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Therapeutic Optimization in Acute Heart Failure with Reduced Ejection Fraction: Experience from the Strong HF Study Adapted to the Cameroonian Hospital Setting

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Abstract

Introduction: Nearly half of patients with acute heart failure (AHF) and reduced ejection fraction (HFrEF) are readmitted within 6 months [1]. Rapid therapeutic optimization is vital [2] [3], yet many patients never receive the doses recommended by clinical guidelines [4] [5]. Our study aimed to evaluate therapeutic optimization in patients hospitalized for a first episode of HFrEF in Yaoundé, using a model adapted from the STRONG-HF study. **Methods:** A prospective longitudinal study was conducted over 9 months (November 2024-August 2025) in three cardiology departments in Yaoundé. Clinical, echocardiographic, and therapeutic evaluations were performed at inclusion (M0, six weeks post-treatment initiation) and at three months (M3 ± 2 weeks). **Results:** Ninety-eight patients were included (mean age 64.5 ± 10.4 years; sex ratio 1.2). Hypertension and hypertensive cardiomyopathy were the predominant factors. At M0, the mean LVEF was 29.9 ± 6.2%. Four-pillar therapy (quadritherapy) was absent in 65.3% of patients, primarily due to undocumented reasons (59.7%) or hypotension (33.3%). The median delay for initiating full four-pillar therapy was 65 days. Its implementation at M0 was associated with age (45 - 55 years, p = 0.042) and health insurance coverage (p = 0.033). By M3, the mean LVEF increased to 34.1 ± 6.9%, and the proportion of patients on four-pillar therapy rose to 54.1%. LVEF improvement was significantly associated with a sequential initiation duration of < 42 days (p =

0.041) and its maintenance at M3 (OR = 2.6 [1.1 - 6.9], p = 0.041 and OR = 4.2 [1.7 - 11], p = 0.02, respectively). **Conclusion:** There is a significant delay and a lack of optimization in initiating four-pillar therapy in Yaoundé. Despite improvement during follow-up, practices remain below recommended standards, highlighting the need for dedicated heart failure centers.

Keywords

Heart Failure, Left Ventricular Ejection Fraction, Therapeutic Optimization, Yaounde

1. Introduction

Heart failure affects more than 64 million people worldwide, a prevalence representing nearly two-thirds of all cancers combined [6]. The five-year mortality rate for chronic heart failure is approximately 50%, with survival rates lower than those for major cancers such as colorectal, breast, or prostate cancer [7] [8]. It remains the leading cause of hospitalization globally [9]. Despite considerable advances in cardiology, readmission rates for heart failure have not improved since the 1980s [4] [9] [10]. Within 60 to 90 days post-discharge, 30% of heart failure patients are readmitted and 15% die [11]. Approximately half of all patients are readmitted within 6 months of their first hospitalization [1].

Consequently, the speed of treatment optimization is a vital factor for patients following acute heart failure (AHF) [2] [3]. Indeed, many heart failure patients never receive optimal therapeutic doses as recommended by clinical guidelines [4] [5]. This was the focus of the STRONG-HF trial (Safety, tolerability and efficacy of up-titration of guideline-directed medical therapies for acute heart failure), a prospective, multinational, randomized, open-label clinical study. It evaluated the safety and tolerability of rapid up-titration to optimal doses of recommended therapeutic classes in patients hospitalized for AHF [10]. In that study, patients were seen at discharge, at one week for the initiation of half-doses, and then between the second and sixth weeks for therapeutic optimization. The primary endpoint—HF readmission at 180 days or all-cause mortality—was assessed at three months. STRONG-HF results demonstrated good tolerability and a reduced risk of death or rehospitalization [10].

The four recommended therapeutic classes (four-pillar therapy) are: 1) Beta-blockers (BB), with Bisoprolol showing a significant 11.8% reduction in mortality [12]; 2) Angiotensin-converting enzyme inhibitors (ACEi)/Angiotensin receptor-neprilysin inhibitors (ARNI)/Angiotensin II receptor blockers (ARB); 3) Mineralocorticoid receptor antagonists (MRA), specifically Spironolactone at 25 mg/day, which demonstrated a 30% reduction in mortality in heart failure with reduced ejection fraction (HFrEF); and 4) Sodium-glucose cotransporter-2 inhibitors (SGLT2i).

