REPUBLIC OF CAMEROON
*Peace – Work – Fatherland*
**********
MINISTRY OF HIGHER EDUCATION
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THE UNIVERSITY OF YAOUNDE I
**********
FACULTY OF MEDECINE AND BIOMEDICAL SCIENCES

REPUBLIQUE DU CAMEROUN
*Paix – Travail – Patrie*
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UNIVERSITE DE YAOUNDE I
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FACULTE DE MEDECINE ET DES SCIENCES BIOMEDICALES

**DEPARTMENT OF INTERNAL MEDICINE AND SPECIALTIES**

# Diagnosis of Heart Failure with Preserved Ejection Fraction in Adults more than 65 years old in Yaounde Using the HFA-PEFF Score

**Thesis written and publicly defended in partial fulfillment of the requirements for the award of *Medicinae Doctor* (MD) degree by :**

**NKOTUH EMMANUEL SHU**

**17M072**

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***Academic year 2023-2024***

**REPUBLIC OF CAMEROON**
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**MINISTRY OF HIGHER EDUCATION**
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**NKOTUH EMMANUEL SHU**

**17M072**

**Defense date: 27/06/24**

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***Academic year 2023-2024***

# PRELIMINARIES

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# DEDICATION

To My parents:

Mr Nkotuh Reuben Fuh *of blessed memory*

And

Mrs Shu Grace Numfor

# ACKNOWLEDGEMENT

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- My family members and all whose names are not mentioned, I sincerely thank you for your respective contributions in my training and the realization of this work.

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| 213 | AKABA Désiré | AP | Human Anatomy |
| 214 | NSEME ETOUCKEY Georges Eric | AP | Legal Medicine |
| 215 | NGONGANG Gilbert Frank Olivier | SL | Legal Medicine |
| 216 | MENDOUGA MENYE Coralie Reine Bertine épse KOUOTOU | SL | Morbid Anatomy |
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| 221 | EUSTACE BONGHAN BERINYUY | SL | Biochemistry |
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| 231 | ONDOUA NGUELE Marc Olivier | L | Pharmacology |
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| 233 | EDOUMA BOHIMBO Jacques Gérard | SL | Stomatology and Surgery |
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| 238 | NOKAM TAGUEMNE M.E. | SL | Dental Medicine |
| 239 | GAMGNE GUIADEM Catherine M | L | Dental Surgery |
| 240 | KWEDI Karl Guy Grégoire | L | Dental Surgery |
| 241 | NIBEYE Yannick Carine Brice | L | Bacteriology |
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| 244 | NGAMENI Bathélémy | P | Phytochemistry/ Organic chemistry |
| 245 | NGOUPAYO Joseph | P | Phytochemistry/Pharmacognosy |
| 246 | GUEDJE Nicole Marie | AP | Ethnopharmacology/Plant Biology |
| 247 | BAYAGA Hervé Narcisse | L | Pharmacy |

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|---|---|---|---|
| DEPARTMENT OF PHARMACOTOXICOLOGY AND PHARMACOKINETICS | | | |
| 248 | ZINGUE Stéphane (HD) | AP | Pharmacy |
| 249 | FOKUNANG Charles | P | Molecular Biology |
| 250 | TEMBE Estella épse FOKUNANG | AP | Clinical Pharmacology |
| 251 | ANGO Yves Patrick | L | Chemixtry of natural substances |
| 252 | NENE AHIDJO épouse NJITUNG TEM | L | Neuropharmacology |
| DEPARTMENT OF GALENICAL PHARMACY AND PHARMACEUTICAL LEGISLATION | | | |
| 253 | NNANGA NGA Emmanuel (HD) | P | Galenical Pharmacy |
| 254 | MBOLE Jeanne Mauricette épse MVONDO M. | SL | Quality control and management of health products and food |
| 255 | NYANGONO NDONGO Martin | SL | Pharmacy |
| 256 | SOPPO LOBE Charlotte Vanessa | SL | Quality control of Drugs |
| 257 | ABA'A Marthe Dereine | L | Drug Analysis |
| 258 | FOUMANE MANIEPI NGOUOPIHO Jacqueline Saurelle | L | Pharmacology |
| 259 | MINYEM NGOMBI Aude Périne épouse AFUH | L | Pharmaceutical Regulation |

KEY:

- HD= Head of Department
- P= Professor
- AP= Associate Professor
- SL= Senior Lecturer
- L= Lecturer

# PHYSICIAN'S OATH

Declaration of Geneva adopted by the Geneva Assembly of the World Medical Association in Geneva, Switzerland, September 1948 and amended by the 22nd World Medical Assembly, Sydney, Australia (August 1968)

*On admission to the medical profession:*

*I will solemnly pledge myself to consecrate my life to the service of humanity*

*I will give my teachers the respect and gratitude which is their due*

*I will practice my profession with conscience and dignity*

*The health of my patients will be my first consideration*

*I will respect secrets confided in me, even after the patient has died*

*I will maintain by all the means in my power the honor and noble traditions of the medical profession*

*My colleagues will be my brothers*

*I will not permit considerations of religion, nationality, race, party politics or social standing to intervene between my duty and my patient*

*I will maintain the utmost respect for human life from the time of conception, even under threat I will not use my medical knowledge contrary to the laws of humanity*

*I make these promises solemnly, freely and upon myhonour.*

# ABSTRACT

**Background**: Heart failure is a major public health problem which affects approximately 2% of the world's population. HFpEF is increasingly frequent with the most common symptom being exertional dyspnea. It is common in older adults and its prevalence is unknown in our milieu. Moreover, the diagnosis of HFpEF in older adults is challenging due to the presence of multiple comorbidities, some of which can mimic HFpEF signs and further confound the diagnosis. Scores have been created so as to ease its diagnosis such as the HFA-PEFF score by ESC.

**OBJECTIVE**: Determine the epidemiological, clinical and paraclinical aspects of HFpEF in a group of older adults in Yaounde using the HFA-PEFF diagnostic algorithm.

**METHODS**: We conducted a hospital based Descriptive cross-sectional study at the Yaounde Central Hospital and Yaounde Biyem-Asi district Hospital. We included older adults aged 65 and above admitted or consulting at the outpatient departments of the Cardiology and Geriatric units presenting with signs and/or symptoms of heart failure within the period of 4 months from February to May. Subjects underwent a 6MWT, echocardiography and electrocardiograms were done and an Nt-pro BNP test in those with increased filling pressures. HFpEF was graded with the HFA-PEFF diagnostic tool. Charlson commobidity score was used to assess for any comorbidities. The quality of life was evaluated using the Minnesota living with heart failure questionnaire. We carried out binary regression to identify factors associated to poor quality of life. The level of significance was set at 5%.

**RESULTS**: Overall, 292 participants were included, of whom 53 (18.2%) were diagnosed with HFpEF. HFpEF made up 58.9% of older adults with HF. The Majority of patients with HFpEF were female (sex ratio 0.43) and the mean age was 74.5± 8.9 years. The most common cardiovascular risk factors were sedentary lifestyle (94.3%), Hypertension (79.2%), Obesity (66%) and Diabetes (24.5%). The most frequent clinical findings were dyspnea (88.7%), fatigue (71.7%) and lowerlimb edema (43.4%). Left ventricular hypertrophy, atrial fibrillation and left bundle branch block were the major findings on electrocardiography in 52.8%, 13.2% and 23.7% respectively. Echocardiography revealed left ventricular hypertrophy and left atrial dilatation in 52.8% and 28.3% of patients respectively. The HFA-PEFF score diagnosed HFpEF in 53 participants (20.8%). 29 (11.4%) had an intermediate score and 173 (67.8%) had a low score. Quality of life (Qol) was poor in 34% of cases with depression being independently associated with poor Qol.

**CONCLUSION**: Heart failure with preserved ejection fraction has an increased prevalence in our region, constitutes the principal phenotype of heart failure in older adults, occurs predominantly in women and precociously in long standing hypertensive patients. The HFA-PEFF score made the diagnosis in a great number of cases (65%) but can be improved upon by diastolic stress test. The quality of life in these patients with HFpEF was poor and they require psychosocial management of depression.

K**eywords**: 6MWT, HFpEF, Older adults, HFA-PEFF score , ESC, Yaounde.

# RESUME

**CONTEXTE**: L'insuffisance cardiaque est un problème majeur de santé publique touchant environ 2 % de la population mondiale. Les différents phénotypes incluent L'ICFEr, L'ICFEmr, L'ICFEP. Cette dernière est une affection de plus en plus fréquente dans la population âgée mais sa prévalence et ses caractéristiques sont méconnues dans notre contexte. Son diagnostic est difficile en raison de la présence chez les sujets âgés de plusieurs comorbidités dont les signes miment ceux de L'ICFEP. Afin d'en faciliter le diagnostic plusieurs scores ont été développés tels que le HFA-PEFF score de l'ESC.

**OBJECTIF**: Déterminer les aspects épidémiologiques, cliniques et paracliniques de L'ICFEP dans un groupe de personnes âgées à Yaoundé en utilisant le score HFA-PEFF comme outil diagnostique.

**METHODOLOGIE**: Nous avons mené une étude transversale descriptive avec un aspect analytique en milieu hospitalier chez des personnes âgées (> 65ans) présentant des signes et symptômes de l'insuffisance cardiaque à l'hôpital Central de Yaoundé et à l'hôpital de District de Biyem-Assi reçus en consultation externe ou hospitalisés sur une période de 4 mois (de Février à Mai). Des données ont été recueillis concernant leurs profil sociodémographiques et cliniques, Des échographies cardiaques et des électrocardiogrammes de repos ont été réalisés, et la Nt-proBNP chez ceux ayant des pressions de remplissages élevées. L'ICFEP a été posée à l'aide de l'outil diagnostic HFA-PEFF. Leur capacité fonctionnelle a été évaluée à l'aide du test de marche de six minutes. La qualité de vie a été évaluée à l'aide du Minnesota living with heart failure questionnaire. Une analyse multivariée par régression logistique a été effectuée pour identifier les facteurs associés à une mauvaise qualité de vie avec une valeur p inferieure à 0.05 considérée comme statistiquement significative.

**RESULTATS**: Au total 292 participants ont été inclus. Le diagnostic de l'IC a été retenu chez 90 personnes. Le score HFA-PEFF a permis de diagnostiquer une ICFEP chez 53 participants, ce qui représentait une proportion de 58,9% parmi la population d'insuffisants cardiaque et une prévalence de 18.2% chez les sujets présentant au moins un symptôme de L'IC. 29 (11,4 %) patients avaient un score intermédiaire et 173 (67,8 %) un score faible. La majorité des patients atteints d'ICFEP étaient des femmes (sex-ratio 0,43) et l'âge moyen était de 74,5± 8,5 ans. Les

principaux facteurs de risques étaient la sédentarité (94.3%), l'hypertension artérielle (79,2 %), l'obésité (66 %) et le diabète (24,5 %). Les symptômes les plus fréquents étaient la dyspnée (88,7 %), la fatigue (71,7 %) et les œdèmes des MI (43,4 %). L'hypertrophie ventriculaire gauche, la fibrillation auriculaire et le bloc de branche gauche étaient les principales anomalies électrocardiographiques avec respectivement 52,8 %, 13,2 % et 23,7 % des cas. L'écho doppler cardiaque Trans-thoracique mettait en évidence une hypertrophie ventriculaire gauche et une dilatation de l'oreillette gauche chez respectivement 52.8% et 28.3% des patients. La qualité de vie était mauvaise dans 34 % des cas, la dépression étant associée de manière indépendante à une mauvaise qualité de vie.

**CONCLUSION**: Le phénotype ICFEP est prédominant dans notre population de sujet âgés. Les femmes sont les plus atteintes et l'hypertension est la principale comorbidité. Le score HFA-PEFF permet de poser le diagnostic mais il peut être amélioré si l'échographie cardiaque de stress est courante. L'amélioration de la qualité de vie chez ces patients passe par une prise en charge psychosociale de la dépression.

Mots clés : ICFEP, score HFA-PEFF, ESC, Yaoundé.

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# ABBREVIATIONS, INITIALS AND ACRONYMS

| | |
|---|---|
| 6MWT | 6 minute walk test |
| ACC: | American college of cardiology |
| AF: | atrial fibrillation |
| AHA: | American heart association |
| AIDS: | acquired immune deficiency syndrome |
| ANOVA: | analysis of variance |
| ARN: | angiotensin receptor/neprilysin inhibitor |
| AVB: | atrioventricular block |
| BNP: | brain natriuretic peptide |
| BP: | blood pressure |
| CCI | charlson's comorbidity index |
| CO: | cardiac output |
| COPD: | chronic obstructive pulmonary disease |
| CHF: | congestive heart failure |
| CKD: | chronic kidney disease |
| ECG: | electrocardiogram |
| EDV: | end diastolic volume |
| EF: | ejection fraction |
| ESC: | European society of cardiology |
| ESV: | end systolic volume |
| HF: | heart failure |
| HFpEF: | heart failure with preserved ejection fraction |
| HJR: | hepato-jugular reflux |
| HRQoL: | health related quality of life |
| JVP: | jugular venous pressure |
| LBB: | left branch block |
| LQH: | left atrial hypertrophy |
| LV: | left ventricle |

| | |
|---|---|
| LVH: | left ventricular hypertrophy |
| MCS: | mechanical circulatory support |
| MR: | mitral regurgitation |
| MLWHF: | Minnesota living with heart failure |
| MRA: | mineralocorticoid receptor antagonist |
| NYHA: | New York heart association |
| PAH: | pulmonary arterial hypertension |
| PASP: | Pulmonary arterial systolic pressure |
| RBB: | right branch block |
| RVH: | right ventricular hypertrophy |
| SV: | stroke volume |
| SBP: | systolic blood pressure |
| DBP: | diastolic blood pressure |
| T2DM: | type 2 diabetes mellitus |
| TEE: | thrombo-embolic events |
| VAD: | ventricular assist devices |
| VES: | ventricular extrasystole |

# INTRODUCTION

## Background and Rational

Heart failure(HF) is a serious condition in which the heart is unable to pump enough blood to meet the body's requirements [1]. It is a clinical syndrome consisting of cardinal symptoms (e.g. breathlessness, fatigue and ankle swelling) that may be accompanied by signs (e.g. pulmonary crackles, elevated jugular venous pressure, and peripheral edema) [2]. It is due to a structural and/or functional abnormality of the heart that results in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise [2]. HF is a rapidly growing public health issue with an estimated prevalence of 64 million people globally (8.52 per 1,000 inhabitants), accounting for 9.91 million years lost due to disability [3], and when adjusted for age it is highest in the older age group [4]. In Africa, a study indicated that between 25.6% and 30% of admissions to cardiology units were attributable to HF, with a 360-day mortality rate of 21.9–51.9% [5]. The healthcare cost due to HF in Africa is estimated at 8.2 million FCFA [6]. In Cameroon, a study done by Kuate *et al.* in 2018 revealed a hospital prevalence of 40.8% with a mortality of 16.4% [7].

Ejection fraction (EF) has been used for sub-classification of this complex clinical entity with preserved EF being ≥ 50% [2]. In Sub-saharan Africa (SSA), Boombhi *et al*. found that HFpEF was more prevalent than HFrEF (45.5% vs. 37.5%) in the HF population and mainly occured in older adults [8]. Globally, in 2022, there were 771 million people aged 65+ years, accounting for 10% of the world's population [9], and in SSA today, 4.8% is older than 60 years [10]. Diagnosing HF in older adults poses specific challenges; false-positive clinical diagnosis are not uncommon [11]. The most common symptom of HFpEF is exertional dyspnea, even though symptoms of reduced exercise tolerance are common in older adults and have been shown to reflect normal physiological changes related to ageing or could be related to non-cardiac etiologies [12]. Moreover, the diagnoses of HFpEF in older adults may be difficult due to the presence of multiple comorbidities, some of which can mimic HFpEF signs and further confound the diagnosis. Many societies such as the European society of Cardiology, suggest the early diagnosis and management of comorbidities in patients with HFpEF for a better overall outcome, and as such, have developed a highly sensitive diagnostic tool, the HFA-PEFF score for its diagnosis [13].

With the growing older population, the prevalence of HFpEF is expected to increase even in low resource income countries including Cameroon. Studies have been conducted on heart failure in Cameroon but emphasis have not been laid on HFpEF in older adults.

# CHAPTER I: PROBLEMATIC

## I.1. JUSTIFICATION OF STUDY

Modernization has resulted in newer drugs, a better approach to treat diseases and an overall increase in life expectancy. There is a gradual shift in population demographics as more people live longer, making a significant proportion of the population affected by non-communicable diseases including heart failure. Symptoms of reduced exercise tolerance are common in older adults and diagnosing HFpEF is challenging due to the presence of multiple comorbidities, some of which can mimic HF signs and further confound the diagnosis of HF. Hence determining the prevalence and describing the clinical profile and paraclinical characteristics will improve upon making the diagnosis of HFpEF in this group. Also, the lack of emphasis regarding HFpEF in older people in our setting warrants research in this population.

## I.2. RESEARCH QUESTION

What is the prevalence of HFpEF in older adults in Yaounde?

## I.3. OBJECTIVES

### General objectives

Study the epidemiological, clinical and paraclinical elements of HFpEF in a group of older adults using the HFA-PEFF diagnostic algorithm.

### Specific Objectives

1) Determine the prevalence of HFpEF in a group of older adults using the HFA-PEFF score.
2) Describe the clinical characteristics of a group of older adults with HFpEF.
3) Describe the paraclinical characteristics of a group of older adults with HFpEF.
4) Identify factors associated with poor quality of life in these older adults with HFpEF.

## I.4. DEFINITION OF TERMS

- ✓ **Older adults**: people aged 65 years and above [14].
- ✓ **Heart failure**: this is a clinical syndrome associating specific or non-specific signs and symptoms, due to structural and/or functional abnormalities of the heart, resulting in high intra-cardiac pressures and/or insufficient flow during exercise and/or at rest. Some patients have exercise intolerance but little evidence of fluid retention, whereas others complain primarily of edema, dyspnea, or fatigue [15].
- ✓ Heart failure with preserved ejection fraction: patients with symptoms and signs of HF, with evidence of structural and/or functional cardiac abnormalities and/or raised natriuretic peptides, with a LVEF ≥50% [16].
- ✓ **Chronic heart failure**: persistent heart failure syndrome over time (more than six months) [15].
- ✓ **HFA-PEFF diagnostic scoring system [13].**

The score has functional, morphological, and biomarker domains. Within each domain, a major criterion scores 2 points or a minor criterion 1 point.

**Table I**: step 2(E): echocardiographic and natriuretic peptide heart failure with preserved ejection fraction workup and scoring system (diagnostic workup) [13].

| | Functional | Morphological | Biomarker (SR) | Biomarker (AF) |
|---|---|---|---|---|
| Major | septal e' < 7 cm/s or lateral e' < 10 cm/s or Average E/e' ≥ 15 or TR velocity > 2.8 m/s (PASP > 35 mmHg) | LAVI > 34 ml/m² or LVMI ≥ 149/122 g/m² (m/w) and RWT > 0,42 # | NT-proBNP > 220 pg/ml or BNP > 80 pg/ml | NT-proBNP > 660 pg/ml or BNP > 240 pg/ml |
| Minor | Average E/e' 9 -14 or GLS < 16 % | LAVI 29-34 ml/m² or LVMI > 115/95 g/m² (m/w) or RWT > 0,42 or LV wall thickness ≥ 12 mm | NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml | NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml |
| Major Criteria: 2 points | ≥ 5 points: HFpEF | | | |
| Minor Criteria: 1 point | 2-4 points: Diastolic Stress Test or Invasive Haemodynamic Measurements | | | |

**Interpretation:** a major criterion = 2points and a minor criterion =1point.

≥5points=HFpEF, 2-4points=diastolic stress test or invasive hemodynamic measurement is necessary. ≤ 1point = no HFpEF.

- ✓ **Co-morbidity**: It is defined as the co-occurrence of more than one disorder in the same individual. The co-morbidities studied here are those of the Charlson comorbidity score (CCI) [17] which include; Myocardial infarction, peripheral vascular disease, history of stroke, dementia, chronic obstructive pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, chronic kidney disease, hemiplegia, diabetes, solid tumour, lymphoma, leukemia and AIDS.
- ✓ **Prognosis**: According to Cambridge University, it is a doctor's judgment of the likely or expected development of a disease or a statement of what the likely future situation is. We evaluated the 10-year survival of patients using the Charlson comorbidity index.

**Table II**: Charlson index and corresponding 10-year survival rate [17]

| **Charlson index** | **10-year % survival (%)** |
|---|---|
| 0 | 98 |
| 1 | 96 |
| 2 | 90 |
| 3 | 77 |
| 4 | 53 |
| 5 | 21 |
| 6 | 2 |
| >6 | 0 |

- ✓ **Six Minute Walk Test**: It is a sub-maximal exercise test used to assess aerobic capacity and endurance. It evaluates the functional capacity of the individual and consists of measuring the maximum distance an individual covers after a six-minute walk at normal pace [18].
- Theoretical distance calculated from Trooster as thus; Theoretical distance = 218 + [5.14 x height in cm] – [5.32 x age] – [1.8 x weight kg] + [51.31 x sex] (0 for women and 1 for men) and interpreted as follows; ≤73% for severe functional limitation, 74-81% for moderate functional limitation, 82-90% for good functional mobility, ≥90% for excellent functional mobility.
- The VO2 max calculated using the Cahalin's formula $VO_{2\ peak}$ = 0.03 * distance (m) + 3.98 [19].
- ✓ **Functional capacity**: the ability of an individual to perform aerobic work as defined by the maximal oxygen uptake.

- ✓ **Quality of life**: It is a concept which aims to capture the well-being, whether of a population or individual, in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns at a specific point in time. QoL differs from the public health measure health-related quality of life in that the latter is a measure that explores the connection between health and QoL. In this case, HFpEF was the health condition. It was assessed here using the Minnesota Living with Heart Failure Questionnaire (MLHFQ) which has physical, socioeconomic, and emotional components to assess the impact of the disease on the daily lives of patients within a month [20].

**Table III**: MLWHF score and corresponding quality of life [20]

| MLWHF score | Quality of life |
|---|---|
| <24 | Good |
| 24-45 | moderate |
| >45 | poor |

- ✓ **Depression**: otherwise known as depressive disorder, is a common mental disorder. It involves a depressed mood or loss of pleasure or interest in activities for long periods.

The four questions Geriatric Depression Scale (GDS-4) provides a quick and reliable screen for depression as shown [21];

-Are you basically satisfied with your life?

-Do you feel that your life is empty?

-Are you afraid that something bad is going to happen to you?

-Do you feel happy most of the time?

**Interpretation** [22]

**GDS = 0**: This is not indicative of a depressive status, however the patient should be monitored further for any more signs displayed and also for their evolution.

**GDS = 1**: This score is not consistent with a depressive status, however, there should be some concerns raised in regard to the mental health of the patient and further assessment is required.

**GDS ≥ 2**: This score is indicative for the presence of a depressive status. The patient needs to be referred to further specialist consultation.

- ✓ **Diastolic dysfunction:** LV diastolic dysfunction is usually the result of impaired LV relaxation with or without reduced restoring forces (and early diastolic suction), and increased LV chamber stiffness, which increase cardiac filling pressures [23].

  **Grade I diastolic dysfunction:** E/A ≤ 0.8 + E ≤ 50cm/s.

  **Grade II diastolic dysfunction:** E/A ≤ 0.8 + E ≤ 50cm/s or 0.8< E/A< 2 and at least two of the following:

  - Average E/e'>14
  - TR velocity >2.8m/s
  - LA volume index >34ml/$m^2$

  **Grade III diastolic dysfunction:** E/A ≥ 2 [23].

# CHAPTER II: LITERATURE REVIEW

# II.1. KNOWLEDGE REVIEW ON HEART FAILURE

## II.1.1. Definition

According to the European Society of Cardiology (ESC), Heart failure is not a single pathological diagnosis, but a clinical syndrome consisting of cardinal symptoms (e.g. breathlessness, ankle swelling, and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles, and peripheral edema). It is due to a structural and/or functional cardiac abnormality that results in elevated intra-cardiac pressures and/or inadequate cardiac output at rest and/or during exercise [2]. This definition of HF restricts itself to stages at which clinical symptoms are apparent. Before clinical symptoms become apparent, patients can present with asymptomatic structural or functional cardiac abnormalities [systolic or diastolic left ventricular (LV) dysfunction], which are precursors of HF.

Heart failure corresponds to the continuity of most cardiac pathologies and heart failure with preserved ejection fraction (HFpEF) is an extremely common condition in the elderly. The definition adopted by the European Society of Cardiology [16] is based on the presence of 3 criteria:

- Presence of symptoms and/or signs of heart failure (at rest or on exertion).
- LVEF $\geq$ 50%.
- Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides.

### II.1.2. Epidemiology

- **World**

An estimated 64.3 million people are living with heart failure worldwide. In developed countries, the prevalence of known heart failure is generally estimated at 1% to 2% of the general adult population. In the United states based on data from Medicare beneficiaries in 2007-2014 of individuals aged ≥ 65 years, an estimated incidence rate of HFpEF increased considerably with age, from 3.1 (2.9–3.4) cases per person-year in the age group 65–69 years to 14.5 (13.6–15.4) cases per person-year in the age group >80 years [24]. Not withstanding variances in diagnostic criteria, most studies estimated that over half of all heart failure patients in the general population have a preserved LVEF and that this proportion is increasing [3]. HF is thought to have contributed to 1 in 8 deaths in 2017 [25]. HFpEF is a syndrome marked by substantial morbidity and mortality, including a 35% two-year rate of HF hospitalization and 14% two-year mortality. Importantly, HFpEF has been rising over the past decade by 10% relative to HFrEF, and this gap is projected to increase owing to the aging of the population [25].

- **Africa**

In Sub-saharan Africa some studies indicated that between 25.6% and 30% of admissions to cardiac units were attributable to HF ranging from 12% in Sudan [26], to 28.6% in Togo [27]. In South Africa, the hospital based prevalence of HFpEF is estimated to be 13.3% [28].

- **Cameroon**

Some earlier studies in Cameroon found the prevalence at about 30% in Cameroon by Kingue *et al.* [29] and recently, a prevalence of 40,8 % was obtained by Kuate *et al.* for hospitalized patients [7], meanwhile in 2021 Boombhi *et al.* found that HFpEF was more prevalent than HFrEF (45.5% vs. 37.5%) [8].

- **Gender**

Men have a higher incidence of heart failure, but the overall prevalence rate is similar in both sexes since women survive longer after the onset of heart failure. Women tend to be older when diagnosed with heart failure (after menopause), they are more likely than men to have diastolic dysfunction, and seem to experience a lower overall quality of life than men after diagnosis [30].

Patients suffering from HFpEF are older, mostly female and obese, and exhibit a lower prevalence of coronary artery disease (CAD) than patients with HFrEF [31].

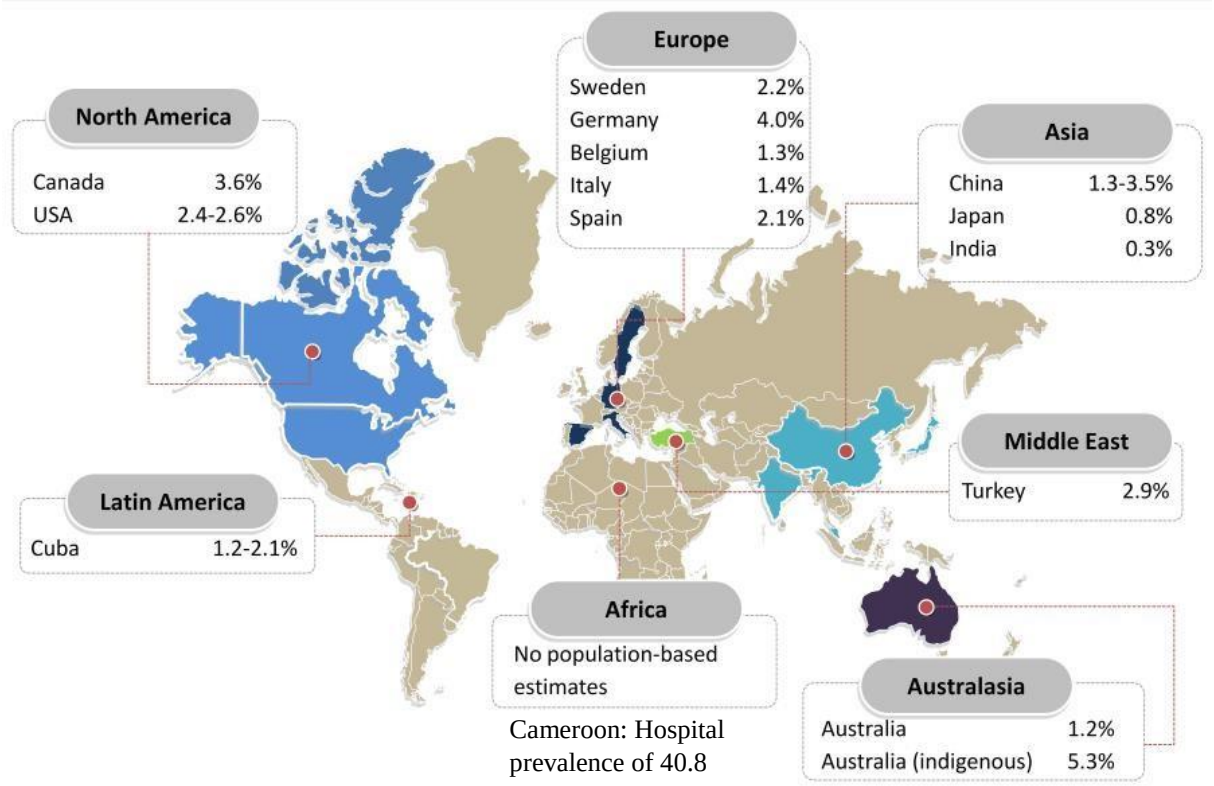



**Figure 1:** heart failure prevalence in population-based studies around the world, in percentage per region [24].

- **Risks factors**

HF risk factors vary substantially across world regions, with hypertension being highly associated with HF in all regions but most commonly in Latin America, the Caribbean, Eastern Europe, and sub-Saharan Africa, and with a minimal association of IHD with HF in sub-Saharan Africa [32,33]. Ischemic heart diseases (IHD) prevalence among HF patients is highest in Europe and North America but rare in sub-Saharan Africa, whereas hypertension prevalence among HF patients was highest in Eastern Europe and sub-Saharan Africa, valvular and rheumatic HD prevalence among HF patients was highest in East Asia and Asia-Pacific countries [32]. HF is common throughout sub-Saharan Africa. According to a meta-analysis, the most common pathogenesis is hypertensive HD in 39.2% (95% CI, 32.6%–45.9%), followed by cardiomyopathies in 21.4% (95% CI, 16.0%–27.2%) and rheumatic HD in 14.1% (95% CI, 10.0%–18.8%), whereas IHD was reported in only 7.2% of cases (95% CI, 4.1%–11.0%) [34].

