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CLINICAL PROFILE OF HEART FAILURE PATIENTS FOLLOWED UP IN OUTPATIENT CARDIAC CLINIC AT KING FAISAL HOSPITAL

Dissertation submitted to the college of Medicine and Health Sciences, School of medicine and pharmacy in partial fulfillment of the requirement of the award of a Master's degree in Internal medicine, University of Rwanda.

Kigali, August 30, 2021

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Declaration

I hereby declare that this dissertation titled “CLINICAL PROFILE OF HEART FAILURE PATIENTS FOLLOWED UP IN OUTPATIENT CARDIAC CLINIC AT KING FAISAL HOSPITAL” is my original work. Except where acknowledged; it has passed through the anti-plagiarism system and found to be compliant and this is the final version of my thesis.

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Date: August 30, 2021

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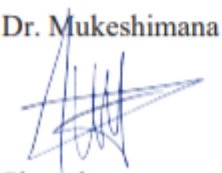

Signed

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Dedication

To the almighty God, my beloved wife Nise Sandra, and my beautiful baby girl Selah; in you, I find my daily inspiration.

To my Late Dad, whose non-resilience keep motivating me and pushing me to become the best version of myself.

To my mum, my siblings, and friends you made me a better person.

Abstract

Introduction: Heart failure is a disease that exerts great stress on patients, caregivers, and healthcare systems. In sub-Saharan Africa, it causes multiple readmissions and a high-cost economic burden; this is not different from Rwanda. This study aims are to have a clinical profile of HF patients in outpatient cardiac clinic, to assess the adherence to guideline recommended medical therapy in chronic heart failure with reduced, mid-range and Preserved Ejection fraction with eccentric Left ventricular remodeling, and to have an insight into the need for cardiac device therapy in the studied population, in a country with a scarce resource on advanced therapy.

Method: This was a prospective observational study conducted at King Faisal Hospital, Kigali, Heart failure enrolled patients from June 1, 2020, to January 31, 2021, were followed up for a period of 6 months. We recorded their social demographic status, class of heart failure, comorbidities, initial NYHA functional status, three and six months NYHA functional status, medications used, combination anti-remodeling modalities, up-titrated and target maximum anti-remodeling medication at enrollment, at three and 6 months in heart failure with reduced, mid-range and Preserved ejection fraction with LV remodeling.

Results: 86 participants were enrolled in the study, 10 were lost to follow-up, 3 died and 3 didn't sign the consent. The median age was 51 years, female made the majority 53 % of the studied population,44 % were overweight,69% were coming from the city of Kigali. 37%,24%,20%,19 %, are percentages of HFrEF, HFpEF, HFmrEF, and Right-sided heart failure respectively, among all HF patients; cardiomyopathies was the most prevalent, followed with Rheumatic heart disease with (64 %,21%) respectively.

Hypertension and diabetes were highly predominant comorbidities with 26% and 16% of the population respectively. The majority in this cohort, came initially in NYHA class II (44%) and class III (41%) there was improved functional status at 6 months with 66% in NYHA class I and 28% in NYHA class II. In HFrEF/HFmrEF/Preserved EF with LV remodeling; the use of anti-remodeling was used during the whole 6 month's follow-up with RAS I (average 96 %), Bblocker (average 92%), MRA (86% average), SGLT-2 I (2% average).

In HFrEF, ACE I+ Bblocker +MRA was the predominant combination at enrollment,3 and 6 months with 65%,50%, and 42%, respectively.

At 3 months, only 2 classes of anti-remodeling attain maximum target doses; in HFrEF patients, those on aldactone attain maximum with 86% followed with ACE I with 50% at target maximum dose for those in the group of HFrEF/HFmrEF/Preserved EF with LV remodeling.

At 6 months, 3 classes of anti- remodeling attain maximum target doses; in HFrEF patients, those on aldactone attain a maximum with 91 % followed by Bblocker attain target maximum dose of 68 % and with ACE I that attain a maximum of 62% in the group of HFrEF/HFmrEF/Preserved EF with LV remodeling.

The need for device therapy was found to be low (CRT 15%, ICD 7%).

Conclusion: We found that HFrEF was the most prevalent subtype of heart failure, cardiomyopathies was the leading class. The functional status went improving during the follow-up with NYHA Class I being the most prevalent at 6 months, the need for cardiac devices was found to be low and the adherence to GDMT in chronic heart failure in HFrEF/HFmrEF/Preserved EF with LV remodeling is relatively satisfactory, though the dosage to achieve the target is suboptimal especially at 3months.

Key words: Clinical profile; outpatient heart failure patients; guideline directed medical therapy adherence; need of device therapy; King Faisal Hospital Kigali.

List of abbreviations

ARB: Angiotensin receptor blocker

ACE I: Angiotensin-converting enzyme inhibitor

ARNI: Angiotensin receptor –Neprilysin inhibitor

Bblocker: Beta blocker

CMR: Cardiac magnetic resonance

CT: Computer tomography

COPD: Chronic obstructive pulmonary disease

CRT: Cardiac resynchronization therapy

GDMT: Guideline directed medical therapy

HFrEF: Heart failure with reduced ejection fraction

HFmrEF: Heart failure with mid-range ejection fraction

HFpEF: Heart failure with preserved ejection fraction.

HF: Heart failure

HHD: Hypertensive heart disease

ICD: Intra-cardiac defibrillator

IHD: Ischemic Heart disease

LV/RV: Left ventricle/Right ventricle

LVEF: Left ventricle ejection fraction

LVEDV/LVESV: Left ventricular end-diastolic volume /left ventricular end-systolic volume

MRA: Mineralocorticoid receptor antagonist

MR: mitral regurgitation

NYHA: New York heart association

OSA: Obstructive sleep apnea

OPD: Outpatient patient department

PASP: Pulmonary artery systolic pressure

PADP: Pulmonary artery diastolic pressure

PND: Paroxysmal nocturnal dyspnea

RAS I/ RAAS I: Renin angiotensin/aldosterone system Inhibitor

RHD: Rheumatic heart disease

RV: Right ventricle

SV: Stroke volume

TAPSE: Trans-annular plane systolic excursion

TTE: Transthoracic echocardiography

TR: Tricuspid regurgitation

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1. INTRODUCTION

1.1. Background

Heart failure is regarded as a progressive disease that unable the heart to generate enough cardiac output to meet metabolic demands to under perfused tissues, or it ability to do so at higher filling pressures.

Heart failure is classified according to the ejection faction ,presence or not of structural heart disease ,any diastolic dysfunction and presence of elevated natriuretic peptides ,its classification has changed recently in to three subtypes and according to their ejection fraction : HFrEF, HFmrEF, HFpEF(1)

26 million of people in the world population are affected by Heart failure, per that it has been classified as a global pandemic. (1)

Heart failure burden to health care system is asserted to rise as lifestyles are changing, deleterious lifestyles, sedentary, and increase life expectancy, hence heart failure burdens not only the health systems but also the next of kin and the patient in person. (2)

Heart failure population are stated to rise from 2012 to 2030 with 2.42% to 2.97% respectively;
Adding on that, its prevalence is stated to rise from 2012 to 2030 with 46%, with a total of more than 8 million of adult population more than 18 years of age. (association, 2019) (3)

Heart failure is regarded as the primary cause of hospitalization in the elderly.(4) (5)

In the United States of America, 8.5% of cardiovascular mortality are attributed to HF. An average per year of new cases of HF is estimated to be 960,000 cases, with a rate per year of 309,000 death originates from HF roughly calculated to be one in eight deaths.(6)

In the European Union, an estimate of more than 10 million has HF within it 510 million people.

An average of 15 million of the population in Europe lives with HF, this has been stated by The European society of cardiology 2008 guidelines for the management and diagnosis of decompensated and chronic HF.(7)

A study aiming to approximate the value in regards to HF in 24 countries within the European union ushered by a group of researchers at Imperial college of London and the International center for circulatory health, found that the cost per year was estimated to be 33.14 billion US$ which is approximatively €29 billion.(8)

In the Sub-Saharan Africa , HF cases ascends with recurrent hospital admissions and high economic cost burden and Disability –Life years.(9)

Heart failure in Sub-Saharan Africa in contrast to western countries; it is a progressive disease with more frequency in the young and middle age group. Hypertensive heart disease (number one with 39.2%), cardiomyopathies (22.7%), rheumatic heart disease (13.8%) are predominating; these three etiologies have 75% pertaining to HF etiologies ; IHD account for 7.2%.(9)

An approximate of 12 million people have RHD in Sub-Saharan Africa, and the mortality rate per year is approximated to be 400.000 deaths. (9)

In Sub-Saharan region; among the most frequent and contemplated cardiomyopathies: Dilated, endo-myocardial fibrosis and peri-partum are most prevalent. other cardiomyopathies are less common.(9)

Hypertension in Africa is contemplated as the cornerstone of cardiovascular diseases. (10)

Hypertension in Africa cases rose from 1990 to 2010 with 54.6 million to 130.2 million cases respectively; expectations by 2020 rose up to 216.8 million patients.(11)

The heavy load in Africa of RHD, infective endocarditis is enhanced by a widespread presence of rheumatic fever, which is usually preventable and amenable but enhanced by a high burden of socio-political precariousness, poor nutrition ,unavailability of infrastructures and above all poverty.(12)

A retrospective chart review done in Rwanda, conducted in 3 non-communicable disease clinic (NCD) from 2006 to 2017 enrolled 719 patients with HF. The overall median age was (including pediatrics and adults) was 27 years, adults median age was 42 years. Adults were the predominating population with 64 %, females were in majority with 68% of adult population.

3 etiologies were predominating in the adults; with cardiomyopathy, RHD, HHD with 40% ,27% and 13% respectively. No records of IHD were found . (2020) (13)

1.2 Problem statement

Based on anecdotal observation, heart failure is a common condition in Rwanda referral hospitals.

There is a paucity of data on its classification and subtypes, outpatient follow-up, medication, and advanced therapies need.

1.3 Research question

1.3.1 General question

What are the demographics characteristic, classification, and subtypes of heart-failure patients followed in the OPD cardiac clinic at King Faisal Hospital?

1.3.2. Specific questions

1.What is the functional status of patients with HF on follow-up at enrollment,3 months, and at 6 months.

2. Which class of heart failure are they in, what are the sub-types (HFrEF, HFmrEF, vs HFpEF vs Right-sided heart failure), and what is their estimated ejection fraction during the follow-up?

