Original Article

Survival rate and predictors of 36-month mortality in patients with heart failure in Sub Saharan Africa: insights from the Douala Heart Failure Registry (Do-HF)

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Background: Heart failure (HF) is a growing public health concern with a high mortality rate in sub-Saharan Africa. However, few studies have reported the long-term predictors of mortality in this region. This study sought to determine the 3-year mortality rate and the predictors of mortality amongst HF patients in Douala, Cameroon.

Methods: We conducted a prospective analysis on patients recruited in the Douala Heart Failure (Do-HF) registry, an ongoing prospective data collection on patients with HF at four cardiology units in Douala, Cameroon. Patients included were followed for 36 months from the index date of inclusion, with all-cause mortality as the primary outcome. Cox proportional hazard regression models were used to determine predictors of mortality.

Results: Out of the 347 participants included, 318 (91.6%) completed follow-up. The mean age was 64±14 years, 172 (49.6%) were men. Hypertensive cardiomyopathy and dilated cardiomyopathy were the most frequent causes of heart failure. The median follow-up was 33 months, and 150 (47.2%) patients died. Independent predictors of mortality included New York Heart Association functional class III & IV (aHR 2.23; 95% CI: 1.49–3.33; P<0.001), presence of pulmonary rales (aHR 1.87; 95% CI: 1.30–2.68; P=0.005), chronic kidney disease (aHR 2.92; 95% CI: 1.79–4.78; P<0.001), enrolment as inpatient (aHR1.96; 95% CI: 1.17–2.54; P=0.005), no formal education (aHR 2.06; 95% CI: 1.28–3.33; P=0.003), and a monthly income of at most three minimum wage (aHR 2.06; 95% CI: 1.28–3.33; P=0.003).

Conclusions: This study shows that almost half of HF patients die after 36 months of follow-up. Also, late presentation and poverty-related conditions were associated with poor outcomes. These findings suggest prioritizing preventive strategies that target early diagnosis and socioeconomic status to improve the prognosis of HF.

Keywords: Heart failure (HF); mortality; outcome; predictors; Sub Saharan Africa

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Introduction

Heart failure (HF) is a growing public health concern, especially in sub-Saharan Africa (SSA), where the burden is high due to the double effect of infectious and non-infectious causes (1,2). Non-infectious causes of HF are partly due to urbanization and the ongoing epidemiological transition, reflected in the rise (3) of several cardiovascular risk factors in this region (3). Despite the advances in HF management (4-6), SSA still presents the highest mortality rates compared to other regions (7).

Regional disparities are described regarding the etiology of heart HF. Ischemic causes are frequently reported in high-income countries, whereas non-ischemic etiologies are predominant in low to middle-income countries (7-9). In addition, HF patients in low to middle-income regions are a decade younger than in high-income countries (10). Albeit the burden of HF in SSA, few studies have reported long-term outcomes for these patients in this region.

Although the THESUS-HF was the largest cohort of HF patients in SSA, follow-up was achieved over six months (11). THESUS HF reported heart rate and patient location as significant predictors of patient outcome (11). The International Congestive Heart Failure Study (INTER-CHF) study remains one of the few extensive cohort studies providing data on long-term (one-year) follow-up and predictors of outcome in patients with HF in SSA (7). The INTER CHF reported chronic kidney disease, New York Heart Association stage of HF, and other factors as predictors of outcome(7).

The Douala Heart Failure (Do-HF) registry prospectively follows, providing local clinical features, treatments, and long-term outcomes for HF patients in a limited-resource setting. In this analysis, we described the 36-month mortality and associated factors. We present the following article in accordance with the STROBE reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-22-166/rc).

Methods

Study design and clinical setting

The Douala Heart Failure (DoHF) registry is a prospective, multicenter, observational data collection on HF patients since 2016 in 4 cardiology centers in Cameroon, Central Africa. We selected centers based on the availability of a cardiologist who can conduct echocardiography with experience in conducting cohort studies.