In addition to older age, male sex, and ethnicity, multiple other factors indicate increased risk for development of HF as follows [35]:

- **Major clinical risk factors**: Age, sex, hypertension, LV hypertrophy, myocardial infarction, valvular heart disease, obesity, diabetes.
- **Minor clinical risk factors**: Smoking, dyslipidemia, chronic kidney disease, albuminuria, sleep-disordered breathing, anemia, increased heart rate, dietary risk factors, sedentary lifestyle, low socioeconomic status, psychological stress.
- **Toxic risk precipitants:** Chemotherapy [anthracyclines, cyclophosphamide, 5-fluorouracil (5-FU)], targeted cancer therapy (trastuzumab, tyrosine kinase inhibitors), cocaine, nonsteroidal anti-inflammatory drug (NSAIDs), thiazolidinediones, doxazosin, alcohol.
- **Morphological risk predictors**: Increased LV internal dimension, mass, asymptomatic LV dysfunction.
- **Biomarker risk predictors**: Immune activation (e.g. insulin-like growth factor 1 (IGF1), tumor necrosis factor (TNF), interleukin-6 (IL-6), C-reactive protein (CRP), natriuretic peptides (e.g. brain natriuretic peptide (BNP) and N-terminal BNP (NT-BNP), high sensitivity cardiac troponin.

## II.1.3. RECALL

### II.1.3.1. Aging and the Cardiovascular system [36]

Aging is characterized by a progressive organ dysfunction that complicates the maintenance of homeostasis. The older adults are defined by an age greater than 65years old, and physiological changes occurring with aging do not appear at any definite time [14].

**Structural changes** [36]**.**

- ✓ With aging, a moderate increase in thickness of the LV wall is observed even in the absence of arterial hypertension or another cause of afterload increase. it is a concentric hypertrophy, characterized by hyperplasia of myocardial cells due to parallel addition of sarcomeres. When the hypertrophy concerns the interventricular septum, it leads to LV outflow obstruction and thus to a further increase in afterload.
- ✓ Valvular changes such as; aortic regurgitation increases with age as a result of calcification of the aortic cusps, aortic stenosis due to stiffening, scarring and calcification of the aortic valve leaflets, and mitral annular calcification.
- ✓ The action potential and thus the duration of contraction are prolonged due to the prolongation of cytoplasmic $Ca^{2+}$ release. The extension of the action potential is due to deceleration of the deactivation rhythm of L-type $Ca^{2+}$ channels and the decreased outflow of $K^{+}$. Also, the $Ca^{2+}$ reuptake from the sarcoplasmic reticulum is decreased, while the activity of the Na+-Ca2+ exchange pump is increased. These changes in the Ca2+ cycle influence myocardial relaxation and are accountable for deceleration of the premature diastolic filling rhythm in aging.
- ✓ With the increase in age, a vital reduction of the sinoatrial node's pacemaker cells is observed, probably due to apoptosis, so that less than 10% of cells remain up to 70 years of age. In addition, the increased deposition of adipose tissue, amyloid and collagen, leads to sinus nodal disease.

**Functional changes** [36]

- ✓ At rest the end-diastolic and end-systolic diameters of the LV are not changed with aging. Also, at rest the heart rate is not greatly altered, or is slightly decreased in aged persons. Thus, systolic function and cardiac output remain normal.
- ✓ In contrast to systolic function, LV diastolic function is altered in old people. The changes in the calcium cycle influence myocardial relaxation and are accountable for the deceleration of the premature diastolic filling rhythm that characterizes aging. The delayed relaxation, combined with the decreased compliance of aged myocardium leads to an increase in end-diastolic pressure, a decrease in the early passive diastolic filling phase, and an increase in the late energetic phase of

diastolic filling. Possible mechanisms that explain the reduction of velocity of the early diastolic filling are the extracellular matrix accumulation, fibrosis and the deceleration in calcium activation from the preceding contraction.

✓ In aging, the response of the cardiovascular system to adrenergic stimulation is decreased.

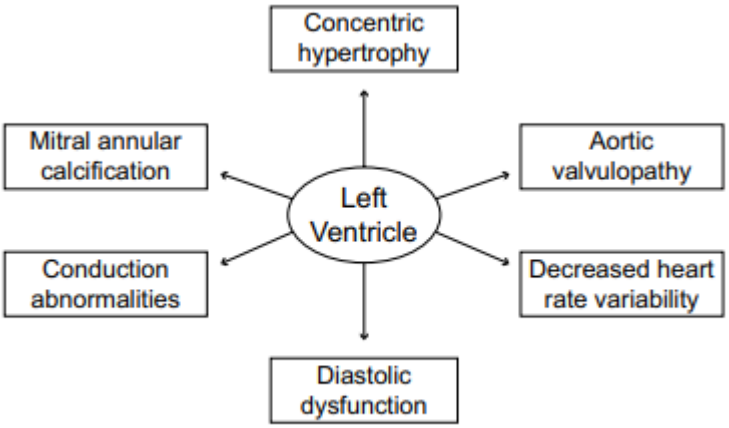



**Figure 2**: left ventricular changes due to aging **[36]**.

**Vessels** [36]

✓ Macroscopically the main changes observed are dilation and convolution of large arteries (dilation is more severe in the aorta, proximal to the myocardium and in its large branches, but smaller in the muscular arteries) and enlargement of the vascular lumen and thickening of the vascular wall.

✓ Microscopically, endothelial cells become irregular in shape and increase in height. In addition, hypertrophy, proliferation and migration of smooth muscle fibers is observed in the subendothelial space, which is infiltrated by collagen deposits, while there is also a decrease and fragmentation of elastin as well as calcification. It is known that agents involved in the inflammatory/atherosclerotic processes, such as adherence molecules, matrix metalloproteinases, growth factors and cytokines, can occur in the tunica intima of arterial wall of old people.

✓ At the cellular level, there is increasing expression of vasoconstrictive factors (such as endothelin-1 and angiotensin-II) and decreasing expression of vasodilator substances (such as estrogens and nitric oxide.

✓ The above mentioned structural changes lead to arteriosclerosis resulting in stiffening of the large arteries and an increase of pulse wave velocity (PWV). The increase in arterial stiffness with age is also responsible for changes in arterial pressure. Systolic blood pressure increases steadily,

especially after the sixth decade, while diastolic pressure reaches a plateau after the fifth decade and decreases slightly after the sixth.

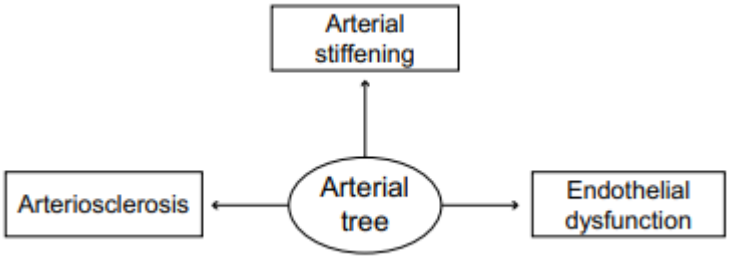



**Figure 3:** arterial changes due to aging **[36]**.

### II.1.3.2. Anatomy of the Heart [37]

The heart is a muscular organ having the shape of a recumbent pyramid and about the size of a fist, located just behind and slightly left of the breastbone.

The sides of the pyramid are:

- A lower diaphragmatic face on which the pyramid rests
- An anterior face (sternocostal) facing forward
- A right pulmonary side
- A left pulmonary side

The heart weighs between 250 and 350g, and lodges in the mediastinum (central cavity of the thorax). It extends obliquely from the second rib to the fifth intercostal space and measures 12 to 14 cm.

Layers of the heart:

The wall of the heart is made up of three tunics, all richly vascularized:

- The epicardium (external coat): is the visceral layer of the serous pericardium. It is often infiltrated by fat, especially in the elderly.
- The myocardium (muscle of the heart): forms the intermediate tunic. It is made up primarily of cardiac muscle cells and forms most of the mass of the heart.
- The endocardium: (internal tunic): is an endothelium (simple squamous epithelium).

**Chambers**

The heart pumps blood through the network of arteries and veins called the cardiovascular system. The heart has four chambers:

- The right atrium receives blood from the inferior and superior vena cava and pumps it to the right ventricle.

- The right ventricle receives blood from the right atrium and pumps it to the lungs, where it is loaded with oxygen.

- The left atrium receives oxygenated blood from the lungs and pumps it to the left ventricle.

- The left ventricle (the strongest chamber) pumps oxygen-rich blood to the rest of the body. The left ventricle's vigorous contractions create our blood pressure.

Two coronary arteries arise from the aortic sinuses in the initial portion of the ascending aorta and supply the muscle and other tissues of the heart. They circle the heart in the coronary sulcus, with marginal and interventricular branches, in the interventricular sulci converging towards the apex of the heart.

The returning venous blood passes through cardiac veins, most of which empty into the coronary sinus. This large venous structure is located in the the coronary sulcus on the posterior surface of the heart. The coronary sinus empties into the right atrium between the opening of the inferior vena cava and the right atrioventricular orifice. A web of nerve tissue also runs through the heart, conducting the complex signals that govern contraction and relaxation. Surrounding the heart is a sac called the pericardium [37].

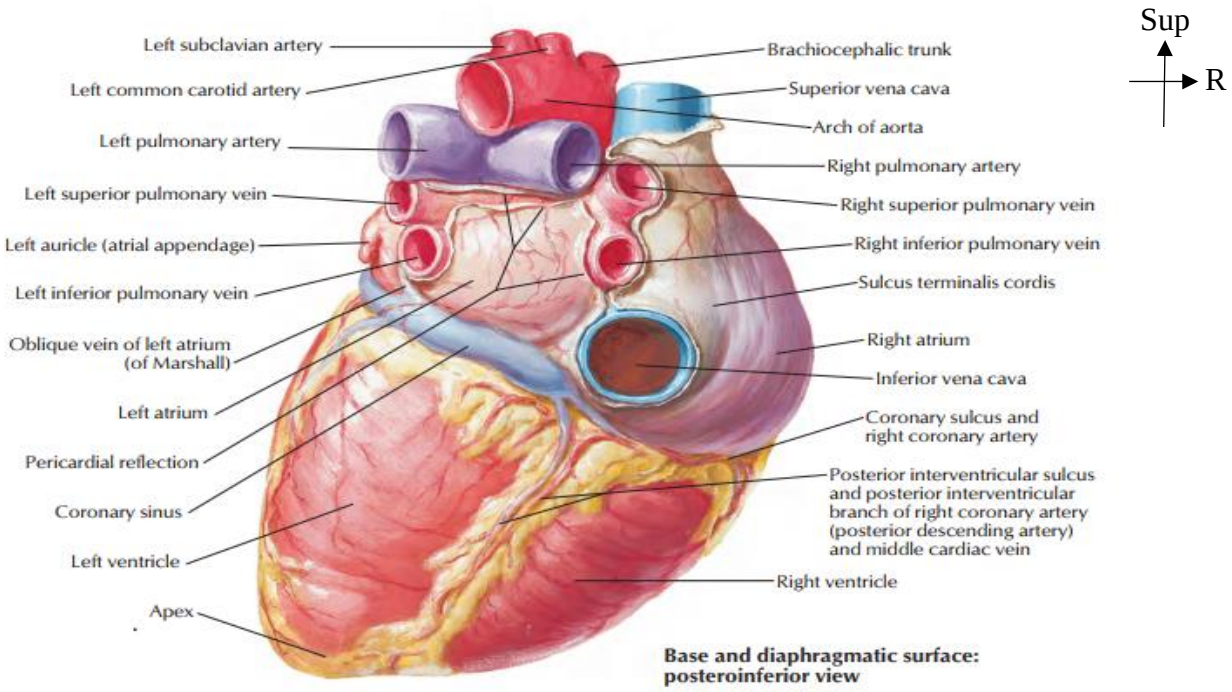



**Figure 4:** anatomy of the heart posterior view [37]

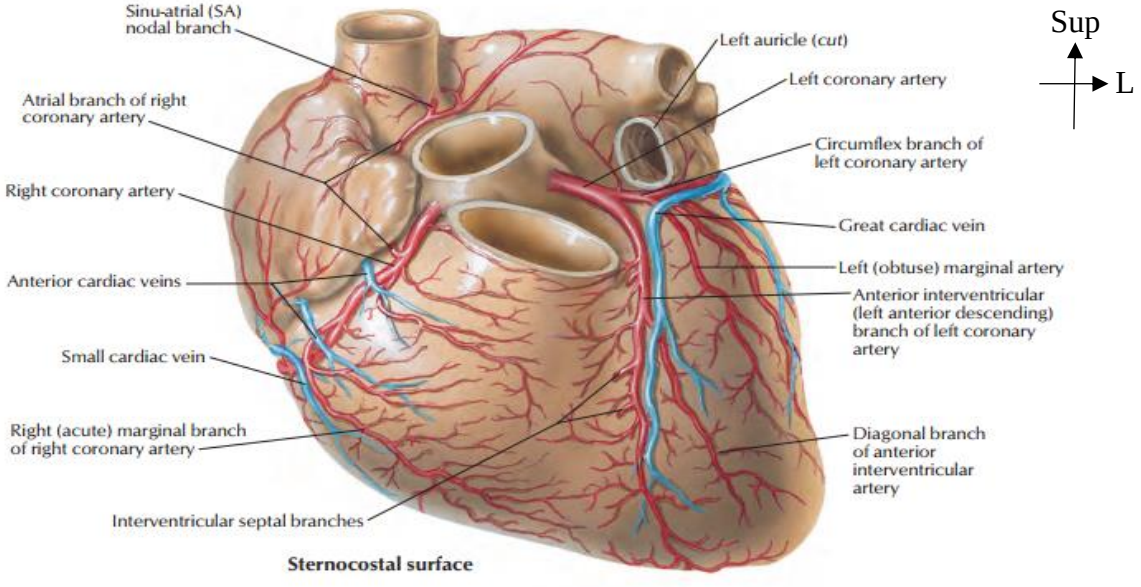



**Figure 5:** vessels supplying the heart [38].

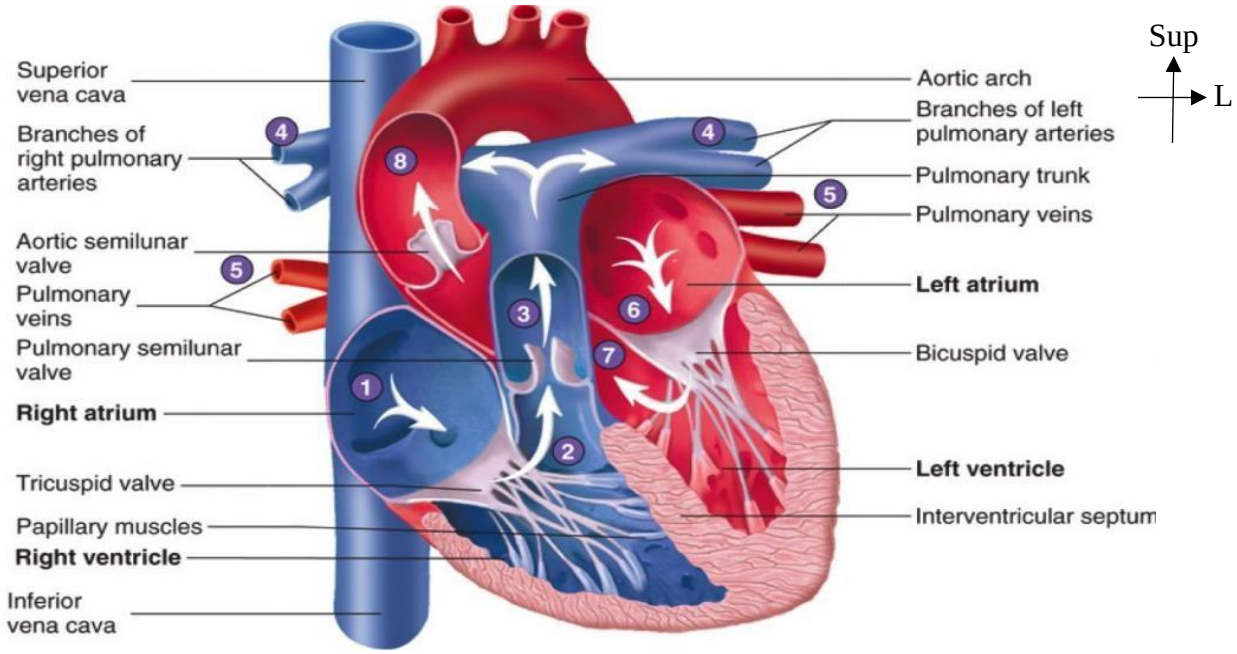



**Figure 6:** direction of blood flow in the Heart [38].

### II.1.3.3. Physiology

The cardiac output (CO) is the amount of blood ejected from the left ventricle, and normally it is equal to the venous return. It is gotten from the equation;

CO = stroke volume (SV) x heart rate (HR)

CO also equals the rate of oxygen consumption divided by the difference in arterial and venous oxygen content. The stroke volume is the amount of blood pumped out of the heart after one contraction. It is the difference in end-diastolic (EDV) and end-systolic volume (ESV). It increases with increased contractility, increased preload, and decreased afterload. Also, contractility of the left ventricle increases with catecholamines by increasing intracellular calcium ions and lowering extracellular sodium.

The preload is the pressure on the ventricular muscle by the ventricular EDV.

Frank-Starling law describes the relationship between EDV and SV. This law states that “the strength of the heart’s systolic contraction is directly proportional to its diastolic expansion, with the result that under normal physiological conditions the heart pumps out of the right atrium all the blood returned to it without letting any back up in the veins”. As venous return increases, there is a larger EDV in the left ventricle, which leads to further stretching of the ventricle. Further stretching

of the ventricle leads to a larger contraction force and a larger SV. A larger stroke volume leads to a larger CO, thus equalizing CO with venous return.

Next, the afterload is the pressure that the left ventricular pressure must exceed to push blood forward. Mean arterial pressure best estimates this. Also, afterload can be estimated by the minimum amount of pressure needed to open the aortic valve, which is equivalent to the diastolic pressure. Thus, diastolic blood pressure is one of the better ways to index afterload. Finally, the ejection fraction (EF) is equal to SV/EDV. EF of the left ventricle is an index for contractility. A normal EF is greater than or equal to 50%.

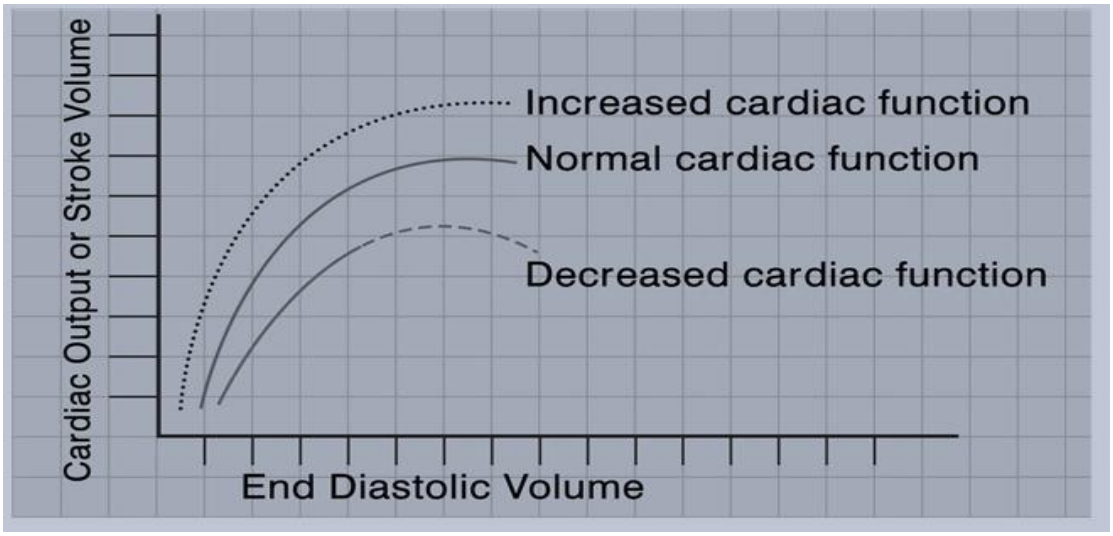



**Figure 7:** graph illustrating Frank-Starling law [39].

**Heart Cycle**

The cardiac cycle is a series of electrical and mechanical events that occur during the phases of heart relaxation (diastole) and contraction (systole) [40]. The normal duration of a cardiac cycle for a heart rate of 75 beats/minutes is 0.8 seconds.

**Electrical events**

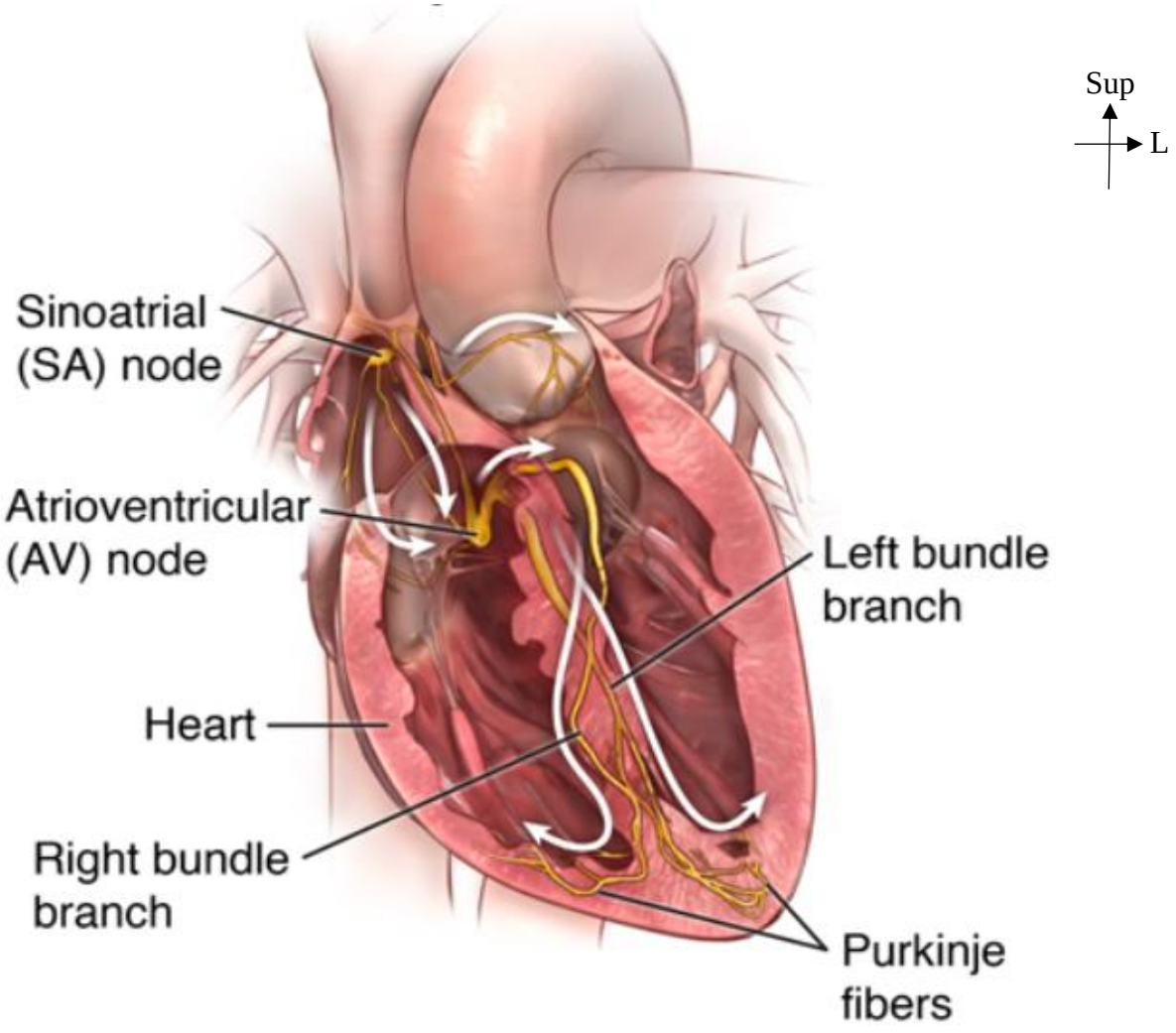



**Figure 8:** electrical system of the heart [41].

The figure above shows the impulse-generating and impulse-conducting system of the normal heart. The cardiac cycle begins with depolarization of the sinoatrial node in the upper right atrium and spread of the action potential through the atria, resulting in atrial systole. The connective tissue of the atrioventricular (AV) groove prevents cell-to-cell conduction of the electrical impulse from atrium to ventricle, permitting this only through the specialized cells of the AV node. This region

of slow conductance delays activation of the bundle of His, allowing completion of ventricular filling. The impulse then passes via the right and left bundle branches to each muscle cell, producing an orderly sequence of ventricular contraction. The ECG records the summation of the spread of the electrical potentials. The specialized cells of the sinoatrial node, the AV node and Purkinje tissue have an inherent rhythmicity. Unlike other myocardial cells, these cells do not maintain a diastolic intracellular potential of about –90 mV, but depolarize spontaneously. The sinoatrial node has the fastest inherent depolarization rate and normally determines the heart rate. When this does not function, pacemaker tissue in the AV node, bundle of His or Purkinje system assumes this role, but the heart rate is then considerably slower[42].

**Mechanical events**

The cardiac cycle may be divided into phases in any number of methods, for instance four phases or seven phases. In the four phases method, the opening and closing of the heart valves explains this method of the cardiac cycle. These phases are:

- **Phase I:** Filling period - the inlet valve is opened to fill the ventricle and the outlet valve is closed. The volume of blood in the ventricle increases from about 45 mL (from previous cycle) to about 115 mL.
- **Phase II:** Period of isovolumetric contraction -both valves are closed, blood volume is constant but the blood pressure increases to about 80 mmHg.
- **Phase III:** Period of ejection -the outlet valve of the ventricle is opened and the inlet is closed and due to more contraction, the blood pressure rises.
- **Phase IV:** Period of isovolumetric relaxation -both valves are closed and intraventricular pressure decreases without any blood volume changes [43].

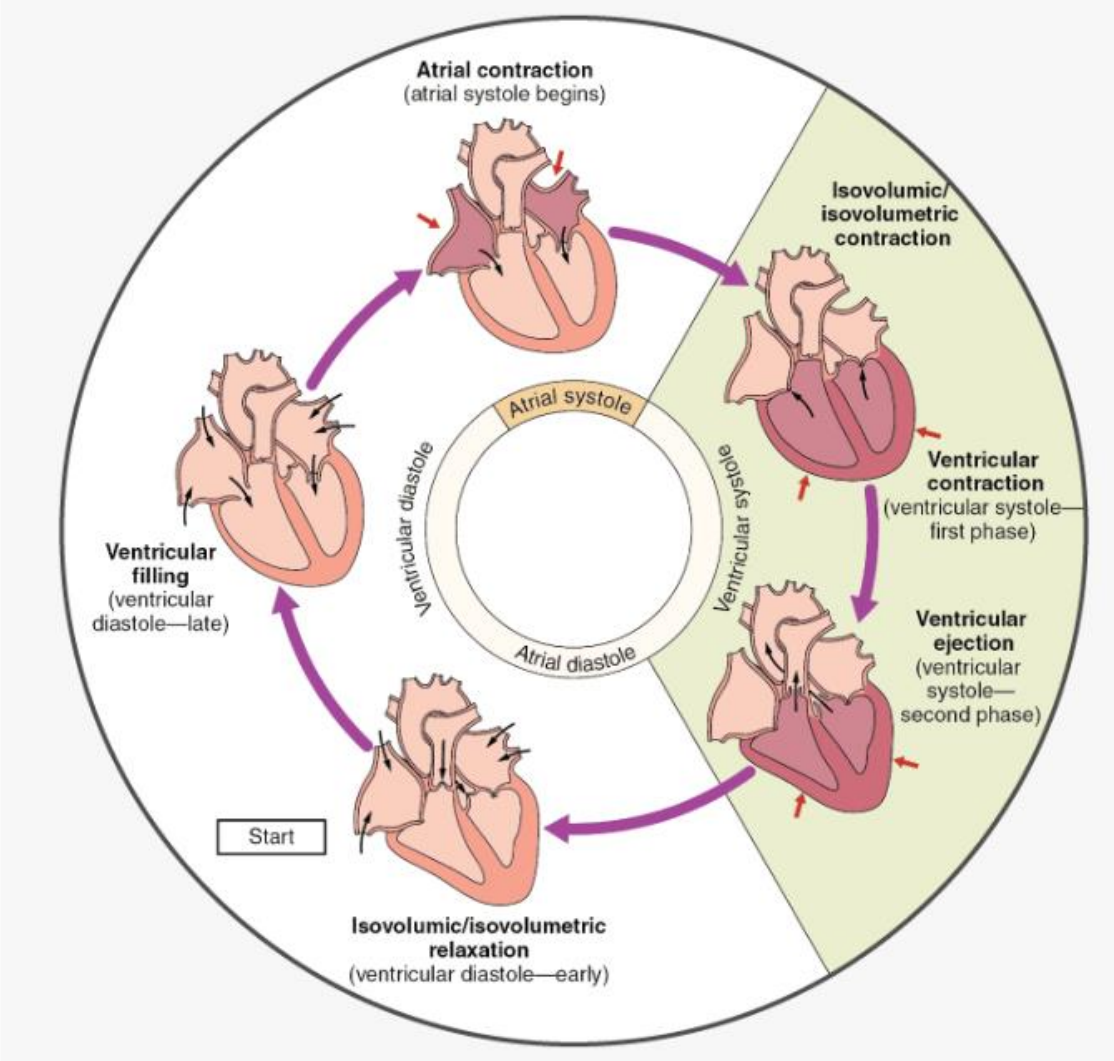



**Figure 9:** cardiac cycle [43].

### II.1.3.4. Pathophysiology of Heart Failure with Preserved Ejection Fraction (HFpEF)

The heart acts as the pump that, through coordinated muscle activity, supplies the organs and tissues of the body with oxygenated blood. To function properly, it must undergo proper relaxation to aid appropriate filling of blood during diastole, and have coordinated contraction dependent on a functional heart muscle (or myocardium) during systole [44].