3.Which medications are they taking? Is it up-titrated to the maximum effective dose (especially in HFrEF, HFmrEF, and Preserved EF with left ventricular remodeling)?

4.How many require advanced therapy (cardiac devices); despite optimal medical therapies?

1.4. Hypothesis

We expect anti-remodeling therapy use at the target dose to be sub-optimal. We expect the need for Cardiac devices to be high.

1.5. Objectives.

1. To have a database of classification of heart failure patients followed in King Faisal hospital's cardiac clinic.
2. To see the trend of anti-remodeling up titration and target doses achievement especially in HFrEF, HFmrEF, and Preserved EF with left ventricular remodeling at 3 months and 6 months.
3. To have an overview of functional status using NYHA, at baseline, at 3 and 6 months.
4. To have an overview of echocardiographic finding of LVEF, diastolic function, and TAPSE at enrollment, at 3 and at 6 months.
5. To have an overview of the need for cardiac devices in cardiac patients followed at King Faisal Hospital (KFH) in the same cohort.

2. LITERATURE REVIEW

2.1. Definition

HF is defined as a cluster of signs and symptoms, arising from the heart incapacity to fulfill body energy requirements, either due to an impairment on its framework or its inaptitude to relax or to generate sufficient cardiac output.
Clinical diagnostic criteria have generally included history, physical examination, and imaging studies (chest radiograph,transthoracic echocardiography/cardiac MRI …)

HF can be classified as:

- low output (decrease cardiac output) vs High output (High stroke volume and high cardiac output)
- Left-sided or right-sided
- Systolic (inability to expel sufficient blood) vs diastolic (inability to relax and fill normally)
- Based on EF assessment in to (Heart failure with reduced EF (<40%), Heart failure with mid-range EF (40-49%) and Heart failure with preserved EF (>50%).

2.2. Pathogenesis (14)

HF can be viewed as a gradual dysfunction triggered by an index event that can be either acute, like in case of myocardial infarction or gradual onset like in case of cardiomyopathies; this index of event endpoint is loss of myocyte function to generate sufficient cardiac output to meet metabolic demands.

Several accommodating changes are switched on in the existence of myocyte impairment in the setting of left ventricular systolic dysfunction; allowing patients to modulate in a period of months to years until the heart fails and the patient becomes symptomatic which increases morbidity and mortality rates if not treated.

The conversion of HF in becoming symptomatic is associated with an increase activity in various systems including: neuro-hormonal, adrenergic, and cytokines.
These changes have a direct effect within the myocardium both at a cellular level and molecular level, these cluster of changes are called left ventricular remodeling.

Ventricular remodeling happens when there is an alteration in left ventricular mass ,geometry following the index of event or in the case of hemodynamic overload.
Increasing LV dilatation results in mitral valve incompetence due to tethering of papillary muscle and resulting in functional mitral regurgitation; which will increase the hemodynamic load on the heart, hence the progression of heart failure.

In HFrEF, the turnaround of left ventricular remodeling can be attained using medical and device therapy, owing to an amelioration of HF symptoms and life expectancy. One of the anti-remodeling medication objectives in heart failure is to prevent or reverses the remodeling of the heart. (14)

2.3. Clinical manifestations

Some of the fundamental symptoms of HF include fatigue and dyspnea.
Low output: fatigue, exercise intolerance, mental status changes, and anorexia
Congestive features:

- there can be left-sided (dyspnea, orthopnea, PND)
- there can be right-sided (peripheral edema, right upper quadrant discomfort, bloating, early satiety)

physical examination depends if there are congested or not, usually, they can have Cheyne stoke respiration, low pulse pressure, raised jugular venous pressure, S3 or S4 sound shifted PMI, added sounds on auscultating areas, congestive hepatopathy, jaundice, decreased breath sounds bilaterally, stony dullness, pulmonary edema.

2.3.1 Functional classification and severity stages

2.3.1.1. The Functional classification system (15)

Used as a measure of quantification of functional status limitation in HF patients was first developed by the NYHA.

- Class I- Patients with cardiac disease without limitations of physical activity.
- Class II- Patients with cardiac disease with slight limitation of physical activity.
- Class III- Patients with cardiac disease with marked limitations in physical activities but not at rest.
- Class IV- Patients with cardiac disease with limitations in any physical activities even at rest.

2.3.1.2 Stages in the development of HF

The American college of cardiology foundation and American Heart association guidelines highlighted various stages in HF progression (15) :

- Stage A – High risk of HF without structural heart disease or HF symptoms.
- Stage B – Presence of structural heart disease without signs and symptoms of HF
- Stage C – Presence of structural heart disease without signs and symptoms of HF either current or prior.
- Stage D – Refractory HF requiring special interventions.

2.4. Diagnosis

Clinical diagnostic criteria have generally included history using the Modified Framingham criteria (2 Major or 1major and 2 minors), physical examination and imaging studies (chest x-ray, Transthoracic echo, ECG, right heart catheterization, cardiac Mri vs CT ….)
Initial laboratory tests include: Full blood count, blood urea nitrogen (BUN), creatinine, electrolytes, thyroid function, serum albumin, and transaminases, NT-proBNP

2.4.1. Role of Imaging studies

- **Echocardiography:**

A transthoracic echocardiogram (with or without ultrasound contrast) alone does not establish nor excludes HF detection; but it is helpful to recognize findings consistent with HF and determine it etiologies.

- **Cardiac Mri:**

Volumetric CMR imaging is considered more accurate and reproducible compared to 2D TTE and doesn't use ionizing radiation as cardiac CT.

CMR help identify other HF etiology; it helps by giving an accurate assessment of cardiac structures, myocardial perfusion, viability, and presence of fibrosis. (16)

A patient who requires serial evaluation of left ventricular systolic function (patient undergoing potential cardio toxic chemotherapy) needs CMR, because small change may affect management.

- **Radionuclide ventriculography (RVG)**:

It may be considered if scarce imaging modalities, but exposes to ionizing radiation (6-7 mSv); may be particularly useful when there are remarkable wall motion abnormalities, deformed framework, or when TTE has poor image quality. Given its high reproducibility, it is helpful when serial evaluations are needed (eg, patients undergoing potentially cardio toxic chemotherapy). (17)

- **Cardiac Ct-scan:**

Enables assessment of coronary arteries, pulmonary embolus as well as LV function; but uses ionizing radiation (4-10 mSv)

- **Single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI):**

Assessing the LV function is generally not the primary reason for referral for SPECT-MPI, but SPECT-MPI does provide information on LV function when evaluating the presence myocardial ischemia and when analyzing its viability.(17)

2.4.2. Measures of left ventricular systolic function

- **LVEF (Left ventricular ejection fraction):**

It is the percentage scale of pumped blood during contraction in correlation with the amount of blood in the ventricle before the heart contracts.

SV = LVEDV – LVESV

LVEF (%) = SV/(LVEDV/100)

Hyper dynamic (>70%), normal EF (50-70%), mild dysfunction (40-49%), moderate dysfunction (30-39%), severe dysfunction (<30%). Several methods are stated in regards of the LVEF measurement and the linear method on the parasternal long axis view. The modified Simpson method using area tracings of the LV cavity is among the favored for assessing left ventricle volume quantification and measurement of LVEF.

- **Myocardial velocities, strain, strain rate:**

The term "strain" reflects the deformation of a structure and refers to the fractional or percentage change in the structure's dimension corrected for its original dimension.
Strain and strain rate can be calculated for various myocardial loci in radial, circumferential, and longitudinal directions.
Parameters such as strain and strain rate may prove to be more sensitive, reliable, and reproducible than LVEF.(18)

2.4.3. Measure of left ventricular diastolic function

Diastole has the following phases: Iso-volumetric relaxation (when both aortic and mitral valve are still closed), early left ventricular filing (when pressure in the L atrium is more than in the l ventricle and mitral valve opens), mid slow filling phase and Left atria kick (left atrial expulse all the blood content).
The echocardiogram is the key diagnostic modality for identifying diastolic dysfunction as well as identification of confounding factors and concurrent disorders.
It should be assessed in patients with HF and history of underlying heart disease.

It can happen in those with HFrEF or HFpEF.
Assessing diastolic dysfunction by echocardiography includes on top of assessing LVEF, LA&LV volume, PASP, PADP aim to assess:

- Trans mitral Doppler inflow velocity patterns
- Tissue Doppler velocities

2.4.4. Measures of Right ventricular function.
TTE with Doppler plays an important role in assessing RV function, it is readily available and gives information on R atrial size, inferior vena cava measurements and changes with respiratory movements, strain analysis and doppler velocities studies; however, if the result of TTE is suboptimal or limited other additional imaging modalities are there to assess RV function and structure like Cardiac Mri (CMR), cardiac CT, Radionuclide imaging, right heart catheterization.(19)

2.5. Approach to heart failure subtypes

The prior definition of systolic heart failure vs diastolic heart failure has been changed to Heart failure is subdivided in HFrEF (<40 %) which has increase LV volume, low EF, HFmrEF (41-49%), and HFpEF (> 50%) which has elevated filling pressures, normal LV volume and evidence of diastolic dysfunction.

- **HFpEF:**

Incidence of HFrEF has decreased across 20 years distant past, whereas HFpEF incidence rose by 45 percent ; this was demonstrated by several studies including the cardiovascular health study together with the Framingham Heart study.(20)(21)

Prevalence is equally distributed in both men and females, HFpEF is a disease of aging, and women live longer than men on average, providing more exposure time to develop HFpEF. (22)
TTE is paramount to help calculate H2FpEF score (estimate PASP and E/e' ratio) that help in the diagnosis of HFpEF.
Management of HFpEF is to treat the comorbidities associated and diuretics use for fluid overload.

2.6 General Management of heart failure

The primary aims in HF management are to lower complications associated with HF including repetitive hospital admissions, HF symptoms, ameliorate quality of life and minimize HF related deaths.
Tackle etiologies of HF and treat comorbidities associated, monitoring by serial routine follow-up, preventive care, heart failure self-care management, pharmacologic therapy, device therapy and advanced therapy all of these are paramount in HF management.
HF therapy depends on the subtypes (HFrEF, HFmrEF, HFpEF or right sided HF) or the presentation either acute or chronic therapy.

