Factors Associated with Mortality in Adults Admitted with Heart Failure at the University Teaching Hospital in Lusaka, Zambia

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Master of Medicine in Internal Medicine

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CERTIFICATE OF APPROVAL

This dissertation entitled "Factors Associated with Mortality in Adults Admitted with Heart Failure at the University Teaching Hospital, Lusaka, Zambia" by PAMELA N. CHANSA is approved in partial fulfilment for the award of the Master of Medicine degree in Internal Medicine by the University of Zambia.

	Name	Signature	Date
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Examiner 3	.....	.....	.....

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.

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DEDICATION

To all the heart failure patients

who participated in this study

God bless you

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ABSTRACT

Background

Heart failure is a major public health problem and has been recognized as an important cause of morbidity and mortality for several years. It is one of the leading non-infectious causes of death among hospitalized patients at the University Teaching Hospital (UTH) in Lusaka, Zambia. This study aimed to investigate the predictors of 30-day mortality in heart failure patients admitted to the medical wards at the UTH using routinely obtained clinical data.

Methods

We enrolled 390 heart failure patients and followed them up over a period of 30 days. Data collected included demographic characteristics (age, sex), medication use and co-morbidities (hypertension, diabetes mellitus, HIV). Clinical data included vital signs, blood urea, serum sodium, serum potassium, serum creatinine, and haemoglobin level. Trans-thoracic echocardiographs and electrocardiographs were also done to determine LVEF and to check for the presence of arrhythmias. Patients were dichotomized into those with preserved (LVEF>=40 percent) and reduced (LVEF< 40 percent) systolic function. Recruited patients were then prospectively followed up to determine outcome by day 30 (i.e. dead or alive). Cox proportion Hazard regression analysis (on Epi Info software version 3.5.3) was used to analyse the effect of each of these parameters on outcome.

Results

Of the recruited patients, 59% were female (95% CI 54-64). The median age was 50 years (IQR 33-68). A significant proportion of patients had not been previously hospitalized with heart failure (64%, 95% CI 59-69). 138 patients (35%, 95% CI 31-40) died within 30 days of admission. 94 (68%) of these deaths occurred in-hospital.

The factors shown to be independent predictors of death on multivariate logistic regression analysis were LVEF<40 percent (OR=2.86, 95%CI 1.68- 4.87), NYHA class IV (OR=2.15, 95%CI 1.27- 3.64), serum urea above 15mmol/L (OR=2.48, 95%CI 1.07-5.70), and haemoglobin level below 12g/dL (OR=1.79, 95%CI 1.11-2.89). The additional factor associated with increased risk of mortality on univariate analysis was systolic blood pressure below 115mmHg (OR=1.63, 95%CI 1.05- 2.51). However, serum creatinine (OR=1.49, 95%CI 0.49-4.48) and HIV status (OR=0.96, 95% CI 0.53-1.72) had no bearing on the risk of death in this patient population.

Conclusions

LVEF <40 percent is a predictor of poor 30-day outcome in hospitalised heart failure patients at the UTH. In order to help improve survival, heart failure patients admitted to hospital need to be triaged according to risk in order to monitor patients closely and institute potentially life-saving measures when indicated.

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LIST OF ACRONYMS AND ABBREVIATIONS

ACE	Angiotensin Converting Enzyme
AFC	Adult Filter Clinic
AIDC	Adult Infectious Disease Center
AIDS	Acquired Immunodeficiency Syndrome
ARB	Angiotensin Receptor Blocker
BMI	Body Mass Index
CI	Confidence Interval
CONSENSUS	Cooperative North Scandinavian Enalapril Survival study
COPD	Chronic Obstructive Pulmonary Disease
DCM	Dilated Cardiomyopathy
DBP	Diastolic Blood Pressure
ECG	Electrocardiogram
Echo	Echocardiogram
EF	Ejection Fraction
GFR	Glomerular Filtration Rate
GWTG-HF	Get With The Guidelines Heart Failure
FBC	Full Blood Count
Hb	Haemoglobin
HF	Heart Failure
HHD	Hypertensive Heart Disease
HIV	Human Immunodeficiency Virus
HR	Heart Rate
ICD	Implantable Cadioverter Defibrillator
IV	Intravenous
IQR	Interquartile range

LBBB	Left Bundle Branch Block
LVEF	Left Ventricular Ejection Fraction
QT_c	Corrected QT interval
MAW	Medical Admission Ward
NYHA	New York Heart Association
OR	Odds Ratio
RBBB	Right Bundle Branch Block
SBP	Systolic Blood Pressure
SOLVD	Studies on Left Ventricular Dysfunction
TB	Tuberculosis
U/E	Urea, Electrolytes
UTH	University Teaching Hospital
WHO	World Health Organisation

CHAPTER 1

1.0 INTRODUCTION:

The clinical syndrome of heart failure is characterised by dyspnoea, fatigue, and fluid retention which may develop as a consequence of cardiac disease.[1, 2] The aetiology is varied[3] and ultimately results in impaired diastolic or systolic function.[1]

Heart failure is an important public health problem. It has been recognised as one of the major causes of morbidity and mortality for several years.[3,4] The burden of heart disease and cost of management of patients is high.[4,7] In North America almost 20 percent of admissions to hospital are due to heart failure and between 2.1 and 21.9 percent of these patients die.[7] In Europe heart failure accounts for 5 percent of admissions to hospital medical wards and the mortality is estimated at about 13 percent.[19] Unfortunately, the magnitude of this problem in Africa is not well studied as few population based studies have been done on the prevalence of heart failure and the mortality rates.

The use of prognostic indicators in predicting disease progression and the probability of death is important in clinical practice. Early recognition and treatment of reversible factors indicative of a poor outcome could aid in reducing deaths.

Several studies done in different populations have reached varying conclusions regarding the most accurate predictors of mortality in heart failure patients. Some of these studies are population-based and describe the long-term probability of death. Such a study was the landmark Framingham heart failure which was a long-term follow-up study started in the 1940s. This study as well as subsequent studies which used data derived from it helped highlight the importance of prognostication in heart failure. Most recently, studies on prognosis in heart failure have focused on the identification of factors which are likely to be indicative of a poor outcome in hospitalised patients. These studies utilise data which is routinely collected on admission to hospital in order to aid clinicians triage patients and provide effective intervention measures.

Some of the documented independent factors associated with high risk of death in heart failure patients include the patient's age, sex, race, heart rate, blood pressure, New York Heart Association class, haemoglobin level, serum sodium, serum urea, serum creatinine

levels, presence of arrhythmias, and the left ventricular ejection fraction. Recently, the use of biomarkers (Brain Natriuretic Peptide, Cystatin C, Troponin T and Growth differentiation factor 15) to predict mortality has been investigated, particularly in the western world with varying conclusions regarding the biomarker with the most accurate prediction of poor outcome. Medications such as angiotensin converting enzyme inhibitors, angiotensin receptor blockers, aldosterone antagonists, certain beta blockers, and the combination of hydrallazine with nitrates significantly have been shown to reduce long term mortality rates in chronic heart failure patients.

The University Teaching Hospital (UTH) is the largest public referral institution in Zambia with a catchment population of 2 million people. For the past 5 years, heart disease has been amongst the top ten causes of morbidity and mortality. According to hospital records, in 2008, the proportion of deaths in heart disease patients had increased to 44.3 percent and was the third commonest cause of death amongst adult medical patients.

The aim of this study was to establish some of the factors associated with early mortality in patients admitted with heart failure at the UTH using routinely collected clinical data in order to aid reduce deaths.

CHAPTER 2

2.0 LITERATURE REVIEW:

The clinical prognostic determinants in heart failure can be categorised into the following: (1) patient characteristics and co-morbidities; (2) laboratory parameters; (3) functional parameters and ventricular function; and (4) interventions received.[5, 9]

2.1 Effect of patient demographics and comorbidities on mortality:

Studies have shown that age has a bearing on in-hospital mortality in heart failure patients.[13,15,19] Most studies in North America and Europe found that patients who were above the age of 65 years were more likely to die while in hospital than their younger counterparts. In the United Kingdom, the prevalence of heart failure is about five times higher in elderly patients compared with the general population.[6] However, in the developing world, patients with heart failure tend to be younger due to the high prevalence of rheumatic heart disease and HIV cardiomyopathy.[10, 11]

The role of gender in prognosis of heart failure patients is inconclusive. Population based long term follow-up studies have shown that females with heart failure have a better prognosis than their male counterparts. [21-23] However, according to a European Heart Failure Survey and a study in Singapore, female gender carried adverse prognosis.[19, 36]

Diabetes and chronic obstructive pulmonary disease have a bearing on mortality in heart failure. In one long term study it was found that diabetes significantly increased all-cause mortality in patients with ischemic cardiomyopathy.[26] Patients with Chronic Obstructive Pulmonary Disease (COPD) or corpulmonale were also found to be more at risk of death while in hospital.[15] However, the influence of malnutrition and AIDS defining illnesses, which are common in our setting, on outcomes in heart failure have been poorly studied.