**LV Structure and remodelling**

The left ventricular (LV) diastolic dysfunction plays a fundamental role in HFpEF and entails an increase in vesicular-elastic stiffness, a decrease in relaxation efficiency or both, resulting in increased filling pressures at rest or during activity. Initial observational studies revealed a common occurrence of concentric hypertrophy of the left ventricle alongside a normal chamber size. However subsequent population-based investigations have shown that many HFpEF exhibit either concentric remodeling without hypertrophy or even maintain a normal LV geometry. Cardiomyocytes in HFpEF appear thicker and have a less elongated shape and contain increased collagen content [45].

**LV Diastolic limitations**

Diastolic dysfunction is the inability to fill the ventricle to an adequate preload volume (EDV) at acceptably low pressures. Diastolic function is often conceptualized as the totality of an active process of pressure decay during early diastole related to myofilament dissociation and calcium reuptake and passive stiffness related to the viscoelastic properties governed by mechanical changes. The rate of LV pressure decay during isovolumetric relaxation is prolonged in HFpEF and when the heart rate increases, the left ventricle fails to enhance relaxation to allow for more rapid pressure decay contributing to LV and LA pressure elevation. In addition to delayed relaxation, during early diastole; the extent and velocity of mitral annular longitudinal motion, the LV recoil and the end systolic volume (ESV) achieved in the preceeding contraction cycle are all impaired. This is significant particularly during the stress of exercise , such that left ventricular filling is reliant on high LA pressure. Despite the high LV filling pressures in patients with HFpEF, at rest or with exercise, LV preload (EDV) is generally not compromised [45].

**LV Systolic limitations**

Ejection fraction is the measure that is used most often to asses systolic function. It is more often appropriately viewed as a reflection of ventricular-arterial coupling. It can be normal even when contractile function is impaired when afterload is low. Although ejection fraction is preserved at rest, enhancement in ejection fraction with stress is markedly limited in HFpEF, primarily owing to the inability to reduce chamber volume to a sufficiently low ESV rather than to a limitation in the increase in EDV. Diminished reductions in ESV impair early diastolic suction, promoting left atrial hypertension, while also blunting the normal increase in forward stroke volume that is required with exercise. Limited stroke volume reserve in HFpEF, coupled with the common presence of chronotropic incompetence significantly limits cardiac output in response to exercise in HFpEF, which is inadequate to meet the increased metabolic demands associated with locomotion [45].

**Atrial Dysfunction**

The left atrium (LA) functions as an important barrier between the LV and the pulmonary circulation, by facilitating LV filling through its conduit and booster functions and by shielding the pulmonary vasculature from wide LV pressure oscillations in concert with the mitral valve apparatus. In healthy hearts, about 80% of LV filling occurs during early diastole and the remaining 20% occurs with atrial contraction. Patients with HFpEF might be more reliant on LA contraction to achieve LV filling. In more advanced stages of HFpEF, progressive atrial dilatation and loss of atrial contractile reserve occurs, particularly with stress. Atrial dilatation precedes atrial fibrillation and is associated with chronic LV diastolic dysfunction [45].

**RV Dysfunction and Pulmonary vascular resistance**

Pulmonary hypertension is common in patients with HFpEF, particularly during exercise, because downstream elevations in LA pressure add to components of pulmonary vascular load related to arteriolar resistance and cardiac output. Studies have shown that RV function is impaired in HFpEF, even when accounting for the degree of pulmonary hypertension, and that the RV seems to demonstrate enhanced afterload sensitivity, and like the LV, the RV in HFpEF also displays increased diastolic stiffness [45].

In patients with HF, cardiac output (stroke volume multiplied by the heart rate) could be reduced at rest or with exercise. As a result, neurohormonal regulated compensatory mechanisms are activated [46]:

- Sympathetic compensatory mechanism – the baroreceptors sense a decrease in blood pressure (BP), leading to the release of catecholamine (noradrenaline), which stimulates beta-1 adrenoceptor cells in the heart. This culminates in an increased heart rate, contraction and stroke volume, which will increase the cardiac output. Although it can be helpful in the short term to maintain cardiac output, in the long term the mechanism can be damaging and actually exacerbate HF;

- Renin-angiotensin-aldosterone (RAA) compensatory mechanism – the under perfusion due to reduced BP is detected by the kidneys. This activates the RAA pathway, leading to increased concentrations of renin, plasma angiotensin II, and aldosterone. Angiotensin II is a potent vasoconstrictor of the renal (efferent arterioles) and systemic circulation, where it stimulates release of noradrenaline from sympathetic nerve terminals, inhibits vagal tone, and promotes the release of aldosterone. This leads to the retention of sodium and water and the increased excretion of potassium. In addition, angiotensin II has important effects on cardiac myocytes and may contribute to the endothelial dysfunction that is observed in heart failure. In the short term, this maintains organ perfusion, but in the long term, it exacerbates cardiac dysfunction and remodeling.

- Atrial natriuretic peptide (ANP) is released from the atria in response to stretch, leading to natriuresis and vasodilatation. Brain natriuretic peptide (BNP) is also released from the heart, predominantly from the ventricles, and its actions are similar to those of atrial natriuretic peptide. C-type natriuretic peptide is limited to the vascular endothelium and central nervous system and has only limited effects on natriuresis and vasodilatation. The atrial and brain natriuretic peptides increase in response to volume expansion and pressure overload of the heart and act as physiological antagonists to the effects of angiotensin II on vascular tone, aldosterone secretion, and renal-tubule sodium reabsorption

- Endothelin is secreted by vascular endothelial cells and is a potent vasoconstrictor peptide that has pronounced vasoconstrictor effects on the renal vasculature, promoting the retention of sodium.

- Antidiuretic hormone (vasopressin) concentrations are also increased in severe chronic heart failure. High concentrations of the hormone are particularly common in patients receiving diuretic treatment, and this may contribute to the development of hyponatraemia.

These compensatory mechanisms are able to modulate LV function within a physiologic/homeostatic range so that the functional capacity of the patient is preserved or is minimally depressed. Thus, patients may remain asymptomatic or minimally symptomatic for a period of years; however, at some point, patients become overtly symptomatic [47].

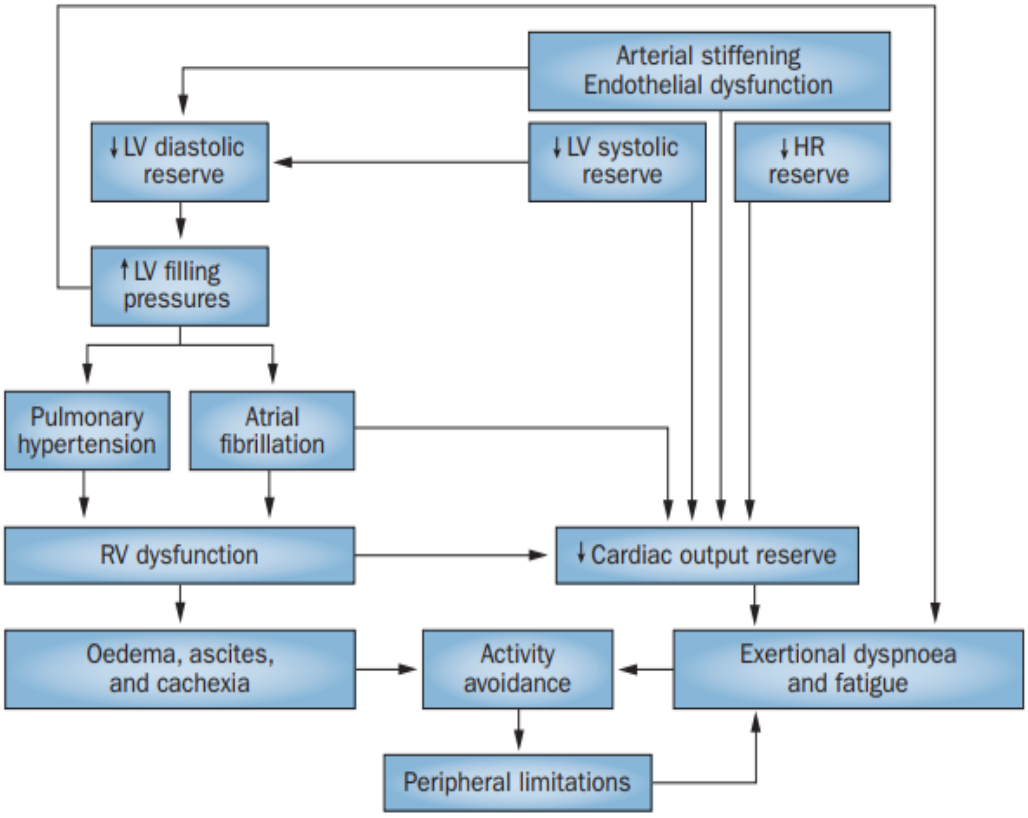



**Figure 10:** pathophysiology of heart failure with preserved ejection fraction. Arrows show causal inter-relationships between components [34].

The table below shows aetiologies of heart failure [48].

**Table IV:** aetiologies of heart failure (part 1)

| **Systolic heart failure** | **Diastolic heart failure** |
|---|---|
| Arterial hypertension | Arterial hypertension |
| Coronary artery disease | Diabetes mellitus |
| Valvular heart disease (Volume load) | Valvular heart disease (pressure load) |
| Arrhythmia | Hypertrophic cardiomyopathy |
| Inflammatory diseases | Restrictive cardiomyopathy |
| Idiopathic cardiomyopathy | Constrictive pericarditis (alcohol) |
| Toxic cardiomyopathy | Amyloidosis (storage disease) |

**Table V:** aetiologies of heart failure (part 2)

| **Left-sided heart failure** | **Right-sided heart failure** |
|---|---|
| Coronary artery disease | Coronary artery disease (right ventricle MI) |
| Hypertension | COPD |
| Myocarditis | Pulmonary hypertension |
| Heart valve disease | Pulmonary valve stenosis |
| | Pulmonary embolism |
| | Tricuspidal regurgitation |
| | Pneumothorax |
| | Pericardial effusion |

**Table VI:** potential specific aetiologies underlying heart failure with preserved ejection like syndrome [13]. (part 1)

| **Abnormalities of the myocardium** | | |
|---|---|---|
| Ischaemic | | Myocardial post-infarction/scar<br>Myocardial stunning, Epicardial coronary artery disease, Microvascular and endothelial dysfunction |
| Toxic | Recreational substance abuse | Such as alcohol, cocaine |
| | Heavy metals | Such as Iron, lead, copper (Wilson) |
| | Medications | Such as chloroquine, ergotamine, cytostatic drugs (e.g anthracyclines) |
| | Radiation | Mean cardiac radiation doses > 3 Gy |
| Immune and Inflammatory | Related to infection | Such as cardiotropic viruses, HIV, Hepatitis, parasites e.g chagas |
| | Not related to infection | Lymphocytic myocarditis, autoimmune diseases (e.g rheumatoid arthritis), connective tissue disorders like scleroderma |
| Infiltrative | Related to malignancy | Direct infiltrations and metastatis |
| | Not related to malignancy | Amyloidosis, sarcoidosis, primary and secondary hemochromatosis, storage diseases (e.g Fabry disease) |
| Metabolic | Hormonal | Such as Thyroid diseases, parathyroid diseases, Addison disease, conn's disease |
| Genetic | Diverse forms | Such as HCM, restrictive cardiomyopathies |
| Endomyocardial | | Endomyocardial fibrosis , Hypereosinophilic syndrome (Loffler's endocarditis) |

**Table VII:** potential specific aetiologies underlying heart failure with preserved ejection like syndrome [13]. (part 2)

| **Abnormalities of loading conditions** | | |
|---|---|---|
| Hypertension | | Primary and secondary forms of hypertension |
| Valvular and structural defects | Acquired | Heart valve diseases |
| | Congenital | Septal defects |
| Pericardial and endomyocardial pathologies | Pericardial | Constrictive pericarditis and pericardial effusion |
| | Endomyocardial | Endomyocardial fibrosis, hypereosinophilic syndrome |
| High output states | | Severe anaemia, sepsis, thyrotoxicosis |
| Volume overload | | Renal failure and fluid overload |
| Rhythm disorders | | Atrial/ ventricular arrhythmias, conduction disorders |

### II.1.4. Clinical Presentation

In evaluating patients with HFpEF, the following comorbidities and/or risk factors are assessed: Previous myocardial infarction, Valvular heart disease, familial heart disease, Alcohol use, Hypertension, diabetes, dyslipidemia, coronary/peripheral vascular disease, sleep-disordered breathing, Collagen vascular disease, rheumatic fever, pheochromocytoma, thyroid disease, substance abuse (previous/current history), history of chemotherapy/radiation to the chest.

**Predominant Left-Sided Heart Failure**

**Symptoms**

The New York Heart Association (NYHA) classification of heart failure is widely used in practice and in clinical studies to quantify clinical assessment of heart failure.

- **Dyspnea:** Shortness of breath is the most common manifesting symptom in patients with HFpEF. It generally begins with effort and then worsens during the evolution of the pathology to be present at rest; first in a lying position then it becomes permanent. It manifest with progressively increasing severity as the following (NYHA):
  - **Class I:** the patient is asymptomatic both at rest and during ordinary physical activity. Dyspnoea appears for unusual major efforts; no discomfort is felt in everyday life.
  - **Class II**: the patient is moderately limited in physical activity, but asymptomatic at rest. Dyspnoea appears with usual heavy exertion, such as brisk or uphill walking or climbing stairs (> 2 floors).
  - **Class III:** the patient is limited in his ordinary activity, but asymptomatic at rest. Dyspnoea appears for low intensity efforts of everyday life, such as walking on flat ground or climbing stairs (≤ 2 floors).
  - **Class IV:** the patient is symptomatic at the slightest effort, and sometimes even at rest. Dyspnoea can be permanent at rest.
- **Orthopnea**: this is dyspnoea occurring in the lying position, partially improved by the semi-sitting position due to the reduction in venous return.
- **Paroxysmal nocturnal dyspnea:** it is a dyspnoeic attack occurring during the night, often accompanied by fits of coughing without expectoration, forcing the patient to get up.
- **Cardiac asthma**: It is a predominantly expiratory bradypnea, wheezing, where cough and sputum are often absent. It is secondary to congestion of the bronchial wall.

The typical heart failure symptoms such as ankle swelling, exertional hepatalgia and bloating, generally indicate advanced HFpEF with right-sided heart failure, but are often not present. Other

possible presentations include chest pain/pressure, palpitations and non specific symptoms such as; anorexia, nausea, weight loss, fatigue are present [49–51].

### II.1.4.1.Physical Examination

A physical examination is generally insensitive for HFpEF. Signs of left sided heart failure could be present meanwhile right sided heart failure signs are indicative of advanced HFpEF.

- **Cardiac signs:**

Palpation: apex beat, spread and lowered in case of cardiomegaly Auscultation:

- frequent, irregular tachycardia in case of arrhythmia
- left galloping noise: fundamental sign to look for carefully at the apex or at the end-apex in left lateral decubitus; This is an added noise that can be proto diastolic (B3) or end diastolic (B4) or summation.
- frequent systolic murmur of mitral regurgitation, especially during attacks.
- snapping of B2 at the pulmonary focus, indicating the existence of pulmonary arterial hypertension. Blood pressure is normal for a long time, but often low, especially in severe forms due to the decrease in cardiac output. Differential blood pressure is pinched.

- **Pulmonary signs:**

Percussion can reveal liquid pleural effusions which are frequent, often bilateral and of variable abundance.

Pulmonary auscultation may show crackles or sub-crepitating rales localized to the bases or more extensive, due to increased oncotic pressure in pulmonary circulation and the leaking of fluid into the interstitial spaces of the lungs. sometimes wheezing.

**Predominant Right-Sided Heart Failure**

- **Symptoms:**

- Exertional hepatalgia: heaviness-like pain, occurring on exertion, located in the epigastrium or in the right hypochondrium, giving way when the effort is stopped, sometimes accompanied by digestive disorders.
- Spontaneous right flanc pain, permanent right flanc pain in advanced forms.

- **physical signs:**
- cardiac signs

On palpation: Harzer's sign, infundibulo-pulmonary systolic elevation.

On auscultation: tachycardia, xyphoid gallop sound, systolic murmur of tricuspid regurgitation, burst of the second sound in the pulmonary focus in the event of pulmonary arterial hypertension.

- peripheral signs

- Spontaneous turgidity of the jugular veins.
- Sensitive, even painful hepatomegaly, of firm consistency with a soft lower edge, giving rise to hepato-jugular reflux. The liver is expansive in systole in case of tricuspid insufficiency.
- Edema of the lower limbs white, soft, pitting, bilateral, predominant in the dependent parts, responsible for weight gain.
- At an advanced stage, anasarca with ascites, pleural effusion, edema of the lower limbs [52].

**Global heart failure**

It is an association of both left and right HF.

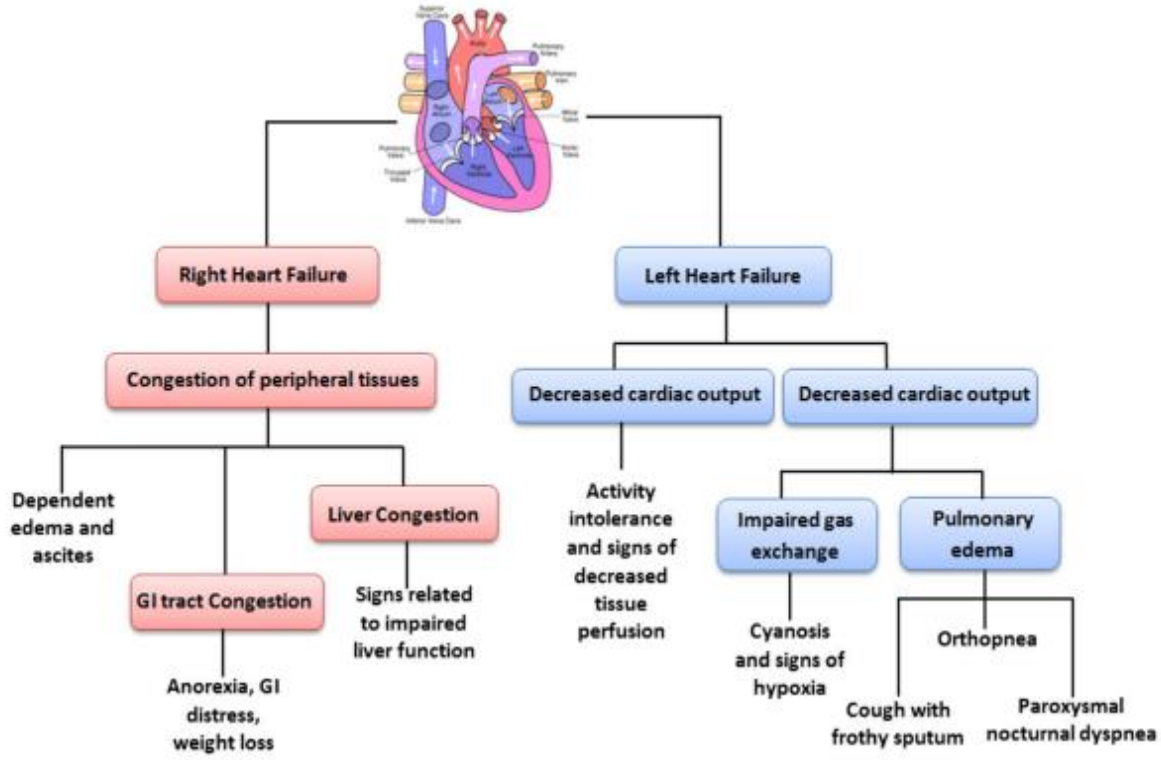



**Figure 11:** consequences of Heart failure [37].

### II.1.4.2. Diagnostic Workups [2]

**Biological exams:**

- **Natriuretic Peptides**

Measurement of NPs are recommended, if available. A plasma concentration of B-type natriuretic peptide (BNP) <35 pg/mL, N-terminal pro-B-type natriuretic peptide (NT-proBNP) <125 pg/mL, or mid-regional pro-atrial natriuretic peptide (MR-proANP) <40 pg/ml make a diagnosis of HFpEF unlikely [2].

**Morphological exams:**

- **Transthoracic echocardiography**

It is the key examination allowing the positive diagnosis, very often the etiological diagnosis, and the prognostic evaluation. This examination allows the positive diagnosis by detecting a systolic dysfunction (decreased left ventricular ejection fraction) and/or a diastolic dysfunction (raised left ventricular filling pressures). It measures the ejection fraction of the left ventricle and therefore distinguishes heart failure associated with systolic dysfunction of the left ventricle from heart failure with preserved systolic function (LVEF ≥ 50% and elevations in blood pressure).

**Measure**: left ventricular diameters and volumes, cardiac output. Left ventricular diameters and volumes should also be recorded.

A diagnosis of HFpEF is suggested if there is a non-dilated LV with a normal EF, concentric remodelling or LVH, and left atrial enlargement [13].

- **Electrocardiogram (EKG):**

An electrocardiogram (ECG/EKG) may be used to identify arrhythmias, ischemic heart disease, right and left ventricular hypertrophy, and presence of conduction delay or abnormalities (e.g. left bundle branch block). Although these findings are not specific to the diagnosis of HFpEF, a normal ECG virtually excludes left ventricular systolic dysfunction.

- **Frontal chest X-ray:**

The cardiac silhouette:

- Cardiomegaly with a cardio-thoracic index greater than 0.50.
- Elongated lower left arch with sub-diaphragmatic point.
- Convex left mid arc indicating left atrial dilation or PAH
- Right overhang with appearance in double contour testifying to a dilation of the left auricle.

- A normal cardiac silhouette does not exclude the diagnosis of heart failure.
- Straight overhang (dilation of the right auricle).
- Convex upper right arch (dilation of the superior vena cava) The cardiac lung:

The radiological signs are graded according to the elevation of the pulmonary venocapillary pressures:

- **Stage 1**: dilation of the upper lobar pulmonary veins (redistribution of venous blood to the apices)
- **Stage 2**: interstitial oedema: Enlargement of the pulmonary hiles Filling of fissures Frequent pleural effusion Kerley lines
- **Stage 3**: alveolar oedema: fluffy opacities, poorly limited, bilateral, predominantly peri-hilar.
- After this stage we can have pleural effusions [53].

- Right and left cardiac catheterization and left coronary catheterization
- Right heart catheterization:

Invasive examination, venipuncture. It allows the measurement:

- central venous, right ventricular, and pulmonary pressures (systolic, diastolic and mean pulmonary arterial pressure).
- pulmonary capillary pressure.
- cardiac output and pulmonary arteriolar resistance. Right heart catheterization is not systematic and is performed less and less. It is indicated in a few situations such as the diagnosis of pre-capillary pulmonary hypertension, suspicion of constrictive pericarditis, and very rarely during valvulopathy in case of diagnostic doubt if ultrasound is not contributory.

• **Left heart catheterization**.

There are two entities in left coronary catheterization which are [13];

- left ventricular angiography (or ventriculography) Invasive examination, involving arterial puncture. It permits: the study of the systemic and left ventricular end diastolic pressures (catheterization). LV filling pressures at rest (LVEDP $\geq$ 16mmHg) confirms definite evidence of HFpEF.
- measure the ejection fraction of the LV and study the segmental systolic function of the LV (ventriculography).

- **Coronary angiography**

It permits the study of the coronary network. It is carried out only in case of suspicion of ischemic heart disease.

- Right heart catheterization should be considered for the structured workup of suspected HFpEF, especially when left heart pressures are not available. A resting mPCWP ≥15 mmHg confirms definite evidence of HFpEF [13].

• Cardiac magnetic resonance imaging (MRI):

- Allows in case of non-contributory echocardiography (low echogenic patients):
- Measurements of left ventricular volumes, LVEF, and LV mass.
- The study of segmental systolic function, perfusion, and late enhancement.
- To help in the etiological diagnosis: congenital heart disease, tumours, myocarditis, arrhythmogenic dysplasia of the right ventricle, sequelae of infarction, etc.

• **Stress test:**

In clinical practice, exercise testing has limited diagnostic value. However, normal exercise capacity in an untreated patient makes the diagnosis of heart failure unlikely. The interest of the effort evaluation is in fact mainly prognostic.

The metabolic stress test is a stress test coupled with the measurement of gas exchange with in particular the measurement of the peak of oxygen consumption (peak of VO2). A low VO2 peak (recall < 10 mL/kg/min) is a poor prognosis, while a higher VO2 peak (recall > 18 mL/kg/min) identifies patients at lower risk of mortality. The 6-minute walk test consists of measuring the distance covered by the patient for 6 minutes. A short distance travelled is associated with a poor prognosis.

Exercise Stress echocardiography : the diastolic stress test. The parameters that have been studied most often, during or immediately after exercise, are the mitral E/e' ratio and the TR peak velocity, which indicate increases in mPCWP and PASP, respectively [13].

- **Other workups**

Basic investigations such as serum urea and electrolytes, creatinine, full blood count, liver and thyroid function tests are recommended to differentiate HFpEF from other conditions, provide prognostic information, and to guide potential therapy.

**Decompensation factors**

Chronic heart failure assumes a longer and slower course over weeks, months, or even years, during which coping mechanisms have time to develop. Patients may remain asymptomatic or minimally symptomatic for a long time. Patients may remain asymptomatic or minimally symptomatic for a long time. Then, heart failure often progresses by flare-ups during which signs of water and sodium retention or peripheral hypoperfusion appear, interspersed with phases of relative stability. These episodes are often favoured by aggravating factors that it is essential to seek systematically:

- Anaemia
- Interruption of treatment or departure from the low-salt diet
- The occurrence of arrhythmias, first and foremost atrial fibrillation, which is also a common cause of an acute attack.
- Infections
- A flare of acute myocardial ischemia.
- Finally, certain associated pathological states (fever, anemia, onset of hyperthyroidism or renal insufficiency) can promote an acute attack by increasing cardiac work or blood volume [52].

**Differential diagnosis**

- Left heart failure:

Mainly dyspnoea:

- Psychogenic dyspnoea
- Of pulmonary origin (COPD, asthma, pleurisy, pneumothorax, foreign body).
- Of neuromuscular origin (amyotrophic lateral sclerosis, myasthenia gravis)
- Anaemia, dehydration, hyperthermia…

- Right heart failure:
  - Faced with painful hepatomegaly:

Other causes of painful hepatomegaly: primary or secondary tumoral liver, infectious liver (hepatitis, hepatic amoebiasis, hydatid cysts), cirrhosis

  - In front of oedemas:

Oedema of the lower limbs of non-cardiac origin: renal, hepatic, chronic venous insufficiency, lymphatic involvement, neoplastic obstacle, malabsorption syndrome (hypoalbuminemia).

**Table VIII:** disease staging and classification [54]

| ACC/AHA stages of heart failure | | NYHA functional classification | |
|---|---|---|---|
| Stage of heart failure based on structure and damage to heart muscle | | Severity based on symptoms and physical activity | |
| Stage A | At high risk for developing heart failure. No identified structural or functional abnormality; no signs or symptoms. | Class I | No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnoea |
| Stage B | Developed structural heart disease that is strongly associated with the development of heart failure, but without signs or symptoms. | Class II | Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnoea |
| Stage C | Symptomatic heart failure associated with underlying structural heart disease | Class III | Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results in fatigue, palpitation, or dyspnoea. |
| Stage D | Advanced structural heart disease and marked symptoms of heart failure at rest despite maximal medical therapy | Class IV | Unable to carry on any physical activity without discomfort. Symptoms at rest. If any physical activity is undertaken, discomfort is increased |

### II.1.5. Diagnostic algorithms for HFPEF

There are two types of probability tests in which HFpEF is present in patients with dyspnea based on the findings obtained in clinical settings: the HFA-PEFF score and the $H_2$FPEF score. Although both scores include echocardiographic indices, the $H_2$FPEF score focuses on comorbidities, whereas the HFA-PEFF score includes natriuretic peptide levels [55].