2.6.1. Management of HFrEF, HFmrEF

HFmrEF is more similar than HFrEF, in some respects with a greater frequency of coronary artery disease.(23)

Generally, HFmrEF respond to medical therapy in the same manner as HFrEF rather than HFpEF, the difference that there was no benefit found in the use of **Ivabradin**e as secondary pharmacological therapy in HFmrEF.(24)

No current evidence on benefits by device therapy in HFmrEF was shown in sudden cardiac death avoidance besides those that will need recurrent pacing, however in HFrEF benefits are tremendous if they meet the criteria for device therapy.

2.6.1.1. Non-pharmacologic management

Includes education and support approach to promote HF self-management, daily weight monitoring (to detect fluid accumulation), vital signs self-monitoring, and lifestyle modification.

In the lifestyle modification:

- Smoking cessation
- Abstinence or restriction of alcohol consumption and avoidance of illicit drugs
- Sodium restriction is usually 3g/day, some times less than 3g/day in acute decompensation .(25)
- Fluid restriction 1,5-2 liters per day at best in refractory HF stage D or NYHA IV or symptomatic hyponatremia and serum sodium $\leq$120 meq/l.(25)
- Avoidance of obesity.

2.6.1.2. Associated condition management

- Hypertension: Therefore, we recommend treatment to a target systolic blood pressure of ≤ 130 mmHg, in agreement with the American college of cardiology and American heart association (ACC/AHA) 2017 heart failure guideline update. (26)

  A stepwise combination therapy approach containing: ACE/ARB/ARNI, diuretic or Bblocker, or second-line therapy containing MRA, hydralazine or amlodipine, or felodipine.
- Coronary artery disease: it a major cause and contributor of HFrEF and HFmrEF, should be treated medically for symptom relief and secondary prevention.
- Arrhythmias and conductions system disorders: mostly A-fib and ventricular tachyarrhythmia; standard therapy for anticoagulation and heart rate/rhythm control as well as Sudden cardiac death (SCD) prevention should be applied.
- Valvular heart disease: Can be regarded as ultimate reason of HF or a secondary phenomenon for patients with function MR or TR in dilated cardiomyopathies. Clinically indicated valve intervention (surgical replacement) can lead to improvement in symptoms and may also improve cardiac function.
- Cardiomyopathy: In patients where coronary artery diseases are excluded a search for non-ischemic cardiomyopathy should be sought since disease-specific therapy is available, genetic causes of dilated cardiomyopathy should be sought especially if family history is suggestive and family counseling for other family members.
- Diabetes: Glycaemia therapy in Diabetes type I with HF is the same as for other adults with comorbidities, however in type II diabetes it is different when there is **NO established cardiovascular risk and without proteinuria Chronic kidney disease:** usual regimen is applied with metformin as a core initial therapy and management according to HB1AC.
- **Established cardiovascular risk and proteinuric Chronic kidney disease:** The GLP-1 receptor agonists demonstrated favorable atherosclerotic cardiovascular and renal outcomes(27), (28)

  The SGLT-2 I dapagliflozin, empagliflozin has also demonstrated benefits for cardio renal outcomes, especially for heart failure hospitalization, risk of kidney disease progression, and mortality.(29)

2.6.1.3. Pharmacological management

Initial pharmacological therapy:

Initial pharmacologic therapy of HFrEFand HFmrEF; includes a combination of, an excess of fluid drug management (diuretic), RAS I (ARNI, ACE inhibitor, ARB), and a beta blocker. When renin-angiotensin system inhibitor is not tolerated an alternative combination of hydralazine/nitrate is used.

Combining anti-remodeling therapy decreases the rate of hospitalization and cardiovascular mortality.

The cornerstone of HFrEF and HFmrEF medical therapy is the blockade of the RAAS and B adrenergic system.

HFrEF patients should take combination of three therapies, ACE/ARB /ARNI, Bblocker, diuretics.

ACE I+Bblocker+MRA had 56% decrease in mortality ,comparing to combination of ARNI+Bblocker+MRA that has the greatest decrease in mortality with 62% versus those on placebo.(30)

Evidence based anti-remodeling drug should be used and up-titrated to target maximum tolerated dose (start low, go slow, aim high).

Target to higher doses is suggestive of a better outcome than lower doses (31) (32)

Once indicated and up titrated to target maximum dose the effect of secondary therapy is seen and there is an improvement on patient survival.

Indication of MRA includes NYHA II-IV with EF <35 % or heart failure post-MI with EF <40 %. (33),(34)

Despite knowledge of guideline-directed medical therapy, achieving target maximum dosage is still suboptimal in clinical practice. (35)

This was also qualified in a study done in turkey assessing adherence to guideline-directed medical therapy in HFrEF .(36)

GDMT refers to dose up-titrating modalities up to the target Maximum doses (from known clinical trial) of anti-remodeling medications. This is associated with improved clinical outcome with decrease in mortality and decrease rate of hospitalization.

This includes the use of ARB, ACE I, ARNI, Bblockers, MRA and aim should be to achieve the target maximum to achieve inhibition of neuro-hormonal and RAAS activation responsible for remodeling on the heart.(14)

ARB, ACE I dose up-titration is to be doubled 1-2week interval, for ARNI double the dose 2-4weeks interval, Bblocker dose should be doubled at 2 weeks' interval, hydralazine and nitrate (use as an alternative to ACE I, ARB, ARNI), the dose should be up titrated 2-4weeks interval until a target dose is reached.

After diagnosis of HFrEF and HFmrEF, health care professionals should have the intention of achieving target maximum anti-remodeling doses usually within 3 to 6 months', within that period an assessment of electrolytes and hemodynamic is mandatory.
After 3-6 months of achieving target maximum tolerated dose of GDMT, a ventricular function reevaluation either by TTE or other imaging modalities is paramount in order to assess the requisite of device therapy (ICD or CRT).(37)

Secondary pharmacological therapy:

Once indicated they are usually added to optimal initial pharmacological therapy and up-titrated to the recommended target maximum doses.
Indication of MRA includes NYHA II-IV with EF <35 % or heart failure post-MI with EF <40 %
If symptoms persist on initial pharmacological therapy plus MRA; another secondary therapy can be added:

- for mortality improvement in type II diabetes or non-diabetes add SGLT-2 inhibitors (Dapagliflozin and Empaglizosin) (38)
  or hydralazine plus nitrate.
- For HF hospitalization reduction: Ivabradine, digoxin
- Vericuguat: can be added in patient in class II-IV NYHA and LVEF ≤45 % despite optimal medical therapy.
- Ivabradine: indicated in patient in sinus rhythm with severe systolic dysfunction and base line HR >70 beats/min; despite maximum tolerated dose on Bblocker

HFmrEF responds to treatment of anti-remodeling medication and dose up-titration as HFrEF, this includes the same effect on initial and secondary pharmacological effect except for ivabradine on decrease rate of hospitalization and decrease in mortality.(39),(40),(41).

2.6.1.4. Device therapy

- **Cardiac resynchronization therapy (CRT**):

It is indicated generally, when there is left ventricular systolic dysfunction with evidence of ventricular dyssynchrony, shown on ECG with electrical dyssynchrony (broad QRS) and provides electrical activation simultaneously or near-simultaneous of left and Right ventricle (biventricular pacing).

They are 2 types: CRT –P (Pacemaker) and CRT-D (Implantable intra-cardiac defibrillator).

In those that meet the criteria, CRT induces a direct effect on hemodynamic benefits, improves left ventricular systolic function, promotes left ventricular reverse remodeling and change in ventricle geometry.

Cardiac resynchronization therapy was linked with increases in LV ejection fraction of 3.7 percent at three months and 6.9 percent at 18 months and decreases in LV end-systolic volume index by 16.7 percent at three months and 29.6 percent at 18 months.(42)

To qualify for CRT, the patient should at least be on GDMT (Guideline Directed medical therapy) at target maximum dose for at least 3 months.

- **Implantable cardiac defibrillator (ICD**):

It primary purpose is to prevent Sudden cardiac death either by primary intention or secondary intention, severe LV systolic dysfunction cardiomyopathies with either ischemic or non –ischemic origin are prone to life threatening arrhythmias (non-sustain Ventricular tachycardia and fibrillation), patients with severe LV systolic dysfunction who are post cardiac arrest survivors owing to life threatening arrhythmias.

It is also indicated as primary prevention in patient structural heart muscle disease and other channelopathies.

Some indications of implantable cardioverter defibrillator as sudden cardiac death primary prevention in patients with Hypertrophic cardiomyopathy include: syncope which are inexplicable, LV wall diameter of more than 30 mm, non-typical hemodynamic (blood pressure) feedback post workout, family history of SCD, gene mutation of myosin heavy chain (MYH7 gene), late gadolinium Cardiac MRI enhancing (a marker of fibrosis).(43)

CRT need is on HF patients on GDMT for ≥ 3 months or on GMDT and ≥40 days after myocardial infarction with still NYHA II-III and ambulatory class IV with LVEF ≤ 35%, sinus rhythm, LBBB with QRS ≥150 m/s, non-LBBB ≥130 m/s, ICD is indicated for sudden cardiac death prevention in patients with LVEF≤35% with no less than 40 days

post myocardial infraction on chronic GDMT still in NYHA II-III and expected to live >1 year , patients with LVEF ≤30 % in NYHA class I with no less than 40 days post-myocardial infraction . (25)

In 2014, another indication of CRT was added by the FDA, in patients with LVEF ≤ 50 % and patients with NYHA I-III on stable target GDMT and AV block (Atrial ventricular) > 40 % of the time that cannot be managed with a usual algorithm(44)

If the need of requiring ventricular pacing >40 % of the time is not met in those patients with LVEF 35% ≤50 % but have heart failure symptoms and have been on target maximum dose of GDMT with minimum of 3 months,40 days post-MI, LBBB (native /paced) QRS >150 m/s and has NYHA III-IV; then they qualify for CRT.(44)

Advance care for heart failure:

- Include LV assisted devices (LVAD), useful as a bridge to transplant (BTT) indication in advanced heart failure on optimal medical therapy with improvement still in NYHA class III-IV, hemodynamically unstable despite inotropic support plus intra-aortic balloon pump.
- Cardiac transplantation indication (45)

    1. Patients with cardiogenic shock which is refractory and require LV assisted devices or intra-aortic balloon pump
    2. Patients with cardiogenic shock in need of inotropic support (Dobutamine, milrinone, etc.)
    3. Peak VO2 <10cc/kg/min
    4. Patients with NYHA class III-IV despite CRT and optimal directed medical therapy.
    5. Frequent arrhythmias which are life-threatening; despite ICD, catheter ablation and antiarrhythmic drugs.
    6. Congenital heart disease without evidence of pulmonary hypertension in end-stage HF
    7. Non manageable angina by medical or surgical possibilities.
- Palliative care in heart failure is a multidisciplinary approach done by specialist nurse, psychosocial, palliative care specialist on the patient with stage D advanced heart failure, it can be done at home or hospice, medical therapy should be continuing because improves the quality of life nor quantity.(46)

3. METHODOLOGY AND MATERIALS

3.1. Study design

This is a prospective observational study on the clinical profile of heart failure patients followed in the KFH outpatient cardiac clinic in a period of 6 months.

