 2 dimensional mode. Pulsed wave, continuous wave and colour flow Doppler studies were used in determining flow velocities and pressures across the mitral valve, left ventricular outflow tract (LVOT), aortic valve, tricuspid and pulmonic valves. The pericardium and the Inferior vena cava were assessed from the subcostal view. A print out of all the measurements was obtained and attached to a standard reporting sheet.

4.3.4 Ankle Brachial Index

The participants were required to expose all the arms and legs. We ensured that the legs were kept warm with a blanket to avoid erroneously obtaining low readings as a result of cold-induced vasoconstriction. Systolic blood pressures were obtained using a standard analogue sphygmomanometer and BT-200 vascular Doppler machine.

All the above procedures were conducted on the same day. Participants with major abnormalities on ECG or ECHO were given a standard report to be submitted to their attending physician. Those found with severely elevated blood pressures were admitted for BP control. Health education was given to all patients found with any traditional cardiovascular risk factors in terms of lifestyle modifications, adherence to medications and regular clinic visits.

Clinical procedure

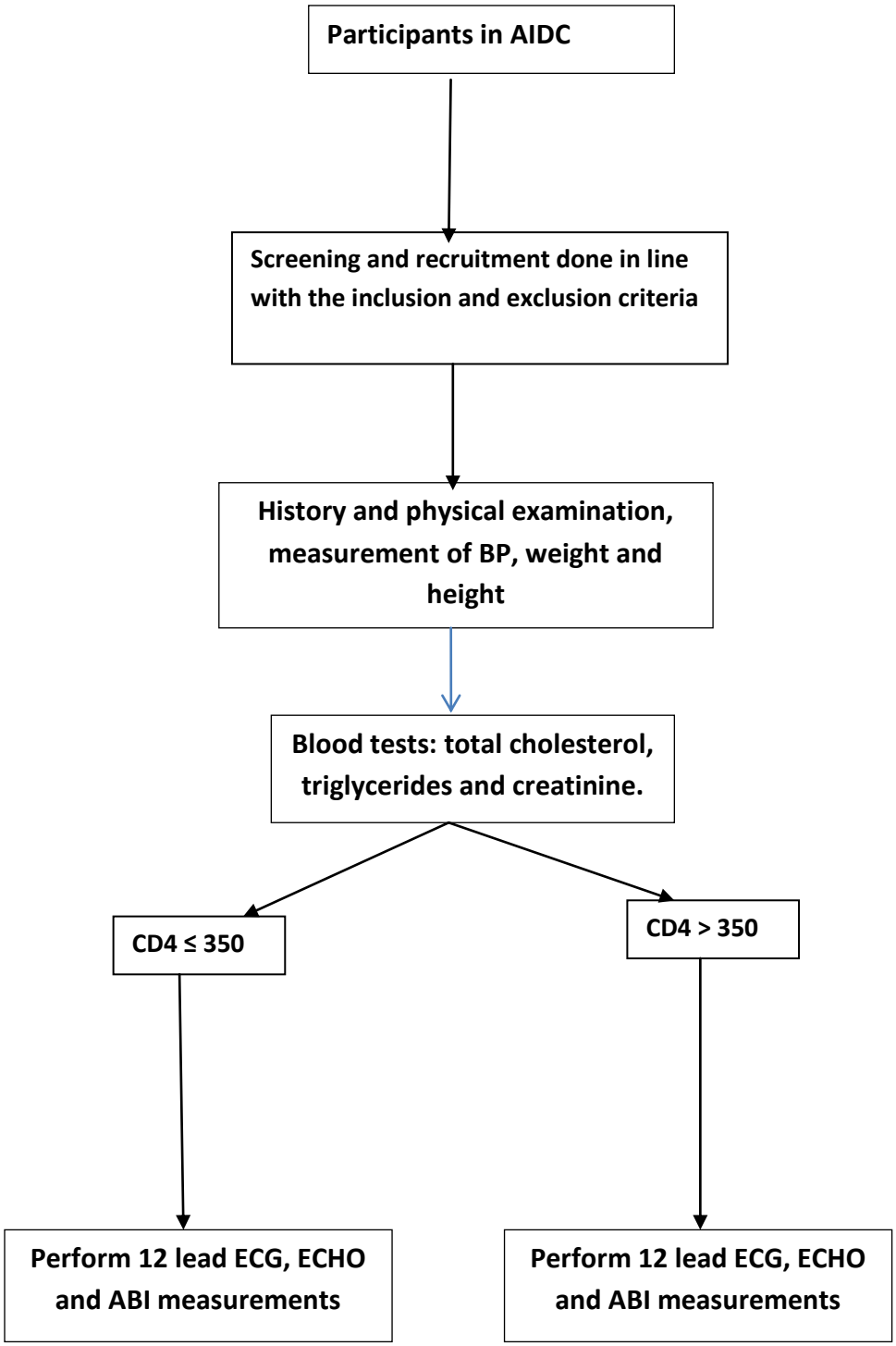


Fig 1 – clinical procedure

4.4 VARIABLES

4.4.1 Dependent variables

These were abnormalities found on ECG, ECHO and ABI

4.4.2 Independent variables

These were age, sex, duration of HIVdiagnosis, ART status, BMI, CD4 count, hypertension, diabetes, known smoker, lipid profile and creatinine clearance

Categorical variables

These included sex, ART status, HIV diagnosis>5 years, hypertension, diabetes and smoking. Some of the continuous variables were categorised and these included CD4≤350, systolic BP>140, Diastolic BP>90 and creatinine clearance<90.

Continuous variables

These included age, systolic and diastolic BP, creatinine, total cholesterol, triglycerides and CD4 count. Note that some of these where further categorised as stated above

4.5 STUDY DEFINITIONS

The following study definitions were used

4.5.1 Subclinical Cardiovascular disease – defined as any abnormality identified on ECG, ECHO or ABI, that has not been documented before and the participant shows no symptoms despite the abnormality.

4.5.2 Abnormal ECG

According to the Minnesota code for interpretation of ECG abnormalities (appendix 4), an abnormal ECG was defined by the presence of the following; left ventricular hypertrophy, arrhythmias, AV conduction defects, ventricular conduction defects, QT prolongation, ST-T changes, p wave abnormalities, abnormal Q waves and abnormal axis deviation.

4.5.3 Abnormal ECHO[48,55]

Using recommendations by the American Society of Echocardiography and European Association of cardiovascular imaging, an abnormal echo was defined by the presence of the following

- Left ventricular systolic dysfunction – ejection fraction less than 52% for males and less than 54% for females
- Left ventricular diastolic dysfunction – abnormalities in the e/a ratio, with e/a<0.8 for impaired relaxation, e/a = 0.8-1.9 for pseudonormal pattern (abnormality unmasked using the vasalva manoeuvre and e/a≥2 for restrictive pattern.

- Left ventricular dilatation (mid cavity diameter at end diastole) - ≥54mm for females and ≥60mm for males
- Left atrial dilatation (diameter) - ≥39mm in females and 40mm in males
- Right atrial dilatation (minor axis) - ≥45 mm for both sexes
- Right ventricular dilatation (basal diameter) - ≥42mm for both sexes
- Right ventricular systolic dysfunction (TAPSE) - ≤17mm for both sexes
- Abnormal Pulmonary valve acceleration time (PVAT) - <100ms
- Presence of pericardial effusion – defined as an echo-free space of >10mm.

Valvular abnormalities in terms of structure and function were defined using standard Doppler measurements.

4.5.4 Abnormal ABI

This was calculated as a ratio of the systolic BP at the ankle (dorsalis pedis artery) to the systolic BP at the arm (brachial artery). A value of <0.9 defined an abnormal ABI[49]

4.5.6 Traditional CVD risk factors[56] – Using data from the Framingham heart study, CVD risk factors were defined as presence of hypertension, diabetes, smoking, and abnormal lipids.

4.5.7 Non traditional CVD risk factors – these were defined as risk factors specific to HIV infected patients that have been shown to increase risk of future CVD events. These were: presence of kidney dysfunction, duration of HIV infection, exposure to protease inhibitors, CD4 count ≤ 350cells/ml, using data obtained from various studies.[10, 13,31,33,53]

4.6 OUTCOMES

4.6.1 Primary outcome

Evidence of subclinical cardiac disease on ECG, ECHO or ABI

4.6.2 Secondary outcomes:

1. Association between CD4 count and presence of subclinical CVD
2. Prevalence of CVD risk factors (traditional and others)
3. Commonest cardiac lesion in the study population

4.7 DATA ANALYSIS

4.7.1 Sample size calculation

Sample size was calculated using the prevalence formula

$$\mathbf{SS = Z^2 \times P \times (1 - P)/W^2}$$

SS – Sample size

Z – Z value (1.96 at 95% confidence interval)

P – Estimated frequency of CVD in HIV patients attending out-patient clinics (20%)

W – Precision of 5%

The prevalence of cardiac disease in HIV infected patients attending outpatient clinics is an estimated average of 40% based on previous work.[12] For a population survey using systematic sampling, this effect with a precision of 5% of the prevalence estimate required a sample size of **239** at 95% confidence interval using Epi-info 7.

4.7.2 Data Entry

Data from each participant was collected on a hard copy data entry sheet. Each participant was assigned a participant identification number (PIN) which was entered onto an electronic data entry excel spread sheet. No participant's names were used, to ensure confidentiality.