#### II.1.5.1. The HFA-PEFF scoring system [13]

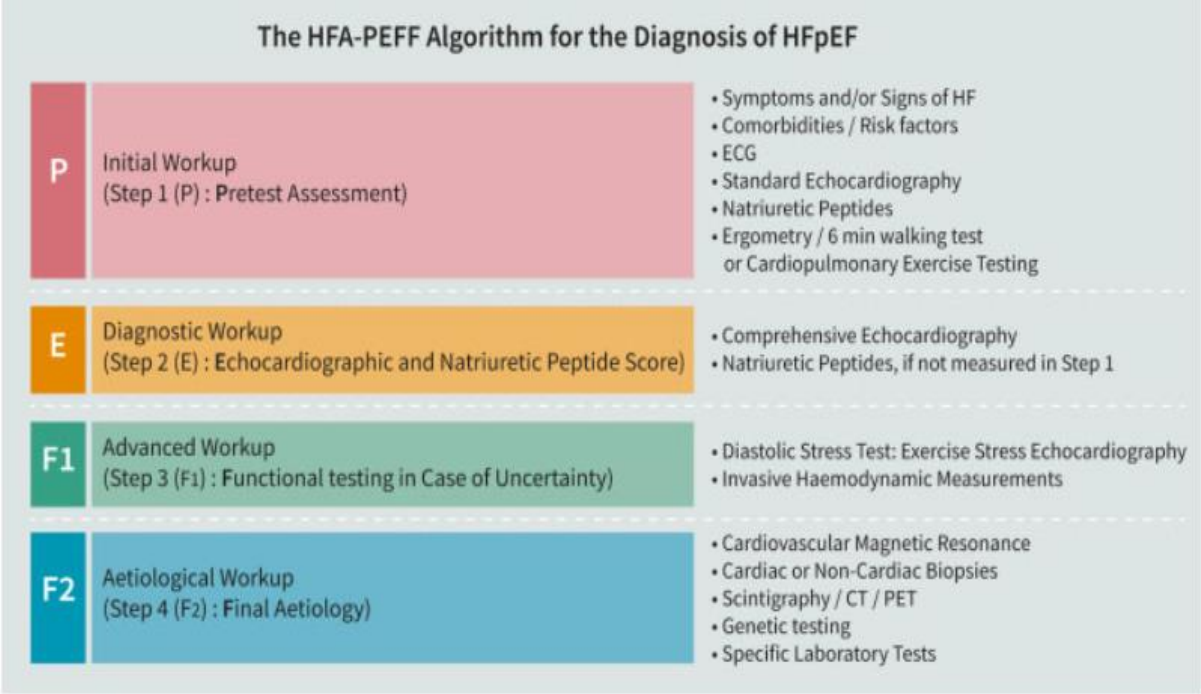
Because HFpEF accounts for more than half of all heart failure hospital admissions, and providing effective management is a major unmet clinical need dependent on a clear diagnosis, a writing committee initiated by the HFA of the ESC in 2019 produced an updated consensus recommendation -the HFA–PEFF diagnostic algorithm for its diagnosis. The key criteria in the HFA recommendations were [13]:

(i) Symptoms and/or signs of HF,
(ii) Normal or only mildly abnormal LV systolic function, and
(iii) LV diastolic dysfunction.

Diagnostic parameters were invasive measurements, echocardiographic indices of LV diastolic function and filling pressures, LV hypertrophy (LVH), left atrial (LA) enlargement, serum natriuretic peptides (NP), and atrial fibrillation (AF).

Cut-offs for key non-invasive parameters are often based on limited data, and may fall in a non-diagnostic intermediate range. The non-invasive diagnosis or exclusion of HFpEF will not depend on a single parameter above or below a certain cut-off, but on a combination of parameters derived from clinical, laboratory, and imaging tests that together will give a probability for the diagnosis. The flow chart below provides an overview of the new diagnostic algorithm comprising the following steps ;

**Table IX:** overview of the diagnostic heart failure with preserved ejection fraction steps 1–4 (P–F) [13].




- **Step 1 (P):** Pre-test assessment

It should be performed in any patient who presents with symptoms and/or signs compatible with a diagnosis of HF. It require a detailed clinical and demographic history; an electrocardiogram (ECG); blood tests; standard echocardiography to exclude other causes such as HFrEF or heart valve disease; and investigations for ischaemia, arrhythmias, anaemia, or pulmonary disease.

- **Step 2 (E):** Echocardiographic and natriuretic peptide heart failure with preserved ejection fraction diagnostic score

There is no single non-invasive diagnostic criterion for HFpEF so a combination of echocardiographic measurements of cardiac structure and function, and NP levels is recommended. Some may already be available from Step 1.

The echographic criteria are listed below ;

- Septal and lateral mitral annular peak early diastolic velocity (e') :

Major criterion: septal e'<7 cm/s; or lateral e'<10 cm/s in subjects < 75 years old or septal e'<5 cm/s; or lateral e'<7 cm/s in subjects >75 years old.

- The ratio of the peak velocity of mitral inflow during early diastole (E), over the average of septal and lateral mitral annular early diastolic peak velocities (e') :

Major criterion: average septal–lateral E/e' ratio ≥ 15

Minor criterion: average septal–lateral E/e' ratio 9 -14

- Tricuspid regurgitation peak velocity (TRV) :

Major criterion: TRV >2.8m/s or Pulmonary artery systolic pressure >35 mmHg.

- Left ventricular global longitudinal systolic strain (GLS) :

minor criterion: GLS < 16%.

- Left atrial volume index (LAVI) :

Major criterion: LAVI >34 mL/$m^2$ in sinus rhythm or LAVI >40 mL/$m^2$ in atrial fibrillation

Minor criterion: 29-34 mL/$m^2$ in sinus rhythm or 34-40 mL/$m^2$ in atrial fibrillation

- Left ventricular mass index (LVMI) and relative wall thickness (RWT) :

Major criterion: LVMI ≥ 149 g/$m^2$ in men or ≥122 g/$m^2$ in women and RWT 0.42;

Minor criterion: LVMI ≥115 g/$m^2$ in men or ≥95 g/$m^2$ in women or RWT >0.42 or LV end-diastolic wall thickness ≥12 mm.

- Natriuretic peptides :

Major criterion: NT-proBNP >220 pg/ml or BNP >80 pg/mL in sinus rhythm or

NT-proBNP >660 pg/mL or BNP >240 pg/mL in atrial fibrillation

Minor criterion: NT-proBNP 125–220 pg/mL, or BNP 35–80 pg/mL in sinus rhythm or BNP 105–240 pg/mL in atrial fibrillation.

**Calculating and Interpreting the HFA-PEFF score**

This score has functional, morphological, and biomarker domains. Within each domain, a major criterion scores 2 points or a minor criterion 1 point. Each domain can contribute maximally 2 points, if any major criterion from this domain is positive, or 1 point if no major but any minor criterion is positive. If several major criteria within a single domain are positive, this domain still contributes 2 points; and if no major but several minor criteria are positive the contribution still is 1 point. Major and minor criteria are not additive in a single domain. Points are added only when they come from different domains.

Interpretation: A total score ≥5 points is considered to be diagnostic of HFpEF, while a score of ≤ 1 point is considered to make a diagnosis of HFpEF very unlikely and to mandate investigations for alternative causes. Patients with an intermediate score (2–4 points) need further evaluation.

**Table X:** step 2 (E): echocardiographic and natriuretic peptide heart failure with preserved ejection fraction workup and scoring system (diagnostic workup) [13].

| | Functional | Morphological | Biomarker (SR) | Biomarker (AF) |
|---|---|---|---|---|
| Major | septal e' < 7 cm/s or lateral e' < 10 cm/s or Average E/e' ≥ 15 or TR velocity > 2.8 m/s (PASP > 35 mmHg) | LAVI > 34 ml/m² or LVMI ≥ 149/122 g/m² (m/w) and RWT > 0,42 # | NT-proBNP > 220 pg/ml or BNP > 80 pg/ml | NT-proBNP > 660 pg/ml or BNP > 240 pg/ml |
| Minor | Average E/e' 9 -14 or GLS < 16 % | LAVI 29-34 ml/m² or LVMI > 115/95 g/m² (m/w) or RWT > 0,42 or LV wall thickness ≥ 12 mm | NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml | NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml |
| Major Criteria: 2 points | ≥ 5 points: HFpEF | | | |
| Minor Criteria: 1 point | 2-4 points: Diastolic Stress Test or Invasive Haemodynamic Measurements | | | |

- **Step 3 (F1):** Functional testing :

  In a typical elderly patient with multiple comorbidities, the presence or absence of isolated cardiac structural and/or functional abnormalities at rest does not always establish or exclude the diagnosis of HFpEF. If invasive testing demonstrates a high LV filling pressure [left ventricular end-diastolic pressure (LVEDP) ≥ 16mmHg, PCWP ≥15mmHg] at rest, then the diagnosis may be confirmed; otherwise, assessment during exercise is recommended, either by non-invasive exercise stress echocardiography or by invasive haemodynamics.

- **Step 4 (F2):** Final aetiology

  Most cases of HFpEF are related to common risk factors and comorbidities, but the possibility of a specific underlying aetiology should always be considered. We postulate that identification of specific HFpEF etiologies will advance the field of targeted therapies.

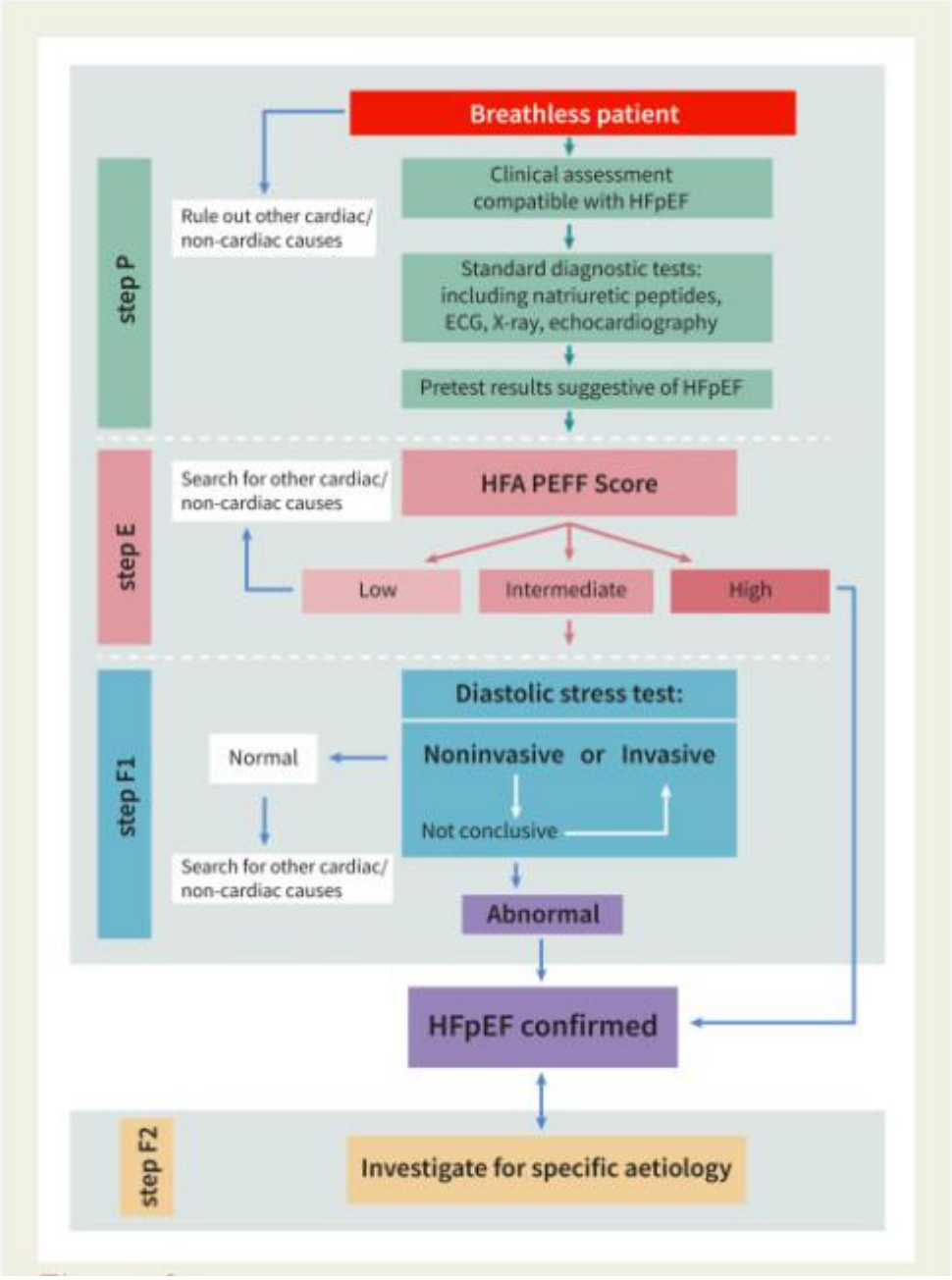


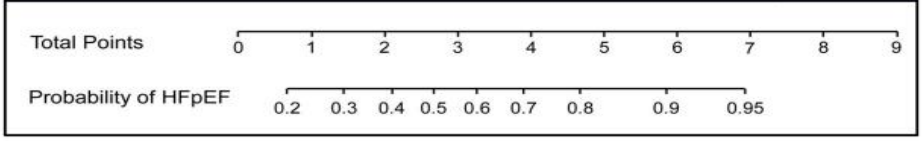

**Figure 12**: flowchart of the HFA-PEFF diagnostic algorithm [13]

### II.1.5.2. The $H_2$FPEF score

The H2FPEF score was developed by Reddy at al. at the Mayo Clinic, Rochester, USA. They built a score using six parameters: obesity, hypertension, atrial fibrillation, age, pulmonary hypertension and elevated filling pressures , the last two measured by echocardiogram . Each parameter is given a score according to the presence of the respective criteria. It enables robust discrimination of HFpEF from non-cardiac etiologies of dyspnea at low and high scores, while identifying patients at intermediate probability where additional testing is needed to refine diagnosis. The final H2FPEF score is calculated by the sum of points, indicating low probability (< 2 points), intermediate probability (2-5 points) or high probability (> 5 points) of HFpEF [56].

**Table XI:** description of the H2FPEF score and point allocations for each clinical characteristic. [56]

| | Clinical Variable | Values | Points |
|---|---|---|---|
| $H_2$ | **H**eavy | Body mass index > 30 kg/m$^2$ | 2 |
| | **H**ypertensive | 2 or more antihypertensive medicines | 1 |
| F | Atrial **F**ibrillation | Paroxysmal or Persistent | 3 |
| P | **P**ulmonary Hypertension | Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg | 1 |
| E | **E**lder | Age > 60 years | 1 |
| F | **F**illing Pressure | Doppler Echocardiographic E/e' > 9 | 1 |
| $H_2$FPEF score | | | Sum (0-9) |




**Tests Sensitivity, Specificity and predictive values of scores**

Studies have compared the accuracy of the two scores, with divergent findings. While two studies showed superior discriminating power with the H2FPEF score, other two showed they were similar, and one study showed superior AUC with the HFA-PEFF score [57].

A Japanese study demonstrated that both high $H_2$FPEF and HFA-PEFF scores showed very high positive predictive values (100% and 83%) to diagnose HFpEF while low scores displayed very high negative predictive values (94% and 100%) [58].

In a Japanese population, a high $H_2$FPEF score (6–9 points) could diagnose HFpEF with high specificity of 97% and PPV of 94%, and a low $H_2$FPEF score (0–1 point) could rule out HFpEF with high sensitivity of 97% and NPV of 93%. HFpEF could be diagnosed with a high HFA-PEFF score (5–6 points; specificity, 84%; PPV, 82%) and ruled out with a low HFA-PEFF score (0–1 point; sensitivity, 99%; NPV, 89%) [59].

### II.1.6. MANAGEMENT of HFpEF [16]

The goals of treatment in patients with HFpEF are to improve their clinical status, functional capacity and quality of life, prevent hospital admission and reduce mortality.

Management of HFpEF focuses on;

1) risk stratification and management of comorbidities, including hypertension, DM, Obesity, AF, CAD, CKD, and obstructive sleep apnea.

2) non-pharmacological management, including the role of exercise and weight loss and the use of wireless, implantable pulmonary artery monitors; and

3) symptom management and disease-modifying therapy with loop diuretic agents, SGLT2is, mineralocorticoid antagonists (MRAs), angiotensin receptor–neprilysin inhibitors (ARNIs), and angiotensin receptor blocker. Treatment includes the following options:

1. **Non-pharmacologic therapy:**

- Oxygen and noninvasive positive pressure ventilation,
- Patient education, self-care, and lifestyle advice

Adequate patient self-care is essential in the effective management of HFpEF and allows patients to understand what is beneficial, and to agree to self-monitoring and management plans. HF patients who report more effective self-care have a better QOL, lower readmission rates, and reduced mortality. Misunderstandings, misconceptions, and lack of knowledge all contribute to insufficient self-care and therefore patient education is vital. Improving patients' knowledge of their condition is fundamental for the development of self-care skills. Education to improve self-care should be tailored to the individual patient and based on, where available, scientific evidence or expert opinion. There is little evidence that specific lifestyle advice improves QOL or prognosis; however, providing this information has become a key component of education for self-care.

2. **Pharmacotherapy** [60]**:**

- **Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2is) :**

The SGLT2is have demonstrated significant cardiovascular benefits in individuals with and without T2DM. This is particularly evident in individuals with HF, as SGLT2is significantly reduce the risk of hospitalization for HF and cardiovascular death across all EF subgroups. Therefore SGLT2i is recommended in all individuals with HFpEF lacking contraindications.

- **Angiotensin receptor-Neprilysin inhibitors (ARNI):** sacubitril inhibits neprilysin, an enzyme that inactivates several important vasoactive peptides that contribute to the pathogenesis and progression of HF, including natriuretic peptides, bradykinin, and substance P. Combination with valsartan is necessary because neprilysin inhibition increases angiotensin levels, which could offset the vasodilatory effect of sacubitril unless also inhibited Sacubitril/valsartan provides modest additional benefit compared with valsartan in individuals with HFpEF.

- **Mineralocorticoid Antagonists (MRAs):** they significantly improve measures of diastolic function in individuals with HFpEF. Spironolactone may reduce the risk of hospitalizations for HF in specific subsets of individuals with HFpEF; however, appropriate monitoring of potassium and kidney function are warranted to reduce the risk of hyperkalemia and worsening kidney function.

- **Angiotensin Receptor Blockers (ARBs):** although an ARNI is likely more effective than an ARB, an ARB may be used when an ARNI is contraindicated (e.g history of angioedema) or lack of affordability impedes access.

**Table XII:** recommendation for treatment of patients with symptomatic HFpEF [16].

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFpEF to reduce the risk of HF hospitalization or CV death.[c] [6,8] | I | A |

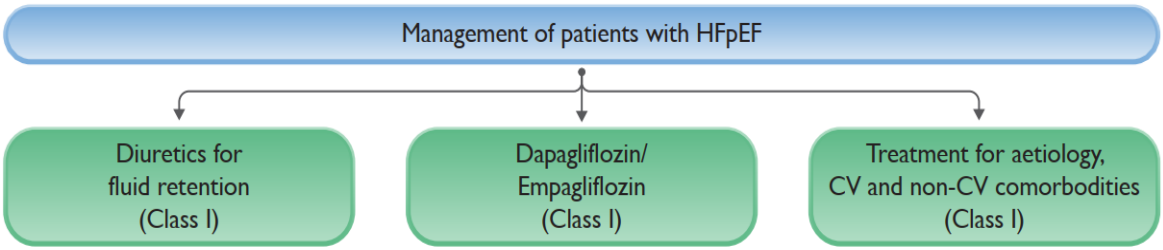



**Figure 13:** managemenet of patients with HFpEF [16]

- **Management of comorbidities:**

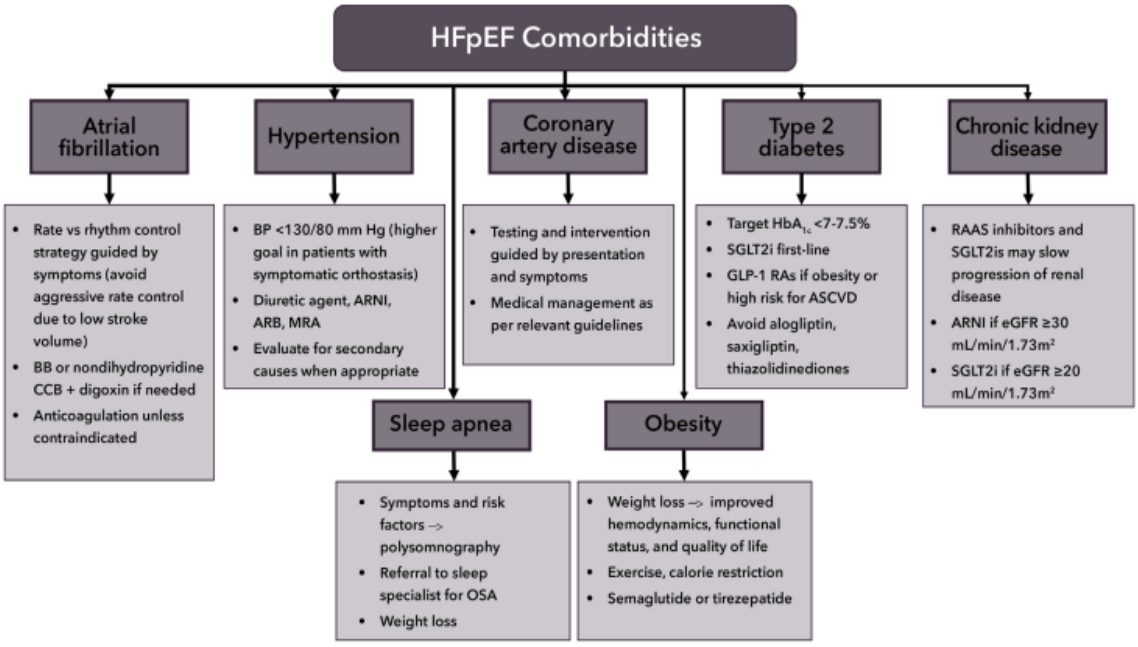



**Figure 14**: management of comorbidities associated with HFpEF [48].

3. Surgical options: they include the following:

- Ventricular assist devices
- Inter-atrial shunt devices
- Cardiac contractility modulation
- Cardiac resynchronization therapy
- Percutaneous pericardial resection
- Heart transplantation

**PROGNOSIS**

In general, the mortality following hospitalization for patients with heart failure is 10.4% at 30 days, 22% at 1 year, and 42.3% at 5 years, despite marked improvement in medical and device therapy [61].

Numerous demographics, clinical and biochemical variables have been reported to provide important prognostic value in patients with heart failure, and several predictive models have been developed. These are listed in the Table below.

**Table XIII**: markers of worse prognosis in patients with HFpEF [47].

| | |
|---|---|
| Demographic data | Older age, male sex, low socio-economic status. |
| Severity of heart failure | Advanced NYHA Class, longer HF duration, reduced peak oxygen consumption, high VE-VCO2 slope, Cheyne–Stoke ventilation, short 6-minute walking distance, reduced muscle strength, poor quality of life. |
| Clinical status | High resting heart rate, low blood pressure, clinical features of fluid overload (both pulmonary congestion and peripheral edema, jugular venous dilatation, hepatomegaly), clinical features of peripheral hypoperfusion, body wasting, frailty) |
| Myocardial remodeling and severity of heart dysfunction | Lower LVEF, LV dilatation, severe diastolic LV dysfunction, high LV filling pressure, aortic stenosis, of heart dysfunction LV hypertrophy, left atrial dilatation, RV dysfunction, pulmonary hypertension, desynchrony, vast area of hypo/akinesias, wide QRS complex, presumed inflammation or infiltration on CMR, inducible ischemia, and poor viability on imaging. |
| Biomarkers of neurohormonal activation | Low sodium, high natriuretic peptides, high plasma renin activity, high aldosterone and catecholamines, high endothelin-1, high adrenomedullin, high vasopressin. |
| Other biomarkers | Markers of renal function, inflammatory markers, cardiac stress markers, cardiac damage markers, metabolic markers, collagen markers, markers of organ damage/dysfunction. |

| | |
|---|---|
| Genetic testing | Certain mutations in inherited cardiomyopathies associated with high risk of sudden cardiac death or rapid HF progression. |
| Cardiovascular co-morbidities | Atrial fibrillation, ventricular arrythmia, non-revascularizable coronary artery disease, previous arterial disease. |
| Non-cardiovascular comorbidities | Diabetes, anemia, iron deficiency, COPD, renal failure, liver dysfunction, sleep apnea, cognitive impairment, depression |
| Non-adherence | Non-adherence with recommended HF treatment. |
| Clinical events | HF hospitalization, aborted cardiac arrest, ICD shocks |

CMR=cardiac magnetic resonance; COPD = chronic obstructive pulmonary disease; HF = heart failure;
ICD = implantable cardioverter defibrillator; LV = left ventricular; LVEF = left ventricular ejection fraction;
VE-VCO2 = ventilatory equivalent ratio for carbon dioxide.

The Charlson comorbidity index is a validated score to estimate mortality in patients with multiple comorbidities. It has been proven to have a significant predictive value for clinical outcome in HF and could be helpful in estimating outcome in HF patient.

## II.2. QUALITY OF LIFE

The World Health Organization (WHO) established the definition of health as "the state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" in 1948. Since then, QoL has been given more consideration in both clinical practice and scientific study.

"Health-related quality of life" (HRQoL) restricts QoL to elements that are related to health. However, there is no widely accepted definition of HRQoL because it is a broad and multifaceted topic. Most definitions of HRQoL centre on two factors. First of all, it is a complex idea that might be considered a latent construct. It outlines the psychological, social, role-functioning, physical, and biological components of health and functioning. Second, unlike QoL, HRQoL allows for both objective and subjective viewpoints within each domain (Testa and Simonson 1996). The objective evaluation, which emphasizes what the person can perform, is crucial in determining the level of health. The subjective evaluation of quality of life takes into account what it means to the individual; in essence, it entails the appraisal of the more objective measurement of health condition into the experience of QoL. People with the same objective health status can report quite variable subjective QoL, which is explained by differences in evaluation [62].

**HRQoL in Heart Failure:**

By limiting the patient's independence and capacity for daily tasks, HF can significantly lower their quality of life (QoL). It can also negatively impact their mental health and emotional well-being.

As such, different questionnaires were devised to evaluate the quality of life.

QUESTIONNAIRE for HRQoF in HF [63].

**Minnesota Living with Heart Failure Questionnaire:**

The MLHFQ consists of 21 questions specific to heart failure and appraises HR-QoL over the period of the previous month. Questions are answered using a Likert scale of 0–5; 0 indicates that the question has no impact on the patient or is not applicable, and 5 indicates the greatest adverse effect. The questionnaires can be divided into three domains: overall QoL domain (score range 0–105), the physical domain consisting of eight questions (score range 0–40), and the emotional domain made up of five questions (score range 0–25). A higher score represents a poorer HR-QoL. The authors recommend the overall total score as the best measure as opposed to the other two domains, which were created following factor analysis. An overall score of less than 24 denotes a high quality of life, between 24 and 45, a moderate quality of life, and beyond 45, a low quality of life. Additionally, the combined scores for the physical and emotional components were determined and divided into

three levels: good, middling, and bad. These classifications represented each dimension's level of functionality. A score of less than nine indicates good physical functioning, a number between nine and seventeen indicates intermediate physical functioning, and a score of more than seventeen indicates poor physical functioning. Scores below 6, between 6 and 11, and above 11 on the emotional component indicated good, moderate, and poor emotional levels, respectively.

## II.3. REVIEW OF PUBLICATIONS ON THE SUBJECT

- **Epidemiology:**

In 2009, Kuznetsova *et al.* [64] conducted a cross-sectional study in the general population in northern Belgium to describe the prevalence and determinants (risk factors) of LV diastolic dysfunction in a general population and to compare the amino terminal probrain natriuretic peptide level across groups with and without diastolic dysfunction. All individuals >18years old were included, Echocardiographic parameters including early and late diastolic peak velocities of mitral flow (E and A ),pulmonary vein flow by pulsed-wave Doppler, and the mitral annular velocities(Ea and Aa) at 4 sites by tissue doppler imaging were assessed. Also examined were sociodemographic characteristics medical history, smoking and drinking habits, and intake of medications. NT-proBNP was measured in plasma samples by a competitive enzyme immunoassay. Overall 539participants were enrolled (50.5% women; mean age, 52.5 years). The number of subjects in diastolic dysfunction groups 1 (impaired relaxation), 2 (elevated LV end-diastolic filling pressure), and 3 (elevated E/Ea and abnormally low E/A) were 53 (9.8%), 76 (14.1%), and 18 (3.4%), respectively. Compared with subjects with normal diastolic function (n=392, 72.7%), group 1 (209 versus 251 pmol/L; P=0.015) and group 2 (209 versus 275 pmol/L; P=0.0003) but not group 3 (209 versus 224 pmol/L; P=0.65) had a significantly higher adjusted NT-probrain natriuretic peptide. The overall prevalence of LV diastolic dysfunction in a random sample of a general population, as estimated from echocardiographic measurements, was as high as 27.3%. This study showed that higher age, body mass index, heart rate, systolic blood pressure, serum insulin, and creatinine were significantly associated with a higher risk of LV diastolic dysfunction.

Murredu *et al.*[65] conducted a population based cross-sectional study to assess the prevalence of both preclinical and clinical heart failure (HF) in the elderly in 2012 in Italy. A sample of 2001 subjects, 65 to 84-year-old residents in the Lazio Region (Italy), underwent physical examination, biochemistry/N-terminal pro brain natriuretic peptide (NT-proBNP) assessment, electrocardiography, and echocardiography. Systolic left ventricular dysfunction (LVD) was defined as left ventricular ejection fraction (LVEF)< 50%.Diastolic LVD was defined by a Doppler-derived multiparametric algorithm. The overall prevalence of HF was 6.7%[95% confidence interval (CI) 5.6 – 7.9], mainly due to HF with preserved LVEF (HFpEF) (4.9%; 95% CI 4.0 – 5.9), and did not differ by gender. A systolic asymptomatic LVD (ALVD) was detected more frequently in men (1.8%; 95% CI1.0 – 2.7) than in women (0.5%; 95% CI 0.1 – 1.0;P=0.005), whereas the prevalence of diastolic ALVD was comparable between genders (men: 35.8%; 95% CI=32.7 – 38.9; women: 35.0%; 95% CI=31.9 – 38.2). The NT-proBNPlevels and severity of LVD increased with age. Overall, 1623 subjects (81.1% of the entire studied population) had preclinical HF (Stage A:

22.2% and stage B: 59.1% respectively). This study showed that, In a population-based study, the prevalence of preclinical HF in the elderly is high. The prevalence of clinical HF is mainly due to HFpEF and is similar between genders.