Our study aimed to evaluate therapeutic optimization in HFrEF patients within

the Cameroonian hospital setting, specifically at six weeks and at three months post-discharge to reduce transportation and medical consultations fees for our patients.

2. Patients and Methods

We conducted a prospective longitudinal study over a 9-month period, from November 5, 2024, to August 5, 2025, in three cardiology departments in Yaoundé.

Patients were enrolled at their first post-hospitalization follow-up visit, which occurred approximately six weeks after initiation of heart failure therapy. This visit was defined as the baseline (M0) for the purposes of this study.

The left ventricular ejection fraction (LVEF) used as the baseline value for the primary endpoint was therefore the measurement obtained at this six-week (M0) visit, rather than at the time of initial hospitalization.

Patients were subsequently followed and reassessed at three months (M3 ± 2 weeks) after treatment initiation.

Inclusion criteria: Patients with a first episode of AHF and reduced LVEF (≤40%) confirmed by echocardiography; initiation of four-pillar HF therapy at least six weeks prior during the study period; and provided informed consent.

Exclusion criteria: Patients with preserved or mildly reduced LVEF (≥40%); pregnant or breastfeeding women; patients with end-stage renal disease or severe liver disease contraindicating treatment optimization; inability to obtain baseline LVEF or initial laboratory tests; and patients with uncorrected severe valvular heart disease. Patients who wished to withdraw or were lost to follow-up before three months were also excluded.

At the M0 visit (6 weeks post-initiation), data collected from medical records included: chief complaint at diagnosis, medical history, comorbidities, underlying heart disease, cardiovascular risk factors, and clinical exam data (NYHA class, hemodynamic and anthropometric parameters). ECG findings were recorded (heart rate, conduction or rhythm disorders, ST-segment changes). Laboratory data included sodium, potassium, and renal function (eGFR calculated via MDRD). Additionally, the status of four-pillar therapy (ACEi/ARB/ARNI, BB, MRA, SGLT2i) was reviewed, including initial doses, initiation mode (sequential titration vs. immediate quadruple therapy), and documented reasons for any therapy absence.

At M3 (± 2 weeks), the follow-up visit assessed clinical and echocardiographic evolution. This included hemodynamic parameters, functional status (NYHA), potential rehospitalizations for heart failure, treatment adherence, and current medication dosages. A transthoracic echocardiogram (TTE) was performed to measure LVEF.

Treatment adherence was assessed at the M3 visit based on patient self-report during the clinical interview. When available, this information was cross-checked with prescription records and medication use reported by the patient. Patients were considered adherent if they reported regular intake of their prescribed medications without interruption since the previous visit.

Echocardiography: All measurements were performed by a single operator to limit variability, in accordance with American Society of Echocardiography (ASE) guidelines. The biplane Simpson's method (Summation of Disks) was used in apical four-chamber and two-chamber views. LVEF was calculated using the formula: LVEF = [(EDV − ESV)/EDV]\100.

Endpoints: The primary endpoint was the change in LVEF between the six-week follow-up visit (M0, defined as baseline) and the three-month visit (M3).

Statistical Analysis: Statistical analysis was performed using SPSS version 26.0. Quantitative variables were expressed as mean ± standard deviation or median [IQR], and qualitative variables as frequencies and percentages.

Associations between variables and LVEF improvement were explored using univariate and bivariate analyses. Odds ratios (OR) with 95% confidence intervals (CI) were calculated.

Given the limited sample size and the number of outcome events, multivariable logistic regression was not performed in order to avoid model overfitting and unstable estimates.

3. Results

A total of 178 patients with suspected HFrEF were initially screened during the study period. Among them, 60 patients residing in remote rural areas were not included due to anticipated difficulties in follow-up.

Of the remaining 118 eligible patients, 20 were excluded: 12 due to missing baseline LVEF data and 8 due to failure to attend the M3 follow-up visit.