The conclusions regarding the influence of race on mortality are also varied. In the Studies on Left Ventricular Dysfunction (SOLVD) trial, mortality was found to be higher in black patients with asymptomatic left ventricular dysfunction or overt heart failure.[24, 25] According to a risk assessment tool developed by the American Heart Association Get-With-The-Guidelines Heart failure (GWTG-HF) study for hospitalised patients, Caucasians carried the

worst prognosis.[15] A study in Singapore found that mortality amongst Southeast Asian heart failure patients was high [36] although a comparative study between Asian and Caucasian heart failure patients found that Asians had a better long-term prognosis.[37]

2.2 Effect of laboratory parameters on mortality:

Decreased kidney function and anaemia are risk factors for all-cause mortality in patients with left ventricular dysfunction, [12, 13, 15, 19, 36] especially when both are present.[27, 28]

2.2.1 Serum sodium, urea and creatinine levels:

Renal function has a bearing on cardiac function and outcome in patients with heart failure. Hypoperfusion of certain vital organs such as the kidney as a consequence of a low cardiac output could lead to cardio-renal syndrome with resultant increase in urea, creatinine and impaired electrolyte and fluid balance.

Hyponatremia is a risk factor for death in heart failure patients [13, 15, 19] as this relates to the severity of cardiac dysfunction and the extent of neurohumoral activation with resultant hemodilution from fluid retention.[80] It has long- and short-term prognostic value in patients who are hospitalized for worsening heart failure.[78, 79]

According to a study done in the United States of America, patients with urea level of greater than 15mmol/L, creatinine level of more than 243*umoL*/L, and systolic blood pressure of less than 115mmHg were more likely to die while in hospital regardless of the patient's left ventricular ejection fraction.[12] The probability of death in a heart failure patient increases significantly if the Glomerular Filtration Rate (GFR) is below 45ml/min.[27]

2.2.2 Haemoglobin level:

About 30 percent of non-hospitalised heart failure patients and 50 percent of hospitalised patients are anaemic.[32]

Several studies indicate that a lower haemoglobin level is associated with increased mortality.[13,15,19,27,29,30-33] Even mild degrees of anaemia were associated with worsened

symptoms, functional status and survival.[30,31] Findings from other studies, however, indicate that haemoglobin level in heart failure does not have a bearing on prognosis.[34,35]

2.3 Effect of functional parameters and ventricular function on mortality:

2.3.1New York Heart Association (NYHA) class:

Long term follow-up studies on heart failure have found that NYHA class III and IV are associated with poor prognosis.[19, 36]

2.3.2 Arrhythmias and conduction defects:

Atrial fibrillation (AF) and heart failure are commonly encountered together, and either condition predisposes to the other, forming a vicious circle.[54,68] The prevalence of atrial fibrillation ranges from 10 to 30 percent in patients with symptomatic heart failure.[69] In the SOLVD study, it was found that the mortality rate was 34 percent higher among patients with atrial fibrillation than among those without it, largely because of a 42 percent increase in the risk of death from pump failure.[69] Direct compromise of cardiac function as a result of the adverse hemodynamic effects, the increased risk of arterial thromboembolism,[70] and the deleterious effects of anti-arrhythmic therapies may all contribute.[68, 71- 75]

Left bundle branch block (LBBB) has been found to impair diastolic function in dilated cardiomyopathy by shortening the time available for the left ventricle to relax, thereby limiting stroke volume.[76] A study in Italy found that 25.2 percent of heart failure patients had LBBB and was associated with increased 1-year mortality from any cause and sudden death.[79] This was independent of the age of the patients, severity of heart failure, and drug therapy received.

2.3.3 Left Ventricular Ejection Fraction (LVEF):

The proportion of chronic heart failure patients with a normal left ventricular ejection fraction, from most studies, has been estimated at 50 percent.[39,56-61] The demographic characteristics in heart failure patients with preserved LVEF was also found to differ

significantly from those with reduced LVEF.[62] Unlike patients with reduced LVEF, those with preserved LVEF were reportedly older, more likely to be female, and often had hypertensive heart disease as the underlying cause of heart failure.[39, 56-62]

Whether overall mortality rates differ between patients with preserved or reduced LVEF is not clear. Some community-based epidemiological studies have shown that the annual mortality rate approaches 15% for both groups of patients; others have shown that the mortality rate was significantly lower in patients with preserved LVEF[62-67] (at 5 percent) than reduced LVEF.[39, 56, 59, 61, 62]

This conclusion was echoed in other similar studies done in different regions in the world. According to a meta-analysis of seventeen studies in Europe on the prognostic significance of heart failure with preserved left ventricular ejection fraction, it was concluded that mortality among patients with heart failure with preserved ejection fraction was half that observed in those with heart failure with reduced ejection fraction, in contrast to previous reports suggesting that mortality may be similar between both groups.[14] However, even patients with preserved systolic function have a five year mortality of 25 percent.[40]

In an African study conducted in Nigeria, poor systolic function with LVEF of less than 40 percent was found to be the best predictor of in-hospital mortality in heart failure patients.[8]

Contrary to the studies mentioned previously, certain studies have found no difference in the risk of death in patients with preserved or reduced left ventricular systolic function.[12,15,38, 39] The results of these studies casts doubt on the usefulness of LVEF as an independent prognostic indicator for both in-hospital- and long term mortality.

2.4 Interventions:

2.4.1 Effect of anti-failure medication on mortality:

Until the late 1980s, treatment of heart failure was confined to symptomatic management with diuretics and digitalis glycosides.[41] However, certain therapies have been shown to have an impact on mortality and are generally recommended for use in heart failure patients unless contraindicated or poorly tolerated.

The administration of inhibitors of the renin-angiotensin-aldosterone system reduces both structural remodelling of the left ventricle, and excess salt and fluid retention in chronic heart failure. This helps relieve the symptoms of heart failure, slows the progression of systolic dysfunction, and lowers mortality. Results from the Cooperative North Scandinavian Enalapril Survival (CONSENSUS) study showed that Angiotensin converting enzyme (ACE) inhibitors reduced morbidity and mortality in symptomatic heart failure patients with NYHA class IV,[42] those with less severe symptoms in the SOLVD study[43] and in asymptomatic patients with left ventricular systolic dysfunction.[6] ACE inhibitors reduce overall mortality by 23 percent in chronic stable heart failure patients.[44] Angiotensin Receptor Blockers (ARBs) have similar efficacy as ACE inhibitors. Candesartan, valsartan and losartan significantly reduce long-term mortality when used as replacement therapy in heart failure patients intolerant of ACE inhibitors.[85-87] Aldosterone antagonists such as spironolactone and epleronone have also been shown to reduce mortality in chronic heart failure patients.[55]

Beta-blockers such as Bisoprolol, Carvedilol, Metoprolol and Nebivolol are beneficial when administered to stable chronic heart failure patients with a significant reduction in re-hospitalisation rates and all-cause mortality by 34 to 35 percent.[45-48] A meta-analysis of 18 trials showed that beta-blockade increased the LVEF by 29 percent and reduced the combined risk of death or hospitalization for heart failure by 37 percent.[53] Beta blockers also reduce the risk of sudden cardiac death from fatal arrythmias.[49-51] There was, however, no improvement in the study patient's NYHA class during long-term follow-up.[52]

Oxidative stress and impaired bioavailability of nitric oxide increase cardiac remodelling and worsens heart failure symptoms.[2,88] Medications such as hydrallazine with nitrates increase nitric oxide levels and cause vasodilatation thus reducing preload. These drugs are particularly useful in black heart failure patients, with or without neurohormonal inhibitors. The A-HeFT trial demonstrated a significant reduction in hospitalisation and mortality in African-American heart failure patients with the addition of hydrallazine and nitrates to standard treatment.[88]

The cardiac glycoside digoxin is traditionally used as a rate-control drug in the treatment of atrial fibrillation. The addition of digoxin for its inotropic effect to standard heart failure management has no impact on mortality.[89] However, its use in chronic heart failure has been shown to reduce the rate of re-hospitalisation, particularly in those with impaired systolic function.[89]

Current data on the efficacy of Niseritide, a recombinant human Brain Natriuretic Peptide (BNP), is limited and not routinely advocated for.[2] Niseritide has however been shown to cause vasodilation and reduce the symptoms of left ventricular failure in the acute setting. Therefore, more research in this area needs to be done.

