Heart failure in a semi-urban setting in Cameroon: clinical characteristics, etiologies, treatment and outcome

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Background: Heart failure (HF) is a major cause of morbidity and mortality in sub-Saharan Africa. There is limited contemporary data on HF in rural and semi-urban settings in Cameroon in this era of epidemiological transition. We aimed at determining the demographic and clinical characteristics, etiologies treatment and outcome of patients admitted for HF in the Buea Regional Hospital.

Methods: We analyzed data from consecutive adult patients admitted for HF to the medical unit of the Buea regional Hospital between June 2016 and November 2017.

Results: Of the eighty-six consecutive patients admitted for heart failure, 48 (55.5%) were females. Their mean age was 59.4±18.3 years. Hypertension, diabetes mellitus and chronic kidney disease were present in 53.4%, 14% and 5.8% of patients respectively. Etiologies of heart failure were hypertensive heart disease (47.7%), Cor pulmonale (11.6%), dilated cardiomyopathy (9.3%), ischemic heart disease (9.3%), and rheumatic heart disease (5.8%). At discharge, treatment included; loop diuretics (97.9%), angiotensin converting enzyme inhibitors (70.9%), beta blockers (36.9%), and aldosterone antagonist (50.6%). The median length of hospital stay was 7 days, and in hospital case fatality was 12.8%.

Conclusions: As reported in other parts of Sub-Saharan Africa, heart failure in this semi-urban Cameroonian population occurs at a younger age, with hypertensive heart disease being the most common cause and associated high in-hospital mortality.

Keywords: Heart failure; semi-urban; Cameroon; Sub-Saharan Africa

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Introduction

Cardiovascular disease is a major health problem both in developed and developing countries. Heart failure is a major growing public health concern worldwide. It affects 1–2% of the general population in developed countries (1,2). In Sub-Saharan Africa, the prevalence of heart failure is increasing as a result of the epidemiological transition with an increase in the prevalence of cardiovascular disease risk factors such as hypertension and diabetes (3). It accounts for 9.4–42.5% of all medical admissions in Africa (4). Patients with heart failure in Sub-Saharan Africa tend to be younger compared to other regions of the world, with most cases occurring around the 5th and 6th decade (5). The etiologies of heart failure vary among world regions and within the

same country. In developed countries, ischemic heart disease stands out as the commonest cause of heart failure (6,7). On the contrary, in Sub-Saharan Africa, heart failure is fuelled by hypertension, cardiomyopathies and valvular heart diseases with ischemic heart disease being less frequent (8-10). A multinational study of heart failure in Sub-Saharan Africa (THESUS-HF) indicated the significant contribution of hypertension (10).

There have been significant advances in the treatment of heart failure in recent decades with disease modifying medications. Despite this improvement in treatment, heart failure remains a main cause of hospitalization, and is associated with significant morbidity and mortality (11).

Heart failure remains largely unexplored in Sub-Saharan Africa. Even though heart failure is common, there is limited contemporary data on their clinical presentation, characteristics, and in hospital outcome in Cameroon with the few studies conducted limited to the two main cities of the country. The aim of this study was to determine the contemporary clinical characteristics, etiologies, treatment, and outcome of patients admitted for heart failure in the Buea Regional Hospital, Cameroon, a semi-urban setting in the South West Region of Cameroon.

Methods

Study design and setting

Between June 2016 and November 2017, we carried out this cross-sectional descriptive and analytic study in the Buea Regional Hospital. This is a secondary level Hospital and serves as one of the two main referral centers in the region, with a bed capacity of 111 beds, and a catchment population of about 200,000 inhabitants. The Hospital also serves as one of the teaching hospitals of the University of Buea. There are 26 doctors including a cardiologist (CN). Facilities for cardiac evaluation at the center include; chest radiography, 12-lead electrocardiograph, and echocardiography. Buea is the capital of the South West region of Cameroon, a semi-urban setting on the slopes of mount Cameroon.

Study population

All eligible patients were consecutively recruited into the study after obtaining oral informed consent. Males and females ≥ 18 years of age, admitted to the medical unit of the hospital between June 2016 and November 2017 with

the admission diagnosis of heart failure (both *de novo* and pre-established diagnosis of heart failure) were included in the study.