In 2006 in Australia, Abhayaratna *et al.* [66] carried out a study to determine the prevalence and predictors of left ventricular (LV) diastolic dysfunction in older adults. Simple random sampling was used to select 1275 Canberra, aged 60 to 86 years (mean age 69.4; 50% men), to constitute the study population. They were assessed for clinical risk factors for heart failure, Echocardiographic parameters were measured and quality of life questionnaire was administered. The prevalence of any diastolic dysfunction was 34.7% (95% CI 32.1% to 37.4%) and that of moderate to severe diastolic dysfunction was 7.3% (95% CI 5.9% to 8.9%). Of subjects with moderate to severe diastolic dysfunction, 77.4% had an LV ejection fraction (EF) > 50% and 76.3% were in a preclinical stage of disease. The prevalence of moderate to severe diastolic dysfunction with an EF >50% and no regional LV wall motion abnormalities was 5.6% (95% CI 4.4% to 7.1%). This study showed that diastolic dysfunction is common in the community and often unaccompanied by overt congestive heart failure. Despite the lack of symptoms, advanced diastolic dysfunction with normal EF is associated with reduced quality of life and structural abnormalities that reflect increased cardiovascular risk.

In 2017, Cui *et al.* [67] carried out a cross sectional study to explore the prevalence and correlates of LVDD and HFpEF in community-based elderly population by data obtained from Shanghai Heart Health study (SHSS) in China. A total of 1274 community residents (769 women, aged≥65 years) participated in the study. Laboratory and echocardiographic data were obtained to analyze correlates of LVDD and HFpEF using univariate and multivariate Logistic analysis. LVDD was detected in 31.9% (406/1274) residents and it was significantly higher in women than in men (34.2% vs. 28.3%, P = 0.027). HFpEF prevalence was 2.8% (35/1274), and increased with aging in the whole cohort. For residents with LVEF≥50% and normal-sized ventricular cavity, female sex (odds ratio [OR] 1.69, 95% confidence interval [CI] 1.24–2.29), heart rate (OR 0.76, 95% CI 0.68–0.86), atrial fibrillation (OR 7.37, 95% CI 3.13–17.36), hypertension (OR 1.32, 95% CI 1.00–1.75), and N-terminal pro-BNP (OR 2.33, 95% CI 1.50–3.61) were independent correlates of asymptomatic LVDD. This shows that LVDD is common in community elderly population, and HFpEF is also not rare.

In 2017, Traore *et al.* [68] carried out a study to describe the epidemiological and etiological features of heart failure with preserved ejection fraction in patients followed at the heart institute of Abidjan over a 12 months period. Heart failure with preserved ejection fraction (HFPEF) was

defined from the symptoms and signs of heart failure, the level of NT-proBNP and from echocardiography data based on the left ventricular ejection fraction (LVEF) > 50%, the dilatation of the left atrium. The diastolic dysfunction of the left ventricle was assessed by the ratio E/E' > 13. The study involved 64 patients with heart failure with preserved ejection fraction out of 257 patients with heart failure that is a prevalence of 25%. The mean age was 57.3 ± 16 years. There was a male predominance that is 52% of cases. Congestive heart failure was predominant in 67%. NT-proBNP levels were 365 pg/ml on average. The average length of stay was 5.5 ± 3.1. Intra -hospital deaths were 4.6%. The etiologies are dominated by high blood pressure in 85.9%, followed by obesity in 28.1%, then by ischemic heart disease in 4.6%. There were no diabetic patients in this group.

- **Clinical data**

In 2021, Boombhi *et al*. [8] investigated a sub-Saharan African population of 201 patients (>18years old) with HFpEF for the clinical, cardiovascular and laboratory findings and therapeutic aspects of HFpEF, compared with those of HFrEF in Yaounde, Cameroon. This prospective multicenter study conducted in three major referral cardiology units of Cameroon found that HFpEF was more prevalent than HFrEF (45.5% vs. 37.5%). Compared with patients with HFrEF, those with HFpEF were older (p=0.003), and had a significantly higher incidence of hypertension (p=0.034) and obesity (p=0.013). HFrEF was significantly more associated with congestive symptoms than HFpEF such as stage 4 NYHA dyspnea (p=0.040), orthopnoea (p=0.005), jugular venous distention (p=0.034), hepatomegaly (p=0.015), hepato-jugular reflux (p=0.018) and ascites (p=0.020). Furthermore, the third sound gallop was significantly more present in patients with HFrEF (p=0.033) [3]. The rate of atrial fibrillation was higher in patients with HFpEF (33.92% vs. 16.9%, p=0.013).

In 2013, Mboup *et al*. [69] conducted a descriptive prospective study in the cardiologic unit of the principal hospital in Dakar Senegal to evaluate the epidemiological, clinical, paraclinical findings and theurapeutic aspects of HFpEF in the sub-Saharan African population. Inclusion criteria was the presence of symptoms and/or signs of HF, EF> 50% and diastolic dysfunction on echocardiography. Overall 587 patients were admitted to the service, 111 patients had a diagnosis of HF (hospital prevalence of 19%) amongst which 32 had HFpEF. The mean age of participants was 65,7 ± 9,1 years; sex ratio;1.28 (18women/14men). All participants were hypertensive with a mean duration of 9.25 ± 3.5years, type II diabetes and current active smoking status found in 13(45%) and 6 patients(9%) respectively. 16 patients (50%) were obese with a mean BMI of 25,55 ± 4,52 kg/m². 10 patients (31%) had a past hospitalization history for HF, 2patients(6%) were previously admitted for myocardial infarction. The most frequent symptom was exertional dyspnea

in 27patients (84%) which could be isolated or associated with either orthopnea and/or paroxysmal nocturnal dyspnea in 13(41%) and 6(19%) patients. signs of congestive HF were present in 13patients (41%). ECG findings of left ventricular hypertrophy and atrial fibrillation occurred in respectively 21(65%) and 4patients(13%).

In 2012 Satomura *et al*. [70] carried out a study to compare clinical features and clinical outcomes between HFpEF and HFrEF over a 3year period in patients older than 80years in Japan. A total of 113patients admitted for HF were enrolled, retrospectively clinical features, laboratory data and echocardiographic parameters were analyzed. In 53 patients (49%), left ventricular ejection fraction was preserved and 58(51%) had HFrEF. In those with HFpEF; the mean age was 84.3 ± 3.92years, 22(40%) were men, the mean BMI was 21.0 ± 3.65kg/$m^2$, 39(71%)patients were hypertensive, 11(20%)patients had dyslipidemia, 14(25%) had type II diabetes, 22(40%)patients had atrial fibrillation and the total death in HFpEF patients was 8(15%). The longterm outcomes of HFpEF in this population was not different from that of HFrEF.

- **Management**

In 2019, Stefan D. *et al.* in Berlin conducted a multicenter, randomized, double-blind parallel-group, placebo-controlled trial study to evaluate the effects of SGLT2 inhibition with empaglifozin on morbidity and mortality in patients with chronic heart failure and a preserved ejection fraction. 5750 patients >18years with HFpEF (EF>400%), with and without type 2 diabetes were randomized to receive a aplacebo or empagliflozin 10mg/day, added to all appropriate treatments for HFpEF and co-morbididities. The primary endpoint was the time-to-first event analysis of the combined risk for cardiovascular death or hospitalization for heart failure, and also they evaluated the effects of empagliflozin on renal function, cardiovascular death, all-cause mortality and reccurent hospitalization events and a wide range of biomarkers that reflect important pathophysiological mechanisms that may drive the evolution of HFpEF. Patients were excluded if they had: a cardiovascular disorder or are receiving treatments that increase the unpredictability of or may change their clinical course, independently of heart failure, if they have an untreated or undertreated cardiovascular condition that may influence the course of HF, or a significant comorbid condition, that may influence the clinical course independently pf HF, or any condition that may jeopardize their safety, limit their participation or undermine the interpretation of trial data. They found that, empagliflozin reduced the risk for cardiovascular death or HF hospitalization and improved glomerular function and slowed the progression of renal disease in patients with type 2 diabetes. They also found out that patients with type 2 diabetes are particularly prone to the development of HFpEF.

- **Prognosis**

In 2022, Nshuti *et al.* [28] carried out a retrospective review of hospital records of all consecutive adults > 18years old admitted to the medical ward at Groote Schuur hospital in Cape town South Africa with a clinical diagnosis of HF during the period of January 2016 to December 2017. Socio-demographic profile (age, gender), medical history (comorbidities), clinical examination findings and laboratory investigations (electrolytes, renal function, haematological parameters) were recorded on all patients who fulfilled the HFpEF criteria. The outcome of interest was the composite of readmission to hospital or death within one year of index admission for HFpEF . A total of 315 potential cases of de novo heart failure were identified for the study period (2016 and 2017), of which 42 patients (13.3%) had HFpEF. The median age of the cohort was 55.5 years (IQR 47-66), with a female preponderance (81.0%). The most common comorbidities were hypertension (85.7%), CKD (40.5%) and diabetes (40.5%). All patients presented to hospital with shortness of breath, with 45.2% and 40.5% of the cohort presenting with New York Heart Association (NYHA) functional class III or IV respectively. The most common finding on physical examination was respiratory crackles (83.3%).the majority of patients (61.9%) had at least one major abnormal finding on the ECG. This included LVH by Sokolow-Lyon criteria and Cornell criteria (both 16.7%), LBBB (11.9 %) and abnormal T wave inversion (38.1%). Atrial fibrillation (2.4%) and atrial flutter (2.4%) were rare. On echo, 81.0% of patients had evidence of concentric LVH and 45.2 % had left atrial enlargement. The majority of participants had evidence of diastolic dysfunction (92.9%). There were 20 patients (47.6%) who had poor outcome. Of these, fifteen patients (35.7%) were readmitted to hospital with decompensated heart failure and five patients (11.9%) died.

In 2017, Kontogeorgos *et al*. [71] carried out a retrospective study to investigate the 5year mortality and its prognostic factors in old hospitalised patients > 65years with HFpEF compared with HFrEF at Sahlgrenska University Hospital/Ostra Sweden. Diagnosis were reviewed and re-evaluated for each patient, the outcome measure was all-cause mortality and collected from May 2007 and 2013. The 5-year mortality was high (67.5%) for the whole study population Age as a continuous variable was estimated to produce a 7.2% higher risk to die for every year to come in the whole cohort (6% for HFrEF and 9% for HFpEF) after adjustment for sex. . After adjustment for age, patients with HFrEF had 42% higher 5-year mortality than HFpEF patients. There were more women in the HFpEF group (56%) than in the HFrEF group (36%).

In 2020 in the United States, Senthil Salvaraj *et al*. [72] carried out a study to describe characteristics and risk of adverse outcomes associated with each score among participants in the

community with unexplained dyspnea. 4,892 Atherosclerosis Risk in Communities (ARIC). Participants aged 67-90years at Visit 5 (2011-2013) without other cardiopulmonary causes of dyspnea were studied. They were categorized as asymptomatic (76.6%), known HFpEF (10.3%), and tertiles of each score among those with ≥ moderate, self-reported dyspnea (13.1%). H2FPEF≥6 and HFA-PEFF≥5. Mean age was 75±5 years, 58% were women, and 22% were black. After a mean follow-up of 5.3±1.2 years, rates (95% CI) of HF hospitalization or death per 1000 person-years for asymptomatic and known HFpEF were 20.7 (18.9-22.7) and 71.6 (61.6-83.3). Among 641 participants with unexplained dyspnea, rates were 27.7 [18.2-42.1], 44.9 [34.9-57.7], and 47.3 [36.5-61.3] (tertiles of H2FPEF-score); and 31.8 [20.3-49.9], 32.4 [23.4-44.9], and 54.3 [43.867.3] (tertiles of HFA-PEFF score). Participants with unexplained dyspnea and scores above the clinical threshold for each algorithm, H2FPEF≥6 and HFA-PEFF≥5, had equivalent risk of HF hospitalization or death compared to known HFpEF, and 28% had “discordant” findings (only high risk by one algorithm), while 4% were high risk by both. In this study, participants with unexplained dyspnea and higher H2FPEF or HFA-PEFF scores face substantial risks of HF hospitalization or death. A significant fraction of patients are classified discordantly by using both algorithms.

# CHAPTER III : METHODS

## III.1. Description of the study

### III.1.1. Study design

This was a descriptive and analytical cross-sectional study.

### III.1.2. Study sites

To carry out this study, we recruited patients from two hospitals: the Yaounde Central Hospital and the Yaounde Biyem-Assi district hospital.

- **Yaounde Central Hospital:**

It is a reference hospital and one of the second-category health facilities in the national pyramid created in 1933. It is located in the centre region, in the Mfoundi Division in Yaounde. It is in the downtown area behind the CENAME and not far from the Messa camp. It offers specialized health care to populations and we find the units and following care services: Medicine and specialty unit, Surgery and specialty unit, Gynaecology and Obstetrics Unit, Intensive care unit, reception, emergencies, Medical-technical unit.

The cardiology service is part of the medicine and specialty unit and consists of consultation rooms, cardiological exploration rooms, echocardiography, ECG, Hospital wards. The medical team consists of: 05 cardiologists, residents and students, 01 major nurse and nurses.

The Geriatric unit has 02 geriatricians, residents, 01 general practitioner, 01 major nurse and nurses. The unit equally has a 9-bedded hospital ward and outpatient consultations.

- **Yaounde Biyem-Assi District hospital;**

It is a 4$^{th}$ degree reference hospital in the health pyramid. It is found in the centre region, in the Mfoundi division, and Yaounde VI subdivision. It is located in Biyem-Assi, and here we find several units including; Internal Medicine unit, Surgery and specialty unit, Obstetrics and Gynaecology unit, pediatric unit, emergencies, reception. It has a hospitalization ward and an out-patient department where we recruited patients.

The cardiology service is part of the medicine and specialty unit and is made of: Consultation rooms, Cardiological exploration rooms: echocardiography, ECG, Hospital wards.

The medical team consists of; 04 Cardiologists, 01 nutritionists, 07 General practitioners, 01 major nurse and nurses.

### III.1.3. Study period

The study was done within 8 months from 1st October 2023, to May 2024. During this timeframe, the following was done: writing of the proposal, obtaining ethical clearance and authorization documents, data collection and analysis, proofreading and publishing of results. Data recruitment began in February 2024 and ended in May 2024 that is a four-month period of data collection.

## III.2. Characteristics of the study population

**III.2.1. Source Population:** All Cameroonian older adults seen at the cardiology and geriatric units in Yaounde, at both in and outpatient departments.

**III.2.2. Target Population:** All older adults with symptoms and signs of heart failure

## III.3. Eligibility criteria

### III.3.1. Inclusion criteria

- People aged 65 years and above.
- With symptoms and/or signs of heart failure
- Given a free-will informed consent.

### III.3.2. Non-inclusion criteria

- Critically ill individuals (WHO performance status class IV).
- Patients with HFrEF or HFmrEF

### III.3.3. Exclusion criteria

- Incomplete data

## III.4. Sampling

We carried out a non-probabilistic consecutive and non-exhaustive sampling from amongst older adults who either consulted or were admitted to the geriatric and cardiology units during our study period.

### III.4.1. Sample size estimation

Our sample size was estimated using the OpenEpi software in https://www.openepi.com/

Data was entered in the sample size calculator;

P was the estimated proportion of HFpEF in older adults = 2.8% as obtained by Cui *et al.* [67] in Shanghai Heart Health study (> 65years).

The population size studied N= 1274 older adults.

Z- was 95% confidence interval (standard value of 1.96).

d- Was the margin of error (precision error) = ±5 %.

Substituting these gave us a sample size; n = 41.

## III.5. STUDY RESOURCES

### III.5.1. Human resources

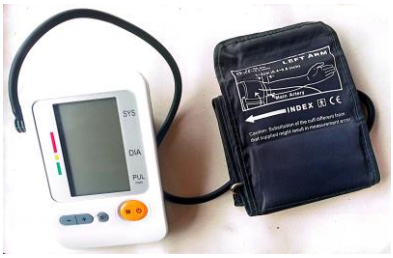
- ✓ Supervisor: Professor NGANOU-GNINDJIO Chris Nadège
- ✓ Co-supervisors: Dr NTSAMA ESSOMBA Marie Josiane
  Dr NDOBO Valérie
  Dr EBENE MANON Guillaume
- ✓ Investigator: NKOTUH Emmanuel Shu
- ✓ A statistician

We worked with the personnel of the various Hospitals concerned.

### III.5.2. Material Resources

- o **For clinical evaluation**
  - Pens and pencils
  - A rim of A4 papers
  - A 3M$^{TM}$ litthmann® Classic III stethoscope [73].

  - A digital blood pressure machine OMRON® HEM-712 Omron Corporation, Tokyo, JAPAN).




  - Scale balance Salter 200 WHGYDR® Premium

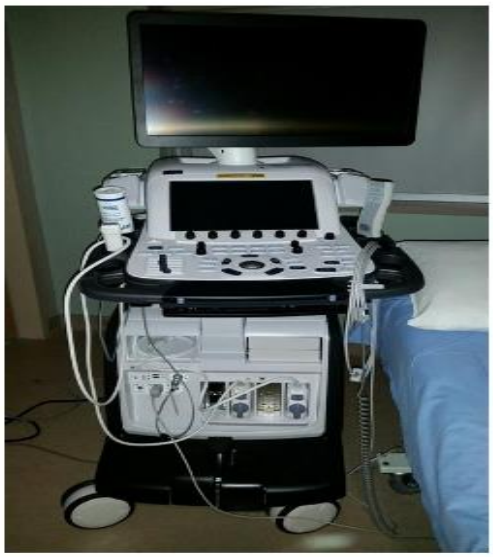
- Non sterile gloves
- Two white lab coats
- Hand sanitizer
- Stadiometer (ADE MZ® mechanical stadiometer)

- An examination room

- **For workups**

- Nt-proBNP tests kits Rapid for Finecare®


- Test tubes
- Syringes
- An echocardiographic machine Winchester® (a Philips IE33 ultrasound machine) [74]



- An electrocardiographic machine Mac 1200 ST electrocardiograph. [75].

- **For the Six Minute walk test**
  - A stopwatch
  - A 30m tract
  - O2 cones
  - 02 chairs
  - A measuring tape
  - A pen
  - Worksheets
- **For data analysis**
  - Laptop computer (acer® AMD Ryzen 3)
  - 16GB USB
  - 04 realms of A4 paper
  - Casio calculator

## III.6. PROCEDURE

### III.6.1. Administrative formalities

A research protocol was written and presented to the supervisors. Thereafter, a request was submitted for ethical clearance from the Institutional ethical Review Board of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I. Authorisation was obtained from the Head of the Yaounde Central hospital, Biyem-Assi District hospital and Yaounde University teaching hospital.

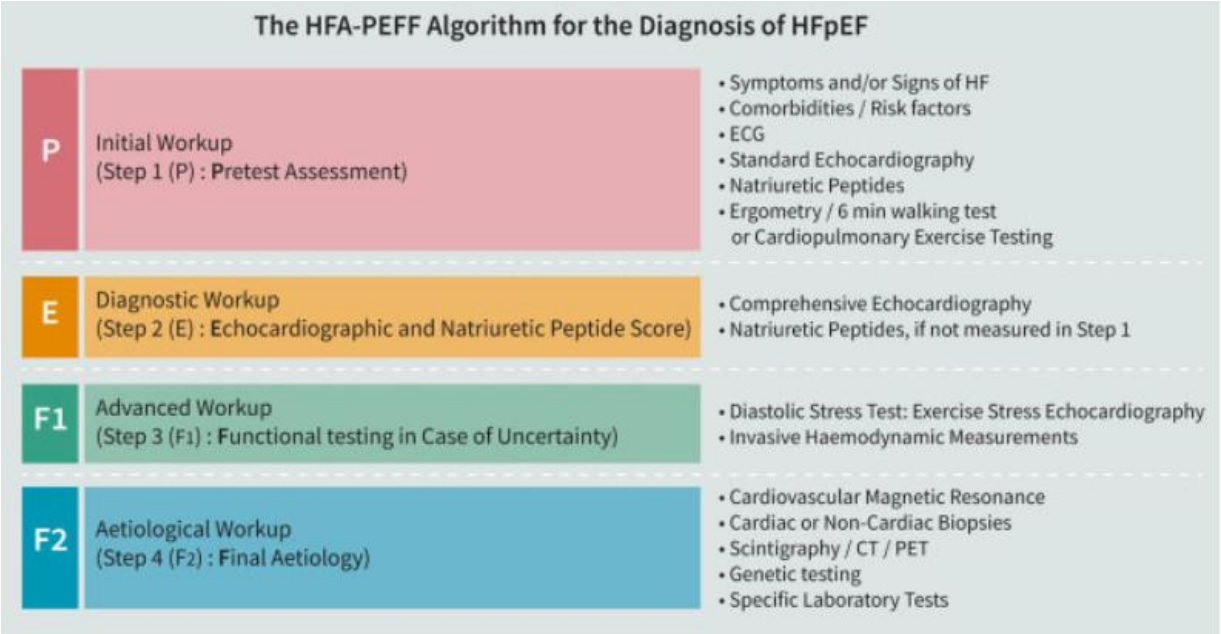
### III.6.2. Recruitment strategy of the study population

Volunteer participants were recruited from the Yaounde Central Hospital and the Yaounde Biyem-Assi District hospital both those admitted in the ward and those for routine visits. To do that we attended cardiology and geriatric consultations in the different hospitals to find patients with symptoms of HF. We also attended rounds in the units to find the hospitalized patients to whom we presented our study by explaining the aims, benefits and possible constraints of the study with the use of an information leaflet available in French and English. Each consenting patient was asked to sign an informed consent form available in French and English.

### III.6.3. General layout of the study

After obtaining the various authorizations and ethical clearance, we proceeded to recruit our study population. Participants with symptoms and/or signs of heart failure were assessed comprising of a clinical assessment that is history taking and physical examination, a six-minute walk test to evaluate exercise capacity. Then morphological evaluations that is, echocardiographic parameters were evaluated with a cardiac echocardiography performed by the Cardiologist in the ward or a 3rd year senior resident in Cardiology under the supervision of a cardiologist and EkG. In patients with a ventricular ejection fraction ≥ 50%, with increased filling pressures and diastolic impairment on echocardiography, blood samples were collected for Nt pro-BNP analysis at the CHU biochemistry laboratory. The values obtained were incorporated into the HFA-PEFF score as seen below, and the corresponding score grading obtained to ascertain the diagnosis of HFpEF. Only steps 1(P) and 2(E) of the algorithm were performed. The data was collected using a pre-established data collection sheet.

**Table IX:** overview of the diagnostic heart failure with preserved ejection fraction steps 1–4 (P–F) [13].




### ➢ Clinical evaluation

For each participant included in the study, a clinical assessment was performed in an appropriate ward in the cardiology units of the YCH and the Biyem-Assi District Hospital.

- History taking: It was done with the help of the pre-established questionnaire. The following were searched:
  - Identification: patient's code, recruitment center;
  - Sociodemographic characteristics (level of education, professional status, marital status, ethnic origin, monthly income.);
  - Data on possible comorbidities using **Charlson comorbidity score** included; age, myocardial infarction, Congestive heart failure, peripheral vascular disease, Cerebrovascular accident or transient ischemic attack, dementia, Chronic obstructive pulmonary disease, peptic ulcer disease, connective tissue disease, liver disease, diabetes mellitus, hemiplegia, leukemia, solid tumour, chronic kidney disease, lymphoma, AIDS.
  - Cardiovascular risk factors: hypertension, diabetes, tobacco, alcohol, dyslipidemia, sedentary lifestyle, race, and psychosocial factors (depression).

**Depression**: otherwise known as depressive disorder, is a common mental disorder. It involves a depressed mood or loss of pleasure or interest in activities for long periods of time [21].

The 4 questions Geriatric Depression Scale (GDS-4) was used for its evaluation. It provides a quick and reliable screen for depression as shown [21] ;

-Are you basically satisfied with your life?

-Do you feel that your life is empty?

-Are you afraid that something bad is going to happen to you?

-Do you feel happy most of the time?

**Interpretation** [22]

**GDS = 0**: This is not indicative of a depressive status, however the patient should be monitored further for any more signs displayed and also for their evolution.

**GDS = 1**: This score is not consistent with a depressive status, however, there should be some concerns raised in regard to the mental health of the patient and further assessment is required.

**GDS ≥ 2**: This score is indicative for the presence of a depressive status. The patient needs to be referred to a specialist for further consultation.

- **Physical examination**
  - Pulse: the radial pules was accessed by palpating the radial artery and counting the number of pulsations during one minute.
  - Respiratory rate: It was assessed on inspection by counting the number of respiratory cycles over a period of one minute. The result obtained was expressed in cycles per minute.
  - **Blood pressure (mmHg) and pulse (per minute):** After 10 mins of rest, in the sitting position with the arm supported at the level of the heart, the systemic arterial blood pressure was measured. The mean of three values was recorded. This was done using an electric sphygmomanometer (OMRON® HEM-712 Omron Corporation, Tokyo, JAPAN).
  - **The weight:** This was taken in a standing position, the patient remaining upright and looking Infront. Subjects were required to remove their shoes, socks, as well as their coats, jackets or pullovers and emptied their pockets and bladders. Before weighing, the scale was adjusted to 0kg. It was expressed to the nearest 0.1kg. An identical device was used for all patients. The device used was the Salter 200 WHGYDR® Premium scale balance.
  - **The height:** This was measured in the erect position after subjects had removed shoes and socks. Height was expressed to the nearest 1cm. Measurements were done using a wall stadiometer. The occiput, shoulder, buttocks and calves were touching the vertical position

of the stadiometer with arms hanging freely alongside the body and palms facing the thigh. With the heels together, the tips of both feet were slightly apart to permit equal weight distribution on both legs. The sliding plate of the stadiometer permitted the upper limit of the subject to be located to the nearest 1cm  The device used was the (ADE MZ® mechanical stadiometer).

- **Body mass index (BMI):** This was calculated using Quetelet's formula; Weight/height$^2$ and expressed as Kg/m$^2$ to the nearest one decimal place.
- **Waist circumference**: Measurements were done in the standing position at the mid distance between the lower costal margin and the iliac crest. This was done using a measuring tape and expressed to the nearest 1cm.

- **Morphological assessment**
  - **Transthoracic echocardiography**

Echocardiography is a common exam done to access the cardiovascular system. it's accuracy, accessibility, safety, reproducibility and cost-efficiency render it a good tool to access the cardiovascular system. It makes use of the principle of reflection of high frequency sound waves as they reflect on different boundaries. A real-time echocardiography provides comprehensive cardiac morphology at very high spatial and temporal resolution. It provides information on volumes, diastolic function, right ventricular function, hemodynamics, and valvular regurgitation. A transthoracic echocardiography was done by the cardiologist in the service or the senior resident in cardiology supervised by the cardiologist for participants in our study to measure the LVEF. Ejection fraction was measured using the Biplane Simpson's method which assumes the LV cavity to be ellipsoidal at all times and involves manual tracing of the LV cavity endocardium at end-systole and end-diastole from the apical 4 chamber view and apical 2 chamber view. Tricuspid regurgitation (TR) maximal velocity was performed with continuous doppler of the TR jet in apical 4 chamber view for measurement of Pulmonary artery systolic pressure or pulmonary acceleration time by pulse wave Doppler on systolic pulmonary arterial flow in parasternal short axis. Transmitral Doppler LV filling recordings were performed from the apical 4-chamber view and analyzed for diastolic filling. Global LV ejection fraction was qualitatively assessed from the 2-dimensional images as preserved (≥50%), mildly reduced (40% to 50%), and reduced (≤ 40%). This was done using a Philips IE33 ultrasound machine.

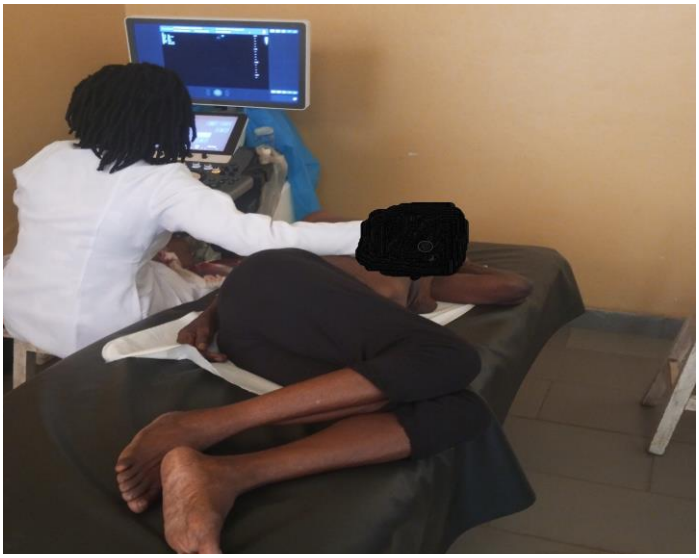


**Figure 15:** a resident in cardiology of the YCH perfoming echocadiography (data from the study).

- **Standard 12-lead resting ECG**

It is a medical examination to record heart activity. It is based on measuring the electrical currents flowing through the heart. In this case, it allowed us to determine rhythm or cardiac conduction disturbances. The undressed patient lied in the supine position on a bed, the electrodes previously covered with the contact gel were positioned on his limbs and his chest. Six leads were vertical (frontal leads I, II, III, aVR, aVL and aVF ), and six were horizontal (precordial leads V1, V2, V3, V4, V5 and V6). The ECG recording was later-on interpreted. This was done using Mac 1200 ST electrocardiograph.