4.7.3 Statistics

All statistical analysis was done using Epi info version 7.

Continuous variables with a Gaussian distribution pattern were expressed as means and standard deviation. A student t-test was used to compare the means. Non-Gaussian type of data was expressed as medians and comparisons were made using the Mann-Whitney U (Kruskal Wallis) test. Categorical variables were expressed as percentages and a Chi square test was used to analyse dichotomous variables.

Cardiovascular outcomes of interest were re-defined as dichotomised categorical variables where "normal" was evaluated against other categories. To determine the association of CD4 count to cardiovascular abnormalities of interest, we dichotomised the variable as CD4≤350 and CD4>350, using data from previous studies. Other continuous variables that were dichotomised include blood pressure, creatinine clearance, total cholesterol and triglycrides. Multivariate logistic regression models were constructed to determine the association between various clinical factors (e.g. hypertension, CD4 count, HIV duration etc) with the CVD outcomes of interest (abnormal EGC, ECHO and ABI), and we used the backward elimination method to derive the final adjusted odds ratio starting with variables with the highest p values.

A p-value of less than or equal to 0.05 was considered statistically significant.

CHAPTER 5

RESULTS

From April 2014 to October 2014, 250 asymptomatic HIV infected patients were recruited into the study. Of these, 4 were excluded for absconding ECHO exam, whilst 2 refused to have an ECG done and 1 participant had woody hard Kaposi Sarcoma in the right leg. A total of 243 patients had all the data required for analysis. Of these 129(53.1%) had CD4≤ 350cells/ml (see fig 2)

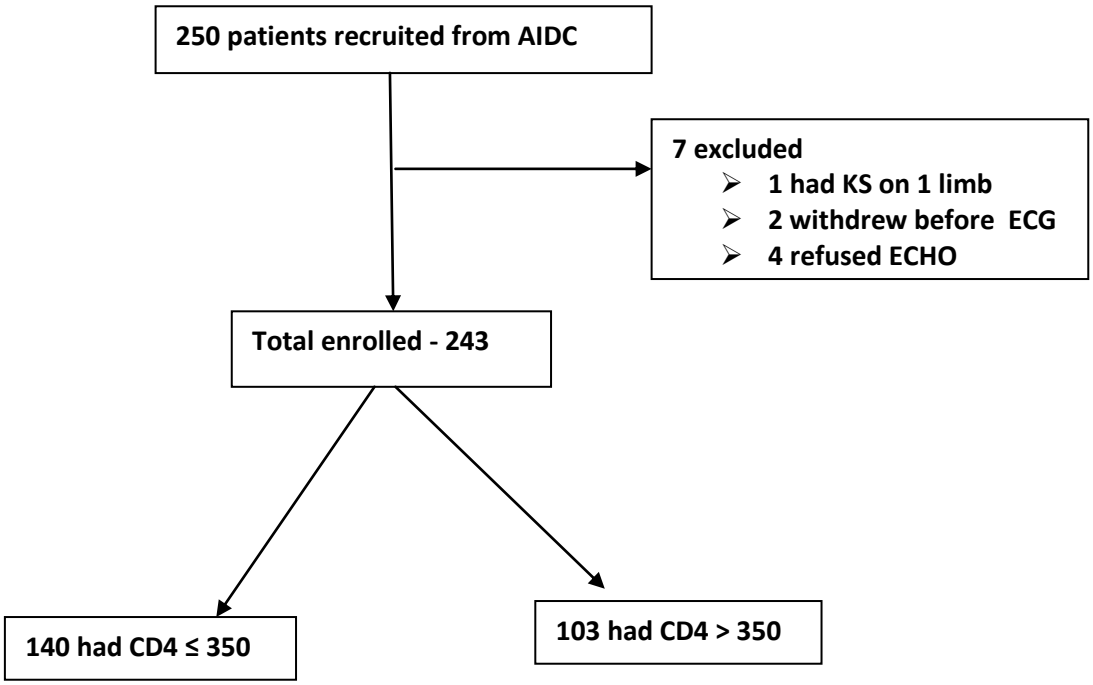


Fig 2 – study participants

5.2 Baseline characteristics of the participants

The baseline characteristics of the participants are shown in table 1. The mean age was 42 years, with age range of 18-86 years and the majority were females. The average CD4 count was 365.5cells/ml. About 90% of the participants were receiving HAART and of these, about 80% were on were on 1st line ART. Approximately 30% of the participants had HIV for longer than 5 years. On history, hypertension was the commonest traditional CVD risk factor and on clinical examination, this increased two fold for both systolic and diastolic hypertension. On the other hand smoking and diabetes were found in less than 10% of this population. The median BMI was within the normal range. About 40% of these patients exhibited laboratory evidence of kidney dysfunction (CrCl<90). Lipid derangements were also observed with more participants having abnormal triglycerides than total cholesterol.

Table 1: baseline characteristics of the participants

Characteristic	Participants n=243	Percentage
Age in years –mean (SD)	42.4	±10.60*
No. of females	143	58.53
Duration since HIV diagnosis > 5 years	80	32.92
Receiving HAART	218	89.71
Regimen: 1st Line	193	79.42
2nd line	22	9.05
3rd line	3	1.23
Diagnosed Hypertension	38	15.64
Diagnosed Diabetic	8	3.29
Current smoker	7	2.88
BMI median (IQR)	23.5	20.8-27.7**
Systolic BP median (IQR)	131	119-149
Systolic BP ≥140mmHg	84	34.57
Diastolic BP median(IQR)	83	74-93**
Diastolic BP≥90mmHg	89	36.63
CD4 count mean(SD)	355.1	±199.9*
CD4 >500	57	23.46
350 – 499	54	22.22
200 – 349	69	28.40
<200	58	23.87
Creatinine median(IQR)	75	61-90**
CrCl<90	96	39.51
CKD STAGE: Stage 1	145	59.67
Stage 2	77	31.69
Stage 3	15	6.17
Stage 4	5	2.06
Stage 5	1	0.41
Cholesterol mean (SD)	4.05	±1.17*
High cholesterol	19	7.82
Triglycerides median (IQR)	0.90	0.67-1.39**
High triglycerides	37	15.23

***standard deviation, **interquartile range*

5.3 Abnormalities on ECG

Figure 3 gives a visual representation of the distribution of various abnormalities seen on ECG in this population.

Left ventricular hypertrophy (LVH) was the commonest abnormality seen, followed by abnormal T waves. Other abnormalities included arrthythmias (atrial flutter, atrial fibrillation, Premature atrial and ventricular conduction), conduction defects (heart blocks of various degrees), bradycardia, ST –T changes, abnormal Q waves and QT prolongation.

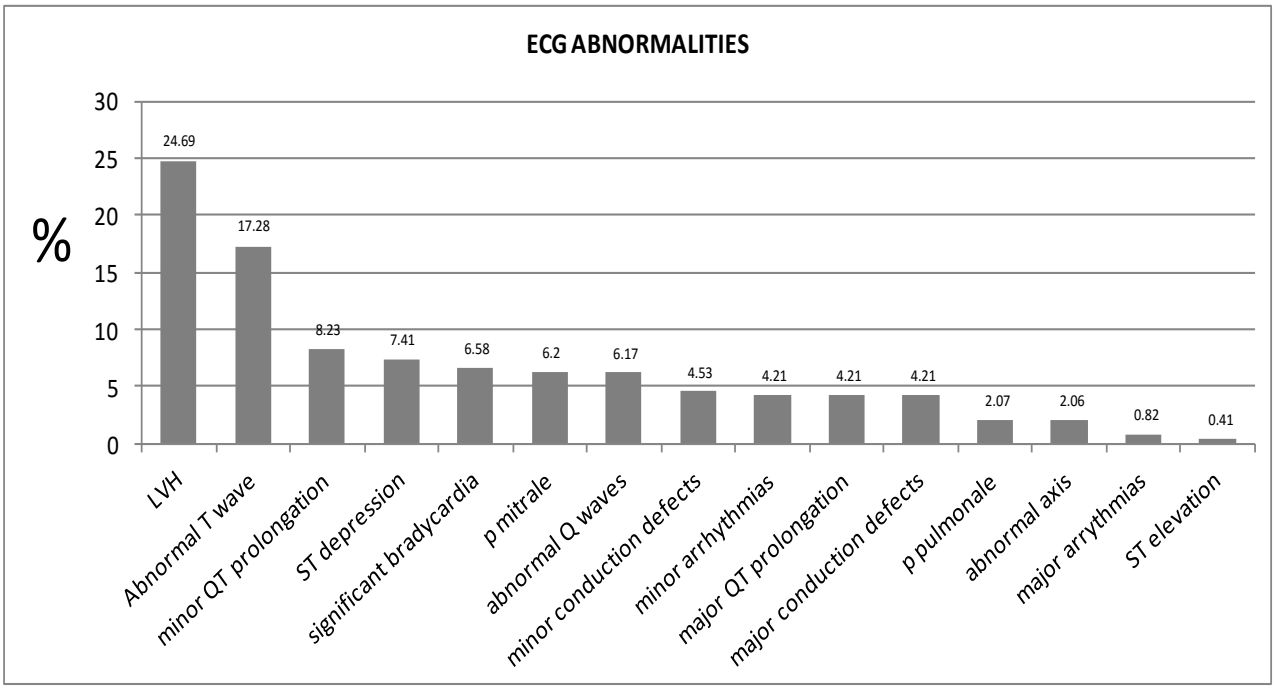


fig. 3 – abnormalities on ECG

5.3.1 ECG abnormalities and relation to CD4 count

Table 2 shows how the various ECG abnormalities related to the CD4 count. Approximately half of the participants had an abnormal ECG, with more than half having major abnormalities such as major arrhythmias (atrial flutter, atrial fibrillation), atrial and ventricular conduction defects, left ventricular hypertrophy (LVH), and major QT prolongation (annex 4).