Data collection

Data from each subject were obtained using a uniform and standardized data collection form. Detailed clinical documentation of newly diagnosed or newly presenting cases or pre-existing cases of HF was carried out. The following data were captured: demographic data, date of diagnosis of HF, and pre-admission history (previous HF-related admissions). Others included New York Heart Association (NYHA) functional class, symptoms, signs, self-reported cardiovascular risk factors, etiology of HF, co-morbidities, blood investigations (hemoglobin, serum creatinine, blood ionogram including serum sodium and potassium, and glycemia), 12-lead ECG, echocardiography, medications, and length of hospital stay and in hospital mortality.

Heart failure was defined according to the Framingham criteria and the European Society of Cardiology (ESC) guideline on the diagnosis and treatment of acute and chronic heart failure (2,12).

Echocardiography was performed with Sonoscape S8 (Sonoscape, China). Two-dimensionally guided M-mode measurements were made according to the recommendations of the American Society of Echocardiography (13). One cardiologist (CN) performed all echocardiographic studies. The etiology of heart failure was based on information obtained from the history, physical examination and echocardiography.

The primary outcome variable was in-hospital death, and the secondary outcomes were a hospital stay >7 days, or the composite of death and or prolonged hospital stay.

The study was approved by the administrative authorities of the Buea regional hospital. We carried out this work in accordance with the declarations of Helsinki. We report this work following the STROBE checklist.

Sample size and statistical analysis

This is the first prospective study of heart failure admissions in a semi-urban setting in Cameroon. A convenient sample of all eligible patients seen during the study period was considered for this study. We analyzed the data with the software Epi Info version 7. We have presented discrete

variables as counts and percentages, and continuous variables as means \pm standard deviation (SD) according to sex. We compared the proportions using Chi squared test or Fischer exact test where appropriate. We have compared mean values using student *t*-test or ANOVA where appropriate. We used univariate and multivariate logistic regression models to identify determinants of the primary and secondary outcomes while adjusting for age, sex, LVEF and use of ACE inhibitors or Spironolactone to look for the determinants of the primary and secondary outcomes. We considered a P value <0.05 to be statistically significant for the observed differences or associations.

Results

Of the 2,201 patients admitted during the study period, 86 (3.9%, 95% CI: 3.1–4.8) had heart failure. Forty-eight (55.5%, 95% CI: 44.7–66.5) of these patients were females. Their mean age was 59.4 ± 18.3 years. There was no significant age difference between men and women (60.9±18.3 vs. 58.2 ± 18.5 , P=0.49). *Table 1* shows the general characteristics of the study population.

Table 2 shows the ECG findings. Sinus tachycardia was present in 30.2% (95% CI: 20.8–41.1) of the patients, 11.6% (95% CI: 5.7–20.3) had atrial fibrillation, and 45.3% (95% CI: 34.6–56.5) had left ventricular hypertrophy on ECG. Table 3 shows the echocardiographic characteristics. The overall mean LVEF was $39.4\% \pm 19.3\%$. Men had a significantly lower LVEF compared to women (P=0.022). About 40.7% (95% CI: 30.2–51.8) patients had a LVEF that was less than 30%. Eccentric left ventricular hypertrophy was more common in women (P=0.048).

Table 4 shows the etiologies of heart failure. Hypertensive heart disease was the most common etiological cause of heart failure responsible for 47.7% (95% CI: 36.8–58.7) of cases. Cor pulmonale (11.6%, 95% CI: 5.7–20.3), dilated cardiomyopathy (9.3%, 95% CI: 4.1–17.5), ischemic heart disease (9.3%, 95% CI: 5.1–17.5), rheumatic heart disease (5.8%, 95% CI: 1.9–13), pericardial disease (2.3%, 95% CI: 0.3–8.1), and HIV cardiomyopathy (2.3%, 95% CI: 0.3–8.1) were less common causes. Other causes of heart failure included peripartum cardiomyopathy (2.3%, 95% CI: 0.3–8.1). Among patients with a valvular etiology, mitral regurgitation was the most common valvular lesion (*Table 5*).

At discharge 97.9% (95% CI: 91.9–99.7) of the patients received loop diuretics, 70.9% (95% CI: 60.1–80.2) received angiotensin converting enzyme inhibitors, 36.9% (95% CI: 27–48.3) received beta blockers, and 50.6% (95%

CI: 40.1–62.1) received an aldosterone antagonist. No patient received digoxin.