Finally, 98 patients were included in the analysis at baseline (M0). During follow-up, all included patients had available data for the primary endpoint (LVEF change between M0 and M3). Mortality during the study period was 11.2% (n = 11). The patient selection process is summarized in a flow diagram (Figure 1).

Although patients from rural areas were less likely to be included due to follow-up constraints, some were retained in the final cohort if they were able to attend scheduled visits, which explains the presence of rural residents in the analyzed population.

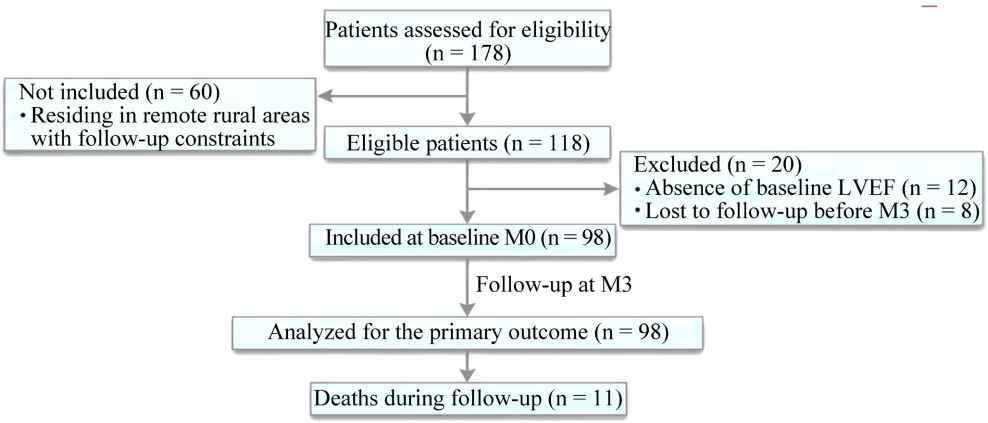


Figure 1. Flow diagram of patient selection and follow-up.

The mean age was 64.5 ± 10.4 years (range 27 - 86) with a sex ratio of 1.22. The majority lived in urban areas; over half had a monthly income exceeding 150 euros and lacked health insurance. Main cardiovascular risk factors were hypertension (54.1%), obesity (38.8%), and diabetes (33.7%).

Hypertensive cardiomyopathy was the most frequent etiology (39.8%). The primary symptom was exertional dyspnea (NYHA III: 59.4%; NYHA IV: 37.5%). Left heart failure signs predominated. The mean LVEF at inclusion was **29.9 ± 6.2%** (range 16% - 40%) (Table 1).

Table 1. Socio-demographic and clinical distribution of patients.

Variables	Population (N = 98)	Fréquence (%)
Sex		
Male	54	55.1
Female	44	44.9
Marital status		
Married	60	61.2
Widow	8	8.2
Widowed	30	30.6
Education level		
Primary	15	15.3
Secondary	26	26.6
Higher education	48	49
None	9	9.2
Monthly income		
<75 USD	4	4.1
[75 - 150 USD[	14	14.3
≥150 USD	46	46.9
None	34	34.7
Résidence		
Urban	61	62.2
Semi-urban	19	19.4
Rural	18	18.4
Health insurance		
Yes	16	16.3
No	82	83.7
Majors cardiovascular risk factors		
Hypertension	53	54.1
Diabetes	33	33.7
Smoking	5	5.1
Dyslipidemia	15	15.3
Sudden death in first degree relative	2	2