Eligibility criteria

Patients 21 years of age or older with clinical signs and symptoms consistent with congestive heart failure (i.e., pedal edema, elevated jugular venous pressure, pulmonary congestion, and tender hepatomegaly) and patients willing to be followed up for a minimum of 36 months were included. Informed consent was obtained from each subject enrolled in the study. Patients were excluded if they refused to give informed consent. We received ethical approval from the Cameroon National Ethical Committee of Research for Human Health before the commencement of the registry by participating institutions (No. 2017/12/959/CE/CNERSH/SP). The study conformed to the principles outlined in the Declaration of Helsinki (as revised in 2013).

Study procedure and data collection

Baseline data were collected from all study participants, including four telephone contacts for subsequent follow-up. Stratification as inpatient or outpatient was based on the participant's hospitalization status at the index date of inclusion. HF was diagnosed by an attending cardiologist per the European Society of Cardiology Guidelines. The study procedure has been described in detail elsewhere (12). Pulmonary hypertension (PH) was diagnosed by the attending cardiologist using echocardiography as a right ventricular systolic pressure >35 mmHg, in the absence of pulmonary stenosis and acute right heart failure (13)

We assessed patients at six-month intervals from the index date of inclusion into the registry. Participants were informed regularly via telephone two weeks before follow-up dates and were invited to their respective study centres for clinic-based follow-up. A telephone-based follow-up was conducted when a participant could not make it to their study centre. Participants were considered lost to follow-up after consecutive weeks of unsuccessful telephone contact

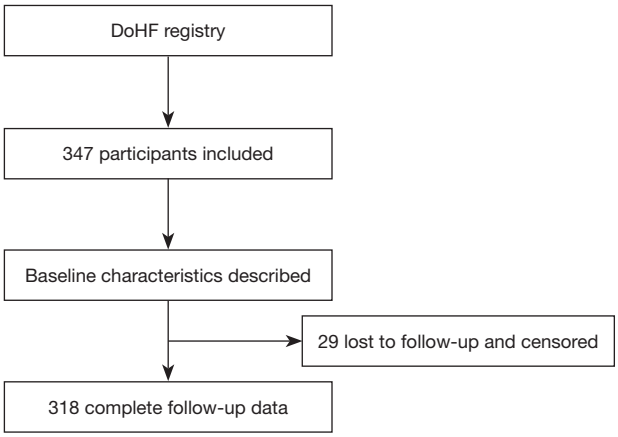

Figure 1 Flow chart of participant recruitment. DoHF, Douala Heart Failure.

with participants or their family members. End of study follow-up was conducted 36 months (±4 weeks) after their inclusion in the registry. All-cause mortality within the follow-up period was our outcome of interest.

Statistical analysis

R version 4.1.2 was used for analysis. Baseline characteristics were compared by New York Heart Association (NYHA) Functional Class. Categorical variables were presented as frequencies and percentages. In contrast, continuous variables were presented as mean and standard deviation as well as the median and interquartile range where necessary for non-missing data. Categorical variables were compared using the Chi-Square test, and continuous variables were compared using an independent *t*-test and Mann-Whitney U-test where applicable. Univariable and multivariable proportional Cox regression models were used to assess the predictors of HF outcomes for time-to-event analysis Participants considered lost to follow-up were included and censored in survival analysis. We selected variables for univariable analysis based on previous predictors described in the literature (7,14,15). Associations (P<0.1) from the bivariable analysis were included in the multivariable while adjusting for gender. Kaplan-Meier curves were used to compare survival in different patient subgroups, and participants considered lost to follow-up were included and censored in both Kaplan-Meier analysis and Cox models.

Results

There were 347 patients included at baseline, with a follow-up rate of 91.6% (*Figure 1*), and the median follow-up was 33 months. The mean age of participants was 64.08 (±14.02) years; 172 (49.6%) were males. Also, 184 participants presented with NYHA class III or IV at baseline, slightly older than those with NHYA class I or II.

