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Markers of Atherosclerosis, Clinical Characteristics, and Treatment Patterns Among Middle-Aged Adult Patients with Heart Failure in Kenya

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Abstract

Background—While risk factors for heart failure are increasingly common worldwide, the contribution of markers of atherosclerosis to heart failure in sub-Saharan Africa is largely unknown.

Objectives—To assess the association between atherosclerotic risk factors and heart failure in a developing country.

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DISCLOSURES

The authors have no conflicts of interest to disclose.

Methods—We performed a case-control study of heart failure in rural Kenya. We assess the risk factors for heart failure using international criteria based on electrocardiogram (ECG), echocardiogram, physical examination findings and laboratory testing. Atherosclerotic risk factors were determined by ECG, echocardiogram, ankle-brachial index (ABI), and lipid testing. We describe the relation of wall motion abnormalities on echocardiogram, ABI <0.9 and ischemic pattern on ECG to presence of heart failure with multivariable logistic regression adjusting for age and sex and using adjusted odds ratios (AORs) and 95% confidence intervals (CIs).

Results—There were 125 cases and 191 controls (n=316); 49% were male. The mean age was 60 (standard deviation 13) years. Most patients had hypertension (53%), and 16% had HIV. Lipids were in the normal range for all. Cases were older than controls (62 vs. 58 years, respectively). The most common abnormality associated with heart failure was dilated cardiomyopathy. Ischemic heart failure was the second most common in men. Cases were more likely to have an ABI <0.9 (46% vs. 31%, AOR 1.99, 95% CI 1.19–3.32), ischemia/infarct on ECG (68% vs. 43%, AOR 3.01, 95% CI 1.43–6.34), and wall motion abnormalities on echocardiogram (54% vs. 15%, AOR 7.00, 95% CI 3.95–12.39).

Conclusion—Ischemic heart failure is more common in Kenya than previously recognized. Non-invasive markers of atherosclerosis are routinely found among heart failure patients. Treatment and prevention of heart failure in sub-Saharan Africa must consider a wide range of causes including those related to atherosclerosis.

Keywords

heart failure; sub-Saharan Africa; atherosclerosis

INTRODUCTION

In 2010, over 41 million people had heart failure (HF) worldwide, a 14% increase from 1990 (1). In the United States, there are more than 3 million physician visits and 1 million hospital discharges yearly for HF (2). Re-admission rates after hospitalization for HF are >50% 6 months after discharge, and 5-year mortality rates are 40–65% in the United States and Europe (3-5). The economic impacts of HF in the United States are astonishing, with costs in 2010 topping $39.2 billion (6). Corresponding data from sub-Saharan Africa are not available owing to challenges in disease classification (7) and lack of population-based studies (8).

Coronary atherosclerosis is the most common cause of HF in high-income settings (9). However, ischemic heart disease (IHD) and atherosclerosis have historically accounted for <2% of the burden of HF in sub-Saharan Africa (SSA) (10). Much of the research showing a low prevalence of IHD in SSA, however, relied on patient report or electrocardiogram (ECG) alone (11,12). Atherosclerotic cardiovascular diseases are becoming more common among patients in SSA with HF according to some studies using contemporary diagnostic techniques in SSA (13,14), but not all (15,16). Epidemiological and clinical data about the causes of HF from most countries in SSA remain unavailable due, in part, to the generally low cardiovascular research productivity from the region (10,17).

To address this unmet need, we designed this study to (1) assess the major abnormality associated with HF using clinical, laboratory and echocardiographic parameters, (2) describe treatment patterns for HF and (3) assess the association between atherosclerotic risk factors and HF in western Kenya. Kenya (population 43.2 million in 2012) is a middle-income country that is marked by a double-burden of communicable and non-communicable diseases (18) and is underrepresented in publications from SSA on HF epidemiology (8). Findings from an economically developing country in the midst of an epidemiologic transition may have local and worldwide relevance for similarly situated countries.

METHODS

Study design

We performed a case-control study to identify associations of markers of atherosclerosis with HF at a national referral hospital in western Kenya. Our methodological approach has three main components: (1) a description of the primary probable etiology of HF adjudicated using clinical, physical examination and radiographic criteria according to society guidelines, (2) a determination of the distribution of risk factors (both atherosclerotic and non-atherosclerotic) for HF in cases and controls, and (3) regression modeling to determine the extent to which atherosclerotic risk factors were associated with higher or lower odds of having HF.