2.4.2 Effect of correction of anaemia and renal function on mortality:

Certain studies have shown that the correction of anaemia in heart failure patients is important. A study done in Israel found that the correction of mild anaemia (Hb 10 to 11.5 g/dL) by administering IV iron or erythropoietin in patients with resistant congestive heart failure and mild to moderate chronic renal failure improved cardiac function and patient functional status, stabilized the renal function and markedly reduce the need for hospitalization.[53]

2.4.2 Effect of implantable cardioverter defibrillators (ICD), left ventricular assist devices and cardiac transplant on mortality:

Implantable cardioverter defibrillators (ICDs) are typically used in post cardiac arrest patients and in those with sustained ventricular tachycardia. However, in some patients with reduced systolic function where medical therapy has been optimised, ICDs have been shown to reduce the risk of sudden cardiac death from fatal arrhythmias and improve survival.[2, 90]

Current data does not support the use of left ventricular assist devices in the long-term management of heart failure.[91] Left ventricular assist devices are recommended for use as bridging therapy in heart failure patients planned for cardiac transplant.

In select patients, cardiac transplantation is the definitive treatment for end-stage heart failure patients. Exercise tolerance and symptoms of heart failure improve post cardiac transplant.[2] Cardiac surgery is therefore, generally accepted as an appropriate intervention strategy for the treatment of end-stage heart failure despite the absence of clinical trial-based data to support it.[2]

The studies mentioned were derived from patients with diverse demographic characteristics and a wide range of co-morbidities. The results of these studies are therefore, unique to the patient population under study and may not be generalised. As such, it is important to investigate factors which increase the risk of adverse outcomes in heart failure patients in

different settings. However, risk stratification provides objective information on the probability of death but does not replace clinical judgement in identifying patients who might benefit from potentially life-saving interventions.[16]

CHAPTER 3

3.0 STATEMENT OF THE PROBLEM:

Admission of patients to the medical wards at the University Teaching Hospital with heart disease is high. According to data from the Hospital Records Department, 8 percent (i.e. 793 of total of 9,915 patients) of patients were admitted with heart disease in 2008. For the same period, 9.4 percent (i.e. 351 of total of 3,737 patients) of the hospital mortalities were attributed to heart failure in patients with various underlying cardiac conditions including Dilated Cardiomyopathy (DCM) and Hypertensive Heart Disease (HHD). During the same period, 44.3 percent of hospitalised heart failure patients died whilst in hospital. The proportion of hospital deaths due to heart failure in our setting is approximately two to three times higher than in North America[15, 16] and Europe[19] respectively. Despite this high mortality, the factors that predict mortality have not been investigated in our patient population.

4.0 STUDY JUSTIFICATION:

Heart failure is important as it is potentially debilitating and could eventually lead to death. Mortality in heart failure patients in our setting is high. Data on the probable prognostic factors in heart failure patients in our setting is limited as most of the documented studies have been done in the western population on patients with different demographic factors, higher socioeconomic status, and better access to diagnostic facilities and medical intervention. Most of the studies on the predictors of both short- and long-term mortality in heart failure use routine clinical data which can be easily obtained in our heart failure patients. Although laboratory resources to measure levels of biomarkers are currently unavailable, basic tests such as haemoglobin levels, urea and creatinine levels, as well as echocardiography and electrocardiography can be done, making such a study feasible in a resource-limited setting.

The information gathered from this study will help stratify patients according to risk with high risk patients being monitored closely and treated more aggressively than those with a low risk of death. In addition, information gathered from this study will also be used to guide

future interventional studies aimed at preventing disease progression in low risk patients and improving outcomes in high-risk patients.

6.0 HYPOTHESIS:

Heart failure patients with reduced systolic function (i.e. Left Ventricular Ejection Fraction of less than 40 percent) admitted to the University Teaching Hospital, have higher proportion of deaths compared to patients with preserved systolic function.

7.0 OBJECTIVES:

7.1 Main Objective:

To determine the predictors of 30-day mortality in heart failure patients admitted to the medical wards at the UTH.

7.2.1 Specific Objectives:

7.2.2 To describe the demographic characteristics of patients admitted to the medical wards at UTH with heart failure;

7.2.3 To compare the proportion of heart failure patients with ejection fraction greater than or equal to 40 percent with those with less than 40 percent on admission;

7.2.4 To estimate the proportion of deaths occurring in heart failure patients within 30 days of admission to the UTH.

CHAPTER 4

8.0 METHODOLOGY:

We conducted a cohort study with a follow-up period of 30 days in the admitting medical wards at the University Teaching Hospital. Enrolment and follow-up of patients was done from November 2010 to September 2011. Purposive sampling method was used in selecting patients. Patients who met the case definition of heart failure were recruited into the study (see section 8.5.1).

8.1 Inclusion criteria:

- Patients who are 18 years old and above (i.e. legal age of consent in Zambia)
- Confirmed heart failure
- Those who consent in writing to participating in the study

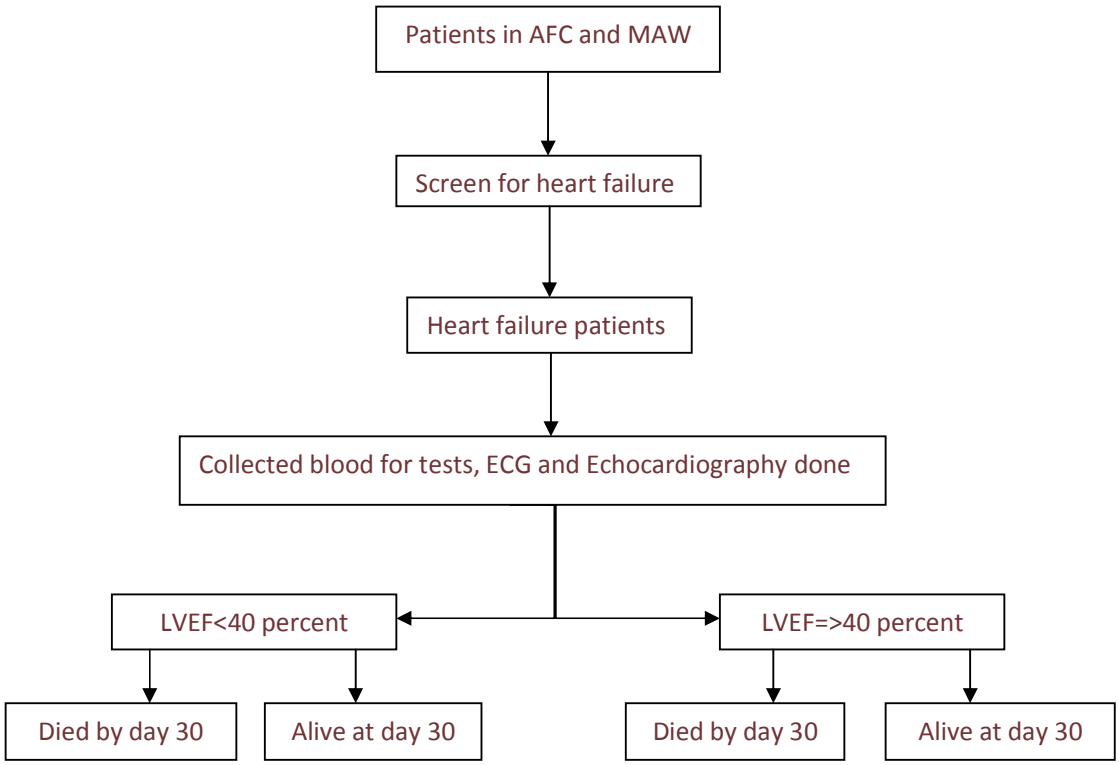
8.2 Exclusion criterion:

- Patients with pericardial disease.

  Despite having features of right-sided heart failure, those with moderate-to-large pericardial effusion and constrictive pericarditis were excluded from this study as definitive management involves either drainage of fluid from the pericardial space or pericardectomy, and treating the underlying cause as opposed to administering standard anti-failure medication.

8.3 Clinical Procedure:

Fig 1: Study process



Recruitment of patients was done during working hours in the admitting medical wards. Written consent was obtained from eligible patients who met the diagnostic criterion of heart failure. Data entry sheets were used to gather the information which included patients' contact phone number, demographic characteristics (age, sex, residence), drug history, past medical history, current medication, functional status (NYHA class) and admission vital signs (blood pressure, heart rate, respiratory rate, and axillary temperature).

8.3.1 Laboratory parameters:

Blood was collected from each patient for blood urea, electrolytes (sodium, potassium), creatinine, and haemoglobin level soon after hospitalisation. Blood for urea, sodium, potassium and creatinine was collected in blood specimen bottles containing heparin. Full Blood Count (FBC) samples were collected in EDTA bottles. An Olympus AU 400 analyzer was used for the determination of biochemistry parameters. PENTRA 80 and XT-2000 was

used for the full blood counts. HIV tests were done using rapid serology tests (i.e. Determine and/or Uni-Gold) following counselling by a qualified counsellor.