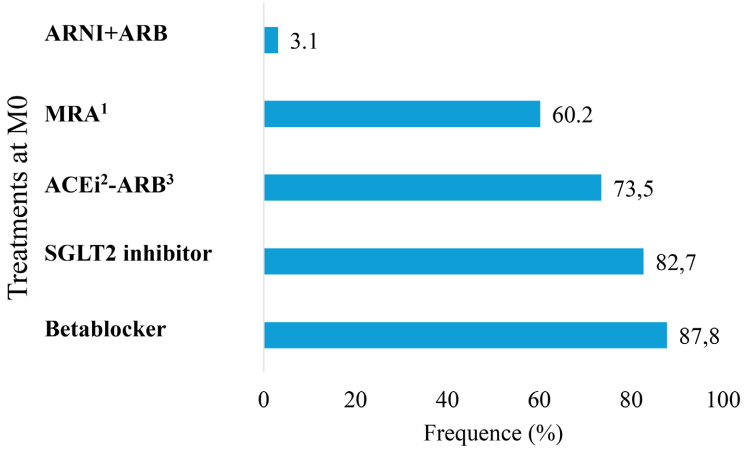
Continued

Other cardiovascular risk factors		
Chronic alcoholism	29	29.6
Obesity (BMI ≥ 30 kg/m²)	38	38.8
Stress	12	12.2
OSA[1]	2	2
NYHA[3] stage	96	98
Stage I	0	0
Stage II	3	3.1
Stage III	36	37.5
Stage IV	57	59.4
Chest pain	14	14.3
Exertional fatigue	88	89.8
Palpitations	9	9.2
Abdominal bloating	0	0
Left heart failure signs	86	87.8
Right heart failure signs	25	25.5

[1]OSA: Obstructive Sleep Apnea, [2]USD; US dollars, [3]NYHA: New York Heart Association.

3.1. Evaluation of Quadritherapy at M0 (Within Six Weeks Following Diagnosis)

At inclusion, 34.7% of patients were not receiving quadritherapy. The most frequently prescribed pharmacological treatment were beta-blockers (94.7%), followed by SGLT2 inhibitors (gliflozins) (83.7%), and ACE inhibitors (51%). Furthermore, a small proportion of patients were receiving the ARB + ARNI combination (3.1%) at M0 (Figure 2).



[1]**MRA:** Mineralocorticoid Receptor Antagonists, [2]**ACEi**: Angiotensin-Converting Enzyme inhibitors, [3]**ARB:** Angiotensin II Receptor Blockers.

Figure 2. Distribution of patients according to therapeutic molecules at M0.

Treatment was initiated in an outpatient setting for 77.6% of patients, compared to 22.4% during hospitalization following an episode of decompensation. Among patients receiving quadritherapy at M0, 12.2% were started on all four molecules simultaneously on the same day at low doses.

Medical reasons justifying the absence of four-pillar therapy at the time of diagnosis included arterial hypotension (33.9%), financial constraints (4.8%), and renal failure (1.6%). However, in 59.7% of medical records, the reason was undocumented. Consequently, these patients were receiving either triple therapy (54.7%), dual therapy (39.1%), or monotherapy (6.2%).

For patients not started on all four molecules immediately within the first six weeks, the mean delay between treatment initiation and complete quadritherapy was 65 days.

Regarding dosing at 6 weeks, doses were lower than the recommended target doses (Table 2).

Table 2. Drug Dosages at M0.

Variables	Median (IQR)	Min – Max
Betablocker	2.5 (1.25 - 5)	1.25 - 50
ACEi[1]	2.5 (2.5 - 5)	1.25 - 25
ARB[2]	40 (25 - 51)	12.5 - 200
ARNI+ARB	-	24 - 49.5
MRA[3]	25 (12.5 - 25)	12.5 - 50
SGLT2 inhibitor (Gliflozin)	10 (10 - 10)	10 - 10

[1]ACEi: Angiotensin-Converting Enzyme inhibitors, [2]ARB: Angiotensin II Receptor Blockers, [3]MRA: Mineralocorticoid Receptor Antagonists.

3.2. Evaluation of Quadritherapy at M3

At M3, 54.1% of patients were receiving quadritherapy, compared to 45.9% who were still not. A progression was observed, with 54.1% of patients on four-pillar therapy at M3 versus 34.7% at M0, representing an increase of 16.7% (Figure 3).

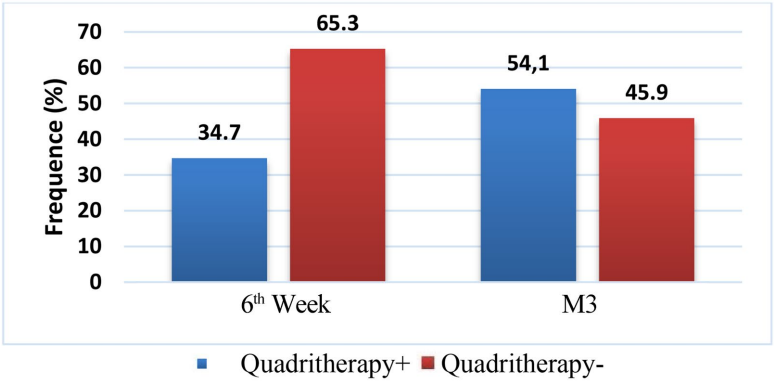


Figure 3. Comparison of quadritherapy at M0 and M3.