The mean length of hospital stay was 8.1 ± 4.2 days (range, 2 to 21 days; median 7 days). Eleven patients died. In hospital case fatality was 12.8% (95% CI: 6.6–21.7). On logistic regression analysis, predictors of in-hospital mortality were a low mean blood pressure and tachycardia. Male sex appeared to be associated with a composite of death and long hospital-stay.

Discussion

This is the first, detailed and contemporary study of heart failure in the South West region of Cameroon. Our results showed that heart failure represented 3.9% of all admissions in the medical unit. It predominantly affected young and middle-aged individuals in the prime of the life. Women were affected more than men. More than two third of the patients presented with severe disease. Hypertensive heart disease was the most important cause of heart failure. The use of disease modifying drugs was sub-optimal. In-hospital mortality was relatively high (12.8%).

Heart failure is a major public health problem in SSA. This is as result of the epidemiological transition SSA is going through with an increase in the prevalence of noncommunicable diseases like hypertension and diabetes (3). The incidence and prevalence of heart failure increases with advancing age (12). The prevalence of heart failure in developed countries is about 1-2% in the general population (14). In SSA the rate of heart failure admission in medical wards varies from one place to another and has been reported to range from 9.4% to 42.5% as shown in a recent systematic review and meta-analysis (4). In our study, the proportion of heart failure among medical admissions was lower than that reported in this systematic review (3.9%). One of the reasons that could explain this lower rate of heart failure admission is the fact that the study was carried out in a general medical ward where we have a high admission rate for HIV infection related opportunistic infections and other noncardiac related conditions. The mean age of heart failure in developed countries is around the 7th decade (15). Compared to developed countries, heart failure in SSA occurs at a much younger age, affecting individuals in the prime of their life who make up the economically active proportion of the population (4). In Sub-Saharan Africa, heart failure occurs most frequently in the 5th and 6th decades (5). The mean age in our study was 59±18 years. This was close to that reported in a

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 Table 1 General characteristics of the study population

Variable	Overall (n=86)	Men (n=38)	Women (n=48)	Р
Age (years), mean ± SD	59.4±18.3	60.9±18.3	58.2±18.5	0.49
Age range (years), n (%)				
<30	6 (7.0)	2 (5.3)	4 (8.3)	0.588
30–39	9 (10.5)	4 (10.5)	5 (10.4)	0.988
40–49	11 (12.8)	5 (13.2)	6 (12.5)	0.932
50–59	14 (16.3)	8 (21.1)	6 (12.5)	0.236
60–69	19 (22.1)	4 (10.5)	15 (31.3)	0.021
≥70	27 (31.4)	15 (39.5)	12 (25.0)	0.150
Hypertension, n (%)	46 (53.4)	21 (55.3)	25 (52.1)	0.77
Past stroke, n (%)	2 (2.3)	2 (5.3)	0 (0)	0.11
Chronic heart failure, n (%)	13 (15.1)	7 (18.4)	6 (12.5)	0.45
Diabetes mellitus, n (%)	12 (14.0)	10 (26.3)	2 (4.2)	0.003
lschemic heart disease, n (%)	1 (1.2)	1(2.6)	0 (0)	0.26
Atrial fibrillation, n (%)	2 (2.3)	1 (2.1)	1 (2.6)	0.87
Current smoking, n (%)	6 (7)	6 (15.8)	0 (0)	0.004
Chronic kidney disease, n (%)	5 (5.8)	3 (7.9)	2 (4.2)	0.46
Alcohol consumption, n (%)	9 (10.5)	9 (23.7)	0 (0)	<0.001
Systolic blood pressure, mean \pm SD	140.3±35.4	146.6±37.8	135.4±32.9	0.16
Systolic blood pressure >140 mmHg, n (%)	37 (43.0)	18 (47.4)	19 (39.6)	0.468
Diastolic blood pressure, mean ±SD	92.5±27.8	94.9±31.1	90.5±25.1	0.477
Diastolic blood pressure >90 mmHg, n (%)	40 (46.5)	17 (44.7)	23 (47.9)	0.768
Heart rate, mean ± SD	96.2±21.9	95.7±18.2	96.7±24.6	0.84
Heart rate >100	34 (39.5)	17 (44.7)	17 (35.4)	0.381
Orthopnea, n (%)	82 (95.3)	35 (92.1)	47 (97.9)	0.20
Peripheral edema, n (%)	77 (89.5)	34 (89.5)	43 (89.6)	0.99
Fatigue, n (%)	86 (100.0)	38 (100.0)	48 (100.0)	1
Rales, n (%)	65 (75.6)	26 (68.4)	39 (79.2)	0.17
NYHA I, n (%)	0 (0)	0 (0)	0 (0)	1
NYHA II, n (%)	5 (5.8)	2 (5.3)	3 (6.3)	0.845
NYHA III, n (%)	44 (51.2)	21 (55.3)	23 (47.9)	0.495
NYHA IV, n (%)	37 (43.0)	15 (39.5)	22 (45.8)	0.733
Hemoglobin(g/dL), mean ± SD	12.3 ±2.4	12.6±2.5	12.1±2.3	0.426
Creatinine (mg/L), mean \pm SD	18.4±20.5	23.5±27.7	14.03±9.7	0.047
Serum Sodium (mmol/L), mean \pm SD	138.8±8.3	139.3±7.8	138.2±8.8	0.633
Serum potassium (mmol/L), mean \pm SD	3.9±0.8	3.84±0.8	3.99±0.7	0.442
Glycemia (g/L), mean ± SD	1.24±0.6	1.32±0.6	1.16±0.6	0.308