8.3.2 Trans-thoracic echocardiography and electrocardiography:

2-dimension trans-thoracic echocardiography (LogiQ 500 pro series and xVision/ MyLab40 2008 model) was used to determine LVEF. The echocardiogram was set in motion-mode and LVEF was determined from left parasternal long axis views using the Quinones formula. Patients were classified as either having reduced systolic function (LVEF<40 percent) or preserved systolic function (LVEF>=40 percent). Electrocardiograms (using the 2007 MAC 1200 version machine) were also done on admission and reported on independently by two clinicians.

8.3.3 Outcome:

Patients were followed up on a daily basis while in hospital. Discharged patients were reviewed in the outpatient clinic and/or contacted by phone on day 30 to determine outcome (i.e. dead or alive). Data collected was then entered into ***epi info*** software and analysed.

8.4 Variables:

8.4.1 Dependent variables:

The outcome of the study patients was described as follows:

Dead: Patients who died within the 30 day of follow-up period (all-cause mortality);

Alive: Patients who were alive at the end of the 30 day follow-up period.

8.4.2 Independent variables:

These included age, sex, NYHA class, blood pressure, heart rate, HIV status, haemoglobin, serum sodium, serum potassium, serum urea, serum creatinine, arrhythmias on electrocardiography, and LVEF on echocardiography.

Categorical variables included sex (Male/Female), NYHA Class (I, II, III, IV), HIV status (Yes/ No), diabetes mellitus (Yes/No), and Hypertension (Yes/No).

Continuous variables included age, admission heart rate, admission blood pressure, respiratory rate, temperature, serum urea, serum sodium, serum potassium, serum creatinine, haemoglobin levels and LVEF.

8.5 Study definitions

For the purpose of this study the following definitions were used.

8.5.1 Heart failure

Case definition:

As adapted from the 2008 European Society of Cardiology (ESC) Guidelines[2]

1. Symptoms (and signs) of heart failure at rest or during exercise. These include fatigue, breathlessness and congestion of systemic veins (orthopnoea, paroxysmal nocturnal dyspnoea, bilateral fine basal crepitations, dependent peripheral oedema, raised jugular venous pressure, and hepatomegaly), and
2. Objective evidence (preferably by echocardiography) of cardiac dysfunction (systolic or diastolic) at rest.

8.5.2 Reduced- or preserved systolic function

The cut-off of 40 percent for LVEF used in this study to categorise heart failure patients as having either reduced or preserved systolic function was adopted from a validated multicentre risk stratification study done in more than 100,000 hospitalised heart failure patients in the United States of America.[14] One of the few documented African heart failure studies on prognosis also utilised the LVEF cut-off of 40 percent.[11]

Reduced systolic function: LVEF less than 40 percent;

Preserved systolic function: LVEF greater than or equal to 40 percent.

8.5.3 Low systolic blood pressure, high serum urea and creatinine

Similarly, the cut-offs for systolic blood pressure, serum urea, and serum creatinine were adopted from the validated risk stratification study mentioned above. High risk patients were identified as having the following abnormal admission parameters:

Low systolic blood pressure: Systolic blood pressure less than 115mmHg

High serum urea: Serum urea above 15mmol/L.

High serum creatinine: Serum creatinine above 243umol/L.

8.5.4 Hyponatremia (2008 ESC Guidelines)[2]

Serum sodium below 135mmol/L.

8.5.5 Hypokalemia (2008 ESC Guidelines)[2]

Serum potassium below 3.5mmol/L.

8.5.6 Anaemia (2008 ESC Guidelines[2] and W.H.O definition)[84]

Haemoglobin level below 12g/dL in females and less than 13g/dL in men.

8.5.7 New York Heart Association functional classification

Adapted from the recommendations made by the Criteria Committee of the New York Heart Association of 1994:[83]

1. Class I: No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnoea.
2. Class II: Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnoea.
3. Class III: Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results in fatigue, palpitation, or dyspnoea.
4. Class IV: Unable to carry out any physical activity without discomfort. Symptoms at rest. If any physical activity is undertaken, discomfort is increased.

8.6 Sample size calculation:

The sample size was calculated using the Pocock formula.[28]

$$N = \frac{P_1(100-P_1) + P_2(100-P_2)}{(P_1-P_2)^2} \times F(\alpha, \beta)$$

N= Sample size calculated

The proportion of patients with either preserved or reduced ejection fraction was estimated at 50 percent each.

P_1= The proportion of patients with preserved ejection fraction (LVEF>= 40 percent) who die in hospital was estimated at 35 percent;

P_2= The proportion of patients with reduced ejection fraction (LVEF<40 percent) was estimated at 50 percent;

F (α, β) is a constant fixed at 7.85

With power of 80 percent and correction factor of 10 percent to account for missing data, the sample size was estimated at **370 patients.**

8.7 Ethical consideration:

The study was approved by the University Of Zambia Biomedical Research Ethics Committee (Certificate Assurance No. FWA00000338). Its purpose was explained to the participants. Written informed consent was obtained from all eligible patients prior to their participation. The participants were informed that they could freely opt-out of the study without compromise to their medical care. None of them received any form of remuneration. No adverse events related to study procedures were experienced.

9.0 DATA ENTRY AND ANALYSIS:

9.1 Data entry:

Data was collected on a hard copy data entry sheet. Each patient was assigned a patient identification number (PTID). The patient's PTID number (not name) was entered on the hard copy data entry sheet in order to ensure confidentiality. Data collected was then transcribed onto a created electronic version of the data entry sheet on ***epi info*** version 3.5.3 and analysed.

9.2 Data analysis:

All statistical analysis was done using ***epi info*** version 3.5.3 dataset at 95 percent confidence interval.

Continuous variables with Gaussian distribution were expressed as means and standard deviation. The student t-test was used to test for statistical significance. Continuous variables with non-Gaussian distribution were expressed as medians and intergroup differences. Kruskal Wallis test was used in this group to test for statistical significance.

Categorical variables were expressed as percentages or proportions. Chi-square test was used to measure the effect of each categorical variable (e.g. LVEF, sex) on the outcome (dead or alive). Some of the continuous variables (e.g. haemoglobin, systolic blood pressure, serum creatinine) were dichotomised before analysis based on values obtained from previous studies. Univariate and multivariate logistic regression analysis was used to analyse the effect of each of the prognostic features (e.g. age, sex, ejection fraction) on outcome in heart failure patients (i.e. dead or alive).

Cox proportion Hazard regression analysis was also used for time-to-event analysis and to determine crude hazard ratios.

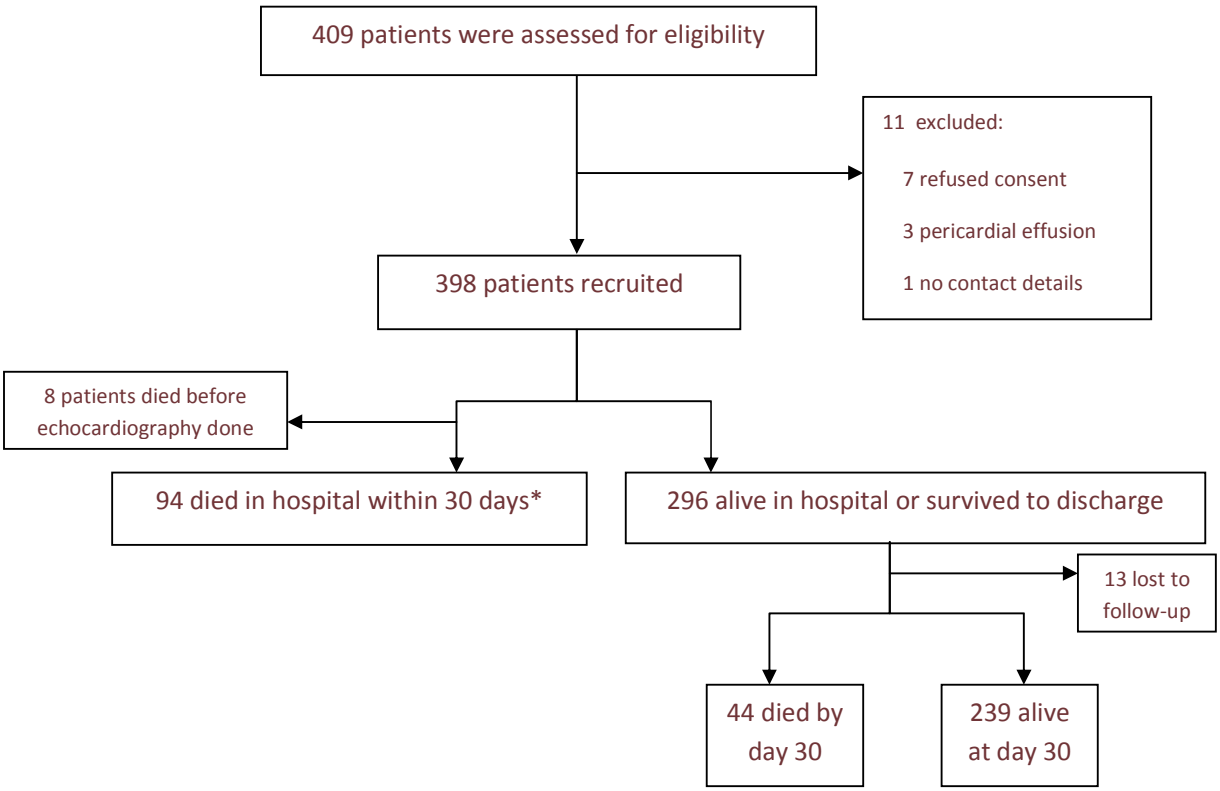
A p-value of less than 0.05 was taken as the level of statistical significance.