**Figure 16:** an electrocadiographic exam (data from the study).

- **BIOLOGICAL WORK UP**

**NT-pro BNP**

Prior to the test, they were no specific diet restrictions. A tourniquet was tied around the patient's arm and blood samples for NT-proBNP measurement were collected by venipuncture into dry plastic tubes. Blood samples were kept at room temperatures in a transport flask and analyzed within 8 hours using the Finecare$^{TM}$ NT-proBNP quantitative test at the CHU biochemistry laboratory under the supervision of a biochemist (Pr Ama-moor). This test uses a sandwiched immunodetection method. When blood sample is added to the sample well of the test, the fluorescence-labelled detector anti-NT-proBNP antibody binds to NT-proBNP antigen in blood specimen. As the sample mixture migrates on the Nitrocellulose matrix of the test strip by capillary action, the complexes of detector antibody and NT-proBNP are captured to anti-NT-proBNP antibody that has been immobilized on the test strip. Signal intensity of fluorescence of detector antibody reflects the amount of NT-proBNP captured and the meter shows NT-proBNP concentrations in blood specimen.

**Figure 17:** carrying out an Nt-proBNP test (data from the study).

- **Functional Capacity**

**The Six-minute Walk Test**

A six-minute walk test was performed on a set track. This was performed using the guidelines established by the American thoracic Society. We set a timer to 6 minutes and the track prepared. The participant was enlightened for the test using the scribe, "The aim of this test was to walk as far as possible for 6 minutes. They walked to and fro in the hallway. Six minutes was a long time to walk. They could probably get out of breath or become tired. They were permitted to slow down, to stop, and to rest when necessary. They could lean against the wall while resting, but resume walking as soon as they were able. They were to walk back and forth around the cones (or poles). They would walk around the cones (or poles) and continue back the other way without hesitation. They watched the way I turned without hesitation." A lap was done on the track for demonstration. The participant was then positioned at the starting line and the timer started. A worksheet was used to keep tract of the laps. The distance covered was recorded and rate of perceived dyspnea and exertion were evaluated using the Borg scale and are recorded at the beginning and end of the exercise [18].

- Absolute contraindications for 6MWT included: unstable angina, myocardial infarction in the last month, syncope, symptomatic severe aortic stenosis, acute pulmonary embolus or pulmonary infarction.

- Relative contra-indications for 6MWT included: a resting heart rate > 120b/m, a systolic blood pressure > 180 mmHg, cardiac conditions like high degree atrio-ventricular block, hypertrophic cardiomyopathy and left coronary stenosis, significant pulmonary hypertension

**Figure 18**: performing a six-minute walk test (data from the study)

**Quality of life**: In this case, HFpEF was the health condition. It was assessed here using the Minnesota Living with Heart Failure Questionnaire (MLHFQ). The MLHFQ is specific to heart failure, consists of 21 questions and appraises HR-QoL over the period of the previous month. Questions are answered using a Likert scale of 0–5; 0 indicates that the question has no impact on the patient or is not applicable, and 5 indicates the greatest adverse effect. The questionnaires can be divided into three domains: overall QoL domain (score range 0–105), the physical domain consisting of eight questions (score range 0–40), and the emotional domain made up of five questions (score range 0–25). A higher score represents a poorer HR-QoL. The authors recommend the overall total score as the best measure as opposed to the other two domains, which were created following factor analysis. An overall score of less than 24 denotes a high quality of life, between 24 and 45, a moderate quality of life, and beyond 45, a low quality of life [20].

- **Patient classification**: This was done using the ESC recommendation guidelines for probability of HFpEF.

**Table II**: step 2 (E): echocardiographic and natriuretic peptide heart failure with preserved ejection fraction workup and scoring system (diagnostic workup) [13].

| | Functional | Morphological | Biomarker (SR) | Biomarker (AF) |
|---|---|---|---|---|
| Major | septal e' < 7 cm/s or lateral e' < 10 cm/s or Average E/e' ≥ 15 or TR velocity > 2.8 m/s (PASP > 35 mmHg) | LAVI > 34 ml/m² or LVMI ≥ 149/122 g/m² (m/w) and RWT > 0,42 # | NT-proBNP > 220 pg/ml or BNP > 80 pg/ml | NT-proBNP > 660 pg/ml or BNP > 240 pg/ml |
| Minor | Average E/e' 9 -14 or GLS < 16 % | LAVI 29-34 ml/m$^2$ or LVMI > 115/95 g/m$^2$ (m/w) or RWT > 0,42 or LV wall thickness ≥ 12 mm | NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml | NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml |

| | |
|---|---|
| Major Criteria: 2 points | ≥ 5 points: HFpEF |
| Minor Criteria: 1 point | 2-4 points: Diastolic Stress Test or Invasive Haemodynamic Measurements |

- **Procedure for data collection**

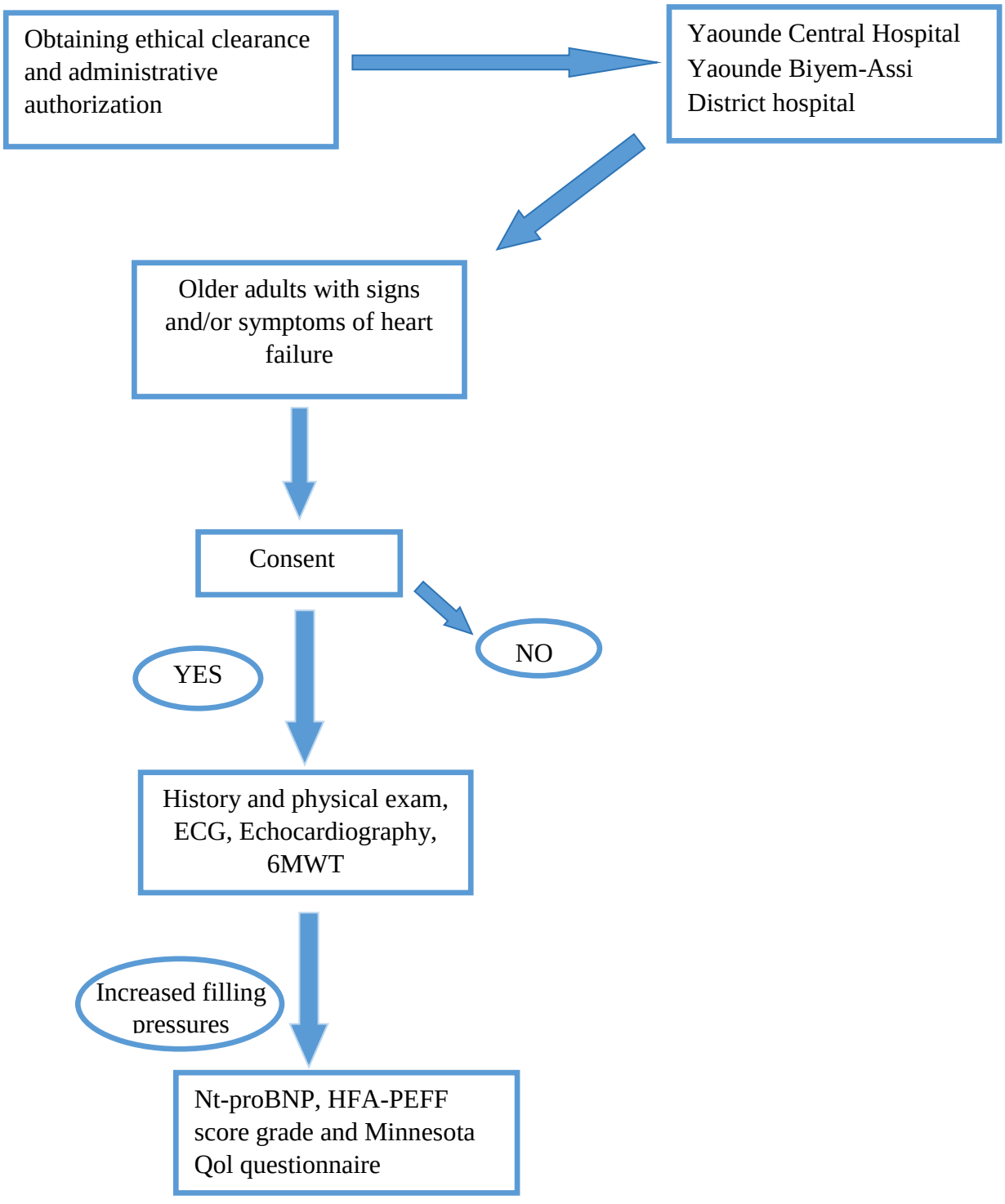



**Figure 19**: flow diagram for data collection

## III.7. Data analysis

The data obtained during the study period was inserted and analysed using IBM Statistical Package for Social Sciences (SPSS) software version 26.

The qualitative variables were expressed in frequency and percentages and were compared using $chi^2$ pearson test or Fischer exact Test as needed. The quantitative variables were expressed in terms of means and standard deviation in the case of a Normal distribution, or medians and interquartile ranges when this was not the case and were compared using Student's t test or U-man Whitney test following the distribution.

A logistic regression was performed to identify factors associated with poor quality of life. A p-value $< 0.05$ was used to define statistical significance.

## 3.9. ETHICAL CONSIDERATIONS

This study was carried out in accordance with the principles of the Declaration of Helsinki of 1964 revised in October 2013 [76].

- Applications for research authorizations were obtained from the institutions concerned:
  - YCH: recruitment authorization;
  - Yaounde Biyema-Assi District Hospital: recruitment authorization;
  - Yaounde University Teaching Hospital : recruitment authorization.
- An ethical clearance was obtained from the Institutional Ethics and Research Committee of the Faculty of Medicine and Biomedical Sciences (FMSB) of the University of Yaounde I (UY1).
- Another ethical clearance was obtained from the Ethics committee for Human health research of the Centre Region.
- **Respects for persons (autonomy):** Prior to inclusion, each participant was informed of the benefits and constraints of the study, and any included participant first signed an informed consent form. Each patient was free to participate in this study and his/her refusal had no effect on his/her follow-up in the hospital.
- **Beneficence**: Patients benefitted from free medical exams and at the end of the research, the test results were given to the participants and explained.
- **Non-maleficence**: No major risk was borne during the study.
- **Justice**: All patients were treated likely.
- **Confidentiality**: Each patient received an anonymous code for data collection. Also, the information collected during the study was kept in strict compliance with medical confidentiality and used only for scientific purposes.

# CHAPTER IV : RESULTS

## IV.1. Recruitment of study population

This study took place in the Geriatric and cardiology departments of 2 hospitals which were the Yaounde Central Hospital, Yaounde Biyem-Assi District Hospital during the period from February 1st to May 2024; i.e.,4 months. The Figure below describes the study population recruitment process.

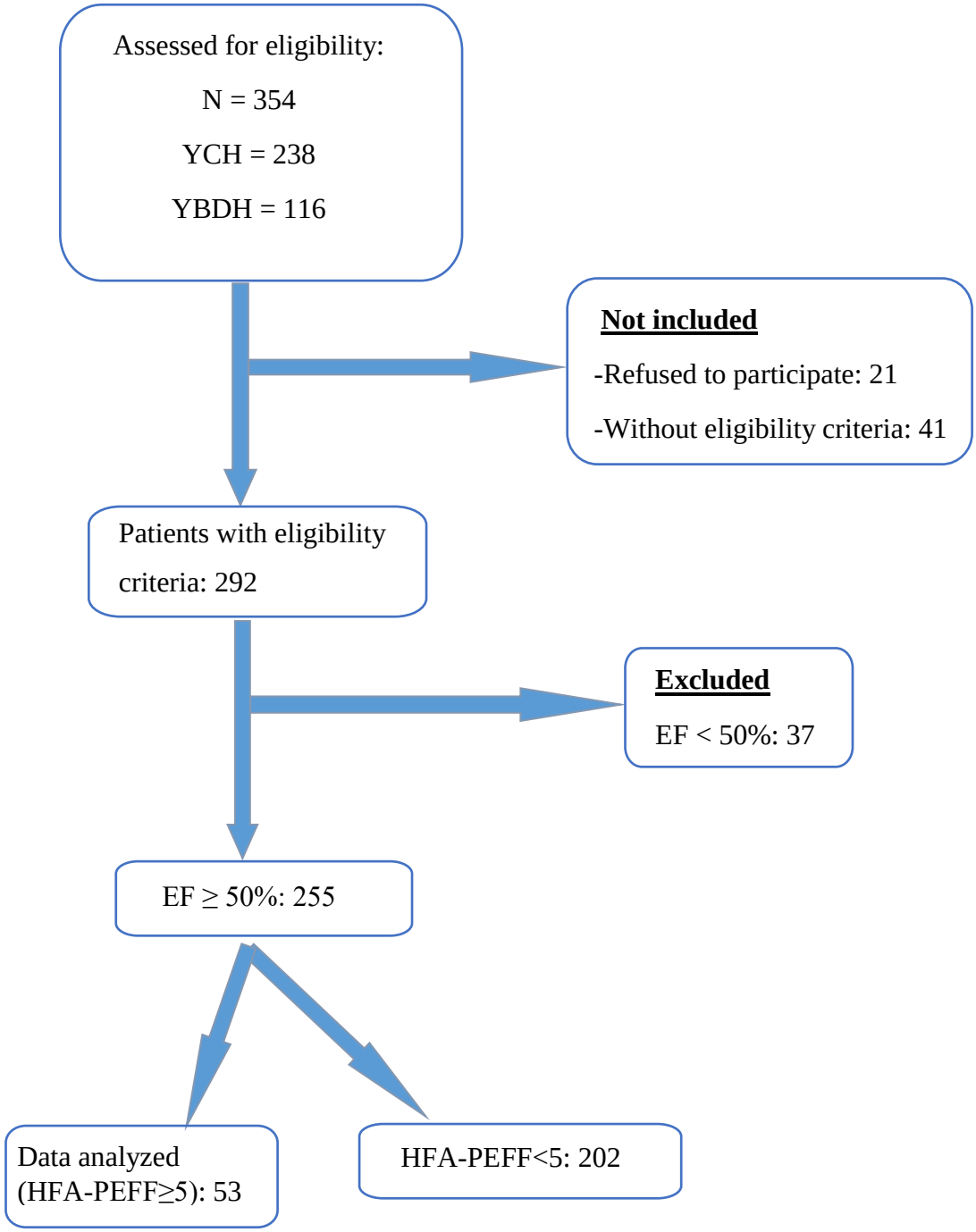



**Figure 20**: flow diagram of participants

## IV.2. Sociodemographic characteristics of the study population

### IV.2.1. Age, gender, marital status and ethnic groups

The mean age of participants was 74.47± 8.94 years, with ages ranging from 65 to 94 years. Most had an age between 65 and 70 years (39.6%), and were female (69.8%), with a sex ratio of 0.43. Concerning the marital status and ethnic group, we found respectively mostly the widows (47.2%) and those from the Bantou ethnic group (54.7%). Table XIV shows this.

**Table XIV**: distribution according to age, gender, marital status and ethnic groups

| Variables | Frequency (N=53) | Percentage (%) |
|---|---|---|
| **Age groups (years)** | | |
| [65-70[ | 21 | **39.6** |
| [70-75[ | 9 | 17.0 |
| [75-80] | 6 | 11.3 |
| [80-85[ | 10 | 18.9 |
| [85-90[ | 3 | 5.7 |
| [90-95[ | 4 | 7.5 |
| **Sex** | | |
| Male | 16 | 30.2 |
| Female | 37 | 69.8 |
| **Marital status** | | |
| Widow | 25 | 47.2 |
| Married | 24 | 45.3 |
| Single | 3 | 5.7 |
| Divorced | 1 | 1.9 |
| **Ethnic groups** | | |
| Bantus | 29 | 54.7 |
| Semi-bantus | 19 | 35.8 |
| Grassfield | 3 | 5.7 |
| Sudanese | 2 | 3.8 |

### IV.2.2.Occupation, educational level and place of residence

The study revealed that majority of the participants did not have an educational background (35.8%), were mostly retired (45.3%) with a monthly income less than 50 000 FCFA (43.4%). As concerns the place of residence, most participants lived in an urban setting. Table XV illustrates this.

**Table XV**: distribution according to educational level, occupation and place of residence.

| Variables | Frequency (N=53) | Percentage (%) |
|---|---|---|
| **Occupation** | | |
| **Retired** | 24 | 45.3 |
| House-wife | 18 | 34.0 |
| Private sector worker | 10 | 18.9 |
| Civil servant | 1 | 1.9 |
| **Level of education** | | |
| None | 19 | 35.8 |
| Primary | 13 | 24.5 |
| Secondary | 16 | 30.2 |
| University | 5 | 9.4 |
| **Socioeconomic status** | | |
| < 50 000 | 23 | 43.4 |
| 50-100 000 | 9 | 17.0 |
| 100 - 150 000 | 19 | 35.8 |
| 150-500 000 | 2 | 3.8 |
| **Place of residence** | | |
| Urban | 20 | 37.7 |
| Semi-urban | 17 | 32.1 |
| Rural | 16 | 30.2 |

## IV.3. Prevalence of HFpEF

In this hospital base setting, using the HFA-PEFF score, 53 out of 292 older symptomatic adults were found to have HFpEF (HFA-PEFF ≥ 5) giving a prevalence of HFPEF of 18.2% . Of these 292 older adults, a total of 90 were diagnosed with HF, Hence a prevalence of HFpEF in HF patients of 58.8%.

- Distribution of the study population according to heart failure types

The major phenotype of heart failure in our participants was HFpEF (18.1%) of cases, meanwhile HFrEF was found in 11.3% of participants. Table XVI below depicts this.

**Table XVI**: distribution of the study population according to Heart Failure types.

| Variables | Frequency (292) | Percentage (%) |
|---|---|---|
| **Patients with Heart failure** | | |
| HFrEF | 33 | 11.3 |
| HFmrEF | 4 | 1.4 |
| HFpEF | 53 | 18.1 |
| Indeterminate | 29 | 9.9 |
| No HF | 173 | 59.3 |

- **Score classification of participants.**

Table XVII below shows that HFA-PEFF score made the diagnosis of HFpEF in 20.8% of participants, ruled out HFpEF in 67.8% of participants and additional testing required in 11.4% of participants. Similarly, $H_2$FPEF score effectively ruled out HFpEF in 72.8% of participants, made the diagnosis in 5.5% and 21.7 % were in the uncertainty zone. Table XVII below.

**Table XVII**: score classification of participants according to diagnostic algorithms.

| Variables | Frequency (N=255) | Percentage (%) |
|---|---|---|
| HFA-PEFF score | | |
| High (≥5) | 53 | 20.8 |
| Intermediate (2-4) | 29 | 11.4 |
| Low (≤ 1) | 173 | 67.8 |

**NB:** We analyzed the 53 participants with HFpEF as diagnosed with the HFA-PEFF score.

## IV.4. Clinical characteristics of the study population

- **Distribution with respect to CV risk factors**

Our study revealed that the principal cardiovascular risk factors were a sedentary lifestyle (94.3%), hypertension (79.2%) and overweight/obesity (66.0%). Figure 21 below shows this.

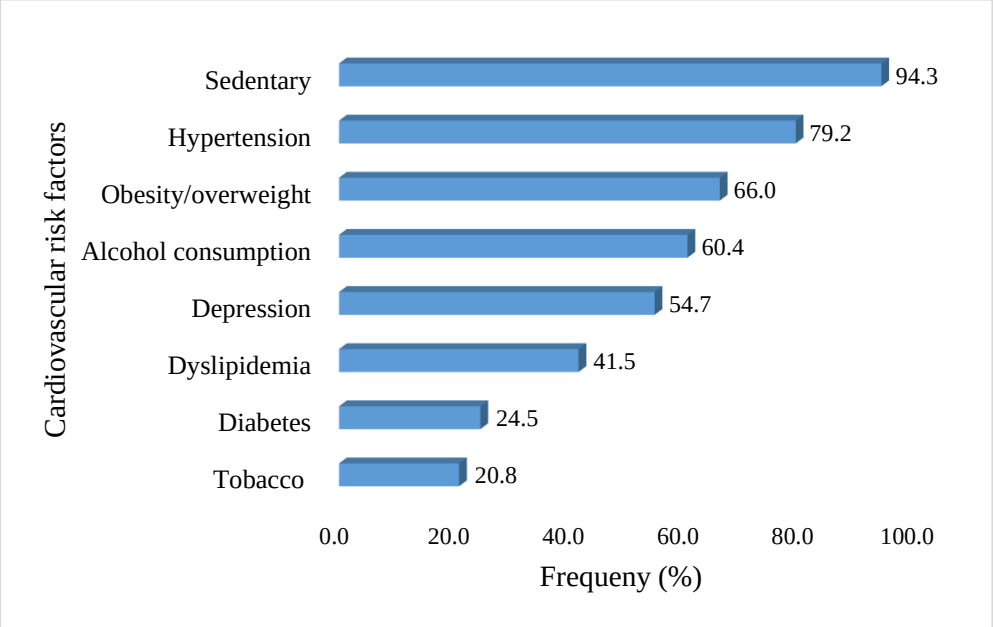



**Figure 21**: frequency of cardiovascular risk factors

➢ **Distribution according to Charlson comorbidities**

Some of the participants (9.4 %) did not have any of the Charlson comorbidities. The majority of patients in our study had Peptic ulcer disease (29.8%), followed by Diabetes (24.5%) and then stroke in 13.2% of the cases. Figure 22 below portrays this.

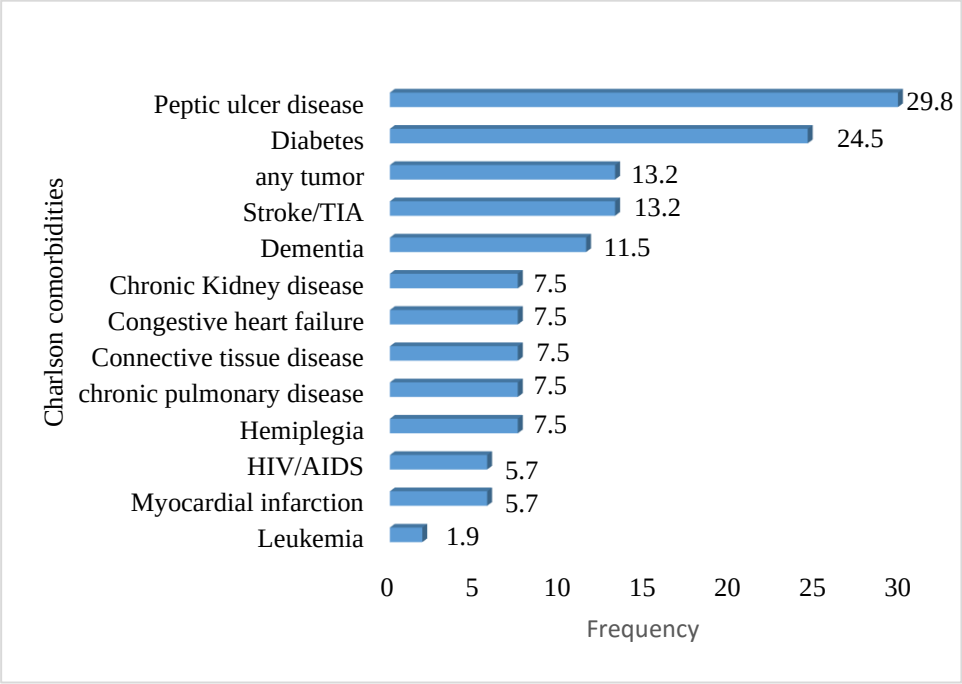



**Figure 22:** percentage of patient comorbidities from Charlson comorbidity score

➢ **Percentage survival: Charlson score**

The mean Charlson comorbidity score was 4.81±2.1. 49.1% of participants had a low 10 year survival probability (<25%). Figure 23 below illustrates this.

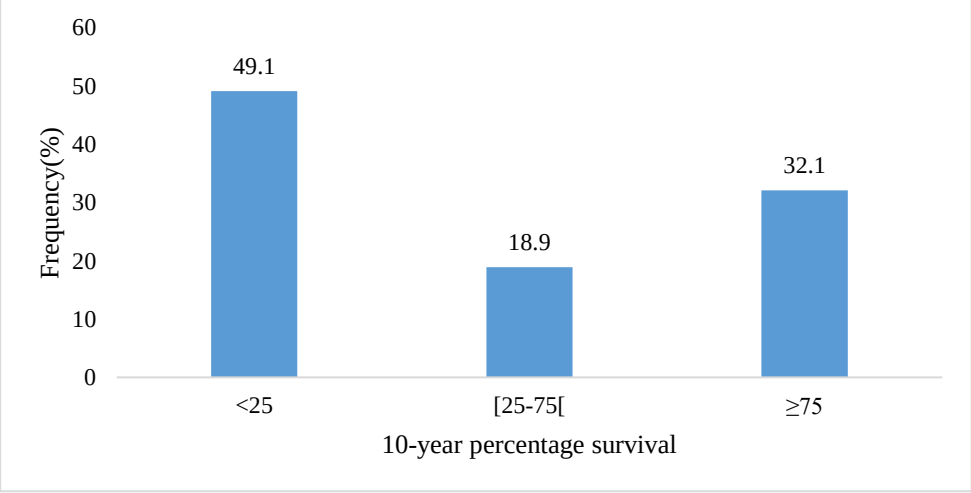



**Figure 23**: 10 year survival probability according to Charlson

- **Frequency of patients with de novo HFpEF**

Table XVIII below reveals that 88.7% of patients were newly diagnosed with HFpEF. Table XVIII below.

**Table XVIII**: distribution of patients with respect to newly diagnosed HFpEF.

| Patient history heart failure | Frequency (N=53) | Percentage (%) |
|---|---|---|
| Old patient | 6 | 11.3 |
| New patient | 47 | 88.7 |

- **BP values of participants**

The mean systolic BP value was 147.8± 27.3 mmHg with extreme values of 90mmHg and 206mmHg. Majority of participants had Grade I HTN (41.5%). As concerns diastolic BP, the mean value was 84.6 mmHg ± 16.4mmHg with extremes of 44 and 115mmHg. 17% of participants had grade II diastolic HTN. Table XIX below shows this.

**Table XIX**: distribution according to BP values

| Variables | Frequency | Percentage (%) |
|---|---|---|
| **SBP** | | |
| Optimal | 9 | 16.9 |
| Normal | 2 | 3.7 |
| High Normal | 4 | 7.5 |
| Grade I HTN | 22 | **41.5** |
| Grade II HTN | 16 | 30.1 |
| **DBP** | | |
| Optimal | 18 | 34 |
| Normal | 8 | 15.1 |
| High Normal | 8 | 15.1 |
| Grade I HTN | 8 | 15.1 |
| Grade II HTN | 9 | 17.0 |
| Grade III HTN | 2 | 3.8 |

- **Distribution according to BMI and abdominal circumference**

The mean BMI value was 28.5 ± 6.1 kg/$m^2$ with a minimum of 18.0kg/$m^2$ and a maximum of 45kg/$m^2$. A great number of participants had class I obesity (30.2%). As for the abdominal gird, the mean was 97.3cm ± 14.3cm. 47.1% had android obesity. This is represented in table XX below.

**Table XX**: distribution of participants according to Anthropometric parameters

| Variables | Frequency (N=53) | Percentage (%) |
|---|---|---|
| **BMI groups** | | |
| Low | 2 | 3.7 |
| Normal | 16 | 30.2 |
| Overweight | 13 | 24.5 |
| Class I obesity | 16 | **30.2** |
| Class II obesity | 3 | 5.7 |
| Class III obesity | 3 | 5.7 |
| **Abdominal Circumference** | | |
| Normal | 28 | 52.8 |
| Android obesity | 25 | **47.1** |

- **Clinical findings of HFpEF**

Dyspnea was the most dominant symptom of left heart failure followed by cough and Displaced apex beat predominated on clinical exam with percentages of 88.7%, 43.4% and 41.5% respectively. As concerns signs of right heart failure, we frequently found bilateral lower limb edema (43.4%) and raised jugular venous pressure (34%). Table XXI below shows this.

**Table XXI**: distribution of participants according to clinical signs.

| Variables | Frequency (N=53) | Percentage (%) |
|---|---|---|
| **Left heart signs and symptoms** | | |
| Dyspnea | 47 | 88,7 |
| Fatigue | 38 | 71.7 |
| Cough | 23 | 43.4 |
| Orthopnea | 16 | 30.2 |
| Chest pain | 10 | 18.9 |
| Palpitations | 14 | 26.4 |
| Paroxysmal nocturnal dyspnea | 12 | 22.6 |
| Displaced apex beat | 22 | 41.5 |
| Lung crackles | 11 | 20.8 |
| Heart murmur | 10 | 18.9 |
| Arrythmia | 10 | 18.9 |
| Left galop rhythm | 10 | 18.9 |
| **Right heart signs** | | |
| Lower limb edema | 23 | 43.4 |
| Jugular vein distension | 18 | 34.0 |
| Abdomino jugular reflux | 11 | 20.8 |
| Right galop rhythm | 5 | 9.4 |
| Right flanc pain | 1 | 1.9 |

- **Classification of HFpEF according to NYHA.**

Table XXII below reveals that NYHA class 2 was the most represented (56.6%) in patients with HFpEF followed by NYHA class III. As shown on table XXII below.

**Table XXII**: distribution of the population according to NYHA classification of Heart failure

| NYHA Classification of heart failure | Frequency (N=53) | Percentage (%) |
|---|---|---|
| NYHA class I | 6 | 11.3 |
| NYHA class II | 30 | 56.6 |
| NYHA class III | 17 | 32.1 |

## IV.5. Paraclinical characteristics of the study population

- **Biological workup**

### IV.5.1. Nt-proBNP measurement

The median Nt-proBNP value was 971.3 [IQ:655.7-1954.8] pg/ml, with a minimum Nt-proBNP value of 171.3pg/ml and a maximum Nt-proBNP value of 7689.7pg/ml.

- **Morphological workup**

### IV.5.2. Transthoracic Echocardiography

- **Aetiologies of HFpEF**

Hypertensive heart disease (64.2%) and Valvular heart disease (32.1%) represented the principal aetiologies of HFpEF and then followed by Dilated and Ischemic heart disease with 17% and 11.3% respectively. Table XXIII below depicts this.