More patients with NYHA III or IV were recruited as inpatients and reported a history of HF for at least two years. Signs of congestion (pulmonary rales and ankle edema) were frequent in patients with NYHA III or IV (*Table 1*). Baseline systolic and diastolic blood pressure were similar in the NYHA subgroups. The NYHA III or IV subgroup participants presented with higher heart rates at baseline.

Hypertension was the most common associated medical condition in patients with HF (65.1%), followed by diabetes mellitus (12.4%) and chronic kidney disease (10.7%), And there was no significant difference in distribution across NHYA classes.

The baseline left ventricular ejection fraction was slightly higher in NYHA I or II participants. Heart failure with reduced ejection fraction (HFrEF) was the most common type of HF (46.7%), and a higher proportion of participants with NYHA III or IV had HFrEF. Also, about half of the study participants presented with valve dysfunction, and pulmonary hypertension was reported in a third of the participants.

Hypertensive cardiomyopathy (46.1%) was the most frequent etiology of HF, followed by dilated cardiomyopathy (32.0%), valvular heart disease (9.5%), and ischemic heart disease (4.9%) (*Figure 2*). Other etiologies accounted for 2.3%.

Diuretics were the most prescribed HF medication at baseline (*Figure 3*). Furosemide (87.6%) was the most frequent diuretic in this cohort; few patients were on furosemide + thiazide diuretics (1.6%) or Bumetanide (1.6%). Digoxin was the least prescribed medication in our cohort of patients. More HF patients with reduced ejection fraction had mineralocorticoid receptor antagonists. In addition, a significantly higher proportion of patients with HFrEF had a combination of beta-blockers, renin-angiotensin system inhibitors, and mineralocorticoid receptor antagonists (*Figure 3*).

Table 1 Baseline clinical characteristics, laboratory and echocardiographic findings of the study population stratified by New York heart association categories

Variable	Overall, N=347	NYHA I/II, N=163	NYHA III/IV, N=184	P value
Socio-demographic and clinical characteristics				
Age (years)				0.004
Mean (SD)	64.1 (14.0)	61.6 (14.2)	66.3 (13.5)	
Gender				0.4
Male	172 (49.6%)	85 (52.1%)	87 (47.3%)	
Female	175 (50.4%)	78 (47.9%)	97 (52.7%)	
Level of education				0.11
None	64 (18.4%)	26 (16%)	38 (20.7%)	
Primary school	112 (32.3%)	46 (28.2%)	66 (35.9%)	
Secondary school	123 (35.4%)	63 (38.7%)	60 (32.6%)	
Post-secondary school	48 (13.8%)	28 (17.2%)	20 (10.9%)	
Health insurance				0.004
Not insured	328 (94.5%)	148 (90.8%)	180 (97.8%)	
Insured	19 (5.5%)	15 (9.2%)	4 (2.2%)	
Monthly income				0.14
≤3 minimum wage*	210 (60.5%)	92 (56.4%)	118 (64.1%)	
>3 minimum wage	137 (39.5%)	71 (43.6%)	66 (35.9%)	
HF past 2 years (yes)	102 (29.4%)	37 (22.7%)	65 (35.3%)	0.010
Patient location				<0.001
Outpatient	264 (76.1%)	144 (88.3%)	120 (65.2%)	
Inpatient	83 (23.9%)	19 (11.7%)	64 (34.8%)	
Tobacco	9 (2.6%)	5 (3.1%)	4 (2.2%)	0.7
Alcohol	112 (32.3%)	64 (39.3%)	48 (26.1%)	0.009
HIV	14 (4.0%)	6 (3.7%)	8 (4.3%)	0.8
History of hypertension	226 (65.1%)	106 (65.0%)	120 (65.2%)	>0.9
Diabetes mellitus	43 (12.4%)	17 (10.4%)	26 (14.1%)	0.3
Chronic kidney disease	37 (10.7%)	13 (8.0%)	24 (13.0%)	0.13
Hyperlipidemia	45 (13.0%)	26 (16.0%)	19 (10.3%)	0.12
Stroke	30 (8.6%)	14 (8.6%)	16 (8.7%)	>0.9
Chronic obstructive pulmonary disease	8 (2.3%)	2 (1.2%)	6 (3.3%)	0.3
Cancer	5 (1.4%)	1 (0.6%)	4 (2.2%)	0.4
Ankle edema	196 (56.5%)	62 (38.0%)	134 (72.8%)	<0.001
Pulmonary rales	134 (38.6%)	28 (17.2%)	106 (57.6%)	<0.001
Heart rate				<0.001
Mean (SD)	87.1 (23.7)	81.9 (21.9)	91.8 (24.4)	