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Table 2 Electrocardiographic characteristics

Characteristic	Frequency (%)
Sinus tachycardia	26 (30.2)
Atrial fibrillation	10 (11.6)
Left ventricular hypertrophy	39 (45.3)
Left bundle branch block	4 (4.7)
Myocardial ischemia	9 (10.5)

 Table 3 Echocardiographic characteristics

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previous study in the capital city of Cameroon by Kingue *et al.* (16). In one of the largest multinational study of heart failure in SSA (THESUS-HF registry), the mean age of patients was 52 ± 18 years, which was also consistent with the finding in our study (10). A recent systematic review and meta-analysis of heart failure in Africa reported that the mean of patients with heart failure ranged from 36.5 to 61.5 years (4). The fact that heart failure occurs at a younger

Variable	Overall	Men	Women	Р
Interventricular septum (mm). Mean ± SD	10.4±2.9	10.4±2.4	10.4±3.2	0.938
Posterior wall (mm), mean ± SD	10.3±2.5	10.3±2.3	10.3±2.7	0.982
Left ventricular end-diastolic diameter (mm). Mean \pm SD	56.96±11.2	59.4±9.8	55.01±12	0.071
Relative wall thickness (mm), mean \pm SD	0.39±0.16	0.36±0.11	0.41±0.19	0.200
Left ventricular mass (g), mean ± SD	243.3±97	258.9±86.9	231.1±104	0.189
Left ventricular hypertrophy, n (%)	61 (70.9)	23 (60.5)	38 (79.2)	0.058
Left ventricular geometry, n (%)				
Normal	18 (20.9)	13 (34.2)	5 (10.4)	0.007
Concentric remodeling	7 (8.1)	2 (5.3)	5 (10.4)	0.391
Concentric hypertrophy	19 (22.1)	9 (23.7)	10 (20.8)	0.748
Eccentric hypertrophy	42 (48.8)	14 (36.8)	28 (58.3)	0.048
Left ventricular ejection fraction (%), mean ± SD	39.4±19.3	34.1±17.7	43.6±19.7	0.022
Left ventricular ejection fraction (LVEF) %, n (%)				
LVEF ≥55	24 (27.9)	8 (21.1)	16 (33.3)	0.252
LVEF 45-54	9 (10.5)	3 (7.9)	6 (12.5)	0.489
LVEF 30-44	18 (20.9)	8 (21.1)	10 (20.8)	0.884
LVEF <30	35 (40.7)	19 (50)	16 (33.3)	0.117
Left atrial area (cm ²), mean \pm SD	24.2±6.9	25.4±6.6	23.2±7.1	0.141
Left atrial area >20 cm², n (%)	65 (75.6)	31 (81.6)	34 (70.8)	0.247
Tricuspid annular plane systolic excursion (mm), mean	15.4±2.3	15.3±2.4	15.4±2.2	0.757
Tricuspid annular plane systolic excursion <17 mm, n (%)	58 (67.4)	22 (57.9)	36 (75)	0.035
Right atrial area (cm²), mean ± SD	20.8±6.9	21.2±6.2	20.4±7.5	0.492
Right atrial area >18 cm ² , n (%)	47 (55.3)	23 (60.5)	24 (51.1)	0.384
Pulmonary artery systolic pressure (mmHg), mean \pm SD	64.1±20.1	61±22.9	66.3±18	0.299
Pulmonary systolic pressure (PAPs) mmHg, n (%)				
PAPs <35	24 (27.9)	13 (34.2)	11 (37.5)	0.752
PAPs 35-44	8 (9.3)	6 (15.8)	2 (4.2)	0.066
PAPs 45-54	9 (10.5)	4 (10.5)	5 (10.5)	1
PAPs ≥55	45 (52.3)	15 (39.5)	30 (62.5)	0.034