Reasons for the absence of four-pillar therapy at M3 included hypotension (33.3%), voluntary treatment discontinuation (6.7%), financial constraints (2.2%), and combined reasons (4.4%). In 53.3% of medical records, no reason was documented.

During the three-month follow-up, 36.5% of patients were hospitalized at least once for cardiac decompensation.

Analysis of LVEF evolution at three months showed that 16.3% of patients showed no improvement. Overall improvement was observed in 81.6% of patients compared to baseline LVEF. This improvement was greater than 5% in 87.4% of patients and greater than 10% in 64.4%. Thus, nearly two-thirds of patients presented an improvement of more than 10% of their LVEF (Figure 4).

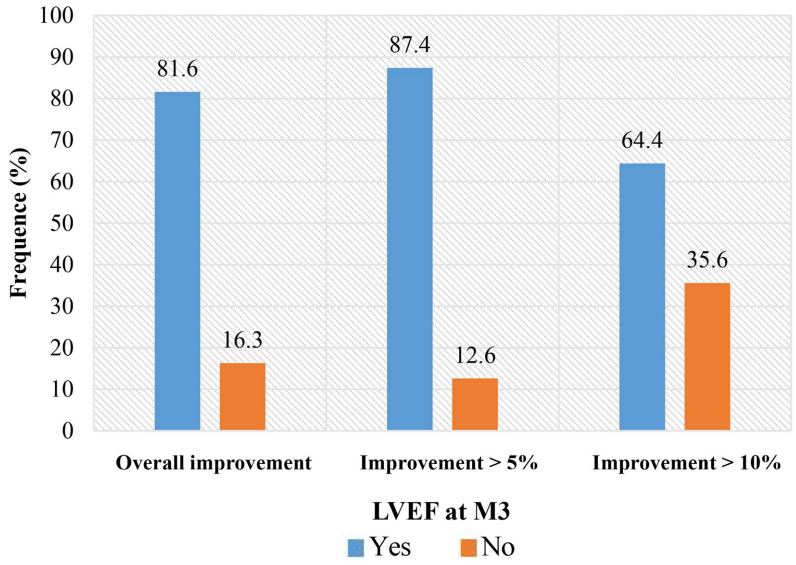


Figure 4. Distribution according to LVEF evolution at M3.

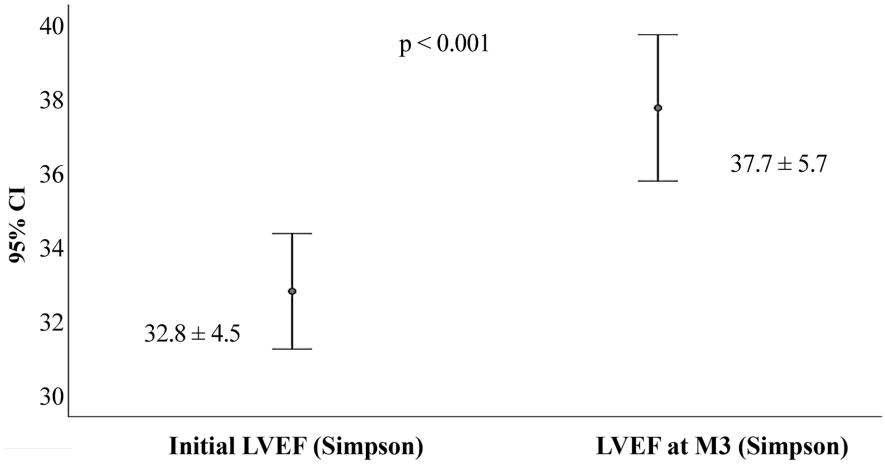


Figure 5. LVEF evolution in patients on quadritherapy at M3.