Table 1 (*continued*)

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Variable	Overall, N=347	NYHA I/II, N=163	NYHA III/IV, N=184	P value
SBP (mmHg)				0.10
Mean (SD)	133.3 (30.5)	135.6 (29.2)	131.4 (31.6)	
DBP (mmHg)				0.5
Mean (SD)	82.4 (18.5)	82.4 (16.7)	82.5 (20.1)	
Body mass index, kg/m^2				0.2
Mean (SD)	26.8 (5.9)	27.2 (6.0)	26.5 (5.8)	
Laboratory measurements				
Potassium, mEq/L				0.7
Mean (SD)	4.2 (0.7)	4.1 (0.6)	4.2 (0.7)	
Sodium, mEq/L				0.6
Mean (SD)	137.5 (6.5)	137.8 (6.2)	137.3 (6.8)	
Creatinine, mg/dL				<0.001
Median (IQR)	1.2 (1.0, 1.6)	1.2 (1.0, 1.5)	1.4 (1.1, 1.8)	
Serum urea, mg/dL				0.015
Median (IQR)	34.0 (25.0, 54.0)	30.0 (24.2, 40.9)	39.0 (25.5, 59.1)	
eGFR, mL/min/1.73 m^2				<0.001
Mean (SD)	62.0 (25.2)	69.2 (24.0)	56.4 (24.8)	
Glucose, mg/dL				0.7
Mean (SD)	105.0 (41.3)	102.3 (35.7)	107.5 (45.8)	
NT-proBNP, ng/L				0.052
Median (IQR)	1,233.5 (832.8, 2,501.2)	1,400.0 (1,196.0, 2,873.0)	971.0 (537.0, 2,190.9)	
Hemoglobin g/dL				0.013
Mean (SD)	11.6 (2.0)	11.9 (1.9)	11.3 (2.1)	
White blood cells, ×10^9/L				0.3
Median (IQR)	5.4 (4.5, 8.0)	5.2 (4.4, 7.0)	5.7 (4.6, 8.0)	
Echocardiographic measurements				
Left ventricular ejection fraction in %				<0.001
Mean (SD)	41.6 (16.6)	45.5 (16.3)	38.1 (16.1)	
Heart failure categories				<0.001
HFpEF	105 (30.3%)	61 (37.4%)	44 (23.9%)	
HFmrEF	80 (23.1%)	51 (31.3%)	29 (15.8%)	
HFrEF	162 (46.7%)	51 (31.3%)	111 (60.3%)	
Right ventricular systolic pressure >35 mmHg	119 (34.3%)	38 (23.3%)	81 (44.0%)	<0.001
Valve dysfunction echo	171 (49.3%)	73 (44.8%)	98 (53.3%)	0.12
Diastolic dysfunction	156 (57.1%)	57 (45.6%)	99 (66.9%)	<0.001

*, Current minimum wage at the time of the research was 57.93 USD. NYHA, New York Heart Association; SD, standard deviation; HIV, human immunodeficiency virus; HF, heart failure; HFmrEF, HF with mildly reduced ejection fraction; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction; IQR, interquartile range; SBP, systolic blood pressure; DBP, diastolic blood pressure.