Setting

One of the 11 NHLBI Centers of Excellence (19) is in western Kenya where Moi University School of Medicine has a 22-year relationship with a consortium of US medical schools. This collaboration, the Academic Model Providing Access to Healthcare (AMPATH) (20,21), partners with Moi Teaching and Referral Hospital (MTRH) (Kenya's second national referral hospital, with 750 beds, and serving a catchment area of 13 million people [Figure 1]) and Moi University School of Medicine. This study was conducted at MTRH between June 2010 and December 2012 in the city of Eldoret.

Participants

All patients ≥40 years old being seen in the inpatient wards, medical outpatient clinic, and cardiology outpatient clinics were eligible for enrollment. Cases constituted patients with a known or presumed diagnosis of HF based on a modified version of the Framingham HF criteria which uses clinical, physical examination and radiographic parameters (22). Controls constituted patients from the same clinical areas with complaints of shortness of breath but no known HF. Symptomatic controls were selected so as to achieve similarities in location of enrollment, healthcare seeking behavior and acuity of illness between groups. Patients were enrolled consecutively and were not matched. Patients were excluded if they were human immunodeficiency virus (HIV) seropositive with a CD4 count level ever <100 cells/mL, within 6 months post-partum, within 3 months of major trauma, or known to have a history of malignancy.

Variables

Enrollment and data collection—The following data were prospectively obtained from each patient: self-reported medical history; socioeconomic status (SES); occupation; residence; alcohol consumption; tobacco use; self-reported history of malaria, tuberculosis, and other recurrent infections; medication use; New York Heart Association (NYHA) functional class; cardiac symptoms and signs; family cardiovascular disease history; and physical activity. Heavy or hazardous alcohol drinkers were identified using the Alcohol Use Disorders Identification Test (AUDIT-C) screening tool (23). SES was measured by an unweighted summary variable accounting for ownership of 5 items (automobile, flushing toilet, television, electricity, and refrigerator) (24).

Clinical evaluation—All patients underwent a thorough cardiopulmonary examination by a physician. Blood pressure was measured in the right arm after the patient had been seated for 10 minutes. Three readings were obtained, each 2 minutes apart. Doppler ultrasound was used to measure ankle systolic blood pressure bilaterally with an HP Sonos 2500 (Philips Healthcare, Bothell, WA) using a linear phased array probe. Ankle-brachial index (ABI) was calculated by dividing the highest of the ankle blood pressures by the ipsilateral brachial blood pressure (25). An ABI <0.9 increases the risk for coronary heart disease 2-4 fold (26).

Electrocardiogram and echocardiogram—A 12-lead resting ECG was recorded for each patient. Echocardiograms were performed by a trained sonographer using a standardized acquisition protocol on a Philips CX-50 machine (Philips Healthcare, Bothell, WA). Images were digitally archived for analysis in the Duke Echocardiography Core Laboratory, which has reported high standards of measurability and reproducibility (27). All echocardiograms were reviewed by one physician or sonographer and approved by one physician overreader.

Echocardiograms included a thorough assessment of left ventricular diameters, wall thicknesses, volumes, ejection fraction, diastolic function, valvular disease, rheumatic heart disease, and right heart function using American Society of Echocardiography (ASE), European Association of Echocardiography, and World Heart Federation guidelines (28-33). Left ventricular volumes and ejection fraction were measured using the biplane Simpson's volumetric method combining apical 4-chamber and 2-chamber views. When images were inadequate for definition of the left ventricular endocardial border, visual ejection fraction was used instead. Using a 17-segment wall motion scoring system, a wall motion score index (WMSI) was calculated according to ASE guidelines (33). Greater scores indicate more wall motion abnormalities. The echocardiographic assessment also evaluated presence and type of congenital heart disease, pericardial effusion size, and presence of stranding within the effusion and cardiac masses or thrombi.

Laboratory analysis—Blood was collected by venipuncture for analysis and storage. The following serum tests were performed in the accredited AMPATH Reference Laboratory in Eldoret, Kenya: C-reactive protein (CRP), total cholesterol, low-density lipoprotein, high-density lipoprotein (HDL), triglycerides, apolipoprotein A1, apolipoprotein B (Apo B), lipoprotein a [Lp(a)], hemoglobin A1c, creatinine, blood-urea nitrogen, hemoglobin,

complete blood count, rapid HIV-1 antibody testing and ELISA if positive, and CD4 count. Higher lipid values are associated with greater risk for atherosclerosis, with the exception of HDL which generally shows the inverse relationship. Clinically relevant values for serum lipids were based on recent guidelines (34). Cut-off values were used for CRP (>75th percentile) and Apo B (>0.9 g/L) as these level predict ischemic cardiovascular events (35,36). Presence of metabolic syndrome was determined by applying International Diabetes Federation criteria (37).