**Table XXIII**: distribution of participants according to aetiologies

| Aetiology of heart failure | Frequency (N=53) | Percentage (%) |
|---|---|---|
| Hypertensive heart disease | 34 | 64.2 |
| Valvular heart disease | 17 | 32.1 |
| Dilated heart disease | 9 | 17.0 |
| Ischemic heart disease | 6 | 11.3 |
| Restrictive cardiomyopathy | 2 | 3.8 |
| Hypertrophic cardiomyopathy | 2 | 3 .8 |
| Inter atrial septal myxoma | 1 | 1.9 |

- **Echocardiographic measurements**

The mean LVEF was 63± 9.5% with a minimum of 50% and a maximum of 87%.

The table below shows the measures of central tendency of certain echocardiographic findings.

Table XXIV below illustrates this.

**Table XXIV**: distribution of position and dispersion of echocardiographic parameters.

| Variables (n=53) | Median [IQ] | Min | Max | Mean±St.dev |
|---|---|---|---|---|
| LVEF (%) | | 50 | 87 | 63± 9.5 |
| Lateral e' value (cm/s) | 6.4 [4.7-8.6] | 1.1 | 10.0 | |
| E on e' ratio | 13.5 [10.0-15.9] | 9.0 | 27.0 | |
| E on A | 1.20 [0.9-1.5] | 0.75 | 3.9 | |
| Tricuspid regurgitation peak velocity (m/s) | 3.1 [2.5-3.3] | 2.0 | 4.0 | |
| Left atrial volume index (ml/m²) | 33.8 [30-36.5] | 27.0 | 57.2 | |
| Left ventricular mass index (g/m²) | 120 [100-138] | 65.0 | 347.3 | |
| Relative wall thickness | 0.4 [0.3-0.6] | 0.3 | 7.0 | |
| Left ventricular wall thickness (mm) | 12 [10-14] | 9.4 | 20.0 | |
| Pulmonary artery systolic pressure (mmHg) | 43.0 [28.5-51.6] | 20.0 | 57.0 | |

- **Functional abnormalities**

Concerning the ratio of the peak velocity of mitral inflow during early diastole (E) to the average mitral annular early diastolic peak velocity (e'), it was abnormal in 67.9 % of cases, As concerns the pulmonary arterial systolic pressure, mild pulmonary hypertension was found in 60.4 % of cases. Grade II diastolic dysfunction was found in 45.2% of cases. Table XXV below shows this.

**Table XXV**: distribution of the population according to some functional abnormalities

| Variables | Frequency (N=53) | Percentage (%) |
|---|---|---|
| **Left ventricular filling pressure** | | |
| **Interpretation E/e'** | | |
| Intermediate | 17 | 32.1 |
| High | 36 | **67.9** |
| **Pulmonary artery systolic pressure** | | |
| Normal | 21 | 39.6 |
| Mild pulmonary hypertension | 32 | 60.4 |
| **Diastolic dysfunction** | | |
| Grade I | 11 | 20.8 |
| Grade II | 24 | **45.2** |
| Grade III | 10 | 18.9 |
| Indeterminate | 8 | 15.1 |

- **Some morphological cardiac abnormalities**

The morphological abnormalities were most at times a severe left ventricular hypertrophy in(43.4%) and concentric (43.4). Mild left atrial dilatation was found in 37.8% of cases and moderate left atrial dilatation in 43.4%. Table XXVI below portrays this.

**Table XXVI**: distribution of participants according to morphological abnomalities

| Variables | Frequency (N=53) | Percentage (%) |
|---|---|---|
| **Left atrial volume index interpretation** | | |
| Normal | 4 | 7.5 |
| Mild dilatation | 20 | 37.8 |
| Moderate dilatation | 23 | 43.4 |
| Severe dilatation | 6 | 11.3 |
| **Left ventricular mass index** | | |
| Normal | 12 | 22.6 |
| Mild hypertophy | 11 | 20.8 |
| Moderate hypertrophy | 7 | 13.2 |
| Severe hypertrophy | 23 | 43.4 |
| **Type of hypertrophy** | | |
| No hypertrophy | 7 | 13.2 |
| Concentric hypertrophy | 23 | 43.4 |
| Excentric hypertrophy | 18 | 34.0 |
| Concentric remodeling | 5 | 9.4 |

### IV.5.3.EKG Characteristics

Majority of the participants were in sinus rhythm (83%) Left ventricular hypertrophy was found in 52.8% of cases, and Left atrial dilatation in 20.8% of cases. As concerns rhythm and conduction disorders, atrial fibrillation was found in 13.2 % of cases, left bundle branch block in 23.1% of cases, type 1 atrio-ventricular block in 5.7% of cases. Tables XXVII and XXVIII represent this.

**Table XXVII**: distribution of the population according to EKG findings part 1

| Variables | Frequeny (N=53) | Percentage (%) |
|---|---|---|
| **Rhythm disorders** | | |
| Heart rhythm | | |
| Sinus | 44 | 83.0 |
| Non sinus | 8 | 15.1 |
| Heart rate | | |
| Normal | 44 | 83.0 |
| Bradycardia | 2 | 3.8 |
| Tachycardia | 7 | 13.2 |
| Atrial fibrillation | | |
| Yes | 7 | 13.2 |
| No | 46 | 86.8 |
| **Cavity hypertrophy** | | |
| Left atrial hypertrophy | | |
| Yes | 15 | 28.3 |
| No | 38 | 71.7 |
| Right atrial hypertrophy | | |
| Yes | 4 | 7.5 |
| No | 49 | 92.5 |
| Left ventricular hypertrophy | | |
| Yes | 28 | 52.8 |
| No | 25 | 47.2 |
| **Conduction disorders** | | |
| Atrio-ventricular block | | |
| No block | 50 | 94.3 |
| AVB 1 | 3 | 5.7 |

**Table XXVIII**: distribution of the population according to EKG findings (part 2)

| Variables | Frequency (N=53) | Percentage (%) |
|---|---|---|
| **Conclusion on QRS duration and axis** | | |
| Normal | 41 | 77.4 |
| Incomplete Bundle branch block | 9 | 17.0 |
| Complete bundle branch block | 3 | 5.7 |
| **Repolarisation abnormalities** | | |
| ST segment displacement in at least 2 leads in the same territory or q-wave of necrosis. | | |
| Yes | 12 | 22.6 |
| No | 41 | 77.4 |

### IV.5.4. Six mimutes walk test and maximum $VO_2$

After performing the 6minutes walk test, severe functional limitation was frequent in patients accounting for 26.4% of cases. As for the maximum volume of $O_2$ consumed, it was poor in several cases (62.3%). This is shown in table XXIX below.

**Table XXIX**: six minutes walk test and maximum $VO_2$

| Variables | Frequency (N=53) | Percentage (%) |
|---|---|---|
| **Six minutes walk distance interpretation** | | |
| Excellent functional mobility | 3 | 5.7 |
| Good functional mobility | 2 | 3.8 |
| Moderate functional limitation | 14 | 26.4 |
| Severe functional limitation | 26 | **49.1** |
| Indeterminate | 8 | 15.1 |
| **VO2 max interpretation** | | |
| Poor | 32 | **60.4** |
| Fair | 12 | 22.6 |
| Good | 1 | 1.9 |
| Indeterminate | 8 | 15.1 |

### IV.5.5. Quality of life in the study population

As shown on figure 25 below, quality of life was moderate in majority of cases (43.4%). Poor quality of life was observed in 18patients (34%). Figure 24 below.

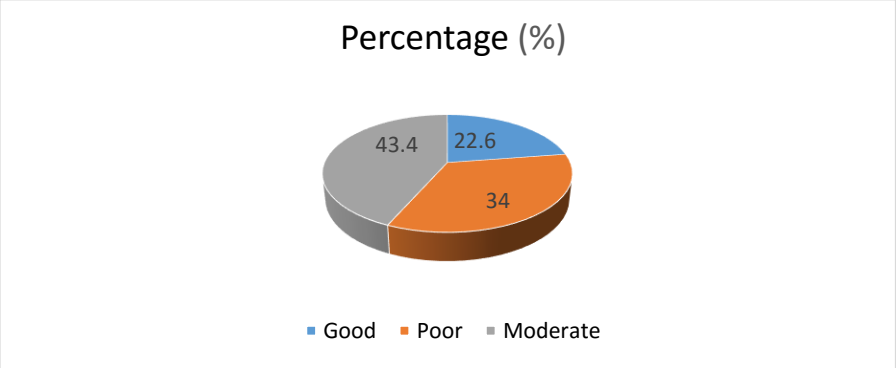



**Figure 24:** distribution of the population according to the quality of life

### IV.5.5.1. Factors associated to poor quality of life

#### IV.5.5.1.1. Univariate analysis

- **Correlation of the quality of life score with demographic and socio-economic characteristics of patients.**

As shown below, neither age, nor sex, nor marital status, nor educational level were significantly associated with poor quality of life of patients with HFpEF ($p \geq 0.05$). This is shown in table XXX.

**Table XXX**: sociodemographic factors associated with poor quality of life.

| Variables | Poor quality life | | OR | p |
|---|---|---|---|---|
| | Yes | No | (CI at 95%) | value |
| | N=18 ; n(%) | N=35 ; n(%) | | |
| **Age groupes (years)** | | | | |
| [65-75[ | 9 (30.0) | 21 (70.0) | 0.66 (0.21-2.09) | 0.342 |
| [75-85[ | 5 (31.3) | 11 (66.8) | 0.83 (0.23-2.94) | 0.522 |
| ≥ 85 | 4 (57.1) | 3 (42.9) | 3.04 (0.60-15.45) | 0.167 |
| **Sex** | | | | |
| Male | 7 (43.8) | 9 (56.3) | 1.83 (0.54-6.18) | 0.248 |
| Female | 11 (29.7) | 26 (70.3) | 1 | |
| **Marital status** | | | | |
| Married | 5 (20.8) | 19 (79.2) | 0.32 (0.09-1.10) | 0.060 |
| Unmarried | 13 (44.8) | 16 (55.2) | 1 | 0.06 |
| **Level of education** | | | | |
| None or primary | 11 (24.4) | 21 (65.6) | 1.04 (0.32-3.35) | 0.589 |
| Secondary | 6 (37.5) | 10 (62.5) | 1.25 (0.36-4.25) | 0.478 |
| University | 1 (20.0) | 4 (80.0) | 0.45 (0.04-4.41) | 0.442 |
| **Level of income (F CFA)** | | | | |
| < 50 000 | 6 (26.1) | 17 (73.9) | 0.52 (0.16-1.72) | 0.222 |
| 50 000-100 000 | 5 (55.6) | 4 (44.4) | 2.98 (0.68-12.90) | 0.133 |
| ≥ 100 000 | 7 (33.3) | 14 (66.7) | 0.95 (0.29-3.05) | 0.589 |
| **Place of residence** | | | | |
| Urban | 6 (30.0) | 14 (70.0) | 0 .75 (0.22-2.46) | 0.434 |
| Rural/semi urban | 12 (36.4) | 21 (63.6) | 1.33(0.40-4.38) | 0.434 |

- **Risk factors, comorbidities and clinical signs associated with poor quality of life**

Lifestyle did not show any association with the patients' quality of life. Nevertheless, patients with depression had a poor quality of life risk multiplied by 3.9. As seen on table XXXI below.

**Table XXXI**: risk factors and comorbidities associated with poor quality of life.

| Variables | Poor quality life | | uOR | p |
|---|---|---|---|---|
| | Yes | No | (CI at 95%) | value |
| | N=18 ; n(%) | N=35 ; n(%) | | |
| **Risk factors** | | | | |
| Alcohol consumption | 12 (37.5) | 20 (62.5) | 1.50 (0.45-4.91) | 0.356 |
| Tobacco smooking | 3 (27.3) | 8 (72.7) | 0.67 (0.15-2.93) | 0.443 |
| Sedentary lifestyle | 18 (36.0) | 32 (64.0) | 0.640 (0.53-0.79) | 0.279 |
| Depression | 8(57.1) | 6(42.9) | **3.86 (1.08-13.9)** | **0.037** |
| **Chronic diseases** | | | | |
| Dementia | 8(36.4) | 14(63.6) | 1.20 (0.38-3.79) | 0.491 |
| Hypertension | 11(26.2) | 31(73.8) | **0.20 (0.05-0.83)** | **0.026** |
| Diabetes | 4 (30.8) | 9(69.2) | 0.82 (0.21-3.168) | 0.530 |
| Obesity | 9(34.6) | 17(65.4) | 1.05 (0.34-3.30) | 0.576 |
| Stroke | 2(28.6) | 5(71.4) | 0.75 (0.13-4.3) | 0.555 |
| Hemiplegia | 2(66.7) | 1(33.3) | 4.25 (0.35-50.39) | 0.263 |
| Myocardial infarction | 2(66.7) | 1(33.3) | 4.25 (0.35-50.39) | 0.263 |
| Peptic ulcer disease | 5(26.3) | 14(73.7) | 0.57 (0.16-1.98) | 0.285 |

- **Clinical signs and etiologies of HF associated with poor quality of life**

Amongst the heart failure signs present at the time of inquiry, we found patients with orthopnea (p = 0.028) or paroxysmal nocturnal dyspnea (p = 0.09) with about 4times the risk of having a poor quality of life. On the contrary, patients having Hypertensive heart disease as etiology had a low risk of having a poor quality of life (OR : 0.18 ; p = 0.007). This is portrayed on table XXXII below.

**Table XXXII**: clinical signs and etiologies of HF associated with poor quality of life.

| **Variables** | **Poor quality life** | | **uOR** | **p** |
|---|---|---|---|---|
| | **Yes** | **No** | **(CI at 95%)** | **value** |
| | **N=18 ; n(%)** | **N=35 ; n(%)** | | |
| **Clinical signs of HF** | | | | |
| Palpitations | 4(28.6) | 10(71.4) | 0.71 (0.18-2.70) | 0.44 |
| Fatigue | 15(39.5) | 23(60.5) | 2.6 (0.62-10.82) | 0.152 |
| Right flanc pain | 0 | 1(100) | 1.52 (1.25-1.86) | 0.660 |
| Chest pain | 4(40) | 6(60) | 1.38 (0.33-5.69) | 0.459 |
| Orthopnea | 9(56.3) | 7(43.8) | **4,00 (1.15-13.83)** | **0.028** |
| Paroxysmal nocturnal dyspnea | 7(58.3) | 5(41.7) | **3.81 (1.01-14.57)** | **0.049** |
| Ankle edema | 11(47.8) | 12(52.2) | 3.01 (0.92-9.77) | 0.058 |
| **Etiology of HF** | | | | |
| Hypertensive heart disease | 7(20.6) | 27(79.4) | **0.18 (0.05-0.64)** | **0.007** |
| Ischemic heart disease | 4(66.7) | 2(33.3) | 5.07 (0.82-31.16) | 0.081 |
| Restrictive cardiomyopathy | 2(100) | 0 | 3.33 (2.18-5.09) | 0.103 |
| Hypertrophic cardiomyopathy | 1(50) | 1(50) | 2.12 (0.12-36.18) | 0.551 |
| Dilated heart disease | 4(44.45) | 5(55.6) | 1.84 (0.42-8.01) | 0.323 |
| Valvular heart disease | 7(41.2) | 10(58.8) | 1.75 (0.52-5.88) | 0.274 |

#### IV.5.5.1.2. Multivariate analysis: binary logistic regression

Depression was the only independent risk factor for poor quality of life (ORa: 4.72 ; adjusted p = 0.043) and hypertensive heart disease as aetiology of heart failure was a protective factor (ORa : 0.23 ; adjusted p = 0.039). Table XXXIII below shows this.

**Table XXXIII**: independent factors associated to poor quality of life

| **Variables** | **Poor quality life** | | **aOR** | **Adjusted** |
|---|---|---|---|---|
| | **Yes** | **No** | **(CI at 95%)** | **p value** |
| | **N=18 ; n(%)** | **N=35 ; n(%)** | | |
| **Chronic diseases** | | | | |
| Depression | 8(57.1) | 6(42.9) | **4.72 (1.05-21.23)** | **0.043** |
| Clinical signs | | | | |
| Orthopnea | 9(56.3) | 7(43.8) | 3.14 (0.49-19.97) | 0.225 |
| Paroxysmal nocturnal dyspnea | 7(58.3) | 5(41.7) | 1.28 (0.18-8.66) | 0.800 |

# CHAPTER V : DISCUSSION

## V.1.1. DISCUSSION

We carried out a descriptive cross-sectional study with an analytical part to determine the epidemiological, clinical and paraclinical elements of HFpEF in a group of older adults in yaounde and their quality of life. We recruited patients from hospitalization and out-patient consultation who presented with symptoms and/or signs of HF. They underwent a series of work ups including Echocardiography, ECG, and Nt-proBNP , from which diagnosis was ascertained using the first 2 steps of the HFA-PEFF diagnostic algorithm. We got our data within the period of 3 months 2weeks , that is from the 1st of February to the 14th of May 2024.

### LIMITATIONS TO OUR STUDY

Before we discuss the above results, certain considerations have to be taken with respect to the scope and nature of this study.

1) This was a cross sectional study; therefore, temporal relationship cannot be established from our results.
2) We did not definitively diagnose cognitive impairment in the study subjects.
3) One factor that could contribute to a deceptive low-likelihood score is obesity. It is well known that obesity correlates with lower NT-proBNP levels, consequently classifying some of the obese HFpEF patients with a 'false' low score as to the actual number of HFpEF patients.
4) Definitive diagnosis could not be made in several patients with an intermediate score requiring further testing.

#### Prevalence of HFpEF

In this hospital based cross-sectional study, 53 out of 292 older symptomatic adults were found to have HFpEF (HFA-PEFF $\geq 5$) giving a prevalence of HFPEF in older adults of 18.2%. Of these 292 older adults, a total of 90 were diagnosed with HF, Hence a prevalence of HFpEF in HF patients of 58.8%. This is not very different from that in the study carried out by Martinez *et al.* [77] in Spain in 2015 who found 72.2% as prevalence of HFpEF in older adults with Heart failure with a mean age of 81±6.6 years old. Also, OTERO *et al.* found a prevalence of HFpEF of 61% in the GALICAP study in older adults with a mean age of 61years old [78]. Deepak Gupta *et al.* in the Atherosclerosis risk (ARIC) study in African-Americans, HFpEF was found in 72% of older adults with HF [79].

This is different from a prevalence of HFpEF of 13.3% found in South Africa by Nshuti *et al*. in a hospital based population > 55years old [28]. These differences could be explained be a more aging western population than the African population.

**Demographic characteristics**

The mean age of the participants was 74.5 ± 8.9 years, with ages ranging from 65 to 94 years. There were more females with a sex ratio of 0.47. This is not far from a study done by Seo *et al.* in Japan which revealed a mean age of 79.4 ± 4.4 years, with more women with a sex ratio of 0.83 [80]. The mean age is higher than that obtained in studies done in developing countries like the study done by Mboup *et al.* in Senegal who had a mean ages of 65.7 ± 9.1years and more women with a ratio of 0.78. Nshuti et al in South Africa also found a mean age of 55.5 years (IQR 47-66) with a female preponderance of 81%. This could be because developed countries have an ageing population and people live longer with the disease due to better health facilities and the studies conducted in Africa considered a much younger population with minimal ages of 45 years and 55 years respectively as in the studies above .

The female preponderance could be due to the fact that in Cameroon, life expectancy of women is more than that of men (62 vs 58 years), so we expect to see more women in the older age group [81].

Most patients were retired with a percentage of 45.3%, with a level of income < 50000FCFA (43.4%). All these can contribute to a decrease in the quality of life of patients living with heart failure.

**Clinical Profile**

**Cardiovascular risk factors and chronic conditions.**

Our study showed that most patients had a sedentary lifestyle (94.6%) as the main cardiovascular risk factor followed by Hypertension (79.2%).This was similar to Mboup *et al* who had 100% of their patients being hypertensive [69]. It could be explained by the fact that long standing hypertension leads to hypertensive heart disease characterized by the onset of left ventricular hypertrophy with an increase in arterial and ventricular stiffness and subsequently impaired relaxation. Sedentary lifestyle could also be explained by the fact that most of our patients were retired and spent most of their time in sedentary positions watching tv, while others with sedentary jobs forced them to stay in those positions for long hours spending little energy (<1.5 metabolic equivalents). This could be the reason many of the patients were overweight and obese (66.0%) with a mean population BMI of 28.5 ± 6.1 kg/$m^2$ . Similar results were found in a causation study

by Aizpurua *et al* where in the mean body weight of older adults with HFpEF was 30.5 ± 5.7 Kg/$m^2$ [82] and 30.9Kg/$m^2$ by Adebayo et al in Nigeria [83]. We found type II diabetes in 24.5%. This was quite low compared to 45% found by Mboup *et al*. in Senegal and can be as a result of many patients not aware of their diabetic status at the time of study . Excess adipose tissue can produce impairments relevant to HFpEF by enhanced pericardial restraint, and also produce a plethora of adverse systemic/metabolic effects, including promoting inflammation, HTN, insulin resistance, and dyslipidemia and impairing cardiac, arterial, skeletal muscle, and physical function [84].

**Comorbidities**

The most frequent Charlson comorbidity was Peptic ulcer disease in 29.8% of cases, followed by Diabetes in 24.5%, Stroke in 13.2% and Chronic Kidney disease (CKD) in 7.5% patients. Nshuti *et al*. found 40.5% with CKD [28] meanwhile Mboup *et al.* found CKD in these HFpEF patients secondary to Nephroangiosclerosis with Hypertension. The significantly low prevalence of CKD findings in our study could be attributed to the constant close range follow up of individuals with HTN. In addition, there could be the possibility of survival bias. Nshuti *et al*. had a much younger population and about half of their patients demised within 1 year so much that the association of CKD and HFpEF might be more fatal than HF alone, so those with both conditions died and only those with HF alone progressed to older ages in our population.

The high prevalence of chronic illness in the elderly has been attributed to the physiological processes involving aging and to chronic inflammations resulting from lifestyle practices and acquired patent diseases whose pathophysiology takes many years before clinical manifestations.

The most frequent presenting complaint was dyspnea in 88.7% of cases with NYHA class II (56.6%) grossly represented, followed by NYHA class III (32.1%) associated with orthopnea (30.2%), and Paroxysmal nocturnal dyspnea (22.6%). Mboup *et al*. also found exertion dyspnea as the most frequent symptom in 84% of case [69]. The slight difference could be due to the fact our study population was slightly older with increased cardiovascular modifications occurring with age. We found signs of congestion in 43.4% of cases similar to Mboup *et al*. who had 41% of congestive signs [69]. On the other hand Nshuti *et al* found 68.8% of patient to be congestive. This discrepancy could be explained by the fact that all their patients were hospitalized and most of ours were found in the out patient departments.

**Paraclinical characteristics**

The most frequent morphological abnormality found on echocardiography was left ventricular hypertrophy in 86.8% of patients with a median left ventricular mass index (LVMI) of 120g/$m^2$ [100-138] min.65g/$m^2$, max. 247g/$m^2$ of whom 43.4% were concentric hypertrophy. The left atrium was moderately to severely dilated in 54.7% of cases in whom it was taken with a median Left atrial volume index (LAVI) of 33.8ml/$m^2$ [30-36.5]. Mboup *et al*. found a mean LVMI of 114.0 ± 33.7 g/$m^2$ which was not very different from ours but with a Mean LAVI of 52.5±3.53ml/$m^2$ [69]. This gross difference in LAVI could be explained by the severity and chronic nature of left ventricular diastolic dysfunction.

Grade II and III diastolic dysfunction were found in 50.9% and 20.7% of our patients respectively while grade I diastolic dysfunction was found in 13.2% of patients. Nshuti *et al*. found grade 1 dysfunction in 74.4%, grade II dysfunction in 7.7% and grade III in 17.9% [28]. Mboup *et al*. found grade II dysfunction in 28%, grade I in 41% and grade III in 31% [69]. We don't have any clear explanation for the discrepancy observed although diastolic dysfunction is better expressed with exercise making for a greater proportion of patients with grade I diastolic dysfunction upon resting echocardiography.

The most frequent etiology was Hypertensive heart disease (64.2%), followed by Valvular heart disease(17%) and Ischemic heart disease (11.3%). Aizpurua *et al.* in the Maastricht study found hypertensive heart disease in 86%, valvular heart disease in 44%, coronary artery disease (25%) [82]. This could be explained by ventricular hypertrophy and stiffness with hypertensive heart disease, a high prevalence of degenerative valvular heart disease and calcification associated with aging, and decreased ATP supply for myocardial function with coronary artery disease.

Upon EKG exam, 83% of patients were in sinus rhythm, 13% had tachycardia, atrial fibrillation was found in 13.2%, 1$^{st}$ degree AV block in 5.7% and 22.7% of patients had a left bundle branch block. Mboup *et al.* found atrial fibrillation in 13% similar to our findings. Atrial dilatation is a major predisposing factor for the onset of atrial rhythm disorders. Seo *et al*. in Japan found a higher occurrence of atrial fibrillation in 26% of cases.

75.5% of our study population had moderate to severe functional limitation following the six-minute walk test. 49% of these patients had severe functional limitation. This is similar to a study carried out by Nganou *et al.* [85] in 2021, who found 39.2% of patients with heart failure with a poor physical condition. This could be explained by muscle deconditioning syndrome in heart failure caused by a reduction in nutritive blood flow to skeletal muscles and specific impairment in mitochondrial oxidative metabolism and characterized by the onset of symptoms of exercise

intolerance like exertional fatigue and cramps in these patients. Hence a corresponding poor maximum Volume of $O_2$ (62.3%) consumed with minimal aerobic exercise after estimation from Cahalin's equation.

**Quality of life**

Poor quality of life was found in 34% of our patients. Ndobo *et al*. had similar findings in 2023 when they found 21.2% of older adults in their study population with poor quality of life. This is due to a high prevalence of chronic diseases which have a considerable impact on their physical capacities and sometimes on mental faculties [86].

The lone independent factor for poor quality of life found was depression (ORa : 4,72 ; adjusted p = 0,043). Similar findings were found by Bekfani *et al.* as they found elevated anxiety and depression scores in patients with HFpEF [87]. These findings could be due to the fact that these older adults have a low functional capacity, loss of interest or pleasure in normal activities, low self care and most often need assistance. These could affect their quality of life negatively.

# CONCLUSION AND RECOMMENDATIONS

## V.1.2. CONCLUSION

At the end of the study, we can state the following.

1- The hospital prevalence of HFpEF in older adults was as high as 18.2% and it's the main type of heart failure in older adult patients with heart failure 58%

2- The mean age of persons with heart failure with preserved ejection fraction was 74,47 ±8,94 years with female predominance, with sedentary behaviour and overweight/obesity as the most prevalent cardiovascular risk factors. Hypertension was the most often identified cause of HFpEF, The main clinical findings were fatigue and dyspnea NYHA class II with or without orthopnea or paroxysmal nocturnal dyspnea. Congestive signs were not always frequent.

3- The main etiology of HFpEF was hypertensive heart disease, findings of Left ventricular hypertrophy, atrial dilatation and diastolic dysfunction were common. The most frequent rhythm abnormality was Atrial fibrillation (13%).

4- Many patients are still in the intermediate range 35% (29) and require further investigations.

5- More than half of the patients had a moderate quality of life 43.4%. We observed that Depression was directly associated with poor quality of life in HFpEF patients.

## RECOMMENDATIONS:

### To the Ministry of Public health

- Continue sensitisation on hypertension as it is still the main cause of HFpEF in our milieu.
- To increase diagnostic tools such as stress echocardiographic machines in main centers and to ease the access to invasive diagnostic tools like heart catheterization.
- Continue to make available drugs used for treating heart failure and reagents necessary to diagnose co-morbidities.

### To the scientific committee

- To conduct comparative and prospective studies on larger populations and community studies to further diagnose HFpEF in older adults.
- The use of HFA-PEFF diagnostic score for diagnosis of HFpEF as it made the diagnosis in 64% of cases.

To Clinicians and Teaching Hospitals

- Continue early detection of hypertension and management as it is the leading cause of HF in our milieu.
- Continue to educate and raise awareness on sedentary behaviour and weight loss as most patients were overweight.
- Continue diagnosing depression in older adults and other conditions that could affect quality of life in older adults. Management of HFpEF should be holistic laying emphasis on the psychosocial management of depression.

### To patients

To consult a physician should in case they have exertional dyspnea or fatigue and not always attribute these to the physiological ageing process.

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# APPENDICES

**I.1.1** APPENDIX 1: Applications for ethical clearance

Nkotuh Emmanuel Shu

7th year general medicine,

Faculty of Medicine and Biomedical Sciences,

University of Yaoundé 1.

P.O Box 1364 Yaoundé.

Phone numbers; 6515 59 861/ 621 117 440

Email; emmanuelshu12@gmail.com

8th February 2024

The President,

Centre Regional Ethics Committee for Human Health Research, National Ethics Committee for Human Health Research.

Subject; An application for ethical clearance.

Dear Professor,

We are honored to write you to seek ethical clearance to carry out our research study. We are working on the topic; Diagnosis of heart failure with preserved ejection fraction in older adults more than 65years in yaounde, under the supervision of Professor NGANOU-GNINDJIO, Doctor NTSAMA ESSOMBA and Doctor EBENE MANON.. Thank you.

Yours sincerely,

Nkotuh Emmanuel Shu

Nkotuh Emmanuel Shu

7th year general medicine,

Faculty of Medicine and Biomedical Sciences,

University of Yaoundé 1.

P.O Box 1364 Yaoundé.

Phone numbers; 6515 59 861/ 621 117 440

Email; emmanuelshu12@gmail.com

3rd April 2024

The President,

Institutional Ethical Review Board,

Faculty of Medicine and Biomedical Sciences, University of Yaounde 1.

Subject; An application for ethical clearance.

Dear Professor,

We are honored to write you to seek ethical clearance to carry out our research study. We are working on the topic; Diagnosis of heart failure with preserved ejection fraction in adults more than 65 years in yaounde using HFA-PEFF score, under the supervision of Professor NGANOU-GNINDJIO, Doctor NTSAMA ESSOMBA and Doctor EBENE MANON.