Regarding the CD4 count, there was a significant difference in the prevalence of total ECG abnormalities between the 2 groups, with participants with CD4≤350 having a significantly higher prevalence. On the individual abnormalities only LVH and bradycardia were significant for CD4≤350. However, participants with CD4>350 had significantly higher prevalence of QT prolongation, arrhythmias and conduction defects, though the overall numbers were small. The remaining abnormalities were comparable between the two groups.

Table 2 – ECG abnormalities in relation to CD4 count

PARAMETER N (%)	Total n(%) =243(100)	CD4≤350 n=140 (57.6%)	CD4> 350 n=103(42.4%)	P value
ABNORMAL ECG	**131(53.91)**	**82 (58.57)**	**49(47.57)**	**0.045***
MAJOR ABNORMALITIES	79(32.51)	45(32.14)	34(33.01)	0.443
Major arrhythmias	2 (0.82)	1 (0.71)	1 (0.97)	0.424
Major conduction defects	5 (2.06)	1 (0.71)	4 (3.88)	0.060
Abnormal Q waves	15(6.17)	9(6.98)	6(5.26)	0.298
ST elevation	1(0.41)	1(0.78)	0(0.00)	0.531
Left ventricular hypertrophy	**60(24.69)**	**37(28.68)**	**23(20.18)**	**0.027***
Major QT prolongation (>116%)	10(4.21)	3(2.33)	7(6.14)	0.077
MINOR ABNORMALITIES	52(21.4)	43 (33.33)	19 (18.45)	0.171
Significant Bradycardia	16(6.58)	14(10.85)	2(1.78)	**0.002***
Abnormal axis	5(2.06)	2(1.55)	3(2.63)	0.442
ST Depression	18(7.41)	11(8.53)	7(6.14)	0.186
Minor arrhythmias	**10 (4.21)**	**3 (2.41)**	**7 (6.80)**	**0.043***
Minor conduction defects	**11 (4.53)**	**3 (2.14)**	**7 (7.77)**	**0.023***
Abnormal T wave	42(17.28)	23(17.83)	19(16.67)	0.407
Minor QT prolongation (>112%)	20(8.23)	7(5.43)	13(11.40)	**0.049***
P mitrale	15(6.20)	11(7.86)	4(3.92)	0.112
P pulmonale	5(2.07)	3(2.33)	2(1.77)	0.562

***statistically significant

Figure 4 gives a visual representation of the different ECG abnormalities between the two categories of participants.

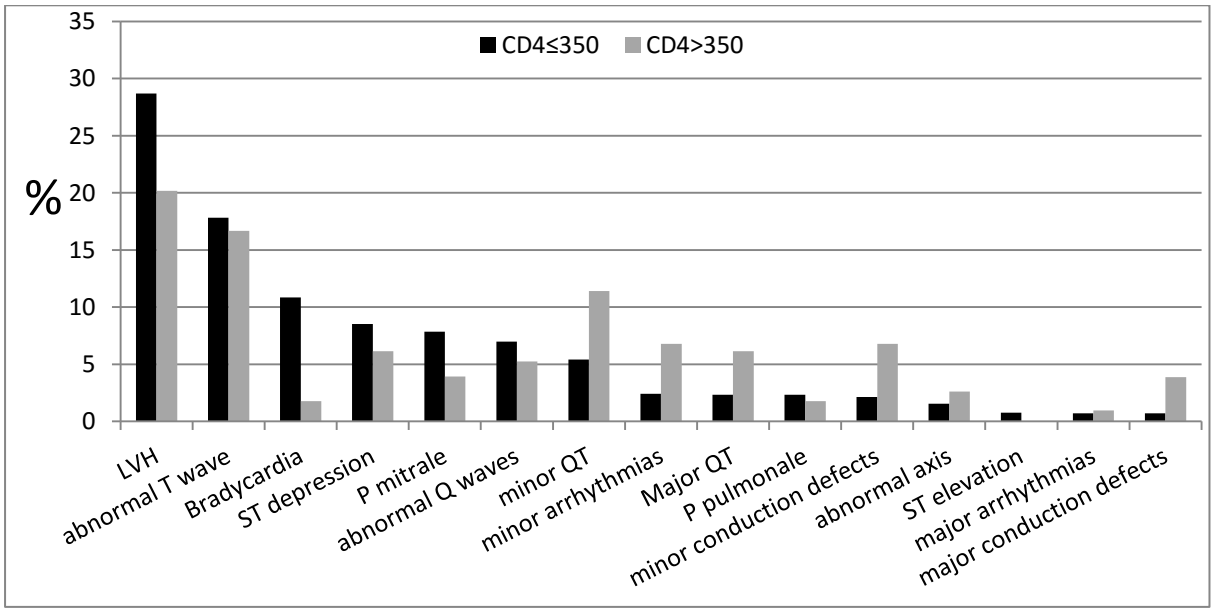


Fig. 4 – ECG abnormalities in relation to CD4 count

5.4 ABNORMALITIES ON ECHO

The distribution of ECHO abnormalities is depicted in figure 5. Once again, left ventricular hypertrophy (LVH) was the commonest ECHO abnormality in this population, followed by left ventricular diastolic dysfunction. Left ventricular systolic function was not so common.

Valvular abnormalities observed in this population were mainly functional in nature, meaning overall valvular anatomy was normal. Right ventricular failure, pulmonary hypertension and pericardial effusion were observed in less than 5% of the participants.

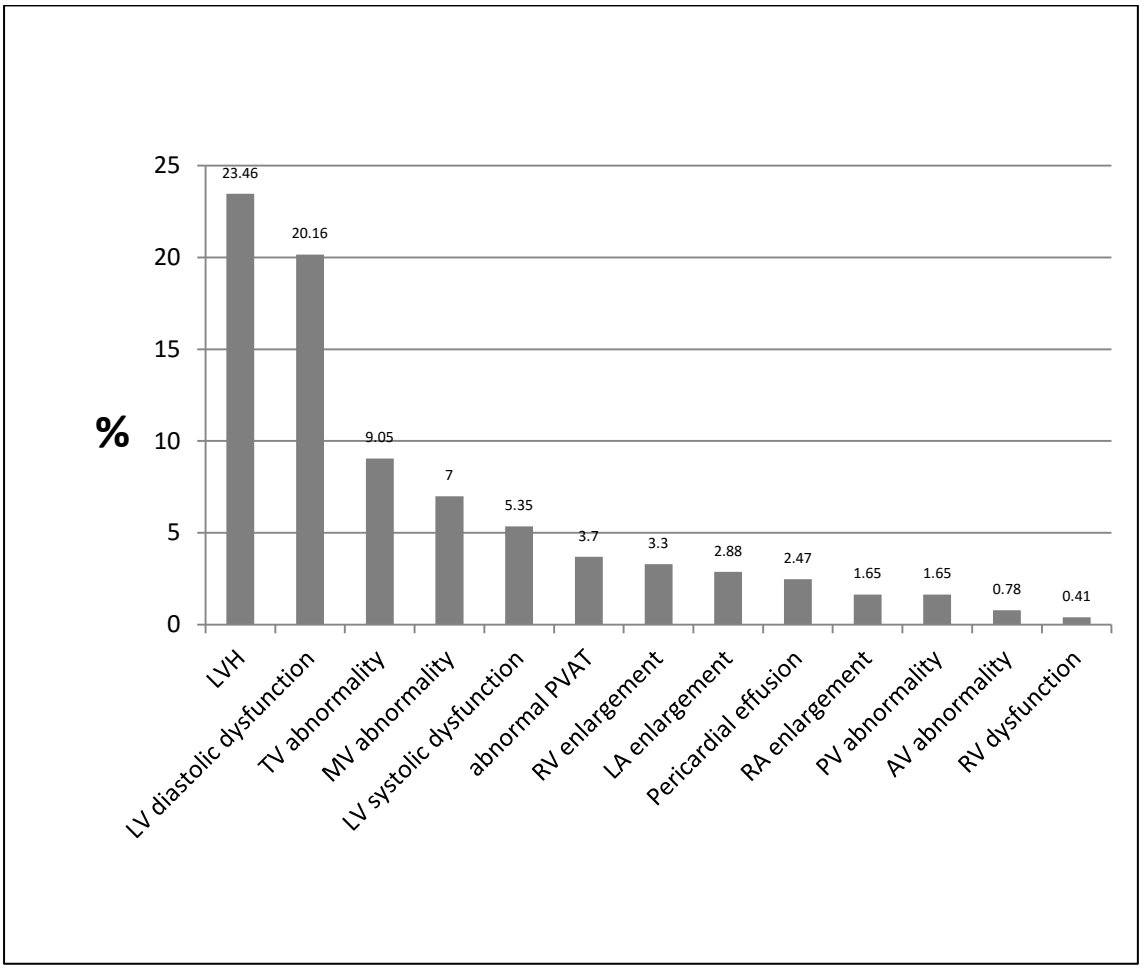


Fig.5 – abnormalities on ECHO

5.4.1- ECHO abnormalities and relation to the CD4 count

Table 3 depicts the various abnormalities seen on echo in relation to the CD4 count. An abnormal ECHO was present in about 45% of the participants, and showed no significant association with CD4≤350 count. However, on the individual abnormalities, participants with CD4 counts ≤350cells/ml had significantly higher prevalence of left ventricular hypertrophy compared to their counterparts. The rest of the parameters were comparable between the two groups.