Statistical analysis

Enrollment of at least 50 cases and 148 controls was defined *a priori* to achieve at least 90% power to detect a statistically significant difference in the proportions of cases versus controls with regional wall motion abnormalities. We based the calculation on a 3:1 sampling ratio of controls to cases and a 1-sided test with a type-1 error rate of 0.05. It was assumed the prevalence of regional wall motion abnormalities would be 10% in the control group and between 25% and 35% among the cases, based on previous estimates (38,39).

Primary probable etiologies of HF were assessed by examining associations between various abnormalities and HF, using clinical, echocardiographic, and ECG criteria and presented as proportion of all cases (Table 1). These criteria incorporate European Society of Cardiology guidelines and HF registry protocols from SSA (13,14,40). Medical history, SES, physical findings, laboratory results, and markers of atherosclerosis were compared between cases and controls. Markers of atherosclerosis were defined *a priori* as WMSI >1.8, ABI <0.9, and ischemic changes on ECG (41,42). Using the case status as the outcome and controls as the reference group, multivariable logistic regression analyses were used to examine the extent to which each HF risk factor and demographic and clinical measurement was associated with higher or lower odds of HF diagnosis. Except for age and sex analyses, all models were adjusted for age and sex. The linearity assumption between the log-odds of HF and the continuous exposures was confirmed using generalized additive models. Results are reported using adjusted odds ratios (AORs) for each measurement and 95% confidence intervals (CIs).

Separate analyses were used to examine the distribution of demographic and clinical risk factors for HF by sex, using only data for the HF cases. Since these measurements were of 3 data types (continuous, binary, or ordinal), 3 types of analyses were required to explore sex as an independent predictor of each risk. Linear regression was used for continuous data, proportional odds logistic regression for ordinal outcomes, and logistic regression for binomial outcomes. Fisher's exact test was used for categorical outcomes with a small number of observations. All models (excluding Fisher's exact test) were also adjusted for age as a linear term.

Ethical considerations

All participants provided written informed consent and the study conformed to the principles outlined in the Declaration of Helsinki. The study was approved by the Institutional Research and Ethics Committee of Moi University College of Health Sciences, the institutional review boards of Duke and Brown Universities, and the NHLBI.

RESULTS

Clinical and demographic characteristics

Of the 5562 individuals we screened, 316 participants—125 (40%) cases and 191 (60%) controls—were included for analysis (Figure 2). Participants were enrolled from the inpatient setting (41%), outpatient clinics (34%), or the casualty department (24%). Mean (standard deviation [SD]) age of cases and controls were 61 (13) and 58 (12) years, respectively (Table 2). About half of the participants were male. Most participants were of low SES, and 41% were farmers. Atrial fibrillation was more common among cases (18%) versus controls (5%, $p<0.01$), but asthma was significantly more common among controls (22%) than cases (12%) ($p<0.05$). A greater percentage of cases (22%) than controls (10%) had chronic kidney disease ($p<0.01$), defined as an estimated glomerular filtration rate <60 mL/min. There were no significant differences in blood pressure, hemoglobin, HIV seropositivity, or heavy alcohol use.

Etiologies of HF

Eight primary probable etiologies of HF were identified. Of 125 cases, 120 had echocardiograms completed, and an etiology of HF could be assigned in 118. Among those, the most common etiologies of HF were dilated cardiomyopathy (19.5%), IHD (17.8%), valvular heart disease (17.8%), hypertension (11.9%), heart failure with preserved ejection fraction (HFpEF, 9.3%), right HF (8.5%), and HIV-associated HF (8.5%). Thyroid disease (2.5%) and pericardial disease (1.7%) accounted for a small portion of cases. There was 1 case of HF due to hypertrophic cardiomyopathy, and 2 cases of unknown etiology.

Figure 3 shows the distribution of HF etiology as a function of sex. Dilated cardiomyopathy and IHD were the most common causes of HF among men, while hypertension and valvular heart disease (mostly rheumatic) were most common among women. IHD occurred in only 10% of women. Right HF, HFpEF, and hypertensive heart disease were more common among women than men. HIV-associated HF was equally common among men and women.