CHAPTER 5

10.0 RESULTS:

Between November 2010 and September 2011, 409 patients were approached as potential candidates for inclusion into the study. Of these, 7 refused to give consent. 3 patients were excluded on the basis of having primary pericardial disease/ effusion and 1 had no contact details for follow-up (see ***Fig.1***). 94 patients died while in hospital. Of the discharged patients, 13 were lost to follow-up and 44 were dead by day 30 with a median time-to-death of 14 days (IQR= 7-25 days).

Fig 2: **Recruited patients**



10.1 Baseline characteristics of the participants

Patient demographics and clinical findings are shown in ***Table 1*** and described briefly here. Majority of the patients were female (59%; 95% CI 54-64). The patients' mean age was 48yrs and 50 yrs for males and females respectively (p=0.9272). A significant proportion of the patients had never been hospitalised previously with heart failure as demonstrated in ***Graph 1*** (64%; 95% CI 59-68). 88 patients were HIV positive (23%; 95% CI 19-27).

***Graph 1*: Previous hospital admissions with heart failure**

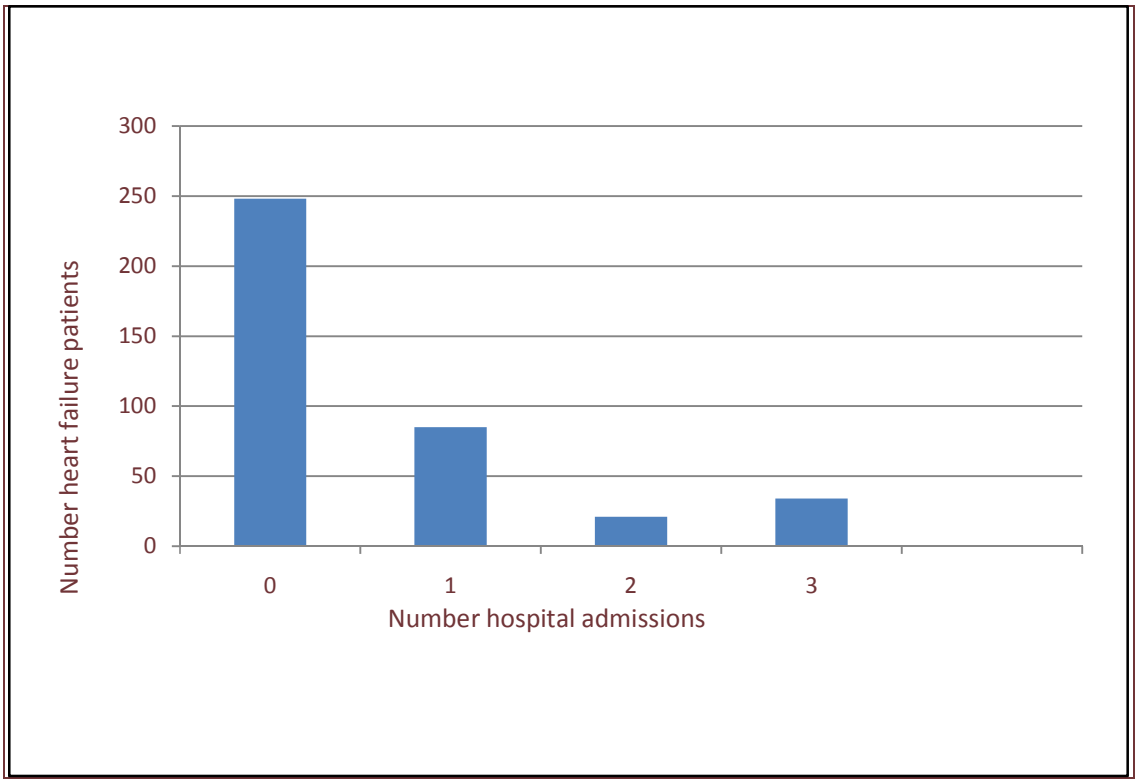


***Table 1*:** Baseline characteristics of heart failure patients and laboratory measurements.

Characteristic	Total n=390	LVEF<40% n=163	LVEF >= 40% n=227	P value
Age, yrs	50 (33-68)	48 (32-69)	52 (34-69)	0.865
Females (No (%))	231 (59)	133 (58)	97 (42)	<0.001*
NYHA class IV (No (%))	119 (31)	118 (72)	153 (67)	0.292
Hypertension (No (%))	130 (33)	49 (30)	81 (38)	0.246
Diabetes mellitus(No (%))	19 (5)	8 (4.9)	11 (4.8)	0.978
HIV (No (%))	88 (23)	42 (26)	46 (20)	0.200
SBP, mmHg	110 (90-130)	100 (90-124)	110 (100-140)	0.001*
DBP, mmHg	70 (60-80)	68 (60-80)	70 (60-81)	0.009*
Heart rate, beats/min	90 (80-100)	93 (80-102)	90 (80-100)	0.040*
Temperature, ^{O} Celsius	36.1 (36-36.8)	36 (36-36.8)	36.3 (36-37)	0.093
Resp Rate, breaths/min	24 (20-28)	24 (20-28)	22 (20-26)	0.013*
Underlying cardiac pathology (No (%)):				
DCM	180 (46)	118 (72)	62 (27)	<0.001*
Corpulmonale	42 (11)	6 (4)	36 (16)	<0.001*
HHD	112 (29)	28 (17)	84 (37)	<0.001*
Valvular heart disease	45 (12)	10 (6.1)	35 (15)	0.005*
Urea, mmol/L	6.7 (4.8-10.1)	7.0 (4.8-10.3)	6.3 (4.8-10)	0.506
Creatinine, umol/L	100 (73-131)	98 (71-118)	102 (74-143)	0.076
Sodium, mmol/L	135 (132-140)	135 (131-139)	136 (132-141)	0.123
Potassium, mmol/L	3.86 (3.40-4.42)	3.73 (3.31-4.37)	3.91 (3.46-4.50)	0.267
Anaemia (Hb <12g/ dL)	166 (43)	69 (42)	97 (43)	0.937

Data are expressed as median (IQR) unless stated otherwise
** Statistically significant*

163 (42%, 95% CI 37-47) of the patients had an LVEF below 40% on trans-thoracic echocardiography. There was no statistically significant difference in age, NYHA class, HIV status or comorbidities such as diabetes mellitus or hypertension between those with reduced and preserved LVEF. As expected, patients with reduced LVEF had lower blood pressures and higher heart rates on admission. A significant proportion of patients with reduced LVEF had dilated cardiomyopathy as the cause of the heart failure. Those with preserved LVEF had either hypertensive heart disease, corpulmonale or valvular heart disease.

The median values for blood urea, creatinine, sodium, potassium and haemoglobin were comparable between the heart failure patients with reduced LVEF and those with preserved LVEF.

10.2 Medication use

***Table 2*: Previous and admission medication**

	LVEF<40%	LVEF>=40%	P value
Previous medication (n=142)			
Loop diuretic	65 (40)	95 (42)	0.696
ACEI or ARB	55 (34)	68 (30)	0.428
Aldosterone antagonist	21 (13)	25 (11)	0.573
B Blockers	3 (1.8)	5 (2.2)	0.804
Admission medication (n=390)			
Loop diuretic	120 (74)	188 (83)	0.028*
ACEI or ARB	86 (53)	144 (63)	0.035*
Aldosterone antagonists	31 (19)	37 (16)	0.486
B Blockers	2 (1.2)	5 (2.2)	0.475
Digoxin	52 (32)	52 (23)	0.048
Aspirin	49 (30)	76 (34)	0.476
Dopamine	39 (24)	22 (10)	<0.001*

Data are expressed as number (percent)
**Statistically significant*

Most of the previously diagnosed heart failure patients were on a combination of loop diuretics with ACE inhibitors (or ARBs) and/or aldosterone antagonists. Only 8 patients were on B blockers (Carvedilol) for chronic heart failure (***Table 2***). Only 62% (n=87) of the previously diagnosed heart failure patients took their anti-failure medication consistently as prescribed by the attending doctor. However, this was self reported data from the patient and may not be accurate.

Loop diuretics and ACE inhibitors/ ARBs were more commonly prescribed in patients with LVEF>=40 percent on admission. Those with LVEF<40 percent were more likely to receive dopamine and digoxin than those with preserved systolic function.