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Table 4 Etiologies of heart failure

Type of heart disease	Overall, n (%)	Males, n (%)	Females, n (%)	Р
Rheumatic heart disease	5 (5.8)	3 (7.9)	2 (4.2)	0.467
Hypertensive heart disease	41 (47.7)	20 (52.6)	21 (43.8)	0.417
Idiopathic dilated cardiomyopathy	8 (9.3)	3 (7.9)	5 (10.4)	0.692
Ischemic heart disease	8 (9.3)	5 (13.2)	3 (6.3)	0.275
HIV cardiomyopathy	2 (2.3)	1 (2.6)	1 (2.1)	0.879
Pericardial effusion/tamponade	2 (2.3)	2 (5.3)	0 (0)	0.107
Cor pulmonale	10 (11.6)	2 (5.3)	8 (16.7)	0.102
Peripartum cardiomyopathy	2 (2.3)	0 (0)	2 (4.2)	0.201
Others	8 (9.3)	2 (5.3)	6 (12.5)	0.254

Table 5 Distribution of valvular lesions

Valvulopathy	None, n (%)	Mild, n (%)	Moderate, n (%)	Severe, n (%)
Aortic regurgitation	78 (90.7)	1 (1.2)	1 (1.2)	6 (7.0)
AS	84 (97.7)	-	1 (1.2)	1 (1.2)
MR	77 (89.5)	1 (1.2)	4 (4.7)	4 (4.7)
MS	84 (97.7)	_	-	2 (2.3)
TR	81 (94.2)	_	5 (5.8)	_

MR was the most frequent valvular heart disease, with 8 (9.4%) of patients having moderate to severe disease.

age in SSA may have serious economic consequences. Heart failure accounted for 3.9% of medical admissions in our study which was lower than the 10% reported in a study in neighboring Nigeria (17). The prevalence of heart failure is generally higher in women. The proportion of women admitted for heart failure in our study was higher than that in men. It was however different from a report in Yaounde where the proportion of heart failure was higher in men (16). In a recent systematic review of heart failure in Africa, it was shown that heart failure affects men more than women (4).

The most common etiological factor for heart failure was hypertensive heart disease. This was consistent with the findings of Kingue *et al.* in the capital city of Cameroon (16). This was also in accordance with findings from the THESUS-HF survey where hypertensive heart disease was the cause of heart failure in 45.4% of the participants (10). In the recent systematic review and meta-analysis of heart failure in Sub-Saharan Africa, hypertensive heart disease was the commonest cause of heart failure with a pooled prevalence of 39.2% (4). Hypertension is a major public problem worldwide. In Cameroon, there is a high prevalence of hypertension, affecting 29.7% of the population (18). Even though the prevalence of hypertension is high in Cameroon, awareness of the disease is low (18). In a recent study in this semi-urban setting, the authors reported that hypertensive heart disease was the most common form of heart disease among patients with heart disease diagnosed on echocardiography (19). Treatment and control of hypertension is associated with a significant reduction in the risk of heart failure and other adverse cardiovascular outcomes (20). However, treatment and control rate of hypertension in Cameroon are low (21). There is an urgent need to develop novel strategies to curb this growing burden of hypertension in Cameroon and SSA.