Table 3 – ECHO abnormalities

PARAMETER	Total n=243	CD4≤350 n=140 (57.6%)	CD4> 350 n=103(42.4%)	P value
Abnormal ECHO	108(44.44)	57(44.19)	51(44.74)	0.465
LV systolic dysfunction	13(5.35)	8(6.20)	5(4.39)	0.275
LV diastolic dysfunction	49(20.16)	22(17.05)	27(23.68)	0.102
LVH	**57(23.46)**	**36(27.91)**	**21(18.42)**	**0.042***
LA enlargement	7(2.88)	3(2.33)	4(3.51)	0.308
RA enlargement	4(1.65)	2(1.55)	2(1.75)	0.268
RV enlargement	8(3.290	3(2.33)	5(4.39)	0.641
RV dysfunction	1(0.41)	1(0.88)	0(0.00)	0.470
MV abnormality	17(7.00)	11(8.53)	6(5.26)	0.167
AV abnormality	3(1.23)	1(0.78)	2(1.75)	0.278
TV abnormality	22(9.05)	15(11.63)	7(6.14)	0.070
PV abnormalities	4(1.65)	3(2.33)	19(9.88)	0.359
Abnormal PVAT	9(3.70)	5(3.88)	4(3.51)	0.446
Pericardial effusion	6(2.47)	3(2.33)	3(2.63)	0.442

***Statistically significant**

Figure 6 is a visual representation of ECHO abnormalities in relation to the CD4 count.

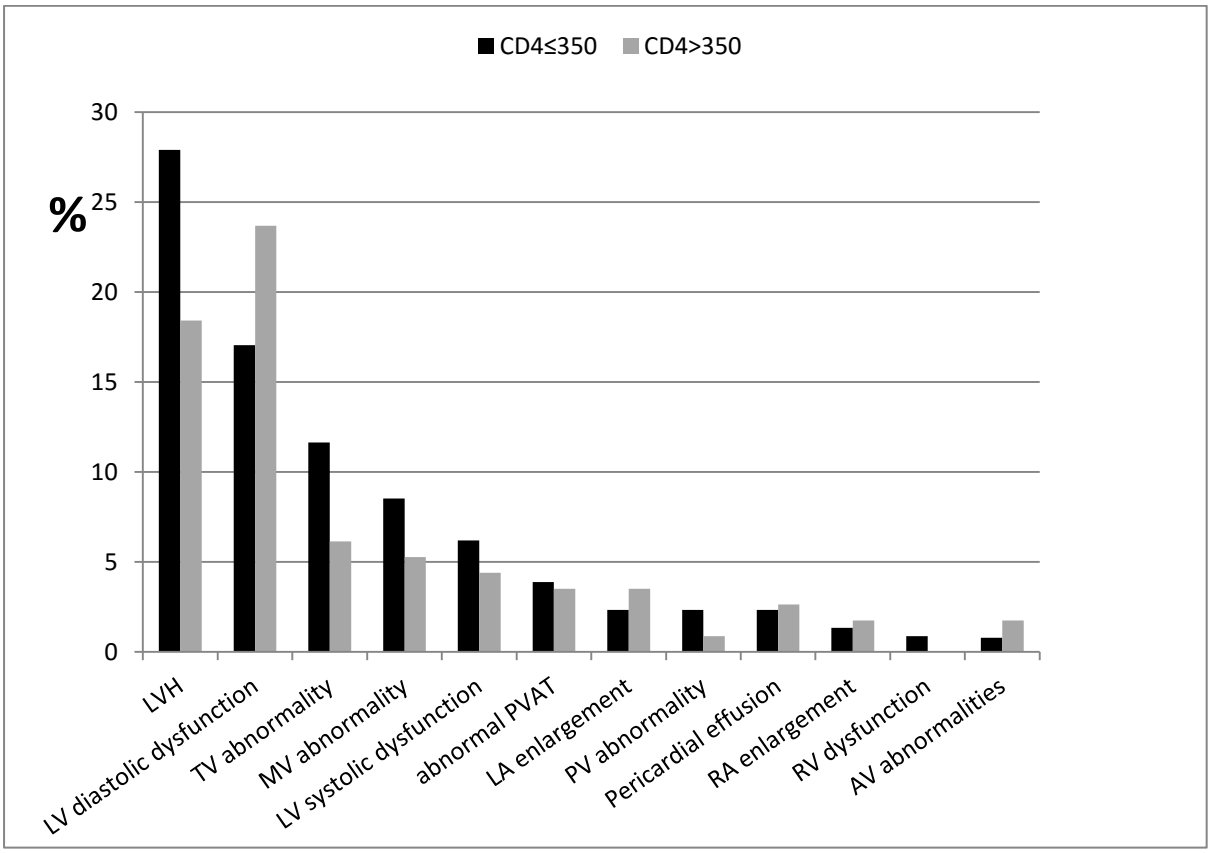


fig.6 – ECHO abnormalities and CD4 count

5.5 Abnormal ABI

Peripheral artery disease as defined by the presence of an abnormal ABI was present in a quarter of the participants (table 4). The majority of those affected showed unilateral limb involvement.

However, in relation to the CD4 count, participants with low CD4 counts had a significantly higher prevalence of peripheral artery disease and had more bilateral limb involvement compared with their counterparts with higher CD4 counts.

Table 4 – Abnormal ABI in relation to CD4 count

PARAMETER	Total n(%)=243(100)	CD4≤350 n=140 (57.6%)	CD4> 350 n=103(42.4%)	P value
Abnormal ABI	49(20.16)	31(24.03)	18(15.79)	0.043*
Limb involvement				
Unilateral	33(13.58)	16(12.40)	17(14.91)	0.287
Bilateral	17(7.00)	15(11.63)	2(1.75)	0.001*

*statistically significant

5.6 Clinical correlates of subclinical CVD on logistic regression

On multivariate logistic regression, clinical factors significantly associated with an increased risk of abnormalities on ECG, ECHO and ABI are shown in table 4.

On ABI, the only clinical factor shown to be predictive of peripheral artery disease was a CD4≤350, which showed a 2 fold increase in risk. On ECG, systolic BP>140 and CD4≤350, doubled the risk of having an abnormality, after adjusting for the other clinical factors known to predict subclinical CVD. On ECHO, only systolic BP>140mmHg was significant for increasing the risk of having an abnormal ECHO.

Diabetes, tobacco smoking and abnormal lipids which are the other known traditional CVD risk factors did not show any association with abnormal findings on ECG, ECHO and ABI.

The other non traditional CVD risk factors particularly applied to HIV infected patients such as duration of HIV infection, exposure to protease inhibitors, creatinine clearance<90, also did not show any association in this population.

Table 5– clinical correlates of subclinical CVD

	PARAMETER	Crude O.R	C.I	Adjusted O.R	C.I
ABNORMAL ABI	CD4 ≤350cells/ml	**2.20**	**1.12 – 4.34$^{\alpha}$**	**2.18**	**1.09 – 4.33$^{\alpha}$**
	Systolic BP≥140	1.67	0.88 - 3.13	2.00	0.87 - 4.50
	Diastolic BP≥ 90	1.08	0.57 - 2.05	0.70	0.81 - 1.55
	Smoker	1.57	0.29 - 8.34	1.61	0.27 - 9.95
	Diabetic	0.54	0.54 - 4.51	0.45	0.17 - 4.51
	Abnormal lipids	1.19	0.56 – 2.54	1.08	0.51 – 2.40
	HIV diagnosis ≥5yrs	1.06	0.55 - 2.05	0.91	0.45 - 1.93
	Exposure to PIs	1.02	0.36 - 2.87	0.94	0.48 - 2.93
	CrCl <90	1.72	0.92 - 3.22	1.69	0.59 - 3.36
ABNORMAL ECG	CD4≤350cells/ml	**1.72**	**1.02 – 2.90$^{\alpha}$**	**1.84**	**1.07 – 3.10$^{\alpha}$**
	Systolic BP≥140	**2.09**	**1.18 - 3.70$^{\alpha}$**	**2.12**	**1.19 – 3.78$^{\alpha}$**
	Diastolic BP≥ 90	**1.87**	**1.07 - 3.26$^{\alpha}$**	1.55	0.71 - 2.95
	Smoker	1.57	0.30 - 8.28	1.57	0.17 - 9.11
	Diabetic	1.04	0.24 - 4.43	0.92	0.23 - 4.82
	Abnormal lipids	0.93	0.49 – 1.79	0.89	0.41 – 1.68
	HIV diagnosis ≥5yrs	0.90	0.52 - 1.55	0.85	0.45 - 1.61
	Exposure to PIs	0.85	0.36 - 2.01	1.21	0.48 - 3.04
	CrCl <90	1.23	0.72 - 2.08	1.07	0.87 - 1.92
ABNORMAL ECHO	CD4≤350 cells/ml	0.86	0.51 – 1.43	0.86	0.50 – 1.47
	Systolic BP≥140	**2.77**	**1.60 – 4.78$^{\alpha}$**	**1.47**	**1.47 - 5.75$^{\alpha}$**
	Diastolic BP≥ 90	**1.83**	**1.08 – 3.10**	0.54	0.54 - 1.88
	Smoker	0.49	0.09 – 2.50	0.12	0.12 - 3.74
	Abnormal lipids	1.07	0.57 – 2.02	0.91	0.45 – 1.99
	HIV diagnosis ≥5yrs	0.90	0.52 - 1.55	0.85	0.45 - 1.61
	Exposure to PIs	0.85	0.36 - 2.01	1.21	0.48 - 3.04
	CrCl <90	1.23	0.72 - 2.08	1.07	0.87 - 1.92