10.3 Outcome and Predictors of 30 day mortality

***Table 3*: Outcome of heart failure patients within 30 days of admission**

	Total n=390	LVEF<40% n=163	LVEF >= 40% n=227	P value
Death from any cause:	138 (35)	77 (56)	61 (44)	<0.001*
In-hospital Mortality	94 (68)	57 (61)	37 (39)	0.006*
Discharged then died	44 (32)	20 (21)	24 (79)	0.181
Alive at day 30:	252 (65)	86 (34)	166 (66)	<0.001*
Alive in hospital	14 (6)	3 (35)	11 (65)	0.006
Discharged, alive at day 30	238 (94)	83 (45)	155 (55)	0.181

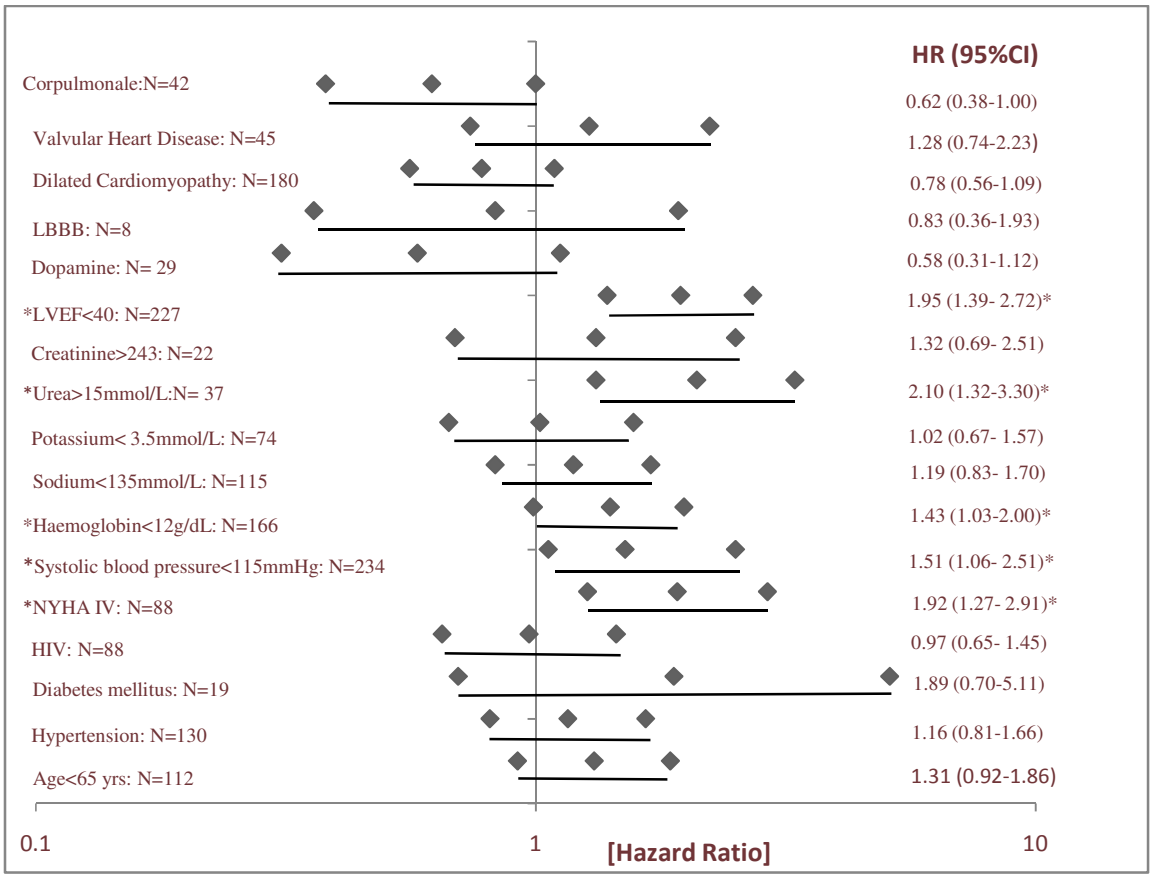
Data are expressed as number (percent)
**Statistically significant*

***Table 4:* Probability of death on logistic regression analysis**

Variable	Crude OR	95% CI	Adjusted OR	95% CI
Age>65 years	1.41	0.90- 2.21	1.72	0.97- 3.04
Hypertension	0.86	0.55- 1.34	1.16	0.66- 2.06
Diabetes mellitus	0.47	0.15- 1.45	0.43	0.13-1.48
HIV	0.99	0.60- 1.63	0.96	0.53- 1.72
NYHA IV	2.22	1.36- 3.62*	2.15	1.27- 3.64*
SBP< 115mmHg	1.63	1.05- 2.51*	1.51	0.84- 2.70
Haemoglobin <12g/dL	1.67	1.10- 2.54*	1.79	1.11- 2.89*
Sodium<135mmol/L	1.26	0.80- 1.97	1.01	0.60- 1.70
Potassium<3.5mmol/L	0.99	0.58- 1.68	0.82	0.45- 1.47
Urea>15mmol/L	3.00	1.50- 5.99*	2.48	1.07- 5.70*
Creatinine<243umol/L	1.56	0.66- 3.72	1.49	0.49- 4.48
LVEF<40%	2.44	1.59- 3.73*	2.86	1.68- 4.87*
Dopamine use	2.14	1.23- 3.73*	1.52	0.79- 2.91
Valvular Heart Disease	0.80	0.41- 1.57	1.26	0.52- 3.07
DCM	1.33	0.88- 2.02	1.00	0.51-1.97
Corpulmonale	1.77	0.93- 3.38	2.17	0.93-5.04

**Statistically significant*

Graph 2: **Predictors of mortality (Crude Hazard Ratios on Cox Proportion Logistic Regression)**

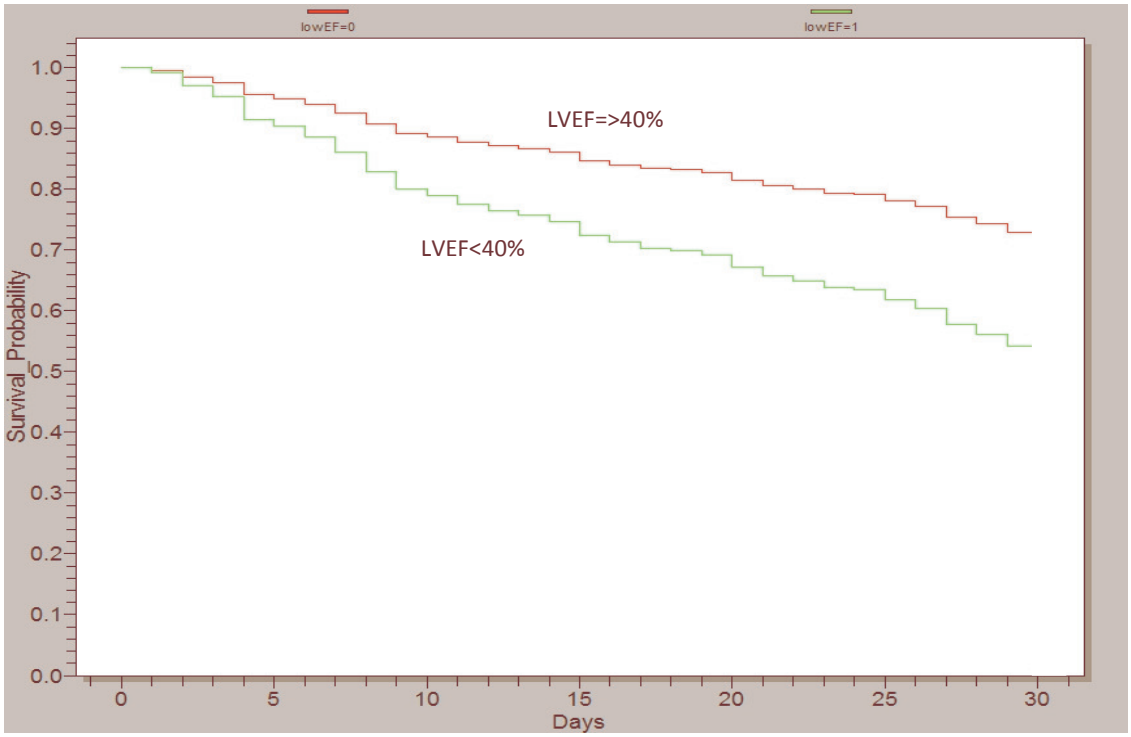


N=number
**Statistically significant*

Table 5: **ECG findings and the probability of death**

Variable	Crude OR	95% CI	Adjusted OR	95% CI
Atrial fibrillation or flutter	1.25	0.58- 2.67	1.24	0.46- 3.33
Premature Ventricular Contractions	1.37	0.77- 2.43	1.40	0.65-2.98
RBBB	2.99	0.42- 21.4	0.26	0.03- 2.13
LBBB	1.20	0.44- 3.23	1.86	0.46-7.59
Long QTc	0.50	0.07- 3.58*	0.45	0.05- 0.47