3.2. Study site

King Faisal Hospital,

The first accredited Quaternary multispecialty Hospital including full-time cardiologists and a cardiothoracic surgeon in the city of Kigali, with 160 beds and with the first and only catheterization laboratory in the country.

3.3. Study population

Adult patients >18 years old consulting the adult KFH cardiac clinic carrying a diagnosis of heart failure

3.4. Selection criteria

3.4.1. Inclusion criteria:

- All consented patients with heart failure (based on Framingham criteria) followed in outpatient adult cardiac clinic.

3.4.2. Exclusion criteria:

- Patients under the age of 18 years (difficult to get their consent).
- Decompensated cirrhosis.
- Refusal to participate in the study
- Lack of relevant information, such as consultation notes.

3.5. Study procedure

Eligible heart failure patients that came between June 1, 2020, to January 31, 2021 were enrolled in the outpatient cardiac clinic and followed prospectively for a period of 6 months, we followed up and review their demographics, initial NYHA functional status,3 months NYHA functional status and 6 months NYHA functional status, recorded the subtypes and classification of heart failure, 2 D heart echo assessment by cardiologists ;(initial, at 3 months and 6 month; assessment of heart chamber diameters, assessment of evidence of valvulopathies, evidence of cardiomyopathies ,evidence of congenital heart defects, assessment of left ventricular systolic Ejection fraction (using Modified Simpson technique or M mode, diastolic function assessment (using the mitral inflow velocities in Apical 4 chamber view and using pulse wave Doppler flow assessing early (E) function and late (A) atrial filling, E/A ratio was assessed and tissue Doppler Imaging assessment; graded form mild to severe Grade I-III , Grade I (E/A ≤ 0.8 and E/e' <10) ,Grade II (E/A >0.8 and E/e' 10-14) and Grade III (E/A ≥ 2 and average E/e' ≥14) , right ventricular systolic function was assessed using the Trans-annular plane systolic excursion (TAPSE) assessed using the M mode on the lateral tricuspid annulus in the Apical 4 chamber view , TAPSE ≥ 1.7 cm is considered normal and <1.7 cm considered reduce ; the term not recorded was used when function was not assessed (either LVEF ,diastolic function or TAPSE) ,the term other medications was used and recorded according to types and doses to Heart failure patients ,anti- remodeling medication was used specifically in the those with HFrEF, HFmrEF and those with Preserved EF with LV remodeling (eccentric) and doses and adherence to GDMT from each class of anti-remodeling was assessed at 3 months and 6 months ; the need of device therapy (CRT/ICD) was assessed in those HFrEF and HFmrEF patients with LVEF <35% and LVEF ≤ 50 % with evidence of evidence of electrical dyssynchrony on ECG (LBBB and QRS>130 m/s or QRS>150 m/s) and 3 months of target GDMT with still NYHA II-III or ambulatory class IV ; The need of ICD was assessed in general in those HFrEF and in those at risk of SCD as primary prevention .

A convenient sampling method was used**.**

3.6. Data collection

- Patients were recruited after meeting inclusion criteria through Electronic medical records (Napier) once they come in the outpatient cardiac clinic.
- After consenting; all data was captured using a pre-established data collection sheet containing (demographic characteristics, comorbidities, BMI, functional status (initial,3 months, and 6 months), medications, classification, and subtypes of heart failure and echocardiography, ECG).
- The questionnaire was kept confidential by the principal investigator to be used only for research purposes and names were tag using code.
- Once enrolled and consent obtained, they were followed up for 6 months, telephonic communication was used solely by the Principal investigator to assess the NYHA functional status and at each visit, medication doses and imaging and ECG modalities were added to the data collection sheet.

3.7. Data analysis

We used Excel for data entry and analysis was done with SPSS 16 version. We draw tables for results and interpretations. Numeral and categorical data descriptive statistics were used**.**

3.8. Ethical considerations

The validity of the study was assessed by Faculty of Medicine staff members who also provided relevant advice to be observed throughout the study. Ethical clearance was obtained from CMHS/IRB &KFH/IRB. Patients were insured confidentiality of the information given and were reserved the possibility to withdraw from the study once decided. Data were collected on a questionnaire secured with codes, then entered in a password excel database.

3.9. Plans for utilization and dissemination of results

A research report was submitted to the University of Rwanda and King Faisal Hospital. It may also be presented as an oral presentation in scientific conferences. Finally, findings from this research may be submitted to Rwanda medical journal, international journals for academic and clinical advancements.

4. RESULTS

Study Design

86 patients in total with HF on follow-up was screened and found eligible between June 1, 2020, and January 31, 2021, and were followed for 6 months' period.
10 lost to follow-up,3 did not sign the consent, and 3 died .70 patients were analyzed.

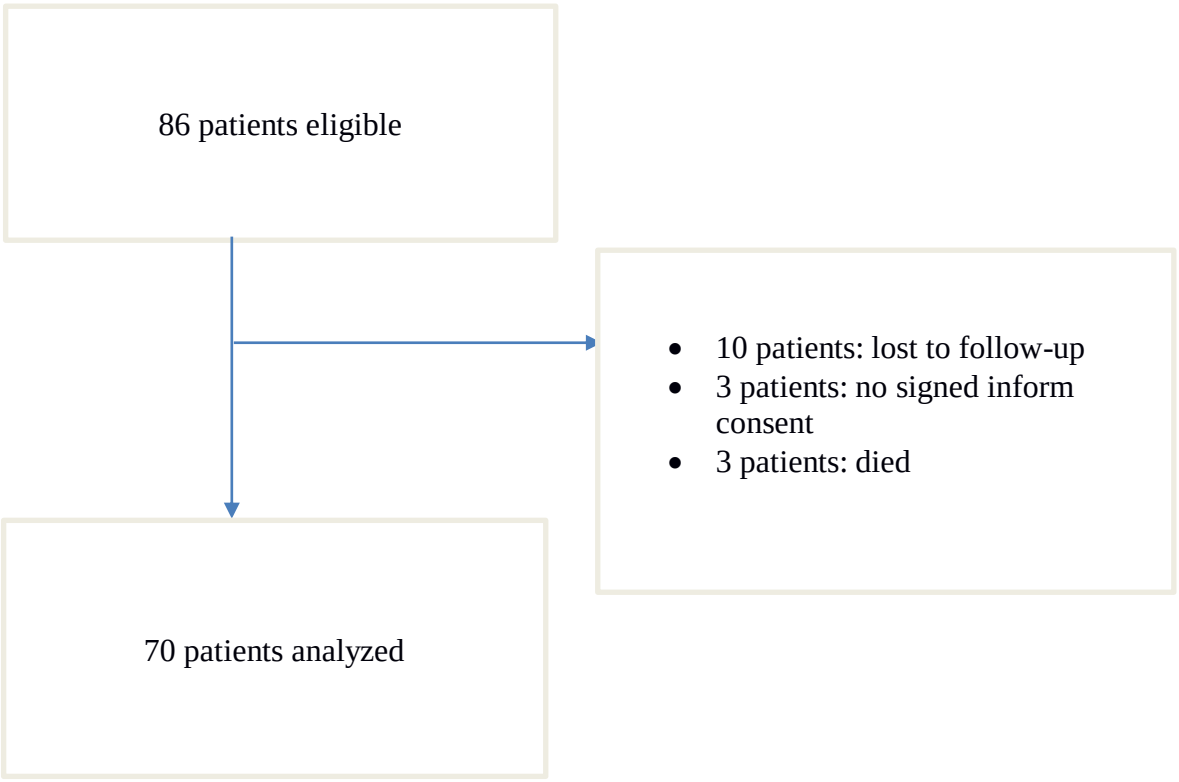

Figure 1 Study Design

Table 1 Demographic characteristics of the participants

Characteristics	Frequency (n)	Percentage (%)	Median (IQR)
Age groups (years)			
≤ 20	4	5 %	-
21-30	8	11 %	-
31-40	13	18 %	-
41-50	9	12 %	-
51-60	10	14 %	-
61-70	12	17 %	-
71-80	11	15 %	-
81-90	1	1 %	-
≥ 91	2	2 %	-
Median (IQR) age, years			51[35-68]
Sex			
Male	33	47 %	
Female	37	53 %	
BMI			
Underweight	2	3 %	
Normal	33	47 %	
Obese class one	8	11 %	
Obese class two	3	4 %	
Overweight	24	32 %	
District			
Kigali	48	69%	
Southern	13	19%	
Northern	3	4%	
Eastern	5	7%	
western	1	1%	

Table 1 shows the demographic characteristic of the population. The majority were female 53% versus 47%. In addition, there was a predominance of adults with a median age of 51[35-68]. Almost a half of the population 47% had a normal body mass index. The origin of the population is mainly in Kigali city with more than half of the population 69%, followed by the southern province with 19%.

