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Research Article

Comparative Analysis of the Clinical Presentations, Cardiovascular & Laboratory Findings & Treatment of Heart Failure with Preserved & Reduced Ejection Fractions in Cameroon: A Multicenter Cross-Sectional Study

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ARTICLE INFO

Article history:

Received: 12 November, 2020

Accepted: 5 December, 2020

Published: 17 December, 2020

Keywords:

Heart failure

preserved

reduced

ejection fraction

clinical

paraclinical

therapeutic aspects

Yaounde

ABSTRACT

Background: Contrarily to past concepts, heart failure with preserved ejection fraction (HFpEF) has become more prevalent than heart failure with reduced ejection fraction (HFrEF). Our objective was to study the clinical, cardiovascular and laboratory findings and therapeutic aspects of HFpEF, compared with those of HFrEF in Yaounde, Cameroon.

Method: This was an analytical cross-sectional study carried-out at the Central Hospital, General Hospital and Military Hospital of Yaounde, from January to April 2018 (4 months). 201 patients aged at least 18 years old with an echocardiography confirmed diagnosis of heart failure had been enrolled. We excluded 12 patients because they had a congenital ventricular septal defect (2), chronic cor pulmonale (4), mitral stenosis (5), and pericarditis (1).

Results: We found that 45.5% of our patients had HFpEF whereas 37.5% had HFrEF. Patients with HFpEF were older and had a significantly higher incidence of hypertension and obesity. HFrEF was significantly more associated with congestive symptoms than HFpEF. The S3 gallop was significantly more present in patients with HFrEF. Patients with HFpEF had significantly higher rate of atrial fibrillation. Furosemide, spironolactone and digoxin were significantly used more frequently in patients with HFrEF.

Conclusion: HFpEF is the most frequent form of heart failure in the hospital setting in Yaoundé, Cameroon. Patients with HFpEF were significantly older and more affected by hypertension and obesity than those with HFrEF. Cardiac ultrasound is indispensable to differentiate between the two entities for better management.

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Introduction

The epidemiological transition of diseases has markedly increased the prevalence of hypertension, diabetes and obesity in low- and middle-income countries located especially in Africa [1, 2]. The improvement in the management and surveillance of these cardiovascular risk factors and their complications has led to an increase in life expectancy of patients suffering from these pathologies. During the past two decades,

there has been a significant increase in the number of cases of heart failure with preserved ejection fraction (HFpEF) in developed countries, due to a high prevalence of these cardiovascular risk factors and an increment in the ageing population [3-5]. Furthermore, despite several studies done on HFpEF in high-income countries, its diagnosis and management remain an ongoing challenge because of the polymorphism of its clinical manifestation and a myriad of nonconclusive clinical trials respectively [3, 4, 6-12]. There is dearth of data done in Africa on

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HFpEF. Hence, we aimed to contribute to this knowledge gap by comparing the clinical and cardiovascular and laboratory findings, and the treatment of HFpEF to that of heart failure with reduced Ejection Fraction (HFrEF).

Methods

I Study Design, Settings and Participants

This was a cross-sectional analytical study conducted in the cardiology unit of three hospitals, namely: Central, General and Military Hospitals of Yaoundé, Cameroon. It was done over a period of 4 months spanning from January 1, 2018 to April 2018. The study population comprised of all consenting consecutive patients aged 18 years and above with a confirmed diagnosis of heart failure, based on clinical and echocardiographic findings hospitalized or followed-up in one of the three aforementioned hospitals. We excluded all patients with a diagnosis of congenital heart disease, cor pulmonale, mitral stenosis or pericarditis.

II Operational Terms

Heart Failure with reduced Ejection Fraction (HFrEF) was defined as the presence of signs and/or symptoms of heart failure with a left ventricular ejection fraction (LVEF) <40%. Heart Failure with preserved Ejection Fraction (HFpEF) was defined as the presence of signs and/or symptoms of heart failure, a LVEF > 50%, a structural heart anomaly (left ventricular hypertrophy and/or left atrial dilation) and/or diastolic dysfunction. A diastolic dysfunction was considered present if: the ratio $E/e' \geq 13$ (ratio between the peak velocity flow E through the mitral valve on pulse wave Doppler heart ultrasound and the velocity e' at early diastole of the flow at the mitral valve on Doppler heart ultrasound) and/or $e' < 9\text{cm/s}$. Left ventricular hypertrophy was defined as a left ventricular mass $\geq 115\text{g/m}^2$ in men and $\geq 95\text{g/m}^2$ in women. Left atrial dilation was defined as a left atrial volume $>34\text{ ml/m}^2$ or a surface area $>20\text{cm}^2$. The signs and symptoms of heart failure considered were those given by the European Society of Cardiology 2016 (ESC 2016) [13].