$^{\alpha}$Statistically significant

CHAPTER 7

DISCUSSION

This study examined the prevalence of subclinical CVD among healthy HIV infected individuals attending their routine out-patient clinic reviews. It also examined the relationship between CD4 count and the prevalence of subclinical CVD. The study population was relatively young with a mean age of 42 years and was mainly composed of female participants. Subclinical CVD was highly prevalent, a finding comparable to many studies done across Africa.[12]

The prevalence of ECG abnormalities was comparable to other major studies (53.91% vs. 51.5%); however, our population showed a fourfold higher prevalence of major abnormalities (29% vs. 7.7%).[47] Studies have found that the presence of major abnormalities on ECG has been associated with an increased risk of incident heart failure[47]. In this study, the major abnormalities found were left ventricular hypertrophy, complete left and right bundle branch blocks, atrial flutter/fibrillation, major QT prolongation and high grades of heart block (2^{nd} and 3^{rd} degree). The high prevalence of hypertension in this population may explain most of the ECG abnormalities especially left ventricular hypertrophy. Systolic arterial hypertension has been associated with development of pathological left ventricular hypertrophy, which may result into ventricular arrhythmias and sudden cardiac death[57]

However, this study also showed an association between CD4≤350 with significantly higher prevalence of ECG abnormalities despite the high prevalence of hypertension. Many factors may be attributed to this; evidence suggests that lower CD4 cell counts are associated with elevated levels of serum inflammatory markers and increased levels of activated CD4 T cells. This inflammatory cascade eventually leads to various forms of vascular damage and in turn causes small areas of myocardial damage.[54] As a result; many electrical abnormalities are prone to occur on ECG, independent of the usual clinical factors such as hypertension. In our study, this has been demonstrated on logistical regression where a CD4≤350 remains significant for ECG abnormalities even after adjusting for the other clinical factors.

This data therefore suggests that ECG can be used as an important tool for predicting subclinical CVD, especially in hypertensive patients with low CD4 counts, as part of their routine care.

ECHO abnormalities where found in 44.44% of our study participants; this finding was comparable to studies conducted across Africa (14 – 55%).[12] The high prevalence of left ventricular hypertrophy and left ventricular diastolic dysfunction were particularly notable. These have been associated with and increased risk of future cardiovascular events by five fold, in the general population.[49] Hypertension may be responsible for these abnormalities.

Pulmonary hypertension and pericardial effusion were not as prevalent as observed in other studies across Africa, despite the high prevalence to tuberculosis, and other HIV associated pulmonary opportunistic infections in Zambia.[58] Uncontrolled HIV infection has also been associated with direct HIV infection of the cardiac myosites, leading to the development of

HIV associated dilated cardiomyopathy (DCM), which is said to progress rapidly to death within 100 days of diagnosis.[21] However in this population, no patient had DCM, except for a few found with left ventricular systolic dysfunction. A low CD4 count did not show an association with increased prevalence echo abnormalities in this population.

ECHO is an important tool for assessing both cardiac structure and function. However, due to its non availability in most hospitals in the country and requirement of particular expertise, using it as a screening tool might be a challenge, notwithstanding the cost implications. As such, only those HIV patients found to have several CVD risk factors, low CD4 counts and major changes on ECG may benefit from a baseline ECHO study.

Peripheral artery disease has been shown to be associated with future incident cardiovascular events particularly ischemic strokes and myocardial infarction.[50, 51] This condition can be screened for using Ankle Brachial Index (ABI). Our study population showed a similar prevalence of abnormal ABI as other major studies (20.1% vs. 19%).[52] In addition, a CD4≤350, was associated with a 2 fold increase in risk. This may be explained as follows; normally, activated CD4 T cells are found frequently in atherosclerotic plaques of patients in the general population. However, the chronic inflammation that accompanies uncontrolled or more advanced HIV disease consists of many of the same inflammatory cells and pro-inflammatory cytokines that destabilize atherosclerotic plaques. In addition, the chemokine receptor CCR5 on the HIV is immunogenic and resides in the intima and media of arteries. It is said to trigger an inflammatory cascade that results in plaque rupture and coronary artery thrombosis by directing monocytes and recruiting T cells to these arteries.[54, 59, 60] Therefore uncontrolled HIV infection is a risk factor for accelerated atherosclerosis. Studies have shown that an ABI<0.9 is associated with stenosis of ≥50% of the affected artery, it is also a marker of systemic atherosclerosis, which predisposes to future coronary artery disease events and ischemic strokes.[52]

ABI is a cheap tool that has been validated by many population studies; [52] it can be easily administered by caregivers at a primary health care level with minimal expertise. As such, all HIV positive patients especially those with CD4≤350 would benefit from a routine measurement of the ABI.

According to the Framingham heart study of 1961, traditional CVD risk factors are hypertension, diabetes, high cholesterol and smoking; these have been associated with increased risk of future CVD events.[54] In our study population, the commonest traditional CVD risk factor was hypertension, and this value increased two fold during physical examination, meaning most of these participants had undiagnosed hypertension. Furthermore, hypertension was the only traditional CVD risk factor which showed a significant association with abnormalities on all the three screening tools used in this study, the other risk factors, in particular, diabetes and tobacco smoking did not. This may however be explained by the low prevalence of these conditions in our study participants. This finding is important in that it draws attention to hypertension as being the most important traditional CVD risk factor in this population, and that more effort needs to be made to screen for it and treat it at every opportunity.

Other non- traditional CVD risk factors among HIV infected patients known to increase risk of CVD as demonstrated by various studies include duration of HIV infection[40], exposure to protease inhibitors[41], kidney disease[53] and low CD4 count[43,54]. In our population, a low CD4 count (≤350cells/ml) was associated with a 2 fold risk of having an abnormal ABI and ECG. The other clinical factors did not show such an association.

7.1 STUDY LIMITATIONS

This was a single centre study, therefore findings cannot be generalised to the entire Zambian HIV population. We were also unable to do viral load test to compare with CD4 counts and how this would relate to subclinical CVD. Most of our blood tests were limited to routine tests done on all HIV patients attending clinic, we were unable to do more specific tests which are biomarkers of heart disease such as d-dimer, C-reactive protein, or test for the presence of opportunistic infections associated with heart disease. All these were due to budgetary constraints.

We did not have a suitable HIV seronegative control group, but however we found higher than expected prevalence rates for subclinical CVD in HIV infected people, compared with general population data.[12]

CHAPTER 8

8.0 CONCLUSION

Subclinical CVD is quite common among clinically healthy HIV infected patients attending their regular out-patient clinic visits at UTH. All 3 tools of measurement used in this study have been able to detect significant numbers of subclinical disease, with ECG showing the highest prevalence. Of the traditional CVD risk factors, hypertension is the most common, while diabetes and smoking have low prevalence. On the non traditional CVD risk factors, CD4≤350 is the most important risk factor in this population.

8.1 RECOMMENDATIONS

In view of the high prevalence of subclinical CVD in this relatively healthy HIV infected population, we make the following recommendations

- Screening for and treatment of hypertension must be conducted at each clinic visit.
- To perform ABI measurements on all patients coming for their first enrollement and on all those with CD4≤350 and BP >140/90mmHg even if they are on treatment. ABI measurement is very simple tool and can be done by primary health care workers at no cost to the patient.
- All patients with CD4≤350 and BP>140/90 should undergo a baseline ECG if available
- All patients with abnormal ECG especially major abnormalities such as left ventricular hypertrophy, major QT prolongation, Q waves, major arrhythmias (complete bundle branch blocks, 2^{nd} and 3^{rd} degree heart blocks, atrial flutter/fibrillation) must undergo a routine baseline ECHO.
- To evaluate the cost effectiveness of using ECG, ECHO and ABI as screening tools for CVD across Zambia.
- A long term study needs to be conducted to determine the outcomes of patients with these various abnormalities.