Table 2 Classification of Heart failure among the population of this cohort

	Frequency	Male	Female	p value
Cardiomyopathies	45(64%)	27(38%)	18(26%)	p<0.001
Dilated	17 (24%)	12 (17%)	5 (7%)	
DCM (peri-partum)	4 (6%)	0	4 (6%)	
Hypertensive	9 (13%)	5 (7%)	4 (6%)	
Hypertrophic	3 (4%)	1(1%)	2 (3%)	
Ischemic	12 (17%)	9 (13%)	3 (4%)	
Restrictive	0	0	0	
Rheumatic heart	15 (21%)	2 (3%)	13 (18.5%)	p<0.001
Aortic				
• Regurgitation:				
Mild	1 (1%)	0	1(1%)	
Severe	2 (3%)	1(1%)	1(1%)	
Mitral				p<0.001
• Stenosis:				
Mild	1(1%)	0	1(1%)	
Moderate	1 (1%)	0	1(1%)	
Severe	4 (6%)	0	4 (6%)	
• Regurgitation:				
Mild	1(1%)	0	1(1%)	
Moderate	3 (4%)	1(1%)	2 (3%)	
Severe	5 (7%)	1(1%)	4 (6%)	
Tricuspid				p<0.013
• Regurgitation:				
Severe	3 (4%)	1(1%)	2 (3%)	
Valvular heart diseases	4 (5%)			p<0.001
Severe aortic regurgitation	1(1%)	0	1(1%)	p<0.001
Moderate mitral regurgitation	3(4%)	1(1%)	2(3%)	
Congenital heart diseases	7(10%)			p<0.001
PDA (Patent ductus arteriosus)	2 (3%)	1(1%)	1(1%)	
ASD (Atrial septal defect)	3 (4%)	1(1%)	2 (3%)	
VSD (Ventricular septal defect)	1(1%)	0	1(1%)	
TOF (Tetralogy of fallot)	1(1%)	0	1(1%)	

Table 2 shows the classification of HF in the population of this cohort. Dilated cardiomyopathy (24%) was the most prevalent. In addition, there was a subgroup of peri-partum dilated cardiomyopathy (6%). Among cardiomyopathies, ischemic (17%) and hypertensive (13%) were the second and third common causes of heart failure. Rheumatic heart diseases (21%) were the second group in the causes of heart failure with the predominance of mitral valve pathologies including severe mitral regurgitation 7% and severe mitral stenosis 6%. Other causes were congenital heart disease with a dominance of ASD (atrial septal defect) (4%)

Table 3 Subtypes of Heart failure

Characteristics N=70	Frequency	Male	Female	p value
	n (%)	n (%)	n (%)	0.068
HFpEF	17 (24%)	6 (8.5%)	11(16%)	
HFrEF	26 (37%)	16(23%)	10(14%)	
HFmrEF	14 (20%)	8 (11%)	6 (8.5%)	
Right sided heart failure and pulmonary hypertension				
Group one	6 (8.5%)	1 (1%)	5 (7%)	
Group two	2 (3%)	0	2 (3%)	
Group three	2 (3%)	1 (1%)	1(1%)	
Group four	3 (4%)	1 (1%)	2 (3%)	

Table 3 shows subtypes of heart failure among the study population. Majority had HFrEF (37%) with predominance of male 23%; p = 0.068. Among the right-sided heart failure, group one was predominant 8.5%.

Table 4 NYHA Functional Class

Initial functional status N=70	Functional status at 3 months	Functional status at 6 months
		P<0.001
Class I 6 (9%)	31 (44%)	46 (66%)
Class II 31 (44%)	34 (49%)	20 (28%)
Class III 29 (41%)	5 (7%)	4 (6%)
Class IV 4 (6%)	0	0

Table 4 demonstrates the patient's functional status by NYHA classification in the population of this cohort. The majority of the population came initially in NYHA class II (44%) and class III (41%). Then after three months, they show an improved NYHA class with 49% in class II and 44 % in class I. Finally, they show an improved functional status at 6 months with 66% in NYHA class I and 28% in NYHA class II

Table 5 Comorbidities associated (N=70)

Characteristics	Frequency n (%)	Male n (%)	Female n (%)	p value
Pulmonary embolism	7 (10%)	2 (3%)	5 (7%)	0.14
Acute coronary syndrome				p<0.001
NSTEMI	5 (7%)	4 (6%)	1 (1%)	
STEMI	4 (6%)	4 (6%)	0	
Asthma	3 (4%)	1 (1%)	2(3%)	p<0.001
Thyroid disorders				p<0.001
Hyperthyroidism	1 (1%)	1 (1%)	0	
Hypothyroidism	2 (3%)	1 (1%)	1 (1%)	
Stroke	2 (3%)	1 (1%)	1 (1%)	p<0.001
Diabetes	11 (16%)	8 (11%)	3 (4%)	p<0.001
Hypertension	18 (26%)	11 (16%)	7 (10%)	p<0.001
CKD	9 (13%)	7 (10%)	2 (3%)	p<0.001
Arrhythmias				0.70
Atrial fibrillation	6 (8%)	1 (1%)	5(7%)	
Atrial flutter	1 (1%)	0	1 (1%)	
HIV	2 (3%)	1 (1%)	1(1%)	p<0.001
SLE	1 (1%)	1 (1%)	0	
Cardiac surgeries				p<0.001
Balloon mitral valvuloplasty	1 (1%)	0	1(1%)	
Mitral and tricuspid valve repair	2 (3%)	0	2(3%)	
Mitral valve replacement	2 (3%)	1 (1%)	1(1%)	
Mitral and aortic valve replacement	1 (1%)	1 (1%)	0	
Septal myectomy	1 (1%)	0	1(1%)	
Having pace makers				p<0.001
CRT-D	2 (3%)	2 (3%)	0	
CRT-P	1 (1%)	1 (1%)	0	
Pacemaker	1 (1%)	1 (1%)	0	
Others				p<0.001
Benign prostate hyperplasia	2 (3%)	2 (3%)	0	
Lyme disease	1 (1%)	1 (1%)	0	
Renal artery stenosis	1 (1%)	0	1 (1%)	
Ventricular tachycardia	1 (1%)	1 (1%)	0	

Table 5 shows the most commonly presented comorbidities among the population in the study. Both hypertension and diabetes were highly predominant, 26% and 16% of the population respectively. Again, CKD (13%), ACS (13%), and pulmonary embolism (10%) were the following group of comorbidities to follow.

Table 6 Cardiac assessment by ultrasound: Left ventricular systolic ejection fraction and LV dimension

	Initial EF	EF at 3 months N=70 p<0.001	EF at 6 months
Male			
≤ 30% (Severe dysfunction)	11(16%)	10 (14%)	5 (7%)
31-39% (Moderate dysfunction)	6 (8%)	2 (3%)	2 (3%)
41-49% (Mild dysfunction)	5 (7%)	2 (3%)	4 (6%)
50-70% (Normal)	9 (13%)	5 (7%)	1 (1%)
≥ 70% Hyper dynamic	2 (3%)	0	1 (1%)
Not recorded	-	14 (20%)	19 (27%)
Female			
≤ 30% (Severe dysfunction)	5 (7%)	2 (3%)	0
31-39% (Moderate dysfunction)	9 (13%)	2 (3%)	2 (3%)
41-49% (Mild dysfunction)	5 (7%)	3 (4%)	2 (3%)
50-70% (Normal)	14 (20%)	9 (13%)	2 (3%)
≥ 70% Hyper dynamic	4 (6%)	1 (1%)	0
Not recorded	-	20 (29%)	30 (43%)

Table 6 demonstrates cardiac assessment by left ventricular systolic ejection fraction. The majority of males 16%, in the studied population group came with severe dysfunction whereas for females 7% only presented severe left ventricular systolic dysfunction. There was a significantly improved left ventricular systolic ejection fraction over time whereby females did not have any severe systolic dysfunction at 6 months and males had only 7% of severe systolic dysfunction.

Table 7. Cardiac assessment by ultrasound: Diastolic function

	Initial n (%)	at 3 months (%) N=70	at 6 months n (%)
	p<0.001	p<0.001	p<0.001
Normal	29(42%)	19 (27%)	12 (17%)
Grade I	5 (7%)	2 (3%)	1 (1%)
Grade II	3 (4%)	1 (1%)	1 (1%)
Grade III	7(10%)	6 (9%)	3 (4%)
Not recorded	26 (37%)	42 (60%)	53 (76%)

Table 7 shows cardiac assessment by diastolic function. Majority, 42% had a normal diastolic function at initial.

Most diastolic function was not recorded at initial, 3 months and 6 months (37%,60%,76% respectively).

Table 8. Cardiac assessment by ultrasound: Right ventricle systolic function (Trans annular plane systolic excursion) (N=70)

	Initial TAPSE	TAPSE at 3 months	TAPSE at 6 months
	p<0.001	p<0.001	p<0.001
Male			
Normal	18 (26%)	11 (16%)	8(12%)
Reduced	18 (26%)	5 (7%)	2(3%)
Not recorded	3 (4%)	15 (22%)	23 (33%)
Female			
Normal	14 (20%)	9 (13%)	5 (7%)
Reduced	12 (17%)	4 (6%)	1 (1%)
Not recorded	5 (7%)	24 (35%)	31 (44%)
TAPSE >1.7 cm normal , ≤ 1.7 cm reduced			

Table 9a. Commonly used anti-remodeling medications

	HFrEF/HFmrEF/Preserved EF with LV remodeling (N=70) (42 patients,60%)		
	Initial	Medications at 3 months	Medications at 6 months
ARB			
Candesartan n (%)	1 (2%)	5 (12%)	5 (12%)
Candesartan /hydrochlorothiazide n (%)	1 (2%)	1 (2%)	1 (2%)
Losartan n (%)	4 (10%)	5 (12%)	5 (12%)
Telmisartan n (%)	1 (2%)	0	0
Valsartan /hydrochlorothiazide n (%)	1 (2%)	1 (2%)	0
Valsartan/hydrochlorothiazide /Amlodipine	0	1(2%)	1(2%)
Beta Blockers			
Bisoprolol n (%)	2 (5%)	3 (7%)	3 (7%)
Carvedilol n (%)	33 (79%)	33 (79%)	30 (71%)
Metoprolol n (%)	4 (10%)	3 (7%)	3 (7%)
Nebivolol n (%)	1 (2%)	1 (2%)	1 (2%)
ARNI n (%)			
(Sacubitril/valsartan)	3 (7%)	4 (10%)	6 (14%)
SGLT 2 inhibitors			
Dapaglifozin n (%)	0	1 (2%)	2(5%)
ACEI			
Captopril n (%)	2 (5%)	2 (5%)	2 (5%)
Enalapril n (%)	15 (36%)	11 (26%)	9 (21%)
Lisinopril n (%)	1 (2%)	1 (2%)	0
Perindopril n (%)	10 (24%)	9 (21%)	9 (21%)
Perindopril /amlodipine n (%)	1 (2%)	0	0
Ramipril n (%)	1 (2%)	1 (2%)	1 (2%)

Table 9. b anti-remodeling used only in HFrEF N:70 (26 patients, 37%)

MRA	initial	3months	6 months
Aldactone n (%)	23 (88%)	22 (85%)	22 (85%)

Table 9 a Demonstrates the most commonly used anti-remodeling medications in HFrEF/HFmrEF/ Preserved EF with left ventricular remodeling;

initially, at three months and 6 months. Beta-blockers were especially carvedilol (79 %) were most commonly used; they were followed by enalapril (36%). **Table 9 b** Demonstrates the use of MRA (aldactone) as anti-remodeling in HFrEF was used at 88%.