III Data Collection

Data were collected from registries of hospitalization and consultation, from patients' medical records, and directly from patients or their families through by interview-administration of pretested structured

questionnaire. Data were recorded using data entry sheets. Variables studied were: sociodemographic (age and gender), past history (hypertension, diabetes mellitus, tobacco abuse, obesity and/or overweight, dyslipidemia, chronic alcoholism, sedentary lifestyle, chronic kidney disease, cerebrovascular diseases), physical findings (blood pressure, pulse, respiratory rate, body mass index, signs and symptoms of heart failure) and treatment modalities.

IV Statistical Analysis

All data collected were entered using CSPro 7.0. Analysis were done using SPSS version 20.0. Qualitative variables were expressed as numbers and percentages, while quantitative variables were expressed as means and standard deviation. The chi-square test was used to find associations between dependent and categorical variables while the student t-test was used to find associations between continuous variables.

Results

A total of 201 patients with heart failure were enrolled in the study. We excluded 12 (5.97%) patients for the following reasons: two had a congenital ventricular septal defect, four had chronic cor pulmonale, five had mitral stenosis and one had pericarditis. Eighty-six (45.50%) patients had HFpEF while 71 (37.57%) had HFrEF. The remaining 32 (16.93%) patients had an intermediate ejection fraction.

I Comparison of the Clinical Findings in HFpEF and HFrEF

The mean age of our study population was 65.69 ± 13.58 years. Patients with HFpEF were significantly older ($p = 0.003$), had hypertension ($p = 0.034$) and obesity ($p = 0.013$). There were also more patients of the female sex, with diabetes, tobacco abuse and dyslipidemia in the group with HFpEF, but these differences were not significant (Table 1). HFpEF was more of sudden onset while HFrEF had a more insidious onset and more congestive signs/symptoms (Table 2). Mean systolic blood pressure was significantly higher in patients with HFpEF ($p = 0.020$) while the heart rate was significantly higher in patients with HFrEF ($p < 0.001$). The S3 galop sound was significantly more present in patients with HFrEF while there was no significant difference in the occurrence of the S4 galop sound in the two groups ($p = 0.376$) (Table 2). Hypertension was identified as the cause of heart failure mainly in patients with HFpEF ($p < 0.001$) (Table 3).

Table 1: Cardiovascular risk factors and past history.

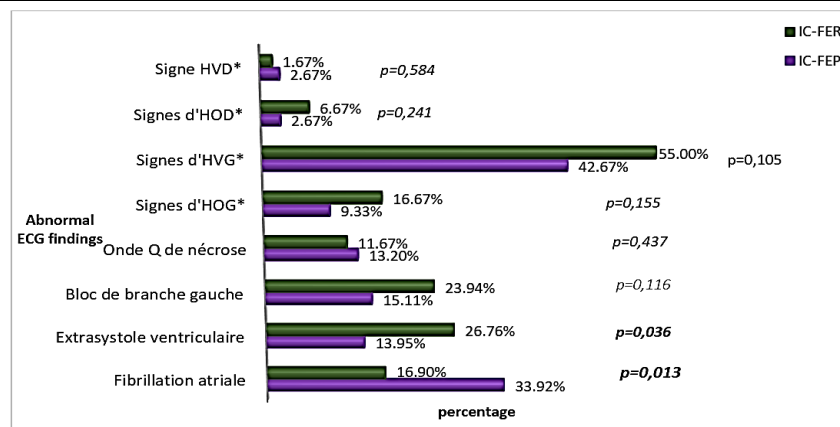
Parameters	HFpEF n(%)	HFrEF n(%)	p value
Age (mean \pm SD)	70,90 \pm 11,88	59,38 \pm 12,87	0,003
Female sex	49(56,98)	35(49,30)	0,081
Hypertension	67(77,91)	45(63,38)	0,034
Type 2 diabetes	31(36,05)	22(30,99)	0,310
Tobacco smoking	13(15,12)	9(12,68)	0,409
Dyslipidemia	43(50,00)	25(35,29)	0,187
BMI ≥ 25	64(74,42)	40(56,34)	0,013
sedentarity	58(67,44)	40(56,34)	0,103
Alcohol intake	26(30,23)	28(39,44)	0,149
Chronic kidney disease	5(5,81)	2(2,82)	0,308
Cerebrovascular disease	5(5,81)	3(4,23)	0,470
hyperthyroidism	2(2,32)	2(2,82)	0,615