***Graph 3*: Kaplan Meier curve: Survival probability based on LVEF**



**Statistically significant*

All-cause mortality was 35 percent with most of these deaths occurring in hospital (see ***Table 3***). The factors shown to be predictive of death on both univariate and multivariate logistic regression analysis, and cox proportion hazard regression analysis (see ***Table 4, Graph 2 and Graph 3***) were NYHA class IV (OR=2.15, 95%CI 1.27- 3.64), serum urea above 15mmol/L (OR=2.48, 95%CI 1.07-5.70), haemoglobin level below 12g/dL (OR=1.79, 95%CI 1.11-2.89), and LVEF<40 percent (OR=2.86, 95%CI 1.68- 4.87). The additional factor associated with increased risk of mortality on univariate analysis was systolic blood pressure below 115mmHg OR=1.63, 95%CI 1.05- 2.51). However, serum creatinine (OR=1.49, 95%CI 0.49-4.48), the use of dopamine on admission (OR=1.52, 95% CI 0.79-2.91), and HIV status (OR=0.96, 95% CI 0.53-1.72) had no bearing on the risk of death in this patient population. The underlying cardiac abnormality was not associated with increased risk of death.

A few patients had conduction defects and arrhythmias. The most frequent findings on ECG were premature ventricular contractions (n=30, 14 percent) and atrial fibrillation (n=18; 8 percent). Only 8 of the patients we studied had LBBB. However, these findings were not associated with an increased risk of death (see ***Table 5***).

CHAPTER 6

11.0 DISCUSSION

Our patient population was mostly female and younger by almost 20 years compared to other cohorts studied in the North America.[12] This finding was similar to other studies done in Uganda and Nigeria[12, 13] and was probably due to the higher proportion of valvular heart disease and dilated cardiomyopathy (presumed to be of infective cause) in our patient population compared to coronary artery disease which is found predominantly in males (and postmenopausal females) in western settings.[1] HIV sero-prevalence in our study population at 23 percent was higher than in the general Zambian population. This suggests some contribution of HIV associated cardiomyopathy as a cause of heart failure. HIV seropositivity however, was not associated with increased risk of death. The proportion of patients with ischaemic heart disease was small and this could be an underestimate. Some patients may have erroneously been labelled as having cardiomyopathy. With the lifestyle changes noted amongst the affluent African population, ischaemic heart disease needs to be thoroughly explored in our patient population.

The proportions of deaths in our patient population during the follow-up period was quite high at 35 percent (n=138). This was much higher than the in-hospital mortalities recorded in other studies (i.e. 3 to 4.1 percent). The magnitude of deaths was also 3 fold higher than that documented in a Nigerian study in patients who were followed-up for a period of 6 months.[11] However, the authors acknowledged that the study's sample size of 79 patients was quite small. Being a tertiary health institution, most of the patients who present to the University Teaching Hospital are critically ill patients referred from primary health care centres and second-level hospitals. In addition, most of the patients present late to health care facilities further contributing to a delay in diagnosis and treatment. Finally, most of our heart failure patients, including those who could benefit from cardiac surgery, have limited access to anti-failure medication as the only readily available treatment option. None of the heart failure patients followed up with poor systolic function had access to ICDs or cardiac transplant. This could explain the higher mortality in patients with poor systolic function in our setting compared to the rest of the world where patients have better access to optimal medical therapy and potentially life-saving surgical interventions.

The independent prognostic predictors of mortality determined from our study included LVEF<40 percent, NYHA class IV, and serum urea above 15mmol/L. Systolic blood pressures below 115mmHg and haemoglobin level below 12g/dL were additional factors indicative of a poor outcome within the 30 day period of follow-up.

The proportion of heart failure patients with LVEF<40 percent from our study was 42 percent (n= 163). This finding was similar to studies done in the developed world[12, 15] which found that about half of the admitted heart failure patients had poor systolic function on trans-thoracic echocardiography. The majority of the long-term follow-up studies done in North America as well as two studies done in Brazil and Nigeria found that patients with LVEF below 40 percent had worse outcomes. However, unlike our study, these studies had varied periods of follow-up ranging between three and six months. Most of these studies recruited chronic stable heart failure patients who were monitored and treated on out-patient basis. Despite the differences in patient populations and periods of follow-up, we found that LVEF less than 40 percent was an important independent prognostic factor in the patients we studied.

The proportion of the heart failure patients recruited with anaemia was slightly lower than was estimated in other studies on hospitalised patients.[32] Anaemia was also an independent prognostic indicator of 30-day mortality.

The prognostic value of high NYHA class has mainly been echoed in long-term follow-up studies on heart failure and not in studies on in-hospital mortality. However, this factor could be of prognostic significance as NYHA class IV on admission indicates poor functional status and significant pulmonary congestion in patients who present with acute decompensation of chronic heart failure.

According to a study done by Fonarow *et al* [12] in-hospital mortality was higher in heart failure patients who had systolic blood pressure below 115 mmHg, serum urea above 15mmol/L and serum creatinine above 243umoL/L. The prognostic value of these factors was independent of the patients' LVEF. The predictability of high blood urea in prognosis was also in keeping with the findings in Petersen's study.[15] However, high serum creatinine was not found to be an important prognostic factor in our study on analysis, even after adjusting for other variables. The contribution of poor renal function to worsening cardiac function and increased risk of death, however, was not fully explored as estimation of creatinine clearance

or GFRs were not done due to logistical problems. It is therefore difficult to conclude from these findings that cardio-renal syndrome does not play a role in the deaths of these patients.

The median serum sodium level of 135 mmol/L and serum potassium level of 3.8mmol/L in our patients was comparable to the findings in other Western studies. Some of our patients however, had deranged electrolyte profiles. 19 percent of the patients in this study had hyponatremia and 30 percent had hypokalaemia of varying degrees. Despite these findings, hyponatremia and hypokalaemia did not contribute to increased risk of death in the patients we studied.

The low number of patients found to have arrhythmias or conduction defects may not be reflective of the actual magnitude of the problem in our heart failure patients as none of the patients we studied had access to continuous cardiac monitoring. Potentially fatal arrhythmias may not have been detected during their hospitalisation. Therefore, the data obtained refuting an association between increased risk of death in the patients with atrial fibrillation or LBBB, in line with major studies, may be inaccurate.

12.0 STUDY LIMITATONS:

None of the patients had continuous monitoring of cardiac rhythm even whilst in hospital due to the limited number cardiac of monitors for inpatients and lack of ambulatory ECG devices for outpatients in order to detect arrhythmias.

Considering that all-cause mortality was used as one of the end-points and that the study protocol did not include post-mortems, it is possible that some deaths may not have been due to cardiovascular cause, contributing to the high mortality reported in this study.

Some important prognostic indicators were not tested for in this study due to limited resources (i.e. cardiac biomarkers such as BNP, cystatin c and troponins).

The information regarding the predictors of long term prognosis in the heart failure patients we studied was not obtained due to the limited follow-up period.

CHAPTER 7

13.0 CONCLUSION

In conclusion, mortality amongst hospitalised heart failure patients at the University Teaching Hospital in Lusaka, Zambia is high.

As hypothesised, LVEF less than 40 percent was found to be a predictor of 30 day mortality in hospitalised heart failure patients at the UTH. Other factors such as NYHA class IV, low systolic blood pressure, high serum urea and anaemia also increased the risk of death of 30 day mortality.

14.0 RECOMMENDATIONS

In view of the high mortality, we recommend that patients be triaged according to risk. In order to improve survival, heart failure patients who are at high risk of death need close monitoring so that potentially life-saving measures can be instituted when indicated.

LVEF, haemoglobin levels, and serum urea should be measured in all admitted heart failure patients. NYHA class must be documented and accurate blood pressure measurements taken on all in-patients in order to assess the risk of mortality.

Patients with LVEF less than 40 percent with refractory heart failure and cardiogenic shock should have access to ICDs and cardiac transplant in order to improve survival.

The presence of anaemia and the its underlying cause in heart failure patients should be investigated and promptly treated in order to reduce the precipitation and worsening of heart failure symptoms and functional status.

Early referral of heart failure patients to tertiary health institutions for evaluation and management should be encouraged as late presentation to hospital could have contributed to the high mortality reported in this study. We also recommend that public health awareness be increased on the need for patients to seek medical help early in order to reduce mortality rates.

Medical therapy needs to be optimised with the use of the recommended beta blockers for chronic stable heart failure, and the combination of hydrallazine with nitrates which are currently underprescribed by attending physicians. There is need to ensure regular supply of essential drugs required for the treatment of heart failure to health institutions.