Thank you.

Yours sincerely,

Nkotuh Emmanuel Shu

**I.1.2** Appendix 2: Applications for authorization at research sites

Nkotuh Emmanuel Shu

7th year general medicine,

Faculty of Medicine and Biomedical Sciences,

University of Yaoundé 1.

P.O Box 1364 Yaoundé.

Phone numbers; 6515 59 861/ 621 117 440

Email; emmanuelshu12@gmail.com

7th February 2024

The Director General,

Yaoundé Central

Hospital,

Subject; An application for authorization to carry out our research study in your prestigious institution.

Dear Professor,

We are honored to write you to seek your authorization and support to carry out our research study in your prestigious institution. We are working on the topic; Diagnosis of heart failure with preserved ejection fraction in older adults more than 65 years in yaounde, under the supervision of Professor NGANOU-GNINDJIO, Doctor NTSAMA EBODE and Doctor EBENE MANON.

We seek your authorization to meet with elderly patients who present in your hospital with symptoms of heart failure from the 15th December 2023 to the 30th April 2024 while expecting a favorable reply receive our warm greetings.

Yours sincerely,

Nkotuh Emmanuel Shu

Nkotuh Emmanuel Shu

7th year general medicine,

Faculty of Medicine and Biomedical Sciences,

University of Yaoundé 1.

P.O Box 1364 Yaoundé.

Phone numbers; 6515 59 861/ 621 117 440

Email; emmanuelshu12@gmail.com

7th February 2024

The Director General,

Yaounde University Teaching Hospital,

Subject; An application for authorization to carry out workups in your prestigious institution

Dear Professor,

We are honored to write you to seek your authorization and support to carry out our research study workups in your prestigious institution. We are working on the topic; Diagnosis of heart failure with preserved ejection fraction in older adults more than 65 years in yaounde, under the supervision of Professor NGANOU-GNINDJIO, Doctor NTSAMA EBODE and Doctor EBENE MANON. In the course of our study, we will need to conduct Nt-proBNP analysis.

We seek your authorization to conduct this lab test at your institution's biochemistry laboratory under the supervision of Professor AMA Moor from February to the 30th April 2024. We will buy the reagents to be used from a supplier. While expecting a favorable reply receive our warm greetings.

Yours sincerely,

Nkotuh Emmanuel Shu

### **I.1.3** Appendix 3: Informed Consent

English version

Mr/ Mrs/ Ms

Topic; Diagnosis of Chronic Heart Failure with Preserved Ejection Fraction in Older adults in Yaounde.

The final year Medical Student, Nkotuh Emmanuel Shu, proposed to me to participate in a research study they are carrying out In Yaoundé Central Hospital and Biyemassi District hospital in view of his M.D thesis in the 2023/2024 academic year. This study has as main aim to determine the epidemiological, clinical and paraclinical elements of HFpEF diagnosis in a group of older adults and improve the quality of life of patients with this condition.

He explained to me that I was free to accept or deny the proposal. I have received and understood the following information

1. The aim of the study
2. The procedure
3. Any constraints

I accept that my medical records be consulted by the research team and used for research purposes only. My participation can be interrupted at any time if the principal investigator deems it necessary or if I wish. All data concerning me will be strictly confidential. Only the research team, and eventually health authority representatives will be given access to my data.

The research proposal for this study has been reviewed and validated by the Ethics and Research committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé 1.

At any time, I can ask for supplementary information from the student investigator using the phone numbers; +237 651 559 861 and 621 117 440.

I hereby accept to participate in the study under the above-mentioned conditions.

Date :

Volunteer’s signature Investigator’s signature

Mr / Mme /Mlle

_____

Sujet: Diagnostique de l'insufisance cardiaque a fraction d'ejection preserver chez les sujets agés plus de 65ans dans la ville de yaoundé.

L'étudiant en septième année de formation médical, Nkotuh Emmanuel Shu, m'a proposé de participer à une étude de recherche qu'ils mènent dans l'Hôpital Central de Yaoundé (HCY), pour sa thèse en fin de formation. L'étude a pour but principal, d'améliorer le diagnostic et la prise en charge de l'insuffisance cardiaque a fraction d'éjection preserver et améliorer la qualité de vie des patients ayant cette pathologie.

Il m'a expliqué que j'étais libre d'accepter ou de refuser la proposition. J'ai reçu et accepter les informations suivantes:

1. Le but de l'étude
2. La procédure
3. Les contraintes

J'accepte que mon dossier médical soit accéder par l'équipe de recherche et utilisé à cette fin uniquement. Ma participation peut être interrompu à tout moment si l'investigateur principal ou moi-même le déicide. Toutes les données me concernant seront maintenu en cofidentialité. Seul l'équipe de recherche et éventuellement les représentants du secteur de la santé seront donner accès aux données contenu dans mon dossier médical.

Cette étude a été révu et validé par la commission d'éthique et de la recherche de la Faculté de Médecine et des Sciences Biomédicales de l'Université de Yaoundé I

A tout instant je peux demander des informations supplémentaires de l'étudiant menant cette étude à travers les contacts ci-après: +237 651 559 861 et 621 117 440.

J'accepte de participer à cette étude sous les conditions mentionnes dessus.

Date _____

Signature de la participante Signature de l'investigateur

**I.1.4** Appendix 4: Questionnaire

Serial code:

Section 1; Identification

| | | | |
|---|---|---|---|
| I.1 | Date of interview | dd/mm/yy | \|__\| \|__\| / \|__\| \|__\| / \|__\| \|__\| |
| I.2 | Sex | Male=1<br>Female=2 | \|__\| |
| I.3 | Patient's phone number | 1: __ __ __ __ __ __ __ __<br>2:__ __ __ __ __ __ __ __<br>Guardian : __ __ __ __ __ __ __ __ | |
| I.5 | Age | | \|__\| |
| I.6 | Marital status | 1= Married 2= Single<br>3= Divorced 4= Widow<br>5= Separated 6= Cohabiting | \|__\| |
| I.7 | Ethnicity | 1= Bantus 4= Grassfield<br>2= Semi-bantu 5= Other<br>3= Sudanese…… | \|__\| |
| I.8 | Occupation | 1= Unemployed 2= Civil servant<br>3= Private sector worker<br>4= Retired 5: Housewife<br>6: Other | \|__\| |
| I.9 | Level of education | 1=None<br>2= Primary<br>3=Secondary (Form 1-5)<br>4=High school(Lower and upper sixth) 5= University | \|__\| |
| 1.10 | Socio-economic status | 1 <SMIG 2= SMIG 3= >SMIG | \|__\| |
| I.11 | Place of residence | 1= urban 2= rural | \|__\| |

SECTION 2: History and risk factors of heart failure

| | | | | |
|---|---|---|---|---|
| 2.1a | Alcohol consumption? | 1=yes<br>2=no | If yes Alcoholic index= | \|__\| |
| 2.1b | Tobacco smoking? | 1=yes<br>2=no | If yes Smoking index= | \|__\| |
| 2.1c | Do you carry out a regular physical activity? | 1=yes<br>2=no | | \|__\| |
| | If yes, for how long? | | 1= < 45mins<br>2= ≥ 45mins | \|__\| |
| 2.1d | Dyslipidemia | 1=yes<br>2=no<br>3=I don't know | | \|__\| |

| | | | | |
|---|---|---|---|---|
| 2.1e | Sedentary lifestyle | 1=yes<br>2=no | | \|__\| |
| 2.1f | Psychosocial factors ( depression,) | 1=yes<br>2=no | | \|__\| |
| 2.1g | Family history of Heart failure | 1=yes<br>2=no<br>3=I don't know | | \|__\| |
| 2.1h | Hypertension? | 1=yes<br>2=no<br>3=I don't know | | \|__\| |
| | If yes N° of anti-hypertensive drugs | | 0=none 1=1<br>2=≥2 | \|__\| |
| 2.2 | Comorbidities | 1=Myocardial infarction | 1=yes 2=no | \|__\| |
| | | 2=Congestive heart failure | 1=yes 2=no | \|__\| |
| | | 3=peripheral vascular disease | 1=yes 2=no | \|__\| |
| | | 4=stroke/transient ischemic attack | 1=yes 2=no | \|__\| |
| | | 5=dementia | 1=yes 2=no | \|__\| |
| | | 6=Chronic pulmonary disease | 1=yes 2=no | \|__\| |
| | | 7=connective tissue disease | 1=yes 2=no | \|__\| |
| | | 8=peptic ulcer disease | 1=yes 2=no | \|__\| |
| | | 9=mild liver disease | 1=yes 2=no | \|__\| |
| | | 10=diabetes | 1=yes 2=no | \|__\| |
| | | 11=hemiplegia | 1=yes 2=no | \|__\| |
| | | 12=Chronic kidney disease | 1=yes 2=no | \|__\| |
| | | 13=any tumor | 1=yes 2=no | \|__\| |
| | | 14=leukemia | 1=yes 2=no | \|__\| |
| | | 15=Lymphoma | 1=yes 2=no | \|__\| |
| | | 16=diabetes with end organ damage | 1=yes 2=no | \|__\| |
| | | 17= moderate/severe liver disease | 1=yes 2=no | \|__\| |
| | | 18=solid tumor | 1=yes 2=no | \|__\| |
| | | 19=AIDS | 1=yes 2=no | \|__\| |
| 2.3 | History of Heart failure? | | 1=yes 2=no | \|__\| |
| | If yes | Year of diagnosis | | /__/__/ |
| | | Base Cardiopathy | | |
| | | Ejection fraction at diagnosis | 1= <50 2=>50<br>3=I don't know | \|__\| |

SECTION 3: Physical Examination

| | | | | |
|---|---|---|---|---|
| Vital signs | PE-1 | Blood pressure: Right arm__ __ __ mmHg | 1=hypotension<br>2=optimal<br>3=normal<br>4=high normal<br>5=grade I hypertension<br>6=grade II hypertension | \|__\| |
| | | Left arm__ __ __ mmHg<br>Sitting position | 1=hypotension<br>2=optimal<br>3=normal 4=high normal<br>5=grade I hypertension<br>6=grade II hypertension | \|__\| |
| | PE-2 | Pulse (bpm) = | 1= < 60<br>2= 60 ≤ HR ≤ 100<br>3= > 100 | \|__\| |
| | PE-3 | Respiratory rate (cpm)= | 1= <12 2= 12 ≤ RR ≤ 20 3>20 | \|__\| |
| | PE-4 | Temperature (°c) = | | \|__\| |
| | PE-5 | $SpO_2$ = | 1= < 90%<br>2= 90 ≤ O2 Sa ≤ 94%<br>3= > 94 % | \|__\| |
| Anthropometric parameters | PE-6 | Weight (kg) = | | \|__\| |
| | PE-7 | Height (cm) = __ __ __. __ | | \|__\| |
| | PE-8 | Mid abdominal circumference (cm) = | Male: 1= <102, 2=102, 3=>102<br>Female: 1=<88, 2=88, 3=>88 | \|__\| |
| | PE-9 | BMI (kg/m2) = | 1=<18 2=18-24.9 3=25-29.9<br>4=30-34.9 5=35-39.9 6=≥40 | \|__\| |
| NYHA functional classification | Class I = 01<br>Class II= 02<br>Class III= 03<br>Class IV = 04 | | /__/__/ | \|__\| |
| Symptoms | 0=asymptomatic | | 1=yes 2=no | \|__\| |
| | 1=dyspnea | | 1=yes 2=no | \|__\| |
| | 2=orthopnea | | 1=yes 2=no | \|__\| |
| | 3=paroxysmal nocturnal dyspnea | | 1=yes 2=no | \|__\| |
| | 4=cough | | 1=yes 2=no | \|__\| |
| | 5=fatigue | | 1=yes 2=no | \|__\| |
| | 6=right flanc pain | | 1=yes 2=no | \|__\| |
| | 7=chest pain | | 1=yes 2=no | \|__\| |
| | 8=palpitations | | 1=yes 2=no | \|__\| |
| | 9=arrhythmia | | 1=yes 2=no | \|__\| |
| Examination findings (physical signs) | 1=Displaced apex beat | | 1=yes 2=no | \|__\| |
| | 2=gallop rhythm | | 1=yes 2=no | \|__\| |
| | 3=heart murmur with characteristics | | 1=yes 2=no | \|__\| |
| | 4=Jugular vein distension | | 1=yes 2=no | \|__\| |
| | 5=abdomino-jugular reflux | | 1=yes 2=no | \|__\| |
| | 6=lung crackles | | 1=yes 2=no | \|__\| |
| | 7= ascites | | 1=yes 2=no | \|__\| |
| | 8=hepatomegaly | | 1=yes 2=no | \|__\| |
| | 9=ankle edema | | 1=yes 2=no | \|__\| |

Section 4: Diagnostic workups

Echocardiogram

| | |
|---|---|
| LVEF | |
| Cardiopathy | |
| Septal peak early diastolic velocity (e')(cm/s) | |
| lateral mitral annular peak early diastolic velocity (e')(cm/s) | |
| average septal–lateral E/e' ratio (ou E/Ea) | |
| Early (E) and late (A) diastolic filling velocities. E/A ratio >2 | |
| Left ventricular global longitudinal systolic strain(GLS) (%) (SLG) | |
| Tricuspid regurgitation peak velocity (TRV)(m/s) (Vmax IT) | |
| Right ventricular outflow tract acceleration time (temps d'acceleration pulmonaire) | |
| Left atrial volume index (LAVI) (ml/$m^2$) (VOG indexe a la surface corporelle) | |
| Left ventricular mass index (LVMI)(m/w)(g/$m^2$) (MVGi) | |
| Relative wall thickness (LVRWT) (epaisseur parietale relative du VG) | |
| Left ventricular wall thickness (mm) Epaiseur parietale telediastolique du VG | |
| Pulmonary artery systolic pressure (PASP)(mmHg) | |

Electrocardiogram

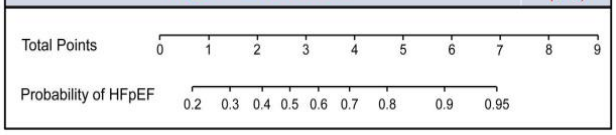
| | | |
|---|---|---|
| Date done | | /__/ __/__/__/ |
| Sinus Rhythm | 1=yes 2=no | \|__\| |
| Heart rate | 1= normal 2= Bradycardia 3=Tachycardia | \|__\| |
| Left atrial hypertrophy | 1=yes 2=no | \|__\| |
| Right atrial hypertrophy | 1=yes 2=no | \|__\| |
| Atrial Fibrillation | 1=yes 2=no | \|__\| |
| Atrial Flutter | 1=yes 2=no | \|__\| |
| Left ventricular hypertrophy | 1=yes 2=no | \|__\| |
| PR interval | 1=<120ms, 2=120-200ms, 3=>200ms, 4=variable | \|__\| |

| | | |
|---|---|---|
| Atrio-ventricular block(AVB) | 1= AVB 1, 2=AVB 2 mobitz 1, 3=AVB mobitz 2, 4=AVB 3 | \|__\| |
| QRS axis | 1=< -30º 2=-30 º ≤ QRS ≤90 º<br>3= QRS > 90º | \|__\| |
| QRS axis conclusion | 1=LAD, 2=normal, 3=RAD | \|__\| |
| QRS duration | 1=<100ms, 2=100-120ms, 3=>120m | \|__\| |
| Conclusion on QRS duration | 1=normal, 2=incomplete BBB, 3=complete BBB | \|__\| |
| If Bundle branch block | 1=LBBB, 2=RBBB | \|__\| |
| QT corrected with bazett formula | 1=<360ms, 2=360-500ms, 3=>120ms | \|__\| |
| Conclusion on corrected QT | 1= short QT, 2=normal, 3= long QT | \|__\| |
| ST segment displacement in atleast 2 derivations in the same territory | 1=yes, 2=no | \|__\| |
| ECG result | 1=normal, 2=abnormal | \|__\| |
| If abnormal, precise pathology | | |

NT-proBNP

| | | |
|---|---|---|
| done | 1=yes 2=no | \|__\| |
| If yes | NT-proBNP value(pg/ml) | |

| | Clinical Variable | Values | Points |
|---|---|---|---|
| $H_2$ | **H**eavy | Body mass index > 30 kg/m² | 2 |
| | **H**ypertensive | 2 or more antihypertensive medicines | 1 |
| F | Atrial **F**ibrillation | Paroxysmal or Persistent | 3 |
| P | **P**ulmonary Hypertension | Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg | 1 |
| E | **E**lder | Age > 60 years | 1 |
| F | **F**illing Pressure | Doppler Echocardiographic E/e' > 9 | 1 |
| | $H_2$FPEF score | | Sum (0-9) |




| | Functional | Morphological | Biomarker (SR) | Biomarker (AF) |
|---|---|---|---|---|
| Major | septal e' < 7 cm/s or lateral e' < 10 cm/s or Average E/e' ≥ 15 or TR velocity > 2.8 m/s (PASP > 35 mmHg) | LAVI > 34 ml/m² or LVMI ≥ 149/122 g/m² (m/w) and RWT > 0,42 # | NT-proBNP > 220 pg/ml or BNP > 80 pg/ml | NT-proBNP > 660 pg/ml or BNP > 240 pg/ml |
| Minor | Average E/e' 9 -14 or GLS < 16 % | LAVI 29-34 ml/m² or LVMI > 115/95 g/m² (m/w) or RWT > 0,42 or LV wall thickness ≥ 12 mm | NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml | NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml |

| | |
|---|---|
| Major Criteria: 2 points | ≥ 5 points: HFpEF |
| Minor Criteria: 1 point | 2-4 points: Diastolic Stress Test or Invasive Haemodynamic Measurements |

$H_2$FPEF score value=……

HFA-PEFF score value=……

Charlson comorbidity score value =……..

A. Calculate Charlson Score or Index (i)

1. Add Comorbidity score to age score
2. Total denoted as 'i' below

B. Calculate Charlson Probablity (10 year mortality)

1. Calculate Y = e^(i * 0.9)
2. Calculate Z = 0.983^Y
3. where Z is the 10 year survival

**Geriatric Depression Scale (GDS)** – 4 Questions Version

1. Are you basically satisfied with your life? (Yes / No)
2. Do you feel that your life is empty? (Yes / No)
3. Are you afraid that something bad is going to happen to you? (Yes / No)
4. Do you feel happy most of the time? (Yes / No)

Total score :

Section 5; Quality of life (MINNESOTA LIVING WITH HEART FAILURE QUESTIONNAIRE)

The following questions ask how much your heart failure (heart condition) affected your life during the past month (4 weeks). After each question, circle the 0, 1, 2, 3, 4 or 5 to show how much your life was affected. If a question does not apply to you, circle the 0 after that question

*MINNESOTA LIVING WITH HEART FAILURE QUESTIONNAIRE*

| Did your heart failure prevent you from living as you wanted during the past month (4 weeks) by | No | Very little | | | | Very Much |
|---|---|---|---|---|---|---|
| 1. causing swelling in your ankles or legs? | 0 | 1 | 2 | 3 | 4 | 5 |
| 2. making you sit or lie down to rest during the day? | 0 | 1 | 2 | 3 | 4 | 5 |
| 3. making your walking about or climbing stairs difficult? | 0 | 1 | 2 | 3 | 4 | 5 |
| 4. making your working around the house or yard difficult? | 0 | 1 | 2 | 3 | 4 | 5 |
| 5. making your going to places away from home difficult? | 0 | 1 | 2 | 3 | 4 | 5 |
| 6. making your sleeping well at night difficult? | 0 | 1 | 2 | 3 | 4 | 5 |
| 7. making your relating to or doing things with your friends or family difficult? | 0 | 1 | 2 | 3 | 4 | 5 |
| 8. making your working to earn a living difficult? | 0 | 1 | 2 | 3 | 4 | 5 |
| 9. making your recreational pastimes, sports or hobbies difficult? | 0 | 1 | 2 | 3 | 4 | 5 |
| 10. making your sexual activities difficult? | 0 | 1 | 2 | 3 | 4 | 5 |
| 11. Making you eat less of the foods you like? | 0 | 1 | 2 | 3 | 4 | 5 |
| 12. making you short of breath? | 0 | 1 | 2 | 3 | 4 | 5 |
| 13. making you tired, fatigued, or low on energy? | 0 | 1 | 2 | 3 | 4 | 5 |
| 14. making you stay in a hospital? | 0 | 1 | 2 | 3 | 4 | 5 |
| 15. costing you money for medical care? | 0 | 1 | 2 | 3 | 4 | 5 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 16. giving you side effects from medications ? | 0 | 1 | 2 | 3 | 4 | 5 |
| 17. making you feel you are a burden to your family or friends? | 0 | 1 | 2 | 3 | 4 | 5 |
| 18. making you feel a loss of self-control in your life? | 0 | 1 | 2 | 3 | 4 | 5 |
| 19. making you worry? | 0 | 1 | 2 | 3 | 4 | 5 |
| 20. making it difficult for you to concentrate or remember things? | 0 | 1 | 2 | 3 | 4 | 5 |
| 21. making you feel depressed? | 0 | 1 | 2 | 3 | 4 | 5 |
| Conclusion | | | | | | |

## Section 7: SIX MINUTE WALK TEST WORKSHEET

Name_____ DOB_____

Test date_____

Gender: M/F Race _____

Height ____m Weight _____kg

Medications taken before the test (dose and time)

_____

_____

Supplemental $O_2$: no yes ____ L/min Assistive device: no yes _____

| Parameter | Pre Test/Baseline | 2min | 4min | 6min |
|---|---|---|---|---|
| $SpO_2$ | | | | |
| HR | | | | |
| BP | | | | |
| Dyspnea (Borg) | | | | |
| Fatigue (Borg) | | | | |

Stopped or paused before 6 minutes completed? Yes, No Duration :_____

Reason_____

Other symptoms at the end of test: angina, dizziness hip, knee, calf pain

Other _____

Number of laps_____(x100 meters) + final partial lap_____ meters= total distance walked in 6 minutes: _____ meters

Comments:

Technician: _____

RATE OF PERCEIVED DYSPNEA

0 Not at all

1 Very Slight

2 Light

3 Moderate

4 Somewhat Hard

5 Severe

6

7 Very Severe

8

9

10 Very, very severe

RATE OF PERCEIVED EXERTION

0 Not at all

1 very light

2 Light

3

4 Somewhat Hard

5

6 Hard

7 Very hard

8

9 Extremely hard 10 Maximum exertion Conclusion :

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COMITÉ INSTITUTIONNEL D'ÉTHIQUE DE LA RECHERCHE
Tel/ fax : 22 31-05-86 22 311224
Email: decanatfmsb@hotmail.com

THE UNIVERSITY OF YAOUNDE I
FACULTY OF MEDICINE AND BIOMEDICAL SCIENCES
INSTITUTIONAL ETHICAL REVIEW BOARD

Ref. : N° 0747 /UY1/FMSB/VDRC/DAASR/CSD

# CLAIRANCE ÉTHIQUE

10 JUIN 2024

Le COMITÉ INSTITUTIONNEL D'ÉTHIQUE DE LA RECHERCHE (CIER) de la FMSB a examiné

La demande de la clairance éthique soumise par :

**M.Mme : NKOTUH EMMANUEL SHU** **Matricule: 17M072**

**Travaillant sous la direction de :**

- **Pr NGANOU-GNINDJIO Chris Nadège**
- **Dr NTSAMA ESSOMBA Marie Josiane épouse EBODE**
- **Dr EBENE MANON Guillaume**

**Concernant le projet de recherche intitulé :** **Diagnosis of heart failure with preserved ejection fraction in older adults more than 65 years in Yaoundé**

**Les principales observations sont les suivantes**

| | |
|---|---|
| Evaluation scientifique | |
| Evaluation de la convenance institutionnelle/valeur sociale | |
| Equilibre des risques et des bénéfices | |
| Respect du consentement libre et éclairé | |
| Respect de la vie privée et des renseignements personnels (confidentialité) : | |
| Respect de la justice dans le choix des sujets | |
| Respect des personnes vulnérables : | |
| Réduction des inconvénients/optimalisation des avantages | |
| Gestion des compensations financières des sujets | |
| Gestion des conflits d'intérêt impliquant le chercheur | |

Pour toutes ces raisons, le **CIER** émet un avis **favorable** sous réserve des modifications recommandées dans la grille d'évaluation scientifique.

L'équipe de recherche est responsable du respect du protocole approuvé et ne devra pas y apporter d'amendement sans avis favorable du **CIER**. Elle devra collaborer avec le **CIER** lorsque nécessaire, pour le suivi de la mise en œuvre dudit protocole.
La clairance éthique peut être retirée en cas de non - respect de la réglementation ou des recommandations sus évoquées.
En foi de quoi la présente clairance éthique est délivrée pour servir et valoir ce que de droit

***LE PRESIDENT DU COMITE ETHIQUE***

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---

CE N°0128/CRERSHC/2024

Yaoundé, the 23 AVR 2024

# ETHICAL CLEARANCE

The Centre Regional Ethics Committee for Human Health Research (CRERSH-Ce) has received the request for an ethical approval for the project entitled: **"Prevalence of Chronic Heart Failure with Preserved Ejection Fraction in Older Adults in Yaoundé"**, submitted by Mr **NKOTUH Emmanuel Shu**.

After evaluation, it appears that the subject is worthy of interest, the objectives are well defined, and the research procedure does not include invasive methods harmful to the participants. In addition, the informed consent form intended for participants is acceptable.

For these reasons, the CRERSH-Ce issued a six (06) months approval for the implementation of the current version of the protocol.

The Principal Investigator is responsible for scrupulous compliance with the protocol and must not make any amendments, however minor, without the favourable approval of the CRERSH-Ce. In addition, the Principal Investigator is required to:

- Collaborate on any descent from the CRERSH-Ce for monitoring the implementation of the approved protocol.
- And submit the final report of the study to the CRERSH-Ce and to the competent authorities concerned by the study.

This clearance may be withdrawn in the event of non-compliance with the regulations in force and the directives mentioned above.

In witness whereof the present Ethical Clearance is issued with the privileges thereunto pertaining. /-

**Copy:** CNERSH.

REPUBLIQUE DU CAMEROUN Comité régional d'Ethique de la Recherche pour la Santé Humaine du Centre CRERSH / C CENTRE MINISTERE DE LA SANTE PUBLIQUE

**THE CHAIRPERSON,**

Pr. Dobo Kuyo Pasinée
Pharmacien

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DIRECTION DE L' HOPITAL CENTRAL DE YAOUNDE
SECRETARIAT MEDICAL

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MINISTRY OF PUBLIC HEALTH
GENERAL SECRETARY
DIRECTORATE OF CENTRAL HOSPITAL OF YAOUNDE
MEDICAL SECRETARY

Yaoundé, le 16 FEV 2024

## ACCORD DE PRINCIPE

Je soussigné **Professeur FOUDA Pierre Joseph**, Directeur de l'Hôpital Central de Yaoundé, marque mon Accord de Principe à Monsieur **NKOTUH Emmanuel SHU** , étudiant de 7ème année de Médecine générale à la Faculté de Médecine et des Sciences Biomédicales de l'Université de Yaoundé I , sous le thème « DIAGNOSIS OF CHRONIC HEART FAILURE WITH PRESERVED EJECTION FRACTION IN OLDER ADULTS IN YAOUNDE » à l'Hôpital Central de Yaoundé, sous la codirection du docteur EBODE NTSAMA ESSOMBA Marie Josiane .

**Pour Le Directeur et par ordre**
**Le Conseiller Médical,**

P.r. Agr Pierre Ongolo Zogo

**Ampliations :**

- Conseiller Médical ;
- Chef service concerné ;
- Intéressé ;
- Chrono/Archives.

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BIYEM-ASSI DISTRICT HOSPITAL
E-mail:hopital_biyemassi@yahoo.fr

N° 108 /AR/MINSANTE/DRSPC/DSBA/HDBA.

# AUTORISATION DE RECHERCHE

Le Directeur de l'Hôpital de District de Biyem-Assi à Yaoundé soussigné, donne autorisation de recherche à **NKOTUH Emmanuel SHU,** étudiant à la Faculté de Médecine et des Sciences Biomédicales de l'Université de Yaoundé 1, à mener une enquête dont l'étude porte sur *« Diagnosis of heart failure with preserved ejection fraction in older adults more than 65 years in Yaoundé»*, supervisée par Dr EBENE Manon, Chef de service de Médecine.

En foi de quoi la présente autorisation est établie et lui est délivrée pour servir et valoir ce que de droit.

Yaoundé, le 13 FEV 2024

Le Directeur

Dr. Daniel Ekoua
Médecin - Cardiologue

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*YAOUNDE UNIVERSITY TEACHING HOSPITAL*
*Tél. : 222 31 25 66* *Fax : 222 31 25 67*

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**DIRECTION GENERALE**

CELLULE D'APPUI PEDAGOGIQUE
DE LA RECHERCHE ET DE LA COOPERATION
BUREAU DE LA CAPRC

N°192/AR/CHUY/DG/DGA/DM/CAPRC/CEAAP/CEARC

## AUTORISATION DE RECHERCHE

Dans le cadre de la rédaction d'un mémoire de fin d'études, en vue de l'obtention du diplôme de Doctorat en Médecine générale, Monsieur NKOTUH Emmanuel SHU est autorisé à mener une recherche au CHUY sur le thème : « **Diagnosis of heart failure with preserved ejection fraction in older adults more than 65 years in Yaoundé** ».

Ces travaux se dérouleront dans le service de Biochimie sous la supervision de Pr. AMA MOOR Vicky Jocelyne, Chef de service.

Toutefois, il devra obligatoirement déposer un exemplaire de mémoire au CHUY (Bureau de la CAPRC).

En foi de quoi la présente autorisation dont la durée de validité est de 03 mois à compter de la date de signature, lui est délivrée pour servir et valoir ce que de droit. /-

Yaoundé, le 11 AVR 2024
**LE DIRECTEUR GENERAL**

REPUBLIQUE DU CAMEROUN Le Directeur Général Centre Hospitalier et Universitaire Yaoundé

Pr. Nkone Engjimo Félicien

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