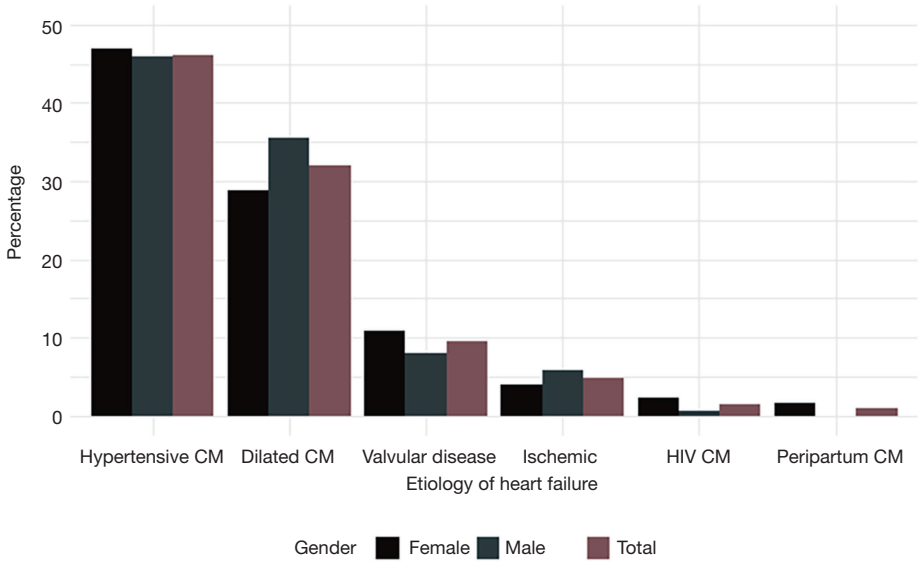

Figure 2 Distribution of cause of heart failure by gender. CM, cardiomyopathy; HIV, human immunodeficiency virus.

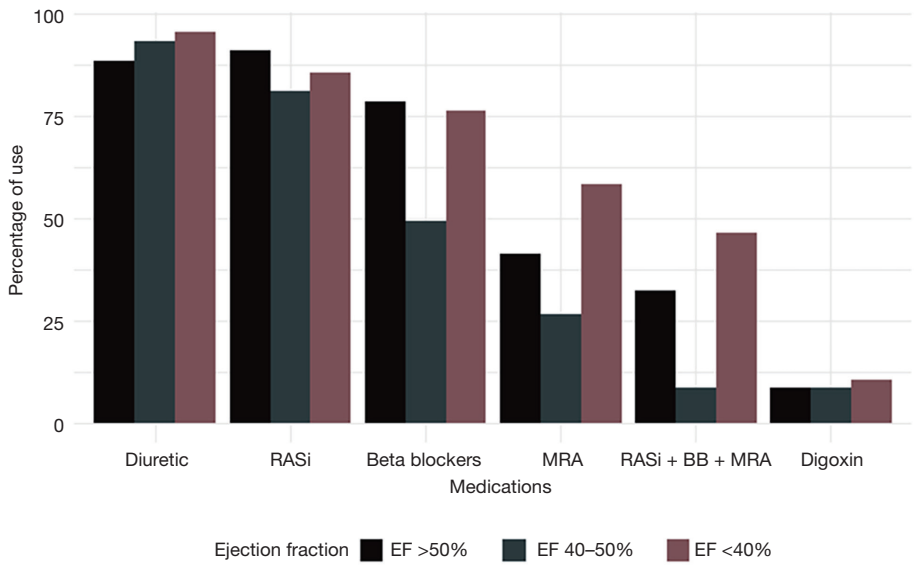

Figure 3 Distribution of medication use by ejection fraction class. RASi, renin-angiotensin system inhibitors; MRA, mineralocorticoid receptor antagonist; BB, beta-blockers.

Predictors of mortality

The median follow-up period was 33 months (IQR: 12–33), of which 318 (91.6%) participants-completed follow-up. Overall, 150 (47.1%) participants died. Age and gender-adjusted KM curves showed no significant difference in mortality across ejection fraction categories (log-rank P=0.24) (*Figure 4*). Participants with New York heart association stage III or IV were more likely to die (log-rank P<0.001), as demonstrated in *Figure 5*.