Table 10 a. Up titrated versus maximum, dose anti-remodeling medications

	HFrEF/HFmrEF/Preserved EF with LV remodeling (N=70) (42patients,60%)		
	Initial	Medications at 3 months	Medications at 6 months
ARB	8 (19%)	13 (31%)	12 (29%)
Up titrated			
Yes		3 (23%)	3 (25%)
No		10 (77%)	8 (67%)
Already max		0	1 (8%)
Maximum dose			
Yes		1 (8%)	2 (17%)
No		12(92%)	10 (83%)
Beta Blockers	40 (95%)	40 (95%)	37 (88%)
Up titrated			
Yes		31(77.5%)	8 (22%)
No		7 (17.5%)	10 (27%)
Already max		2 (5%)	19 (51%)
Maximum dose			
Yes		19 (47.5%)	25(68%)
No		21 (52.5%)	12(32%)
ACEI	30 (71%)	24 (57%)	21 (50%)
Up titrated			
Yes		15 (63%)	5 (24%)
No		7 (29%)	6 (28%)
Already max		2 (8%)	10(48%)
Maximum dose			
Yes		12 (50%)	13(62%)
No		12 (50%)	8 (38%)
ARNI	3 (7%)	4 (10%)	6 (14%)
Up titrated			
Yes		1 (25%)	4 (67%)
No		3 (75%)	2 (33%)
Maximum dose			
Yes		0	1 (17%)
No		4 (100%)	5 (83%)

Table 10a shows up titrated versus maximum, dose anti-remodeling medications for HFrEF/HFmrEF/Preserved EF with left ventricular remodeling, Beta-blockers were among the medications that were up titrated more than others. After three months, Bblockers were up titrated 77.5 % followed by ACE I with 63% else in the study population.

Table 10 b. Up titrated versus maximum, dose anti-remodeling medications

	HFrEF N:70 (26 patients,37%)		
	Initial	Medications at 3 months	Medications at 6 months
MRA	23 (88%)	22 (85%)	22(85%)
Up titrated			
Yes		3 (13%)	0
No		3 (13%)	4 (18%)
Already max		16 (74%)	18 (82%)
Maximum dose			
Yes		19 (86%)	20 (91%)
No		3 (14%)	2 (9%)

Table 10 b, On the other hand, MRA were no longer up titrated at 6 months. The majority of the patients were already at a maximum dose of 74 % for three months and 82% for six months.

Table 11. Combined anti-remodeling Medications

	HFrEF N:70 (26 patients,37%) Initial	HFrEF N:70 (26patients,37%) 3 months	HFrEF N:70 (26 patients,37%) 6 months
Combination anti-remodeling	Combination Initial	Combination 3 months	Combination 6 months
ARNI + B blocker + MRA	2 (8%)	3(12%)	5 (19%)
ARB + B Blocker + MRA	3 (11%)	5 (19%)	4 (15%)
ACEI + B Blocker + MRA	17(65%)	13(50%)	11(42%)
ARB + B Blocker n (%)	2 (8%)	3 (12%)	2 (8%)
ACEI + B Blocker n (%)	1(4%)	1(4%)	0
ARB + MRA n (%)	1(4%)	1(4%)	1(4%)
ARB only n (%)	0	0	1(4%)
ACE only n (%)	0	0	1(4%)
Bblocker only	0	0	1(4%)
	HFmrEF N:70 (14 patients,20 %) Initial	HFmrEF N:70 (1 4 patients,20 %) 3 months	HFmrEF N:70 (14 patients,20%) 6 months
Combination anti-remodeling	Combination Initial	Combination 3 months	Combination 6 months
ACEI + B Blocker n (%)	10 (72%)	8(57%)	7(50%)
ARNI+B Blockers n (%)	1 (7%)	1 (7%)	1(7%)
ARB+B Blocker n (%)	1 (7%)	3(22%)	3(22%)
ACEI +Bblocker + SGLT2 I	0	1(7%)	2(14%)
B Blocker only	1 (7%)	1 (7%)	2 (14%)
ARB only	1 (7%)	1(7%)	1 (7%)
	Preserved EF With left ventricular remodeling N:70	Preserved EF With left ventricular remodeling N:70	Preserved EF With Left ventricular remodeling N:70
Combination anti-remodeling	(17 patients,24 %) initial Combination	(17 patients,24 %) 3 months Combination	(17 patients,24 %) 6 months Combination
ACEI +Bblocker	2 (12 %)	2 (12%)	2 (12%)

Table 11 represents the distribution of combined anti-remodeling medications in the population of this cohort. The majority of HFrEF patients (65%) were on three-combined medications (ACEI + B Blocker + MRA) initially. There was a gradual reduction over time of HFrEF patients under this type of combined anti-remodeling medication and a gradual increase of combination at 6 months of (ARNI+ B blocker+ MRA) at 19%. In addition, for the category of HFmrEF, the combination of ACEI plus B Blocker was commonly used in about 72% of the participants initially.

Table 12. Other medication most commonly used (N+70)

	Frequency	%
Statins		
Atorvastatin	5	(7%)
Rosuvastatin	3	(4%)
Aldosterone antagonist		
Aldactone	12	(17%)
Thiazide		
Hydrochlorothiazide	3	(4%)
Indapamide	1	(1%)
Loop diuretic		
Furosemide	38	(54%)
Torsemide	2	(3%)
Antiarrhythmic		
Digoxin	4	(6%)
Antiplatelet (ADP inhibitor)		
Clopidogrel	5	(7%)
Antiplatelet cox 2 inhibitor		
Aspirin	10	(14%)
Anticoagulant		
Rivaroxaban	9	(13%)
Warfarin	3	(4%)
Beta-blocker		
Atenolol	2	(3%)
Carvedilol	5	(7%)
Metoprolol	2	(3%)
Nebivolol	2	(3%)
Propranolol	2	(3%)
PDE-5 inhibitor		
Sildenafil	2	(3%)
Endothelin receptor antagonist		
Bosentan	5	(7%)
Combination antihypertensive		
Amlodipine/valsartan	1	(1%)
Amlodipine/valsartan /hydrochlorothiazide	1	(1%)
Losartan/amlodipine	1	(1%)
Losartan/hydrochlorothiazide	1	(1%)

Table 12 shows other medications used alone or in addition to anti-remodeling among the population in this cohort. The most commonly used class of medication was loop diuretic where Lasix was used in 54% as an adjuvant to anti-remodeling. The second class of medication used, was aldosterone antagonist, Aldactone (17%) followed by antiplatelet cox 2 inhibitor, Aspirin (14%), and anticoagulant, Rivaroxaban

Table 13. Common ECG findings among the participants in the cohort

	Frequency (N :70)	%
LBBB and QRS more than 130 m/s		
Yes	7	(10%)
No	63	(90%)
QRS more than 150 m/s		
Yes (Paced rhythm)	3	(4%)
No	67	(96%)

Table 14. Need of cardiac devices

Studied population N:70	Frequency %
Need of CRT HFrEF &HFmrEF (40 patients, 57%)	
Yes (CRT-D)	1(2.5%)
Yes (CRT-P)	5(12.5%)
No (Has CRT)	3(7.5%)
No	31(77.5%)
Need of ICD HFrEF +SCD (Sudden cardiac death) prevention (29 patients, 41%)	
Yes	2 (7%)
No	27(93%)

Table 13 shows different ECG findings among the population in this cohort. LBBB and QRS more than 130 m/s were the most ECG findings and accounted for about 10% of the population.

Table 14. Again, CRT-P was needed for about 12.5 % of the studied population whereas 7.5 % had CRT and there was no need for CRT, ICD in the studied group of reduced EF and primary prevention of SCD and in hypertrophic cardiomyopathy were only needed in 7% in the studied population.

5. DISCUSSION

In this present study, the median age was 51 years [35-68], females made the majority 53% of the studied population, this was similar to a meta-analysis by Ogah et all of HF patients in Sub-Saharan Africa; which find the mean age at presentation being between thirtieth and sixtieth years whereas in EuroHF survey the median 69.9 years, in USA 72.4 years in the ADHERE study, in Sub –Saharan Africa the prevalence of females was predominating were cardiomyopathies was the leading cause. (9)

37%,24%,20%,19 %, are the percentages of HFrEF, HFpEF, HFmrEF, and Right-sided heart failure respectively, in HFrEF males was more predominant than females (23 % vs 14%), in HFpEF women were more prevalent than males (16% vs 8.5%) and we did not find it statistically significant P value (0.068) in contrast to a meta-analysis study publication by Carolyn SP Lam et all, on sex differences in heart failure; the reason varies widely from genetic to comorbidities and the pathophysiology of microvascular dysfunction of endothelial inflammation of coronary arteries versus macro vascular in males , history of hypertensive disorders related to pregnancy , peripartum cardiomyopathy , emotional stress , chemotherapy related therapy from breast ca , incidence of diabetes and obesity predispose to HFpEF in females increased fibrosis and stiffness with older ages because of reduced estrogen in contrast younger age at presentation ,obesity, alcohol ,tobacco and illicit drug use predispose to HFrEF in male .(47)

Cardiomyopathies were the most prevalent followed by Rheumatic heart disease with (64 %,21%) respectively this was similar to a 10 years retrospective study, published in 2018 in 3 NCDs clinics in district hospitals in Rwanda by Rusingiza et all with the difference of absence of ischemic cardiomyopathies, this in part was due to more or less on the absence of coronary angiography and other imaging modalities absent at that time. (13)

In our study, among cardiomyopathies ischemic cardiomyopathies were the second leading cause after dilated cardiomyopathies (17%,30 %), this may show the rise of ischemic heart disease in our population.

Among comorbidities hypertension and diabetes were highly predominant, 26% and 16% of the population respectively (P< 0.001). This was similar to a meta-analysis by Ogah et all of HF in Sub –Saharan Africa that find that Hypertension was the pre-eminent reason of

HF; (9); these bring emphasis in treatment of Hypertension and Diabetes according to evidence-based guidelines in order to decrease HF Exacerbation and repetitive hospitalizations.