Figure 4 shows the distribution of etiologies of HF according to age category (< or ≥60 years). Among older patients, dilated cardiomyopathy, IHD, and hypertension were the main probable etiologies of HF. For younger patients, valvular heart disease was the most common etiology.

Atherosclerotic risk factors among cases and controls

The risk factor profile among cases and controls is shown in Table 3. A history of treatment for hypertension was more common among cases than controls (OR 2.55, 95% CI 1.57–4.14). Of the clinical history-based risk factors, there were no statistically significant differences in diabetes, smoking history, family history of early myocardial infarction or reported physical activity. Of the physically measured risk factors, more cases (46%) than controls (31%) had an ABI <0.9 ($p<0.01$).

Analysis of laboratory-based markers revealed that the 75th percentile for CRP was approximately 30 mg/L, and the groups did not differ significantly in the odds of exceeding

this cutoff. Levels of LDL, Apo A1, total cholesterol, triglycerides were in the normal or low range in both groups; however, cases had lower values for these parameters. Lp(a) levels were not statistically significant different between groups. There was no difference in proportion of cases and controls will Apo B ≥0.9 g/L. High-density lipoprotein was significantly lower among cases versus controls (OR 0.67, 95% CI 0.6–0.8) and cases more often met criteria for the metabolic syndrome (OR 1.66, 95% CI 1.04–2.65) indicating greater cardiovascular risk.

Table 4 shows the associations of markers of atherosclerosis with HF. A WMSI >1.8 (OR 7.00, 95% CI 3.95–12.39), low ABI (OR 1.99, 95% CI 1.19–3.32), and ischemic/infarct pattern on ECG (OR 2.68, 95% CI 1.53–4.68) were all significantly more common among cases versus controls ($p<0.01$ for all). Cases were also more likely to have 1, 2, or all 3 of these markers present. There were no significant differences in results when analyses were adjusted for glomerular filtration rate (data not shown).

Electrocardiographic, echocardiographic and treatment parameters

Table 5 shows selected ECG, echocardiographic, clinical, and medication use features according to the main causes of HF. Rhythm and conduction system disturbances were most common among cases of dilated cardiomyopathy or valvular heart disease. The average resting heart rate for HF cases was generally >75 beats per minute. With the exception of cases with HFpEF, most patients presented with advanced NYHA class symptoms. Most HF patients reported taking diuretic medications, and a wide range (29–70%) reported taking angiotensin-converting enzyme inhibitor (ACEi) medications. Less than half of patients with HF reported taking beta-blockers, and ≤20% were taking angiotensin receptor blockers. Antiplatelet medications were used by only 30% of patients with ischemic HF.

DISCUSSION

This study of HF in SSA is unique for a number of reasons. Our study reports probable etiologies of HF in rural Kenya specifically including a variety of modalities to assess communicable and non-communicable etiologies. In addition, we use a case-control design to compare associations between atherosclerotic risk factors and HF. Combining ECG, ABI, and regional wall motion abnormalities on echocardiogram, we specifically assessed the contribution of atherosclerosis to HF in a rural community in western Kenya.

Our findings demonstrate that contemporary probably etiologies of HF in Kenya are myriad. While dilated cardiomyopathy remains the most common form of HF in this patient population, an ischemic etiology is nearly as common. Markers of atherosclerosis appear to exist commonly among patients with HF in rural Kenya in contrast to prior reports (10,43). Our findings challenge prevailing assumptions about the paucity of atherosclerotic disease among patients with HF and provide much needed data on HF in patients from rural SSA. These data have important clinical and public health implications for Kenya and other populations in low- and middle-income countries in the midst of the epidemiologic transition.

Most data from SSA on HF epidemiology demonstrate that patients are, on average, 10– 15 years younger than HF patients in high-income countries. In the largest HF registries from SSA, the average age of participants was 52–57 years; in high-income countries, HF is mostly a disease of septuagenarians (13-16,44). This likely relates to the lower life expectancy in SSA. Rheumatic heart disease, a common cause of HF in SSA, also presents earlier in life. However, it is also clear that, in SSA, IHD presents earlier than in developed countries (45). Thus, many forms of HF are present simultaneously in SSA. The earlier age of presentation with HF has tremendous human and economic implications for the workforce, productivity losses, and caregivers (46).