Table 2 presents the crude hazards from the bivariable analysis. There was an increased mortality rate (adjusted HR =1.93, 95% CI: 1.21–3.07) in participants with no formal education than those with at least primary education. Low monthly income (three or less standard minimum

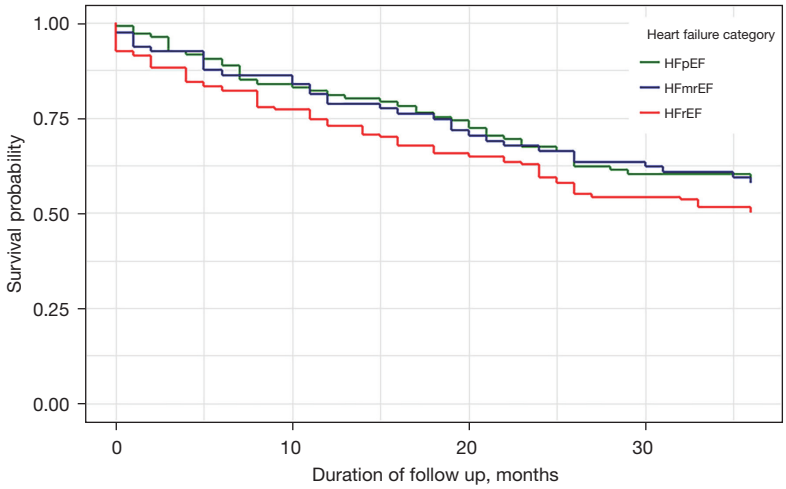

Figure 4 Age and sex adjusted survival curves by European Society of Cardiology HF class. HFpEF, heart failure with preserved ejection fraction; HFmrEF, heart failure with mildly reduced ejection fraction; HFrEF, heart failure with reduced ejection fraction.

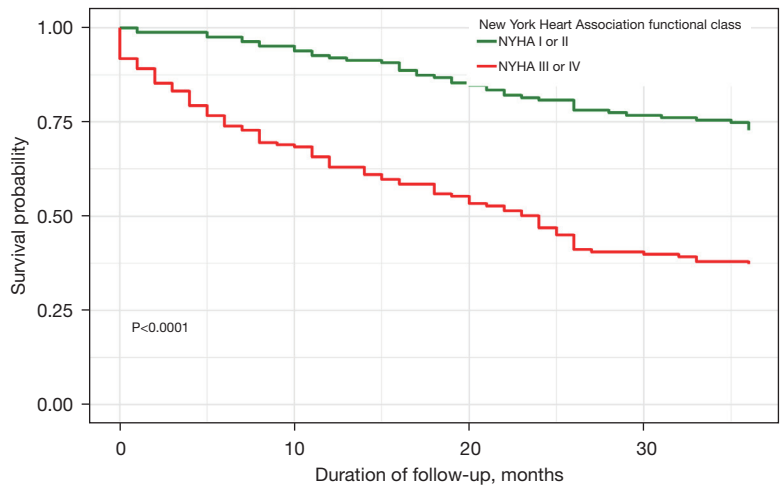

Figure 5 New York heart association and heart failure mortality.

national wages) increased the mortality rate (adjusted HR =2.54, 95% CI: 2.68–3.85).

The mortality rate was significantly higher (adjusted HR =1.48, 95% CI: 1.05–2.10) in participants with a history of at least two years of HF. A similar effect was observed in participants recruited as an inpatient (adjusted HR =1.89, 95% CI: 1.29–1.77). There was a 179% increase in the mortality rate for participants with reported chronic kidney disease (adjusted HR =2.79, 95% CI: 1.71–4.53).