Table 2: Signs and symptoms of heart failure.

Parameters	HFpEF n(%)	HFrEF n(%)	p value
Symptoms			
Total	81(94,19)	70(98,59)	0,156
Sudden onset	44(56,65)	22(30,99)	< 0,001
dyspnea			
NYHA II	16(19,53)	6(8,57)	0,042
NYHA III	23(28,40)	16(27,14)	0,505
NYHA IV	42(51,85)	45(64,29)	0,040
orthopnea	25(29,07)	35(49,30)	0,005
Nocturnal paroxysmal dyspnea	18(20,93)	11(15,49)	0,253
Asthenia	36(41,86)	38(53,52)	0,097
Ankle edema	34(39,53)	34(47,89)	0,187
Night cough	7(8,14)	11(14,49)	0,118
Feeling of weight gain	8(9,30)	9(12,68)	0,336
Palpitation	19(22,09)	17(23,94)	0,465
Syncope	6(6,98)	3(4,23)	0,367
Signs			
Respiratory rate (mean ± SD)	26,61±6,64	30,10±9,46	0,087
Heart rate (mean ± SD)	85,61±24,88	100,01±20,03	< 0,001
Systolic BP (mean ± SD)	145,13±36,18	131,80±34,21	0,020
Diastolic BP (mean ± SD)	86,07±21,35	89,64±24,73	0,335
Jugular venous distention	46(53,49)	48(67,61)	0,034
Hepato jugular reflux	28(32,56)	36(50,70)	0,018
Left deviation of the cardiac apex	11(12,79)	30(42,25)	< 0,001
Galop B3	9(10,47)	16(22,53)	0,033
Galop B4	11(12,79)	7(9,86)	0,376
Peripheral edema	58(67,44)	48(67,61)	0,468
Lung crackles	55(63,95)	48(67,61)	0,298
Tachycardia	28(32,56)	45(63,38)	< 0,001
hepatomegaly	23(26,74)	32(45,07)	0,015
Ascites	8(9,30)	17(23,94)	0,020
Oiguria	3(3,49)	0(0,00)	0,168

Table 3: Causes of heart failure.

Parameters	HFpEF n(%)	HFrEF n(%)	p value
Hypertensive cardiopathy	66(76,74)	34(47,89)	< 0,001
Ischemic cardiopathy	13(15,12)	9(12,67)	0,342
Dilated cardiomyopathy	0	11(15,49)	0,004
Postpartum cardiopathy	0	1(1,41)	0,302
Toxic cardiopathy	0	10(14,08)	< 0,001
valvulopathy	2(2,33)	6(8,45)	0,085
Unknown cause	5(5,81)	0	0,047

**Figure 1:** Electrocardiographic findings in the two groups.

*HOG: Left Atrial Enlargement, HVG: Left Ventricular Hypertrophy, HOD: Right Atrial Enlargement, HVD: Right Ventricular Hypertrophy.

II Comparison of Paraclinical Findings

i Electrocardiographic Findings

Atrial fibrillation was more frequent in patients with HFpEF ($p = 0.013$) and more ventricular extra systoles were occurred in the patients with HFrEF ($p = 0.036$) (Figure 1).

ii Cardiac Transthoracic Doppler Ultrasound Findings

The mean mass of the left ventricle was more important in patients with HFpEF ($p = 0.004$), while the mean area of the left atrium was higher in patients with HFrEF ($p = 0.010$) (Table 4). Left ventricular hypertrophy (LVH) was more frequent in patients with HFpEF ($p = 0.001$) (Figure 2); it was more concentric in patients with HFpEF ($p < 0.001$) and more eccentric in those with HFrEF ($p = 0.006$) (Figure 3). Abnormal relaxation of the right ventricle was more frequent in patients with HFpEF while patients with HFrEF had a more restrictive profile of the mitral valve (Figure 4).