In patients who received four-pillar therapy within six weeks following diagno-

sis, the mean LVEF increased from 32.8 ± 4.55% to 37.7 ± 5.77% at M3. This improvement was statistically significant (p = 0.001), suggesting an association with early and complete initiation of recommended treatment (Figure 5).

Only variables significantly associated with LVEF improvement in bivariate analysis were reported. No multivariable model was constructed due to sample size limitations.

The initiation of immediate four-pillar therapy did not have a significant influence on LVEF improvement. However, LVEF improvement was significantly associated with a sequential four-pillar therapy initiation duration of less than 42 days, as well as the maintenance of four-pillar therapy at M3 (OR = 2.6 [1.1 - 6.9], p = 0.041 and OR = 4.2 [1.7 - 11], p = 0.02, respectively) (Table 3).

Table 3. Factors associated in bivariate analysis with LVEF improvement > 10% at M3.

Variables	LVEF at M3 improved > 10%		OR (95% CI)	P value
	Yes (%) N = 56	Non (%) N = 31		
Immediate quadritherapy				
Yes	8 (14.3)	3 (9.7)	1.5 (0.3 - 6.3)	0.739
No	48 (85.7)	28 (90.3)	-	-
Sequential quadritherapy < 42 jours				
Yes	27 (48.2)	8 (25.8)	2.6 (1.1 - 6.9)	**0.041**
No	29 (51.8)	23 (74.2)	-	-
Quadritherapy at M3				
Yes	41 (73.2)	12 (38.7)	4.2 (1.7 - 11)	**0.002**
No	15 (26.8)	19 (61.3)	-	-

Initiating four-pillar therapy within six weeks following diagnosis was associated with an improvement in NYHA functional class, although this relationship was not statistically significant (OR (95% CI) [1.9 (0.6 - 5.8)], p = 0.247).

Early initiation of four-pillar therapy was significantly associated with a lower risk of rehospitalization the study period (OR (95% CI) [4.1 (1.5 - 11.2)], p = 0.004).

The mortality rate was 11.2%.

4. Discussion

The mean age of our patients was 64.5 ± 10.4 years with a clear male predominance. These data align with those found by Dzudie *et al.* in 2016 in Douala, where the mean age was 64 ± 14 years [13], as well as findings by Kuate *et al.* in 2018 and Ouankou *et al.* in 2024, who reported mean ages of 66 ± 15 years and 64 ± 15 years, respectively [14] [15]. This result is also similar to that reported by Wissal *et al.* in 2021 in Tunisia (61 ± 11 years) [16]. Conversely, in European and North

American registries, the mean age is higher, around 70 years [17] [18]. This difference illustrates the epidemiological transition and the evolution of cardiovascular risk factors in our regions. Regarding male predominance, our study matches African registries where it is well-documented [19] [20]; however, some Western studies report a trend toward gender balance, linked to increased female longevity and the rising frequency of HFrEF in women [21].

Cardiovascular risk factors were dominated by hypertension (54.1%). Our results align with those of Wissal *et al.* in 2021 [15] and Allognon *et al.* in 2023, who found hypertension as a risk factor in 57% and 58% of HFrEF patients, respectively [22]. This observation is close to the THESUS-HF registry data, where hypertension was reported in 43% of cases [23]. Indeed, in Cameroon, hypertension remains a major public health problem; the higher proportion compared to some studies might be explained by our focus on HFrEF specifically [20] [24] [25].

Hypertensive cardiomyopathy was the most represented pre-existing condition (54.1%), followed by dilated cardiomyopathy (35.8%). Uncontrolled hypertension significantly increases the risk of developing heart failure. These results are consistent with Dzudie *et al.* in 2022 [12]. Ischemic etiology was the third most common baseline condition, unlike in industrialized countries where it predominates [26] [27]. A meta-analysis by Shahim *et al.* in 2023 confirmed that ischemic heart disease remains the major etiology of HFrEF in Europe [28].