Cor pulmonale emerged as the second cause of heart failure in our study. This was higher than that reported in two previous from other parts of Cameroon (16,22). Rheumatic heart disease accounted for 5.8% of all heart failure cases in our study. It was the third commonest cause of heart failure in the THESUS-HF registry representing

14.3% of all heart failure cases (10). The recent systemic review and meta-analysis by Agbor *et al.* reported that RHD was the third most common cause of heart failure in SSA but that the prevalence had dropped by 15% over two decades (4). Rheumatic heart disease has virtually disappeared in most developed countries, but continues to be major cause of heart disease in children and young adults in developing countries including SSA (23,24). It is a disease that is 100% preventable, hence there is need to improve public awareness and promote adequate treatment of streptococcal pharyngitis.

Ischemic heart disease was the third most common cause of heart failure in our study together with dilated cardiomyopathy, each representing 9.3%. In other parts of Cameroon, the proportion of IHD among heart failure patients was 2.4% which was lower than that reported in our study (16). In a more recent study in Cameroon, ischemic heart disease represented 6.4% of heart failure etiologies (22). It represented 7.2% of heart failure etiologies in Africa from a recent systematic review and meta-analysis (4). Ischemic heart disease has generally been considered rare in SSA but the prevalence is likely to increase due to the increasing prevalence of cardiovascular risk factors as result of the epidemiological transition (25). The proportion of dilated cardiomyopathy in our study was lower than that previously reported in Cameroon by other authors although it was the third most common cause of heart failure (16,22). This was also in accordance with the recent systematic review of heart failure on the continent (4).

There has been a significant improvement in the treatment of heart failure with disease modifying drugs. More than 90% of the patients in our study received loop diuretics. This was comparable to that reported by Kingue et al. in Yaounde (16). Loop diuretics are widely used drugs for symptomatic relieve in heart failure patients and they are inexpensive. In our study, more than 70% of patients were prescribed angiotensin converting enzymes inhibitors, compared to 60.5% in the capital city of Cameroon. Also, the proportion of patients prescribed spironolactone and beta blocker was higher in our study compared to that reported by Kingue et al. (50.6% vs. 25.1% and 36.9% vs. 19.3% respectively). This low prescription of beta blockers in Africa was highlighted in a recent systematic review and meta-analysis (4). A possible explanation for the low prescription of beta blockers is that it was possible to start this medication as an outpatient follow up. The proportion of patients who received aldosterone inhibitors was higher in the THESUS HF survey (72.4%) (10). No patient received digoxin in our study compared to 60.7% who were prescribed digoxin in the THESUS HF survey (10). Also in a study in Yaounde, 30% of heart failure patients were prescribed digoxin (16). There is still debate regarding the use of digoxin in contemporary heart failure patients. Despite improvement in the treatment of heart failure over the last decades, the prognosis of heart failure is still poor. The in-hospital case fatality for heart failure was12.8% in our study. In other studies from Cameroon, the in hospital mortality has been shown to range from 9.3–18.45% (16,22). The mortality rate in our report was higher than that reported in developed countries with mortality rates of 3.8% to 6.7% (15,26-28). In SSA previous studies on heart failure reported in hospital mortality rates ranging from 3.9% to 25.2%% as shown in a recent systematic review and meta-analysis (4). Lengthy hospital stays are usually required by heart failure patients. The mean length of hospitalstay which was 8.1 days in our study was comparable to that reported in the THESUS-HF survey (10). But this was shorter than that reported in the Yaounde, the capital city of Cameroon (13 days) (16).

Conclusions

Heart failure is a common cause of hospital admission in this semi-urban setting and affects younger individuals. While hypertensive heart disease is the most common cause of HF, Rheumatic heart disease still remains a significant etiology. In-hospital mortality remains high. Low mean blood pressure and tachycardia appeared to be associated with in-hospital death, while the use of ACE inhibitors and spironolactone reduced in-hospital death. Male sex appeared to be associated with a composite of death and long hospital stay.

Limitations and strength

This cross-sectional study was limited by its small sample size. Significant associations could be missed out. It is possible that patients with milder forms of heart failure did not seek medical attention at this tertiary hospital. Also, cases of ischemic heart disease may have been underrepresented as there was no facility for stress test or coronary angiography. We did not capture the readmission rate for heart failure-an important outcome variable. Despite these limitations, our study is the first prospective report on the profile and outcome of heart failure in the South West Region of Cameroon.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the administrative authorities of the hospital. Confidentiality and personal privacy was respected in all levels of the study. Collected data was not be used for any other purpose.

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