Table 4: Distribution of echocardiographic findings in the two groups.

Parameters	HFpEF (%)		HFrEF (%)		p
	Mean	SD	Mean	SD	
Surface of the RA (cm ²)	21,48	14,88	21,73	5,38	0,074
Surface of the LA (cm ²)	24,41	9,91	28,38	6,38	0,010
LV mass index (g/m ²)	120,20	29,46	107,10	25,56	0,004
TDDL (mm)	48,50	7,83	63,47	8,12	<0,001
TSDL (mm)	31,89	8,09	54,36	7,85	<0,001
Valve leaflet retraction (%)	35,30	8,37	14,89	4,93	<0,001
Ejection fraction (Teicholz) (%)	63,93	9,33	27,65	7,19	<0,001
SPAP (mmHg)	44,13	19,01	53,69	17,89	0,010

RA: Right Atrium, LA: Left Atrium, LV: Left Ventricle, TDDL: Telediastolic Diameter Of The Left Ventricle, TSDL: Telesystolic Diameter Of The Left Ventricle, SPAP: Systolic Pulmonary Arterial Pressure.

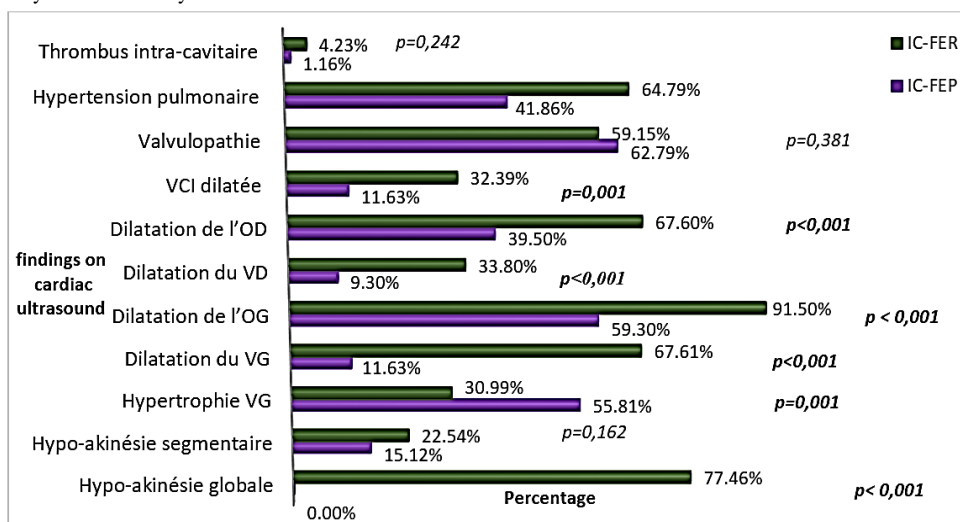


Figure 2: Echocardiographic findings in the two groups.

*VG : Left Ventricle, OG : Left Atrium, VD : Right Ventricle, OD : Right Atrium, VCI : Inferior Vena Cava.