However, a prospective cohort study was done in Tanzania comparing characterization of Heart failure in Tanzania and Sweden population by Abel Makubi et all; find that Hypertension and anemia were more prevalent among comorbidities. (48)

On heart echo assessment on assessment of LV systolic function, diastolic function, and Right ventricular systolic function using (TAPSE), they were an increase of no records of EF done at 3 months and 6 months, this is not following current recommendations on assessing ventricular function at least 3 to 6 months after achieving target dose especially in HFrEF. (49).

In HFrEF Consistency of combination of 3 anti-remodeling ARB/ACE/ARNI, Bblocker and diuretic were used throughout the whole 6 months follow-up period, this was shown to increases patient survival and decrease the risk of hospitalization, however among combination: ACE+ Bblocker +MRA being the most predominant, followed with ARB+Bblocker +MRA and ARNI+Bblocker+MRA being the least predominant despite having the greatest reduction on all-cause of mortality with 62 % reduction, this was confirmed from a 30 years evidence meta-analysis on evidence of drugs in HFrEF by Heather Burnett et all.(30)

This is due to the high cost and continuous availability of ARNI in our settings.

In HFmrEF 2 combinations anti-remodeling ACE+ Bblocker followed with ARB+Blocker HFmrEF responds to medical therapy in the same manner as HFrEF, they receive the same anti-remodeling and dose-up titration modality for a better outcome on mortality reduction and decrease in hospitalization as it was seen in CHARM study and double-blind trial on Bblocker (39),(41).

The proportion of patients on anti-remodeling in the group of HFrEF/HFmrEF/Preserved EF with left ventricular remodeling who are up-titrated at 3 and 6 months ARB was low (27%,25%) respectively and ARNI dose up-titrating is still low at 3months (25%) but went high at 6months for ARNI with (67%); they were high for Bblocker and ACEI at 3 months with (77.5%, 63%) respectively, dose up-titrating decreased at 6 months for Bblocker and ACEI because the majority were already at maximum at 6 months with (51%,48%) respectively.

In the group of HFrEF, MRA dose up titrated was low at 3 months and 6 months because the majority were already at maximum at 3 months and 6 months (74% and 82%) respectively.

Health care provider's goals in HFrEF should be to attain target maximum doses of the GDMT within 3 to 6 months of an initial diagnosis of Heart failure as recommended. (49). Higher doses have better outcomes with decreased mortality and hospitalization than lower doses. (32)

In clinical practice, adherence to GDMT in HF patients is sub-standard (not optimal); this was seen in the QUALIFY global survey a multicenter international prospective study of 15 months in 547 centers in 36 countries including Africa. (35)

Another study was done in Turkey multicenter prospective observational study (ATA study) for 6 months period assessing the adherence to GDMT in outpatient HF patients find that most eligible patients did not receive target doses, the main reason for not using target dose was put into account finding was RAAS inhibitors (symptomatic hypotension, currently in the up-titration and worsening renal function test), Bblockers (Brady arrhythmias, target dose already achieved, symptomatic hypotension, currently in the up-titration), MRA(currently in the up-titration, hyperkalemia worsening renal function test). (36)

In comparison to those cited above studies, in our study, we found that the adherence to guideline medical therapy in chronic heart failure in HFrEF/HFmrEF/Preserved EF with LV remodeling in this study is relatively satisfactory, though the dosage to achieve the target is suboptimal especially at 3months (0% for ARNI, 8% for ARB, 50% ACE I ,47.5% for Bblocker,86% for aldactone), this improved at 6 months (91 % for aldactone,68% Bblocker,62% ACE I,17% ARNI, 17% ARB); effort has to be made to achieve target maximum the early as possible which has advantages on decreasing rate of re-hospitalizations and decreasing mortality, hence improvement of Quality of life and decrease economic burden not only to the family but to the nation in general and this will also help us to assess earlier the need of cardiac device therapy for better outcomes; especially in those with reduced EF with evidence of electrical dissyncchronny and at least on 3 months of optimal GDMT with still NYHA II-III or ambulatory class IV.

The need for CRT in those patients with HFrEF and those with HFmrEF was found to be low in this study with 15 %, and low for ICD with only 7% of patients that qualify those with HFrEF and those for primary prevention of SCD, in this study Hypertrophic cardiomyopathies.

However, some patients with dyssynchrony could qualify if were at target maximum doses at 3 months, and echo assessment of ventricular function was done at 3 months and 6 months as recommended; which were not recorded enough.

6. CONCLUSION AND RECOMMENDATIONS

This prospective observational study at King Faisal Hospital Kigali; find that female was more predominant and HFrEF was the prevalent subtypes of Heart failure, followed with HFpEF and HFmrEF; Cardiomyopathies was the leading class, followed with rheumatic heart disease.

All patients in this cohort functional status went improving in the follow-up, consistency and combination of evidence-based anti- remodeling in HFrEF/HFmrEF/Preserved EF with LV remodeling were satisfactory during the whole follow-up, adherence to guideline-directed therapy was relatively satisfactory, though the dosage to achieve the target is still suboptimal mostly at 3 months, assessment of ventricular function by imaging modalities was unsatisfactory with some function including diastolic function, right ventricular systolic function ,LV dimensions not always recorded at patients visit ,this was also associated with increase of no records at 3months and 6 months and should be done and recorded as per protocol (initially and at least 3 to 6 months) or earlier if the need is found; to assess the need of device therapy once the target doses are achieved .

Further studies are needed, multicenter with longer follow-up emphasizing on the etiologies of dilated cardiomyopathy (as the prevalent class); assessment of reason of not up-titrating anti-remodeling medications in HF patients is paramount.

Based on our results; this is an appeal to all clinicians in Rwanda treating heart failure patients with evidenced of reduced EF and ventricular remodeling are reminded to adhere to the GDMT and aim target maximum of anti-remodeling medications as it has shown to decrease mortality and decrease rate of hospitalizations while also improving symptoms and quality of life ; as long as assessment in the follow-up of ventricular function by TTE at least 3 monthly by experienced physicians/cardiologists in order to assess the need of device therapy.

Increase awareness in treating Hypertension and Diabetes (as leading comorbidities) as per guidelines; in order of improving heart failure patient's care and decrease frequent hospitalization.

Strength of the study

- A first prospective study in Rwanda that assesses HF patients in out-patient cardiac clinic, and assesses the adherence to guideline recommended medical therapy in HFrEF/HFmrEF/Preserved EF with LV remodeling, and assess the need for cardiac devices.
- Study site, first accredited hospital with continuous cardiologist follow-up and best available diagnostic modalities and catheterization laboratory.

Limitation of the study

- The short duration of follow-up and small sample size
- Covid 19 restriction increased loss to follow-up and delays to consult.
- The study did not assess fully the other reasons for not up-titrating except being at the maximum dose of anti-remodeling only.
- Increase of no records on TTE assessment at 3 months and 6 months.

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8. APPENDICES

8.1 Informed consent

8.1.1 Kinyarwanda version

INYANDIKO ISABA UBURENGAZIRA MU KWITABIRA UBUSHAKASHATSI

Nitwa Dr Mulima Nyantabana Yves. Ndi umuganga nkaba n'umunyeshuri mu cyiciro cya gatatu cya Kaminuza y'u Rwanda ishami ry'ubuzima aho nitoza kuba inzobere mu kuvura indwara z'umubiri.

Iyi nyandiko nsabira uruhushya igenewe abantu bose

batumiwe kwitabira ubu bushakashatsi 'Incamake ku barwayi b'umutima bakurikiranwa mubivuza bataha mu bitaro bya King Faisal.'

Ubu bushakashatsi bufite impande ebyiri kureba ibyu burwayi bwose bw'umurwayi w'umutima ,ndetse no gukurikirana uko bagenda bamera mugihe cya mezi atandatu,ubu bushakashatsi buzareba ,ubwoko bw' uburwayi bw'umutima ,imiti umurwayi ariho,ikigero cyo koroherwa agezeho,ndetse kureba gukenerwa k'ubuvuzi bwisumbyeho .

Andi makuru yerekewe uburwayi bw'umurwayi azakurikiranwa ndetse afatwe hakoresheje ikoranabuhanga ribika amakuru y'umurwayi muri mudasobwa ,ndetse hazanifashishwa telephone mugukurina ikigero cy'uburwayi bugezeho (functional status bakoresheje NYHA).

Kwitabira ubu bushakashatsi ni ubushake ,kandi umuntu afite uburenganzira bwo kuyivamo ntagahato;ariko turizera ko muzitabira kubera impavu nziza ubu bushakashatsi bufite.

Ibiza kubirwamo byose mu bushakashatsi ni ibanga ;kandi amazina cyagwa ay'umuryango y'uwitabiriye ntazigera ashirwa ku karubanda. Ntabihembo biteganijwe kuzitabira ubushakashatsi .

Nta ngaruka niwe bizatera umurwayi kwitabira ubushakashatsi .

Imyanzuro yavuye mu bushakashatsi izamenyeshwa ikipe y'ubuvuzi murwego rwo kurushaho kunoza imitangire y'ubuvuzi.

Ku kibazo cyose mwabaza (researchcenter@ac.ur.rw Tel +250 788563311), Dr Mulima Nyantabana Yves mulimayves@gmail.com Tel +250788774914 Dr Willy Mucyo willy.mucyo@gmail.com 0788601823

Njyewe …… nasomye kandi nanyuzwe ibisobanura bya

Dr……. ku bushakashatsi bw' incamake ku barwayi b'umutima bakurikiranwa mubivuza bataha mu bitaro bya King Faisal.' Nemeye nta gahato kwitabira ubu bushakashatsi.

Umukono n'amazina y'umurwayi umukono w'umushakashatsi

Date: …. /……/202…

Nimba utazi gusoma no kwandika

Ndemeza ko umurwayi yasomewe nezaamabwirizi ndetse n'amakuru y'ubu bushakashatsi kandi yagize umwanya wo kubaza ibibazo.Ndemeza ko umurwayi yemeye kw'itabira ubu bushakashatsi nta gahato.

Amazina n'umukono w'indorerezi _____

Igikumwe cy'umurwayi :

Itariki _____

8.1.2 English version

INFORMED CONSENT FORM

Dear Participant

I am called Dr Mulima Nyantabana Yves. I am a student at the University of Rwanda, pursuing Masters in Medicine (Mmed) in Internal medicine and researcher on the Clinical profile of heart failure patients followed in an outpatient cardiac clinic in King Faisal Hospital.