REFERENCES

1. UNAIDS Report on the Global AIDS Epidemic 2010, *ISBN 978-92-9173-871-7 (accessed 24/05/2014)*
2. http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp. *(accessed 24/05/2014)*
3. http://www.usaid.gov/our_work/global_health/aids/Countries/africa/zambia.html
4. UNAIDS. http://www.unaids.org/en/HIV_Data/2006GlobalReport/default.asp
5. Beaglehole R, Yach D. Globalisation and the Prevention and Control of Non-Communicable Disease: The Neglected Chronic Diseases of Adults. *Lancet. 2003; 362:903–8.*
6. Anthony Mbewu and Jean-Claude Mbanya, Disease and Mortality in Sub-Saharan Africa. 2nd edition. World bank, 2006
7. http://www.who.int/cardiovascular_diseases/en/ *(accessed 10/3/2014)*
8. http://www.ichealth.org *(accessed 10/3/2014)*
9. Cohen IS, Anderson DW, Virmani R, et al. Congestive cardiomyopathy in association with the acquired immunodeficiency syndrome. *NEJM, 1986; 315: 628–630*
10. Rerkpattanapipat P, Wongpraparut N, Jacobs LE, Kotler MN. Cardiac manifestations of acquired immunodeficiency syndrome. *Arch Intern Med 2000; 160: 602–608.*
11. Levy WS, Simon GL, Rios JC, Ross AM. Prevalence of cardiac abnormalities in human immunodeficiency virus infection. *Am J Cardiol 1989; 63: 86–89*
12. Magula N.P, Mayosi BM, Cardiac involvement in HIV-infected people living in Africa: a review. *Cardiovasc J S Afr. 2003 Sep-Oct*
13. Pugliese A, Isnardi D, Saini A, et al. Impact of highly active antiretroviral therapy in HIV-positive patients with cardiac involvement. *J Infect. 2000; 40: 282–284.*
14. http://www.zambiahivguide.org (accessed 16/12/2014)
15. Gerard P Aurigemma, John S Gottdiener, Lynn Shemanski. Value of systolic and diastolic function for incident congestive heart failure in the elderly: The Cardiovascular Health study.*J Am CollCardiol. 2001; 37(4):1042-1048.*
16. Rerkpattanapipat P, Wongpraparut N, Jacobs LE, Kotler MN. Cardiac manifestations of acquired immunodeficiency syndrome. *Arch Intern Med 2000; 160: 602–608*
17. Barbaro G, Lipshultz S.E Cardiovascular manifestations of HIV infection. *Circulation 2002; 106: 1420–1425.*
18. Barbaro G, Lipshultz SE. Pathogenesis of HIV-associated cardiomyopathy. *Ann N Y AcadSci 2001; 946: 57–81.*
19. Chariot P, Perchet H, Monnet I,et al. Dilated cardiomyopathy in HIV-infected patients. *NEJM 1999; 340: 732–735.*
20. Hoffman MA, Lipshultz SE, Miller TL. Malnutrition and cardiac abnormalities in the HIV-infected patient. In: Miller TL, GorbachSL,eds. Nutritional Aspects of HIV Infection. *New York: Arnold, 1999:133–139.*
21. Currie PF, Jacob AJ, Foreman AR, Et al. Heart muscle disease related to HIV infection: prognostic implications. *BMJ 1994; 309: 1605–1607.*

22. Heidenreich PA, Eisenberg MJ, Kee LL, et al. Pericardial effusion in AIDS: incidence and survival. *Circulation 1995; 92: 3229–3234*

23. Eisenberg MJ, Gordon AS, Schiller NB. HIV-associated pericardial effusions.*Chest 1992; 102: 956–958.*

24. Moreno R, Villacastin JP, Bueno H, et al. Clinical and echocardiographic findings in HIV patients with pericardial effusion. *Cardiology 1997; 88: 397–400.*

25. Rerkpattanapipat P, Wongpraparut N, Jacobs LE, Kotler MN. Cardiac manifestations of acquired immunodeficiency syndrome. *Arch InternMed 2000; 160: 602–608.*

26. T. AU Maher D, Harries AD, Tuberculous pericardial effusion: a prospective clinical study in a low-resource setting--Blantyre, Malawi, *Int J Tuberc Lung Dis. 1997;1(4):358.*

27. Dronda F, Suzacq C, Pericardial tuberculosis complicated with heart tamponade as presentation form of acquired immunodeficiency syndrome, *Rev Clin Esp. 1997;197(7):502.*

28. Nogueira G, Macedo AJ, Paixão A, Nunes MA et al, Cardiovascular morbidity in children with human immunodeficiency virus infection, *Acta Med Port. 1998;11(12):1051.*

29. SáI, Môço R, Cabral S, Reis AH, Pereira LS et al, Constrictive pericarditis of tuberculous etiology in the HIV-positive patient: case report and review of the literature. *Rev Port Cardiol. 2006;25(11):1029.*

30. Sudano I, Spieker LE, Noll G, Corti R et al, Cardiovascular disease in HIV infection, *Am Heart J. 2006;151(6):1147.*

31. Reinsch, N, Buhr, C, Krings, P, et al. Effect of gender and highly active antiretroviral therapy on HIV-related pulmonary arterial hypertension: results of the HIV-HEART Study. *HIV Med 2008 Jn 16*

32. Sitbon O, Lascoux-Combe C, Delfraissy JF et al, Prevalence of HIV-related pulmonary arterial hypertension in the current antiretroviral therapy era. *Am J RespirCrit Care Med. 2008;177(1):108.*

33. Silva-Cardoso J, Moura B, Ferreira A et al, Predictors of myocardial dysfunction in human immunodeficiency virus-infected patients. *J Card Fail. 1998;4(1):19.*

34. Kanmogne GD, Primeaux C, Grammas P, Induction of apoptosis and endothelin-1 secretion in primary human lung endothelial cells by HIV-1 gp120 proteins. *BiochemBiophys Res Commun. 2005;333(4):1107.*

35. .Limsukon A, Saeed AI, Ramasamy V, Nalamati J, HIV-related pulmonary hypertension Dhuper S. *Mt.Sinai J Med. 2006;73(7):1037*

36. http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/20121120_UNAIDS_Global_Report_2012_with_annexes_en.pdf *(accessed 13/05/2015)*

37. Barbaro G, Fisher SD, Lipshultz SE. Pathogenesis of HIV-associated cardiovascular complications. *Lancet Infect Dis. 2001; 1: 115–124.*

38. Barbaro G. Current Perspective, Cardiovascular Manifestations of HIV Infection, Affiliations *From the Department of Medical Pathophysiology, University "La Sapienza," Rome, Italy*

39. Daniel Periard et al, High Prevalence of Peripheral Arterial Disease in HIV-Infected Persons for the Swiss HIV Cohort Study Angiology and Infectious Diseases Services, University Hospital, and Swiss HIV Cohort Study Data Center, Lausanne, and Hospital Cantonal,Fribourg, Switzerland
40. Birgitt Dau and Mark Holodniy. The Relationship Between HIV Infection and Cardiovascular Disease, *CurrCardiol Rev. 2008 August; 4(3): 203–218.*
41. Pugliese A, Isnardi D, Saini A, et al. Impact of highly active antiretroviral therapy in HIV-positive patients with cardiac involvement. *J Infect. 2000; 40: 282–284.*
42. Canalejo E, Cabello N, Perales I, Allodi S, Sánchez-Purificación A, Asymptomatic peripheral arterial disease detected by the ankle-brachial index in HIV-infected patients: prevalence and associated risk factors, *Enferm Infecc Microbiol Clin. 2011 Nov; 29(9):672-8.*
43. Mehta NJ, Khan IA. HIV-associated coronary artery disease, Angiology. 2003 May-Jun;54(3):269-75. Division of Cardiology, Department of Medicine, Creighton University School of Medicine, Omaha, NE, USA
44. Periard D, Cavassini M, TafféP, Chevalley M et al, High prevalence of peripheral arterial disease in HIV-infected persons, Swiss HIV Cohort Study. *Clin Infect Dis. 2008; 46(5):761.*
45. Ronald J. Prineas, Richard S. Crow, Zhu-Ming Zhang, The Minnesota Code Manual of Electrocardiographic Findings, *2nd ed, 2010, Springer*
46. Journal of the American Society of Echocardiology, 2005.
47. Elsayed Z Soliman, Ronald J Prineas et al, Prevalence and Prognostic Significance of ECG Abnormalities in HIV-infected Patients: Results from the Strategies for Management of Antiretroviral Therapy (SMART) Study, *J Electrocardiol. 2011 November ; 44(6): 779–785*
48. Kristin E. Mondy,1,2 John Gottdiener, High Prevalence of Echocardiographic Abnormalities among HIV-infected Persons in the Era of Highly Active Antiretroviral Therapy, *Clinical Infectious Diseases 2011;52(3):378–386*
49. Gradman AH, Alfayomi. F. From left ventricular hypertrophy to congestive heart failure: management of hypertensive heart disease. *Prog Cardiovasc Dis. 2006 Mar-Apr; 48(5):326-41.*
50. Inqlis SC, Hermis A. Peripheral arterial disease and chronic heart failure: a dangerous mix. *Heart Fail Rev. 2013 Jul;18(4):457-6*
51. Michael H. Criqui, Robyn L. McClelland, The Ankle-Brachial Index and Incident Cardiovascular Events in the MESA (Multi-Ethnic Study of Atherosclerosis), *Journal of the American College of Cardiology, 2010. 04.060*
52. Julián Olalla*1, Daniel Salas, Ankle-brachial index in HIV infection, *AIDS Research and Therapy* 2009. *1742-6405-6-6*
53. Mark J. Sarnak, Cochair; Andrew S. Levey, Kidney Disease as a Risk Factor for Development of Cardiovascular Disease, A Statement From the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention, journal of Circulation, *CIR.0000095676.90936.80*

54. Kenneth A. Lichtenstein,1 Carl Armon, Low CD4+ T Cell Count Is a Risk Factor for Cardiovascular Disease Events in the HIV Outpatient Study, *Clinical Infectious Diseases 2010; 51(4):435–447*

55. Roberto M. Lang, Luigi P. Badano, Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging, Journal of the American Society of Echocardiography January 2015 (update from 2005 guidelines).