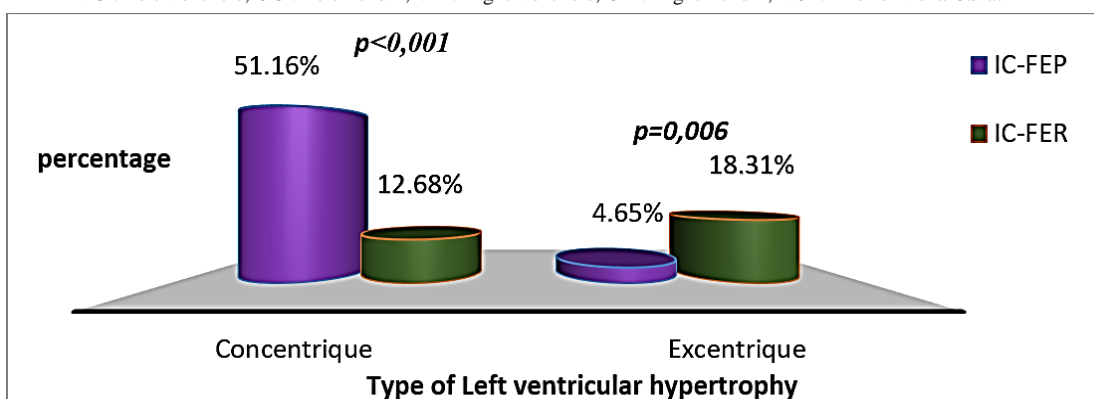


Figure 3: Distribution of patients according to the type of left ventricular hypertrophy.

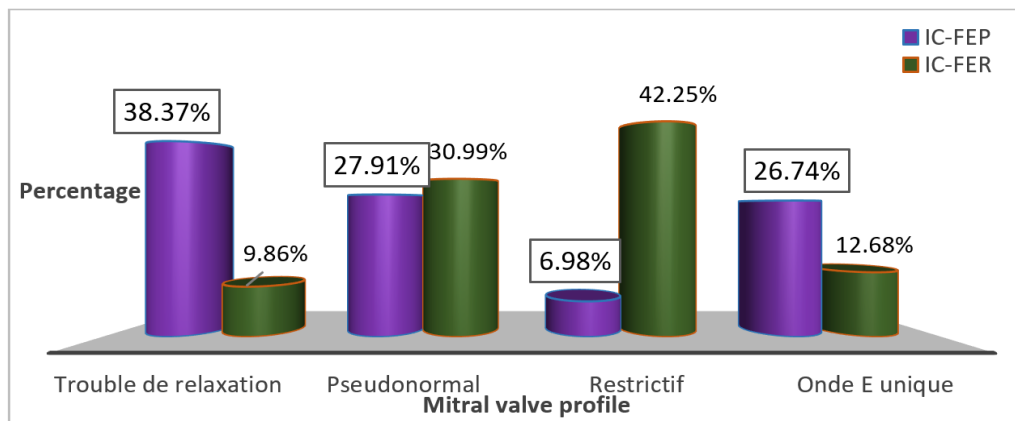


Figure 4: Distribution of patients according to the mitral valve profile.

Table 5: Radiologic findings.

Parameters	HFpEF(N*=40)	HFREF(N*=39)	p value
Cardiac Index (mean ± SD)	0,53±0,05	0,61±0,06	<0,001
Cardiomegaly (%)	31(77,50)	37(94,87)	0,026
Pulmonary congestion (%)	35(87,50)	34(87,18)	0,615
Pleural effusion (%)	7(17,50)	13(33,33)	0,118

N*= Number of patients with a chest X ray.

iii Radiologic Findings

Cardiomegaly was significantly more prevalent in patients with HFREF (p<0.001) (Table 5).

iv Laboratory Findings

There was no significant difference in haemoglobin level, estimated glomerular filtration rate (eGFR) and low-density lipoproteins (LDL) cholesterol between the two groups (Table 6). Anemia was more prevalent in patients with HFpEF and altered kidney function was found more in patients with HFREF, but these differences were not significant (Figure 5).

Table 6: Laboratory findings.

Parameters	HFpEF		HFREF		p value
	Mean	SD	Mean	SD	
Hb (g/l)	12,07	3,18	12,16	2,08	0,848
Blood urea nitrogen (g/l)	0,49	0,34	0,57	0,42	0,519
Serum creatinine (mg/l)	17,95	20,65	16,18	9,31	0,075
GFR (ml/min/1,73 m ²)	67,08	33,92	62,00	25,35	0,321
Total cholesterol (g/l)	1,77	0,50	1,67	0,54	0,495
triglycerides (g/l)	1,00	0,42	0,88	0,40	0,333
LDL cholesterol (g/l)	1,02	0,42	0,90	0,40	0,308
HDL cholesterol (g/l)	0,62	0,63	0,60	0,40	0,589