It is a prospective study for a period of 6 months; this includes patients who are known to have heart failure and followed in cardiac clinic looking for the etiologies, comorbidities associated, functional status, medications, and need of advanced therapy.

Participation in this study is voluntary and you can choose not to enroll in the research and you have the right to withdraw from the study at any time without penalty. However, we hope that you will participate in this study since your views are important.

Whatever information will be gathered will be kept strictly confidential and no reference to your name or other family members will be made public. We wish to compensate for your time used to participate in the study but we will not be able as we do not have the means.

We do not anticipate that there would be any harmful event that would occur with the study, but for any query you refer to the research committee (researchcenter@ac.ur.rw Tel +250 788563311), Dr. Mulima Nyantabana Yves mulimayves@gmail.com Tel +250788774914 Dr. Willy Mucyo willy.mucyo@gmail.com Tel 0788601823

Thank you.

I ……understand the explanation given by Dr…….. about the risks and benefits of this research on clinical profile of heart failure patients followed in the outpatient cardiac clinic, I accept willingly to participate in the research.

Participant's signature Researcher's signature

Date: …. /……/202…

If illiterate

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____

and Thumb print of participant:

Signature of witness _____

Date _____

Verbal Consent

Name of the participant:

8.2. Questionnaire

QUESTIONNAIRE ON CLINICAL PROFILE OF HEART FAILURE PATIENT FOLLOWED IN OUTPATIENT CARDIAC CLINIC IN KING FAISAL HOSPITAL:

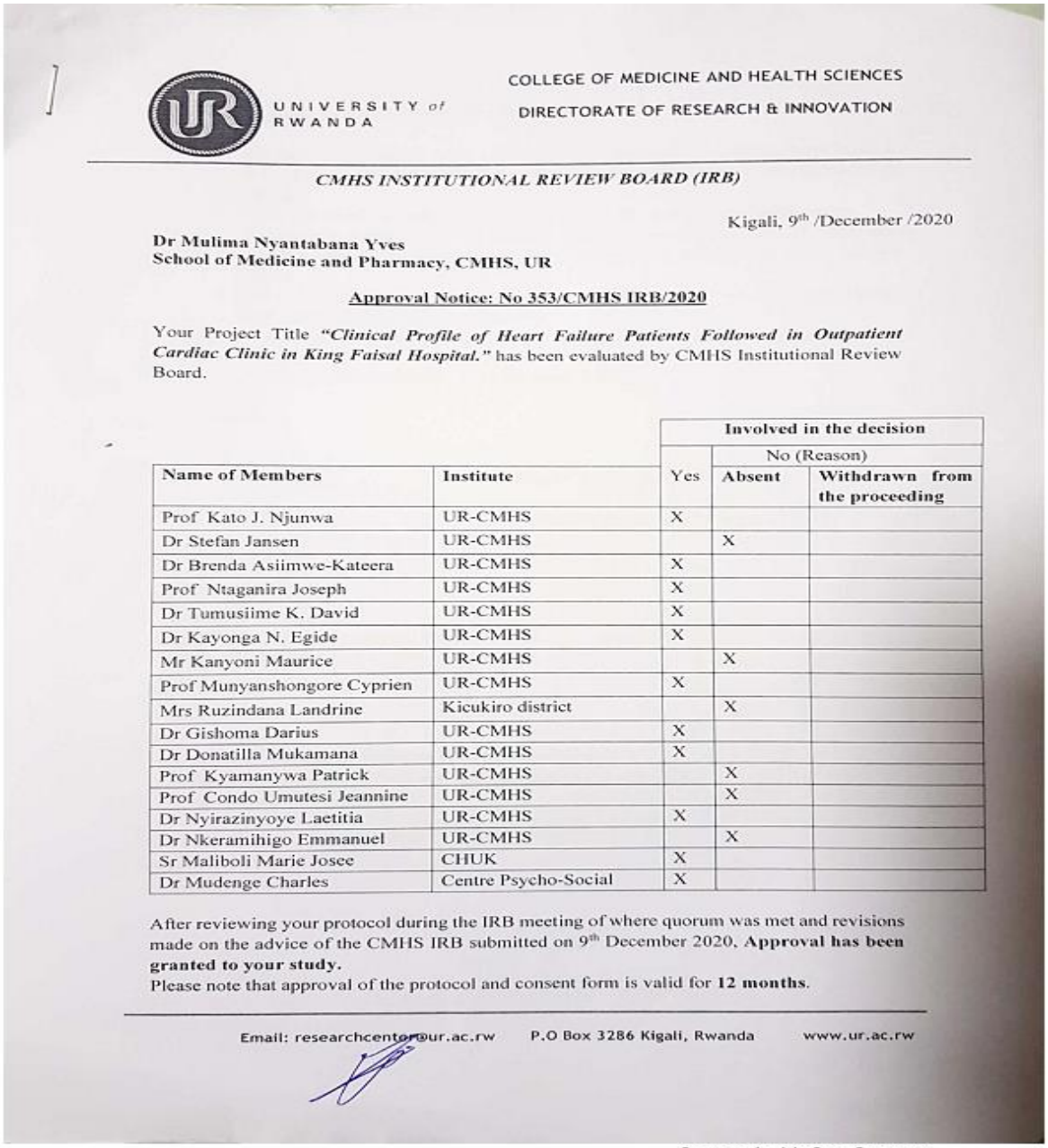
1. Questionnaire number: ……
2. ID: ……..…..
3. Phone N°: ……
4. Enrollment date _DD__/___MM__/__YYYY__
5. Enrolled from: 1. KFH

Patient address					
Code:					
Age:					
Sexe:	Male		Female		
Subtypes of heart failure	HFPEF ☐	HFREF ☐	HFMREF ☐	Right-sided Heart failure ☐	
Classification of heart failure	Cardiomyopathies Dilated ☐ Hypertensive ☐ restrictive ☐ hypertrophic ☐ others ☐	Rheumatic heart disease **Aortic** • Regurg ☐ • Stenosis ☐ • Mixed ☐ **Mitral** • Regurg ☐ • Stenosis ☐ • Mixed ☐ **Tricuspid** ☐ • Regurg ☐ • Stenosis ☐ • Mixed **Pulmonary** ☐ • Regurg ☐ • Stenosis ☐ • Mixed	Valvular heart disease **Aortic** • Regurg ☐ • Stenosis ☐ • Mixed ☐ **Mitral** • Regurg ☐ • Stenosis ☐ • Mixed ☐ **Tricuspid** ☐ • Regurg ☐ • Stenosis ☐ • Mixed **Pulmonary** ☐ • Regurg ☐ • Stenosis ☐ • Mixed	Congenital heart disease	
Comorbidities associated	Diabetes & BMI	Hypertension	ACS history	Thyroid disorders	Others

Heart Echography assessment	**FIRST ECHO** LVEF Diastolic function Tapse	**3 month** LVEF Diastolic function Tapse	**6 month** LVEF Diastolic function Tapse
New York heart Association (NYHA) Functional status			
Anti-remodeling medications &other medication **ACE & Target doses** Captopril 50 mg tid Enalapril 10-20 mg tid Lisinopril 20-40 mg od Ramipril 10 mg od **ARNI & Target doses** Sacubitril/valsartan 97/103mg bid **ARB & Target doses** Candesartan 32 mg od Valsartan 160mg bid Losartan 150 mg od **Bblockers** Carvedilol • 25 mg bid (weight >85kg) • 50 mg bid (weight >85kg) Carvedilol CR 80 mg od Metoprolol 200 mg od Bisoprolol 10 mg od **Hydralazine & nitrate**	**Medications and doses:** Drugs and doses:	**Medications and doses:** Up-titrated In HFREF /HFMREF/ Preserved EF with LV remodeling: **ACE** • Yes ☐ • No ☐ • Already max ☐ **ARB** • Yes ☐ • No ☐ • Already max ☐ **ARNI** • Yes ☐ • No ☐ • Already max ☐ **Bblockers** • Yes ☐ • No ☐	**Medications and doses:** Up-titrated In HFREF/HFMREF/ Preserved EF with LV remodeling: **ACE** • Yes ☐ • No ☐ • Already max ☐ **ARB** • Yes ☐ • No ☐ • Already max ☐ **ARNI** • Yes ☐ • No ☐ • Already max ☐ **Bblockers** • Yes ☐ • No ☐

Isosorbide dinitrate 40 mg tid Hydralazine 100 mg tid **MRA** Aldactone 25-50 mg od Eplerenone 50 mg od **SGT-2 inhibitor** Dapaglifozin 10 mg od Empaglifozin 10 mg od **Sodium guanyl cyclase inhibitor** Vericuguat 10 mg od **Selective sinus node inhibitor** Ivabradine 7.5 mg bid		• Already max ☐ **MRA** • Yes ☐ • No ☐ • Already max ☐ Max in HFREF and HFMREF or Preserved EF with LV remodeling **ACE** • Yes ☐ • No ☐ **ARB** • Yes ☐ • No ☐ **ARNI** • Yes ☐ • No ☐ **Bblockers** • Yes ☐ • No ☐ **MRA** • Yes ☐ • No ☐ **SGLT-2 inhibitor** • Yes ☐ • No ☐	• Already max ☐ **MRA** • Yes ☐ • No ☐ • Already max ☐ Max in HFREF and HFMREF or Preserved EF with LV remodeling **ACE** • Yes ☐ • No ☐ **ARB** • Yes ☐ • No ☐ **ARNI** • Yes ☐ • No ☐ **Bblockers** • Yes ☐ • No ☐ **MRA** • Yes ☐ • No ☐ **SGLT-2 inhibitor** • Yes ☐ • No ☐
ECG			
Need of cardiac devices			

8.3 Ethical approval



UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 9th /December /2020

Dr Mulima Nyantabana Yves
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 353/CMHS IRB/2020

Your Project Title ***"Clinical Profile of Heart Failure Patients Followed in Outpatient Cardiac Clinic in King Faisal Hospital."*** has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Involved in the decision		
		Yes	No (Reason)	
			Absent	Withdrawn from the proceeding
Prof Kato J. Njunwa	UR-CMHS	X		
Dr Stefan Jansen	UR-CMHS		X	
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 9th December 2020, **Approval has been granted to your study.**
Please note that approval of the protocol and consent form is valid for **12 months**.

Email: researchcenter@ur.ac.rw P.O Box 3286 Kigali, Rwanda www.ur.ac.rw

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You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 9th December 2020

Expiration date: The 9th December 2021

Dr Stefan Jansen
Ag. Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

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