56. https://www.framinghamheartstudy.org/risk-functions/cardiovascular-disease/10-year-risk.php *(accesses 13/5/2015)*

57. W. Todd Cade, PT, PhD. HIV- and HAART-related left ventricular dysfunction in persons infected with HIV. *J Cardiometab Syndr. 2008;3:83–87.*

58. Mateyo J.K. Aetiology and presentation of pulmonary disease in severely immuno-suppressed HIV-infected patients at the University Teaching Hospital, Lusaka, Zambia, 2012

59. Chris T. Longenecker and Virginia A. Triant. Initiation of Antiretroviral Therapy at High CD4 Counts: Does it reduce the Risk of Cardiovascular Disease? *Curr Opin HIV AIDS. 2014 January; 9(1): 54–62.*

60. Post W.S, Budoff M, Kingsley L. Associations between HIV Infection and Subclinical Coronary Atherosclerosis: The Multicenter AIDS Cohort Study (MACS). *Ann Intern Med. 2014 April 1; 160(7): 458–467*

APPENDICES

Annex 1

PARTICIPANT INFORMATION SHEET

SPECTRUM OF SUB-CLINICAL CARDIOVASCULAR DISEASE AMONG HIV INFECTED PATIENTS PRESENTING TO UNIVERSITY TEACHING HOSPITAL IN LUSAKA

Introduction

I, Lorrita Kabwe, an MMED student in Internal Medicine of the School of Medicine at the University of Zambia, kindly ask for your participation in the above study. The purpose of the study is in partial fulfilment of the requirements for the award of a Master of Medicine in Internal Medicine. Before you decide whether to participate in the study or not, I would like to explain to you the purpose of the study and what is expected of you. If you agree to take part, you will be asked to sign this consent form in the presence of a witness.

Purpose of the study

This study is being conducted to determine the presence of undetected heart disease among HIV infected patients presenting to the Adult Infectious Diseases Centre (AIDC) in UTH. This is important because it will help us identify patients at risk of developing serious cardiac conditions and to help in putting in prevention measures.

Study procedure

If you agree to participate in this study, we will put your information on a data entry sheet; your name will not be included. We will ask for information regarding the history of your illness, then perform a physical examination that will include checking your blood pressure, pulse, weight and a general physical exam, in strict privacy. Some blood samples will be drawn which will be sent to the laboratory for various tests. You will then be asked to undergo other tests, namely; Electrocardiography (ECG), Echocardiography (ECHO) and Ankle Brachial index.

Risks and discomforts

You will not be exposed to any risks when participation in this study. However, you will experience discomfort from a needle prick during drawing of the blood samples. You may also feel some discomfort during the ECHO test as you may be required to lie down for up to 30 minutes. Be assured that these tests are very safe with no risk of radiation exposure.

Benefits

This study will help us identify various forms of heart diseases in their early stages and thereby give us information that will help set up measures to prevent these diseases from progressing into more serious form.

Confidentiality

All information will be kept strictly confidential. Your name will not be used, but you will be given a study number. Therefore any data obtained will not be traced back to you.

Consent

Participation in this study will be voluntary, with no expectation of payment. Should you decide to withdraw from the study for any reason, you will not suffer any consequences.

Thank you for considering participating in this study. For any questions or concerns, please feel free to contact Dr. Lorrita Kabwe or the ERES Converge IRB office on the following addresses;

Dr Lorrita Kabwe,
University Teaching Hospital,
Department of Internal Medicine,
P/Bag RW1X,
Lusaka,
Zambia.
Cell: +260 979 523309

ERES Converge IRB office
33 Joseph Mwilwa Road
Rhodes Park
Lusaka
Zambia
Email to eresconverge@yahoo.co.uk
Phone +260 955 155633
+260 955 155634

PARTICIPANT INFORMATION SHEET - NYANJA

Pepala ya cizibiso

Spectrum of sub-clinical cardiovascular disease among HIV infected patients presenting to University Teaching Hospital in Lusaka

Kuzibana

Ndine Lorrrita Kabwe, nicita maphunzilo ya minkwala ya mukati pa sikulu la likulu la Zambia, ndikupempani kuti mutengeko mbali ku mapunzilo aya. Cholinga ca aya maphunzilo ni ku kwanisila zofunikila kuti anipe maphunzilo apamwamba mu zamankwala amukati. Mukalibe ku nena ngati muzatengako mbali kapena simuzatengako mbali muma mphunzilo, nifuna kuti niku fotokozeleni cholinga ca maphunzilo ndi zo funikila kwa inu. Ngati mwa vomela kutengako mbali, mupempedwa ku saina ici cipepala pamaso ya opeleka umboni.

Cholinga ca maphunzilo aya

Maphunzilo acitidwa ku ona ngati mungankale matenda yobisika ku mutima ku anthu amatenda yakadoyo ka HIV ku onetsa ku cigawo ca malo amatenda ya akulu (AIDC) ku cipatala cikulu ca UTH. Ici nicacikulu cifukwa cizathandizila ku ziwa odwala amene angathe kudwala matenda yovuta akumutima na ku thandiza kufuna njila zo acingiliza.

Njila yo endetselamo aya maphunzilo

Ngati mwabvomela kutengako mbali kuli aya maphunzilo, tiza lemba zamene muzatiuza pa cipepala cosungila nkani, koma zina lanu sitizaikapo. Tizakupempani kutiuzako pa nkani za matenda yanu, pa mbuyo pake, tizakupimani mu tupi kuikilapo ndi sikelo, BP na mutima, mwa chinsinsi. Tiza micotsa tu magazi tungono twamene tizatumiza kwamene apima magazi. Ndiso muzaphempedwa kucita vipimo vina, monga: ECG, ECHO ndi ankle brachial index.

Zoyofya ndi zododometsa

Simuza ikiwa muciyopeso cili conse pamene muzakala mutenga mbali muli aya maphunzilo. Komabe kapena muzamvela cabe kudodoma polasiwa kanyeleti pocotsa tu magazi. Kapena muganvele kuipa po cita cipimo ca ECHO, cifukwa muzafunika kugona pakanthawi kufika pa ola pakati. Koma zindikilani kuti vopima vonse sivingate kubweletsa vuto lili lonse ngankale radiation sizakukuzani.

Phindu

Maphunzilo aya yaza thandiza kuziwa matenda aku mutima ndi zoyofya zina ndi ku thandiza kuziba mocingiliza matenda kuti asa ende pasogolo nonkala matenda akulu akumutima.

Chinsinsi

Nkani zonse zizakala zachinsinsi. Zina lanu silizaculidwa, koma muzapasiwa numbala yama phunzilo. Ndiye kuti kuyanka kwanu sikungazibike ku anthu ena.

Kubvomela

Kutengako mbali kuli aya maphunzilo ni kuzipeleka, kosaembekezela malipilo. Ngati mwafuna kusiya kutengako mbali nthawi ili yonse, cifukwa cacili conse sikuzakala chilango cili conse.

Zikomo povomera kutengako mbali mumaphunzilo aya. Ngati muli ndi mafunso kenaka maganizo, nkalani omasuka ku funsa Dr. Lorrita Kabwe kenaka the ERES Converge IRB office pa ma keyala osatila.

Dr. Lorrita Kabwe
University Teaching Hospital,
Department of Internal Medicine,
P/Bag RW1X,
Lusaka.
Zambia
Cell: +260 979 523309

ERES Converge IRB office
33 Joseph Mwilwa Road
Rhodes Park
Lusaka
Zambia
Email to eresconverge@yahoo.co.uk
Phone +260 955 155633
+260 955 155634

Annex 2

Consent Form

I, _____ (Full Names of Participant) hereby confirm that the nature of this clinical study has been sufficiently explained to me. I am aware that my personal details will be kept confidential and I understand that I may voluntarily, at any point, withdraw my participation without suffering any consequences. I have been given sufficient time to ask questions and seek clarifications, and of my own free will declare my participation in this research.

I have received a signed copy of this agreement

_____ _____ _____

Name of Participant (Print) Participant's Signature or thumbprint Date

_____ _____ _____

Name of Witness (Print) Witness (Signature) Date

Consent form – Nyanja

Pepala Yovomekeza

Ine,_____ (maina yonse ya otengako mbali) ni simikiza kuti mwamene yalili maphunzilo ani fotokozela bwino. Niziba kuti zonse zo ulusa zaine zizakala zachinsinsi ndinso namvetsa kuti ningate kusiya nthawi iliyonse kopanda kulandila chilango cili conse. Napasiwa nthawi yokwana ku funsa mafunso ndi kunimasulila, mozipeleka neka na vomela kutengako mbali muli aya maphunzilo.