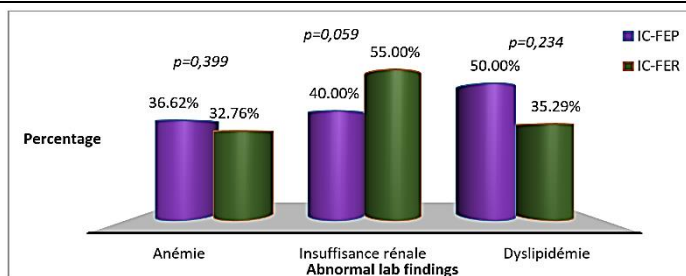


Figure 5: Prevalence of anemia, kidney injury and dyslipidemia in the two groups of patients.

III Treatment

Furosemide, spironolactone and digoxin were used more frequently in patients with HF_rEF ($p < 0.05$). Angiotensin Converting Enzyme

Inhibitors (ACEI), Angiotensin Receptor Blocker (ARB) and beta blockers were also used more frequently in patients with HF_rEF but the difference was not statistically significant (Figure 6).

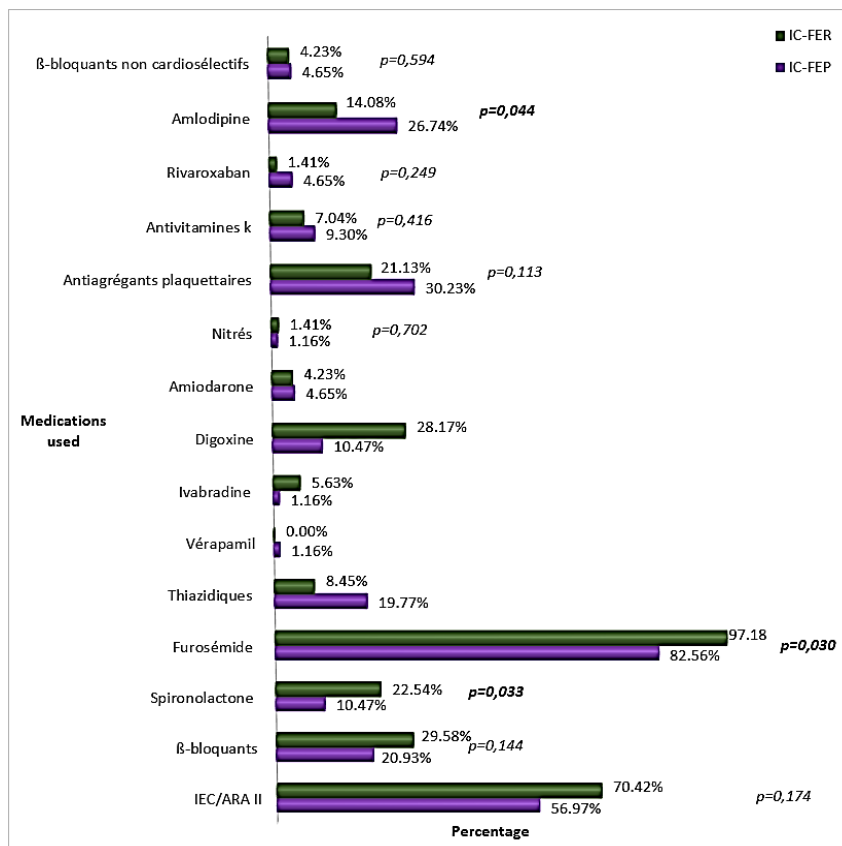


Figure 6: Medications used for treatment of heart failure in the two groups.

Discussion

The current multicenter study conducted in three major referral cardiology units of Cameroon aimed at comparing the clinical presentations, cardiovascular investigations/laboratory findings and treatment of HF_pEF and HF_rEF. We enrolled 201 patients with heart failure among which 45.5% had HF_pEF and 37.5% HF_rEF. Patients with HF_pEF were older and had a significantly higher incidence of hypertension and obesity. Patients with HF_rEF had more signs of fluid overload than those with HF_pEF. The S3 gallop was significantly more present in HF_rEF. Patients with HF_pEF had significantly higher rate of atrial fibrillation. Furosemide, spironolactone and digoxin were significantly more frequent in patients with HF_rEF.