Hospitalised heart failure patients need continuous monitoring of cardiac rhythm. Cardiac monitors should therefore, be procured and placed in the admitting emergency wards. This would aid in the prompt recognition and treatment of life-threatening arrhythmias. Holter monitoring should also be made available for select outpatients at risk of potentially fatal arrhythmias.

Adherence counselling needs to be intensified in order to improve drug compliance. A study on patient adherence to anti-failure medication and related factors should be done to create basis for future interventions.

A cardiac register for the heart failure patients seen at the University Teaching Hospital needs to be developed in order to ensure proper follow-up of patients.

A long term follow-up study on outcome in our patient population with heart failure needs to be done. The state of debility and outcome of these patients post-discharge remains largely unknown. With the current pressure on the few available medical resources in the healthcare system and the human resource crisis, it would be prudent to conduct a long-term follow-up study in order to determine ways of improving healthcare delivery for our heart failure patients in Zambia. Further studies on cardiac biomarkers such as brain natriuretic peptide, troponins, and cystatin C ought to be done in order to determine the contribution of these factors to prognosis in our patient population.

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APPENDICES

ANNEX I

DATA COLLECTION SHEET : Factors Associated with Mortality in Adult Patients Admitted with Heart Failure at the University Teaching Hospital

Instructions : Kindly TICK or CHECK box where applicable. Data should only be collected after the consent form has been signed by the patient or next of kin.

PTID/Study No. **HF** __ __ __ __

Town : _____ Residential area : _____

Phone No (1): _____ Phone No (2) :_____

Date of Admission: _____/_____/_____

HISTORY

1. AGE: _____ yrs
2. SEX: ☐ Male ☐ Female
3. Year of diagnosis of heart failure : _____
4. Number of previous hospital admissions in the last year with heart failure:
   ☐ 0 ☐ 1 ☐ 2 ☐ >=3
5. Date of previous admission due to heart failure: _____/_____/_____
   ☐ Not applicable
6. Drug Hx : Type of antifailure medication received in the last 6 months (Note : Can select more than 1 option):
   ☐ Not applicable ☐ None
   ☐ Diuretics ☐ Aldosterone antagonists
   ☐ ACE inhibitors ☐ β Blockers
   ☐ Dopamine ☐ Dobutamine
   ☐ Other drugs, specify (antibiotics, antiretrovirals):_____
7. Adhérence to medication :
   ☐ Always ☐ Sometimes ☐ Never ☐ Not applicable

8. Type of antifailure medication/ inotropes prescribed on admission (Note : Can select more than 1 option):

☐ Diuretics ☐ Aldosterone antagonists
☐ ACE inhibitors ☐ Beta Blockers
☐ Dopamine ☐ Dobutamine
☐ Other, specify:_____

9. Comorbidities: (Note : Can select more than 1 option):

☐ Diabetes ☐ Hypertension ☐ COPD ☐ HIV
☐ TB ☐ Not applicable

Other, specify: _____

PHYSICAL EXAMINATION (on admission)

10. NYHA Class:

☐ I ☐ II ☐ III ☐ IV

11. Blood Pressure: _____ mmHg
12. Heart Rate: _____ beats/min
13. Respiratory Rate: _____ breaths/min
14. Temperature: _____ ^{o} C

BLOOD RESULTS (on admission)

15. HAEMOGLOBIN LEVEL: _____ g/dL
16. SERUM UREA: _____ mmol/L
17. SERUM SODIUM: _____ mmol/L
18. SERUM POTASSIUM: _____ mmol/L
19. SERUM CREATININE: _____ umol/L
20. CD4 COUNT (if HIV +ve):_____ cells/ml

ELECTROCARDIOGRAM findings:

21. ☐ Normal(if normal, skip Q.23-25) ☐ Abnormal

Note : Can select more than 1 option for Q. 23-25

22. Arrhythmias:

☐ None
☐ Atrial Fibrillation/Flutter
☐ Ventricular fibrillation/tachycardia
☐ Other, specify: _____

23. Ischaemic changes:

☐ None
☐ Q waves
☐ ST elevation
☐ ST depression
☐ T wave inversion

24. Other abnormalities:

☐ Long QTc
☐ Left Bundle Branch Block
☐ Right Bundle Branch Block
☐ Left Ventricular Hypertrophy
☐ Right Ventricular Hypertrophy
☐ Premature Ventricular Contractions
☐ Premature Atrial Contractions
☐ Other, specify: _____

ECHOCARDIOGRAM findings:

25. EJECTION FRACTION: _____ %

26. STRUCTURAL CARDIAC ABNORMALITY:

☐ Valvular Heart Disease ☐ Dilated Cardiomyopathy
☐ Hypertensive Heart Disease ☐ Corpulmonale
☐ Other, specify: _____

DISCHARGE FROM HOSPITAL: (applicable if patient alive within 30 days of admission)

27. ☐ YES ☐ NO

Date of discharge from hospital: _____/_____/_____

OUTCOME:

28. ☐ DEAD BY DAY 30 ☐ ALIVE AT DAY 30

(skip Q.28, 29)

29. Date of outcome: _____/_____/_____

30. Number of days to outcome:

☐ 1 to 7 days
☐ 8 to 14 days
☐ 15 to 21 days
☐ 22 to 30 days

ANNEX II:

CONSENT FORM: Factors Associated with Mortality in Adult Patients Admitted with Heart Failure at the University Teaching Hospital

Introduction

I, Pamela Ng'onga Chansa, an MMED student in the School of Medicine at the University of Zambia, kindly request your participation in the above mentioned study. This study is in partial fulfilment for the award of a Master of Medicine in Internal Medicine. Before you make up your mind whether to take part 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 in this study, you will be asked to sign this consent form in the presence of a witness.

Nature and purpose of the study

This study is being conducted to determine some of the common factors associated with poor outcome in patients with heart failure admitted to the University Teaching Hospital. This is being done in order to identify the factors which are potentially reversible so as to help reduce disease progression.

Procedure of the study

If you agree to participate in this study, we will obtain information using a data entry sheet. Your contact details (telephone number(s)) will be required for easy follow-up. Samples of blood will be taken from you and sent to the laboratory for testing. A qualified HIV counsellor will counsel you before an HIV test is done. Other investigations will include an Echocardiogram and an Electrocardiogram. The results of the tests will be communicated to you and the attending physician if you so wish.

Possible risks and discomforts

You will not be exposed to any risks by enrolling into the study. However, you will experience discomfort from routine collection of blood samples and any other procedures during the course of treatment as part of routine hospital care.

Possible benefits

The information obtained in this study will help in the management of other heart failure patients.

Confidentiality

All the information collected is strictly confidential. Data that will be collected, analysed, and reported on will not include your name and therefore cannot be traced to you.

Consent

Your participation is strictly voluntary. You will not suffer any consequences if you decide not to participate in this study. You may also withdraw from the study at any time for any reason without consequences to you.

Thank you for considering participation in this study. If you have any questions, concerns and clarifications, please contact Dr Pamela N Chansa or The University of Zambia Research Ethics committee on the following addresses;

Dr Pamela Ng'onga Chansa,

The University Teaching Hospital,

Department of Internal Medicine,

P/Bag RW1X,

Lusaka, Zambia.

Mobile phone Number: 260-1-0978700967

Landline Number: 260-1-294499

The University of Zambia Biomedical Research Ethics Committee,

Ridgeway Campus,

P.O Box 50110,

Lusaka, Zambia.

Telephone: 260-1-256067

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 (Signature or thumbprint)	Date

_____	_____	_____
Witness (Print Name)	Witness (Signature)	Date

THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

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Assurance No. FWA00000338
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10 November, 2010
Our Ref: 004-10-10

Dr Pamela Chansa, BScHB, MBChB
Department of Internal Medicine
University Teaching Hospital
LUSAKA

Dear Dr Chansa,

RE: SUBMITTED RESEARCH PROPOSAL: **"FACTORS ASSOCIATED WITH MORTALITY IN ADULTS ADMITTED WITH HEART FAILURE AT THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA"**

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee expedited meeting held on 10 November, 2010 where changes/clarifications were recommended. We would like to acknowledge receipt of the corrected version with clarifications. The proposal is approved.

CONDITIONS:

- This approval is based strictly on your submitted proposal. Should there be need for you to modify or change the study design or methodology, you will need to seek clearance from the Research Ethics Committee.
- If you have need for further clarification please consult this office. Please note that it is mandatory that you submit a detailed progress report of your study to this Committee every six months and a final copy of your report at the end of the study.
- Any serious adverse events must be reported at once to this Committee.
- Please note that when your approval expires you may need to request for renewal. The request should be accompanied by a Progress Report (Progress Report Forms can be obtained from the Secretariat).
- **Ensure that a final copy of the results is submitted to this Committee.**

Yours sincerely,

Dr E. M. Nkandu
CHAIRPERSON

Date of approval: 10 November, 2010 **Date of expiry**: 9 November, 2011