Exertional dyspnea was the major clinical sign, confirming its cardinal role in NYHA functional classification. This expected result aligns with most international registries [19] [26] [27]. Mean LVEF was 29 ± 6.2%, indicating severe dysfunction. These values are close to those reported in pivotal trials like PARADIGM-HF (29%) and DAPA-HF [29] [30]. This highlights late diagnosis in our context, unlike in industrialized nations where screening programs allow for earlier management [31].

At inclusion, the proportion of patients on four-pillar therapy remained limited (34.7%). While this is an improvement over older African data (less than 15% in THESUS-HF), it remains below Western registries where nearly 60% of patients are initiated on four-pillar therapy immediately [32]. These findings confirm the real-world underutilization of evidence-based treatments [31] [33] [37]. Beta-blockers were the most prescribed (94.9%), consistent with Nganou *et al.* [34], likely due to their proven efficacy in HFrEF [35] [36]. SGLT2 inhibitors (gliflozins) were prescribed to 83.7% of patients, possibly due to their low hemodynamic impact. The EMPULSE trial demonstrated that early SGLT2i initiation is safe and offers rapid clinical benefit [33] [36]. Sacubitril/Valsartan was the least prescribed (3.1%) due to limited accessibility and high cost in regions without health insurance [13].

At the three-month reassessment, improvement was observed with 54.1% of patients on four-pillar therapy. This progression shows a positive trend toward therapeutic intensification but remains insufficient relative to current guidelines. Similar trends were seen in the QUALIFY registries, where intensification during

follow-up correlated with better prognosis [19] [37] [38].

We recorded 11 deaths (11.2%) and a 34.7% readmission rate. These data match Mfeukeu Kuate *et al.* in 2021, who reported an in-hospital mortality of 16.4% in Yaoundé [14]. Similarly, Owona *et al.* in 2020 found a 30.6% readmission rate, particularly in older patients with NYHA Stage IV dyspnea [39]. This high rate may be due to the lack of four-pillar therapy initiation, which reduces morbidity and mortality. HFrEF remains a frequent cause of hospitalization with high mortality linked to the severity of LVEF impairment [14].

The 2021 ESC guidelines recommend rapid, concomitant initiation of the four therapeutic classes, ideally within four weeks [33]. However, the average delay in our cohort was 65 days, reflecting significant therapeutic inertia, also due the financial issues in affording medical visits and prescription. This delay may limit the potential benefits suggested by trials such as DAPA-HF and EMPEROR-Reduced, where hospitalization risk reduction was significant within the first weeks of SGLT2i initiation [30] [40]. In PARADIGM-HF, early Sacubitril/Valsartan introduction reduced cardiovascular mortality by 20% [11]. Several factors explain this delay: limited availability of recent molecules (ARNI, SGLT2i) in resource-limited settings [13], high costs [13] [40], the lack of standardized protocols for rapid initiation, and medical inertia often linked to fear of side effects like hypotension or hyperkalemia [14]. These obstacles are not unique to our context; the QUALIFY study showed that even in high-income countries, less than 20% of patients reached target doses [38].

5. Conclusions

There is a significant delay and a lack of optimization in initiating four-pillar therapy among AHF patients with reduced ejection fraction in Yaoundé. Despite improvement during follow-up, practices remain below recommended standards, highlighting the need for dedicated heart failure centers. Furthermore, financial constraints necessitate advocacy for national medical coverage in our context.

Study Strengths

- Updated local data on HFrEF.
- Highlighting the gap between international guidelines and real-world practice.
- Three-month follow-up documenting therapeutic evolution in a representative cohort.

Study Limitations

- Absence of advanced echocardiographic measurements (Global Longitudinal Strain).
- Lack of biological data such as biomarkers (as used in STRONG-HF).
- Small sample size; a more representative sample would provide more actionable results. Financial difficulties were the primary limitation, emphasizing the need for ethical funding.
- The absence of multivariable analysis limits the ability to identify independ-

ent predictors of LVEF improvement. Observed associations should therefore be interpreted with caution.

- Treatment adherence was assessed using self-report, which may be subject to recall and social desirability bias.

Given the observational design of our study and the absence of a control group, the associations observed should not be interpreted as causal relationships.

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Conflicts of Interest

The authors declare no conflicts of interest.

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