The prevalence of HF_pEF (45.50%) in our study is comparable to those reported in Western countries which varies between 24 to 73% depending on the diagnostic criteria used for HF_pEF [6, 14-16]. This prevalence is largely above 10% found by Kingue *et al.* in 2005 in a hospital based study on 167 patients with heart failure in Yaounde, Cameroon and that of Mboup *et al.* in a hospital based study on 32 patients in Dakar, Senegal in 2013 [17, 18]. The differences observed are linked to the methodology used. We did a cross-sectional analytical study, including patients who were either in acute phase or those with chronic heart failure already on treatment; meanwhile, according to reports from France, the ejection fraction tends to increase after the

patient is discharged from the hospital and/or placed on treatment, hence, there is a possibility of overestimation of the prevalence of HF_pEF in the present study [19]. Also, approximately 80 million people had hypertension in sub-Saharan Africa in the year 2000, and this figure is expected to double by the year 2025 [20]. This implies that the prevalence of HF_pEF will also be on a rise since hypertension is one of the main determinants of this pathology [14, 21, 22].

Patients with HF_pEF were significantly older than patients with HF_rEF ($p = 0.003$). This finding is similar to what is described in developed countries where patients with HF_pEF tend to be older (69 to 78 years) compared to patients with HF_rEF (56 to 74 years) [6, 23, 24]. The patients in our study were older than patients in the study done by Mboup *et al.* in Dakar where the mean age was 65.7 years [18]. The number of female patients were higher in the group of HF_pEF, and our results confirmed the fact that more women have HF_pEF (42-85%) and more men have HF_rEF (20-65%) [3, 4, 16, 25, 26]. The fact that this difference was not statistically significant is probably due to a small sample size. Hypertension and obesity were significantly higher in patients with HF_pEF. Our results are similar to studies done in developing countries where hypertension and obesity were significantly more present in patients with HF_pEF [3, 4, 24, 25, 27, 28]. Type 2 diabetes mellitus, tobacco abuse and dyslipidemia were also more frequent in patients with HF_pEF but the difference was not statistically significant. These results are different from studies done in western countries in which these

factors were found to be more associated with HFrEF [4, 16, 24, 25, 28, 29].

Dyspnea was the major presenting complain in both group of patients but was more frequent in patients with HFrEF. Bhatia *et al.*, Maestre *et al.*, and Chinali *et al.* had similar results [4, 28, 30]. The dyspnea was of sudden onset mostly in patients with HFpEF, this can be explained by the mode of evolution of the disease which usually presents with “flash” pulmonary edema, in pauci or asymptomatic patients, due to a precipitating factor [31]. More than half of the patients in both groups were at stage IV of NYHA, but it is more frequent in patients with HFrEF. The fact that most patients were at stage IV illustrates the severity of heart failure in Africa as shown by studies done by Kingue *et al.* in 2005, where 53% of the patients were at stage III or IV [17]. Orthopnea was higher in patients with HFrEF ($p = 0,005$). Likewise, Chinali *et al.*, Bhatia *et al.* and Gupta *et al.* found a higher prevalence of orthopnea in patients with HFrEF but it was not statistically significant [4, 16, 28]. Mean systolic blood pressure was higher in HFpEF while heart rate was higher in patients with HFrEF. Similar findings were reported in studies from high-income countries [24-27, 29, 32].

Jugular venous distention, hepato-jugular reflux, hepatomegaly, and ascites were more frequent in patients with HFrEF. These results are similar to those found in Europe and the US [4, 25, 27, 30]. In several studies notably those of Bhatia *et al.*, Yancy *et al.*, Fanarow *et al.*, and Bishu *et al.*, the occurrence of ankle edema was significantly higher in patients with HFpEF; but in our study, it was not significantly higher in patients with HFrEF ($p = 0.468$) [4, 25, 27, 32]. The S3 galop was predominant in patients with HFrEF ($p = 0.033$) while the S4 galop was predominant in patients with HFpEF ($p = 0.376$). Bhatia *et al.* also had more S3 galop in patients with HFrEF but less S4 galop in patients with HFpEF [4]. Also, in studies done by Yancy *et al.*, Fanarow *et al.*, and Bishu *et al.*, pulmonary crackles were more frequent in patients with HFpEF; but in our study, it was more frequent in patients with HFrEF though not significant ($p = 0,298$) [25, 27, 32]. Arterial hypertension was the major cause of heart failure in both groups, but it was more implicated in the development of HFpEF [33]. Our study shows that hypertension remains the leading cause of heart failure in our milieu and confirms the major role it plays in the pathogenesis of HFpEF as described in the literature [4, 6, 31].