Nalandila pepala yanga yosonyeza ku vomela

_____	_____	_____
Dzina lanu (lembani)	Fyatikani siginecha kapena cikumo	Date

_____	_____	_____
Dzina la mboni (lembani)	siginecha ya mboni	Date

Annex 3

DATA COLLECTION SHEET

SPECTRUM OF SUB-CLINICAL CARDIOVASCULAR DISEASES AMONG HIV INFECTED PATIENTS PRESENTING TO UNIVERSITY TEACHING HOSPITAL IN LUSAKA

Instructions: Please put a cross (X) where applicable

STUDY NO.....

Section 1: History

AGE ☐ years SEX: Male ☐ Female ☐

Month/Year of HIV diagnosis:.....

On HAART: Yes ☐ No ☐

Duration: <1yr ☐ 1 -5 yrs ☐ >5yrs ☐

ARV regimen

1st line ☐ 2nd line ☐ 3rd line ☐

DRUGS

TENOFOVIR ☐ NEVIRAPINE ☐

EMITRICITABINE ☐ EFAVIRENZ ☐

ZIDOVUDINE ☐ LOPINAVIR/r ☐

STAVUDINE ☐ RELTAGRAVIR ☐

ABACAVIR ☐ DARUNAVIR ☐

OTHERS.....

OTHER DRUGS

ATT ☐

SEPTRIN ☐

MULTIVITAMINS ☐

OTHERS……..

CVD RISK FACTORS

Smoking ☐ Hypertension ☐

Diabetes ☐

Section 2: Physical examination

Weight ☐ kgs Height ☐ metres

BMI ☐ kg/m^2 BSA ☐ kg/m^2

Blood Pressure ☐ mm/Hg

Pulse ☐ bpm

Pulse regular ☐ Pulse irregular ☐

Section 3: Laboratory tests

1. CD4 Count ☐ cells/ml

Total cholesterol ☐ mmol/l

Triglycerides ☐

3. **Biochemistry**

Creatinine ☐ ummol/l

CrCl ☐ ml/min

Section 4: Electrocardiogram (ECG)

Rhythm	Sinus	Non-sinus		
Axis	Normal	Left	Right	
voltage	Normal	Low		
P - wave	Normal	p-mitrale	p-pulmonale	
PR interval	Normal (120-200ms)	Short (<120ms)	Prolonged (>200ms)	
QRS	Normal (60 – 120ms)	Short (<60)	Prolonged (>120)	
ST Segment	Normal	Depressed (>1mm limbs, >2mm chest)	Elevated (>1mm limbs, >1mm chest)	
Q – waves	Absent	Present		
T - wave	Normal	Flat	peaked	inverted
QTc	Normal	Short	prolonged	
AV conduction	Normal	Abnormal (specify)		
Ventricular conduction	Normal	Abnormal (specify)		
Miscellaneous				

Section 5: Ankle Brachial Index (ABI)

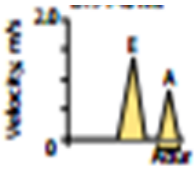
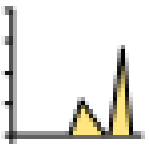
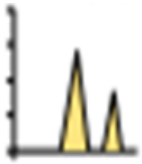
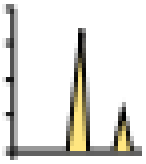
Normal	Low		
>0.9 – <1.2	< 0.9		
	Mild	moderate	severe

	0.7 – 0.9	0.5 – o.7	</=0.4
Limb involvement	Unilateral	Bilateral	

Section 6: Echocardiography (ECHO)

LEFT SIDED CHAMBERS

Ascending aorta	Normal (<30mm)	Dilated and/or calcified		
Left atrium (enlargement – mm)	Normal	Mild	Moderate	Severe
Women	27–38	39–42	43–46	≥47
Men	30–40	41–46	47–52	≥52
LV size	Normal	Mild	Moderate	Severe
1.Volume ml/m2 (S/D)	35-75/12-30	76-86/37-42	87-96/37-42	>97
2.Mass/BSA (g/m2)				
Men	49 – 115	116 -131	132 – 148	>/=149
Women	43 – 96	96 - 108	109 – 121	>/=122
LV function (EF-%)	Normal	Mildly abnormal	Moderately abnormal	Severely abnormal
	>/=55	45-54	30-44	<30
Diastolic dysfunction (E/A)	Normal	Mild (impaired relaxation)	Moderate (pseudonormal)	Severe (restrictive)

	E/A 0.7-1.5)	E/A <0.75	E/A 0.75 - 1.5	E/A >1.5
			 (Unmask with vasalva maneuver)	

RIGHT SIDED CHAMBERS

RV (basal diameter-mm)	Normal	Mild	Moderate	Severe
	20 – 28	29 – 33	34 - 38	>/=39
RA (minor axis dimension – mm)	Normal	Mild	Moderate	Severe
	29–45	46–49	50–54	≥55

VALVES AND PULMONIC PRESSURES

Aortic valve		Mild	Moderate	Severe
Stenosis				
1.AV area (cm2)		>1.5	1.0-1.5	<1
2.Jet velocity (cm/s)		2.6-2.9	3.0-4.0	>4.0
Regurgitation		Central jet width <25% of LVOT	Signs of mild AR – no meeting criteria for severe AR	Central jet width > 65% of LVOT
MV Stenosis		Mild	Moderate	Severe
Valve area (cm2)		>1.5	1.0 – 1.5	<1.0
MV Regurgitation		Small jet < 20% of LA area	Mild but not meeting criteria for major MR	Large jet >40% of LA area
Tricuspid valve	Normal	Mild	Moderate	Severe
TR velocity (m/s)	1.7 – 2.3	2.4 – 2.8	2.8 – 3	>3

Stenosis (mean gradient)				>/= 5mmHg
Pulmonic valve acceleration time PVAT (ms)	Normal >130	Mild 100 - 130	Moderate 80 – 100	Severe <80
		OTHER FINDINGS		
Pericardial effusion	Absent	Minimal (<10mm)	Moderate (10 - 20mm)	Large (>20mm)

ECHO READING FORM

Date of ECHO.....

Study ID No.....

Age/Sex..... Height .....metres Weight.....Kgs

M-Mode 2D Measurements

IVSd: _____(mm)
LVPWd: _____(mm)
LVIDd: _____(mm)
LVIDs: _____(mm)
Fractional Shortening: _____(%)
LV Mass_____ (grams)
Biplanes Simpson EF _____(%)
Teich EF_____(%)
Aortic root diameter_____(mm)
Left Atrial diameter _____(mm)
Right atrial diameter(short axis)_____(mm)
Right ventricular diameter (basal)_____(mm)
Pulmonary artery diameter_____(mm)

Valvular Disease

Mitral Valve ☐ Normal
☐ Stenosis
☐ Regurgitation
☐ Unable to assess

Aortic Valve ☐ Normal
☐ Stenosis
☐ Regurgitation
☐ Unable to assess

Tricuspid Valve ☐ Normal

☐ Stenosis

☐ Regurgitation

☐ Unable to assess

Pulmonic Valve ☐ Normal

☐ Stenosis

☐ Regurgitation

☐ Unable to assess

Doppler Measurements and Calculations

E max vel: _____(cm/sec)

A max vel: _____(cm/sec)

Mitral Valve DT _____ (msec)

Mitral valve PHT_____(msec)

Mitral valve mean gradient_____mmHg

MVOA_____ cm2

Diastolic Function ☐ Normal

☐ Impaired Relaxation

☐ Pseudonormal

☐ Restrictive

☐ Unable to Assess

☐ Indeterminate

AoV mean gradient: _____(mmHg)

AoV PHT_____(ms)

AVOA_____(cm2)

TR max vel: _____(m/s)

PV acc.time_____(ms)

Colour Flow Doppler comments

_____

_____

IVC_____cm

IVC collapse with respiration_____%

Pericardial Effusion ☐ None
☐ Small
☐ Moderate
☐ Large

Overall Test Results: Normal ☐ Abnormal ☐

If Abnormal Clinically Significant: ☐ No
☐ Yes

Echo Comments

_____
_____
_____
_____

Echo done by_____

Verified by_____

ECG READING FORM

STUDY ID NO..... DATE.....

AGE/SEX.....

Recording time

1. Rhythm: Sinus
   Other Specify……..
2. Heart rate..... /min
   Normal ☐ Regular ☐ Irregular ☐
   Tachycardia ☐
   Bradycardia ☐
3. P-wave
   Location……
   Morphology……..
   Duration……..
   Amplitude……..
4. Q and QS pattern (MN codes 1)
   ……
   ……
5. QRS axis deviation (MN code 2)
   ……
   ……
6. ST Segment depression (MN code 4)
   ……
   ……
7. ST segment elevation (MN code 9)
   ……
   ……
8. T-Wave (MN code 5)
   ……
   ……
9. A-V Conduction defects (MN code 6)

……
……

10. Ventricular Conduction defects (MN code 7)

……
……

11. Arrhythmias (MN code 8)

……
……

12. Miscellaneous items (MN code 9)

……
……

ECG diagnosis

……
……
……
……

Read by…….. Date:……..

Verified by…….. Date:……..