Compared to the absence of pulmonary rales at baseline, the presence of pulmonary rales was associated with a significantly higher mortality rate (adjusted HR =1.85, 95% CI: 1.30–2.64). Also, NYHA HF stage III or IV was significantly associated with an increased mortality rate (adjusted HR =2.22, 95% CI: 1.49–3.30).

Discussion

Heart failure is a significant challenge in SSA and has the highest reported mortality compared to other regions. To our knowledge, predictors of all-cause long-term mortality in HF patients in our setting were yet to be explored, and our data reveals some unique characteristics of HF. These findings will guide clinicians in making better decisions to

Table 2 Predictors of mortality

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	aHR[@] (95% CI)	P value
Demographic and income				
Age[$]	1.19 (1.05–1.35)	0.005	1.11 (0.96–1.29)	0.15
Gender (male)	0.96 (0.70–1.33)	0.82		
Health insurance(insured)	0.90 (0.63–1.27)	0.55		
Minimum monthly wage (≤3 minimum wage)	1.93 (1.35–2.78)	<0.001	2.53 (1.67–3.85)	<0.001
Level of education (no formal education)	1.62 (1.12–2.36)	0.01	1.93 (1.21–3.07)	0.006
Patient location(inpatient)	2.28 (1.62–3.21)	<0.001	1.89 (1.29–2.78)	0.001
History				
Hx of hypertension	1.02 (0.73–1.43)	0.90		
Hx of cancer	0.56 (0.11–4.01)	0.56		
Hx of COPD	0.77 (0.25–2.43)	0.59		
Hx of HIV	0.78 (0.32–1.91)	0.59		
Hx of smoking	0.84 (0.31–2.27)	0.73		
Hyperlipidemia	0.81 (0.48–1.37)	0.43		
HF in past 2 years (yes)	1.76 (1.27–2.46)	<0.001	1.48 (1.05–2.09)	0.03
Hx of valvular heart disease	1.37 (0.84–2.24)	0.21		
Hx of diabetes mellitus	1.47 (0.93–2.31)	0.09	1.25 (0.74–2.08)	0.40
CKD (yes)	2.52 (1.64–3.87)	<0.001	2.79 (1.71–4.53)	<0.001
Clinical presentation and echography parameters				
Rales (yes)	2.51 (1.82–3.47)	<0.001	1.85 (1.30–2.64)	<0.001
NYHA stage III or IV	3.39 (2.37–4.86)	<0.001	2.22 (1.49–3.30)	<0.001
Heart rate (10-unit increase)	1.10 (1.03–1.17)	0.004	1.03 (0.93–1.10)	0.48
Ejection fraction[£] %	0.95 (0.91–1.01)	0.06	0.98 (0.93–1.04)	0.46
Pulmonary hypertension[+]	1.52 (1.10–2.11)	0.009	0.98 (0.67–1.38)	0.80
Valvular dysfunction on echo	1.39 (1.01–1.92)	0.04	1.07 (0.75–1.52)	0.72
Diastolic dysfunction	1.31 (0.91–1.93)	0.14		
Baseline medications				
Mineralocorticoid receptor antagonist	0.99 (0.71–1.36)	0.89		
Beta blockers	1.13 (0.78–1.58)	0.46		
RAASi	0.62 (0.42–93)	0.02	0.84 (0.54–1.30)	0.44

[£], 5 unit increase of ejection fraction; [$], hazards ratio per 10-year increase; [+], pulmonary hypertension on transthoracic cardiac echo; [@], adjusted for gender. Hx, history; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; HF, heart failure; CKD, chronic kidney disease; NYHA, New York Heart Association; RAASi, Renin angiotensin aldosterone system inhibitors.

improve patient outcomes.

The mean age of the study participants was 64.08 (SD 14.02) years, a decade older than patients from African HF cohort studies conducted a decade ago (7,16) Although this might reflect the aging of our HF population, the young age of HF patients in Africa remains a striking feature compared with industrialized countries where HF is a disease of the elderly, with a mean age of around 70 years (17).