On ECG, atrial fibrillation was more prevalent in patients with HFpEF, while ventricular ectopic beats were more frequent in patients with HFrEF. Left bundle branch block was more frequent in patients with HFrEF and pathologic Q waves in patients in HFpEF, but these differences were not significant. Our results with the exception of the distribution of pathologic Q waves in the two groups are similar to those described in the literature; a study done by Maestre *et al.* found a higher prevalence of pathologic Q waves in patients with HFrEF. Indeed, Maestre *et al.* found in their studies that a left bundle branch block and a pathologic Q wave occurred respectively in 27.9% and 18.6% of patients with HFrEF against 13.7% and 6.3% HFpEF ($p = 0.037$ and 0.032 respectively) [30]. On cardiac ultrasound, concentric left ventricular hypertrophy was more frequent in patients with HFpEF, while eccentric left ventricular hypertrophy was significantly higher in patients with HFrEF. This pattern is similar to what is described in the pathophysiology of HFpEF and HFrEF, whose causes are hypertension and myocardial dysfunction respectively [21, 23, 34]. Cardiomegaly was found to be more prevalent in patients with HFrEF. The proportion of

pleural effusion was similar in both groups. Our data were similar to the classical findings described in the literature [31, 35].

The group of patients with HFpEF had a higher proportion of anaemia (36.62% vs. 32.72%, $p = 0,399$) while decreased kidney function was found in higher proportion in patients with HFrEF (40% vs. 55%, $p = 0,059$). Distribution of anemia in our study was similar to that observed by Maestre *et al.* and by Steinberg *et al.* [26, 30]. Ather *et al.*, in a cohort evaluating the effect of non-cardiovascular comorbidities on HFpEF and HFrEF, found a significantly higher proportion of anemia in patients with HFpEF [36]. The distribution of altered kidney function in our study was also similar to that found in other studies. Yancy *et al.* found a similar proportion of kidney injury in both groups (26% against 26%, $p = 0,98$), and Chinali *et al.* found a non-significant higher proportion in patients with HFrEF (60% vs. 64%, $p = 0,11$) [25, 28]. Furosemide, spironolactone and digoxin were mostly used in patients with HFrEF ($p < 0,05$); ACEI/ARB and beta blockers were also used more frequently in this group, but the difference was not statistically significant. Similar findings are reported in studies from developed countries [24-27, 29, 32]. Our small sample size might be the reason why there was no significant difference in the usage of ACEI/ARB and beta blockers between the two groups.

Conclusion

HFpEF is the most frequent form of heart failure in the hospital setting in Yaoundé. Patients with HFpEF were significantly older and more affected by hypertension and obesity than those with HFrEF. Cardiac ultrasound is indispensable to differentiate between the two entities for better management.

What is Already Known on This Topic

Heart failure with preserved ejection fraction (HFpEF) is the most frequent form of heart failure. A clear clinical picture has been described in developed countries. This entity concerned patients with several comorbidities like diabetes, obesity and hypertension. There is a challenge in management of these patients with not well-defined therapeutic measures apart symptomatic treatment and management of comorbidities.

What This Study Adds

In Sub Saharan Africa, clinical characteristics of the patients could be the same as abroad with a significantly predominance in older patient, hypertensive and obese. Treatment of these conditions is slightly different from those with HFrEF because in this group patients presented more with congestive heart failure and atrial fibrillation. Most studies are needed to compare outcomes of both groups in our context.

Competing Interests

None.

Author Contributions

Study conception, data collection, analysis and interpretation of the results: JB, AB, BH, CNN, LMK; Critical revision: MNT, DT;

Supervision of all steps: AM, SK. All authors approved the final version of the paper.

Acknowledgements

We acknowledge all participants who accepted to contribute to this study; also, the administrative authorities of all setting where we have recruited patients.

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