Diuretics are recommended by several cardiology clinical society guidelines in HF patients, especially in patients with HFrEF, to alleviate congestive symptoms (18,19). The majority of the participants in this cohort were on diuretics (loop or thiazide). Four standard drug therapies such as angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor/neprilysin inhibitors (ARNIs; sacubitril/valsartan), beta-blockers, mineralocorticoid receptor antagonists (MRAs), and SGLT2 inhibitors are now well established to provide incremental benefit in patients with HF, with a marked reduction in mortality and all-cause hospitalizations (20). Due to unavailability and cost concerns, our patients could only access ACE inhibitors, beta-blockers, and MRAs, and less than 50% of those with HFrEF could access the all 3. In addition, none received interventional or device therapies for personalized treatment of HF, confirming that there is still be a door for improvement of prognosis of our patients using modern therapies as per clinical practice guidelines (18).

The three-year survival probability in this study was 53%. Not many studies have reported HF mortality rate after 36 months of follow-up. Giosofat *et al.* reported a decreased rate of 3-year mortality across different quintiles of periods from 2001 to 2018 (30% Q1 down to 17% Q5) (21). This very high mortality rate compared to those from high-income settings can be attributed to several reasons, including (I) the high and rising burden of uncontrolled cardiovascular risk factors in low-income settings (22), (II) the limited access to effective medications and interventions for cardiovascular diseases (23) and finally the late presentation of our patients.

The etiology of HF in SSA is paralleled by infectious and non-infectious pathologies (7,11,24). The most common cause of HF was hypertensive cardiomyopathy, a similar finding reported in other SSA HF cohorts (11,25-27). Ischemic heart disease contributed only 5% of the etiologies of HF in this study. However, this might have been underestimated due to the limited availability and accessibility to cardiac catheterization in our setting. This prevalence is expected to increase due to the ongoing epidemiological transition causing an increase in cardiovascular risk factors prevalence and the inadequacy of diagnostic facilities in this region (28,29).

This study revealed pulmonary congestion and chronic renal disease predictors of poor patient outcomes. These findings are consistent with INTER CHF and THESUS-HF studies (7,14). Also, patients with signs of congestion with or without renal dysfunction had increased all-cause mortality, similar to the findings of Metra *et al.* and Wattad *et al.* (30,31). Furthermore, patients with a higher NYHA stage of HF (III or IV) had a significantly increased risk of all-cause mortality within a year of follow-up, consistent with findings in previous studies (7,15,32). Frequent HF hospitalizations predict mortality in HF patients (7,33). Hospitalized patients showed increased hazards of mortality.

Several studies have reported low socioeconomic status as a predictor of adverse cardiovascular outcomes (34,35) In this study, no formal education and monthly income less than or equal to 3 national minimum wage (minimum wage in Cameroon at the time of recruitment of participants was 58 US dollars) were independent predictors of poor outcome.

This study, however, had some limitations. Firstly, participants were recruited from specialized cardiology units, impacting the extrapolation of results to the general HF population. Secondly, biological parameters like NT-pro-BNP plasma levels were available only in a subset of patients, which might have precluded an accurate assessment of the predictive role of plasma levels of BNP as described elsewhere (36,37). Our strengths include being one of the first studies that assessed the long-term outcome of HF in SSA patients and with a low rate of loss to follow-up.

Conclusions

This study showed that almost half of HF patients in our setting die after 36 months of follow-up. This high mortality was driven by factors such as late presentation and poverty-related conditions. Preventive strategies that target early diagnosis and socioeconomic status must be prioritized to improve the prognosis of HF patients in our SSA.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://cdt.amegroups.com/article/view/10.21037/cdt-22-166/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-22-166/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Written informed consent was obtained from each subject enrolled in the study. Patients were excluded if they refused to give informed consent. Ethical approval was obtained from the Cameroon National Ethics Committee before the commencement of the registry by participating institutions (No. 2017/12/959/CE/CNERSH/SP), and the study conformed to the principles outlined in the Declaration of Helsinki (as revised in 2013).

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