Non-communicable conditions are the most common causes of HF worldwide (47). A systematic review supports our finding that the contemporary causes of HF in SSA are myriad and include both endemic and emerging causes (8). In low- and middle-income countries, hypertension accounts for 45% (range 15–80%) of cases, while cardiomyopathies and valvular heart disease account for 24% (range 14–40%) and 18% (range 4–53%), respectively. IHD accounts for 8% of cases (range 1–48%) (8). Dilated cardiomyopathy was the most common form of HF in the current study, consistent with the bulk of the literature on HF from SSA (43).

Treatment patterns for patients with HF are poor. In the present study, only 55% of patients with dilated cardiomyopathy were taking ACEi medications, 45% were taking beta-blockers, and 23% were taking digoxin. This mirrors findings from The Sub-Saharan Africa Survey of Heart Failure (THESUS-HF), showing equally poor use of guideline-directed medical therapy (GDMT) (14), and may be related to provider- or patient-level factors. Given the mortality gains from GDMT (48), it is imperative that implementation and monitoring of GDMT for HF patients in SSA be prioritized.

Our methods are notable for a novel approach to identifying markers of atherosclerosis. To determine the extent to which atherosclerosis and ischemia contributed to HF, we used a combination of widely available, non-invasive techniques. We chose this approach based on limitations in access to a broad range of investigative tools and the “erroneously reinforced beliefs that IHD only affects the wealthy and the elderly” in SSA (12). The ABI, ECG, and echocardiogram have a modest to strong correlation to significant coronary artery disease or prior myocardial infarction (41,42). Using this scheme, we identified that markers of atherosclerosis are more common in HF patients in this region than previously described (8,10). Lower HDL, in a clinically meaningful range, and greater proportion of patients with metabolic syndrome also signal greater risk for cardiovascular disease (49). There was a relative paucity of traditional cardiovascular risk factors other than hypertension. It is possible that participants underreported behavioral factors. These factors notwithstanding, this study is one of the first in a rural community in SSA employing specific investigations for markers of atherosclerosis. THESUS-HF demonstrated that IHD was the most common cause of HF in urban Kenya (14), and other studies from the region support the notion of an increasing burden of IHD and risk factors thereof (12,50). These findings underscore the need to develop more accessible tools to diagnose IHD and for clinicians and policy makers to consider varied causes of HF in urban and rural settings.

The strengths of this study include a uniform definition of HF applied to case and control patients who were prospectively identified, a sample size based on power calculations, and the use of an independent echocardiographic core laboratory to analyze images blinded to the clinical information. There are some limitations to our study. We restricted our sample to participants ≥40 years old in order to understand causes of HF in middle-aged adults, but as a result, we may have underrepresented causes that are more common in a younger population. Congenital and rheumatic heart diseases, for example, are more likely in younger age groups. Our study was based at a referral hospital and therefore may not completely represent the community epidemiology. Behavior data elements were self-reported, and participants may have misreported. Lastly, without advanced imaging or functional studies, we were not able to definitively diagnose ischemic HF. The absence of sensitive measures may have resulted in underestimating coronary atherosclerosis. In most of SSA, however, access to invasive imaging techniques is limited. Each of the 3 markers we used (ABI, WMSI, ECG) correlates with coronary atherosclerosis; however, the positive predictive value of this combination for significant coronary atherosclerosis is unknown in SSA.

CONCLUSIONS

Contemporary etiologies of HF in SSA seem myriad and include communicable and non-communicable diseases. Use of GDMT for HF patients in SSA is poor, and strategies to improve its use for HF in SSA are warranted. Markers of atherosclerosis are more common among patients with HF than among patients without. Atherosclerosis is also an African disease and commonly manifests as HF, as it does elsewhere. Inattention to atherosclerosis in SSA risks ignoring an important and common contributor to the cardiovascular disease burden and a missed opportunity for disease prevention.

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ABBREVIATIONS

ABI	ankle-brachial index
ACEi	angiotensin-converting enzyme inhibitor
ECG	electrocardiography
GDMI	guideline-directed medical therapy

HF	heart failure
HFpEF	heart failure with preserved ejection fraction
IHD	ischemic heart disease
SES	socioeconomic status
SSA	sub-Saharan Africa
WMSI	wall-motion score index

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Highlights

- The most common causes of heart failure in western Kenya was dilated cardiomyopathy.
- Markers of atherosclerosis were more common in those with heart failure than without.
- Ischemic heart disease was the 2nd most common cause of heart failure in men.
- Use of guideline-directed medical therapy was low.
- Inattention to atherosclerosis in Kenya may ignore a common cause of heart failure.

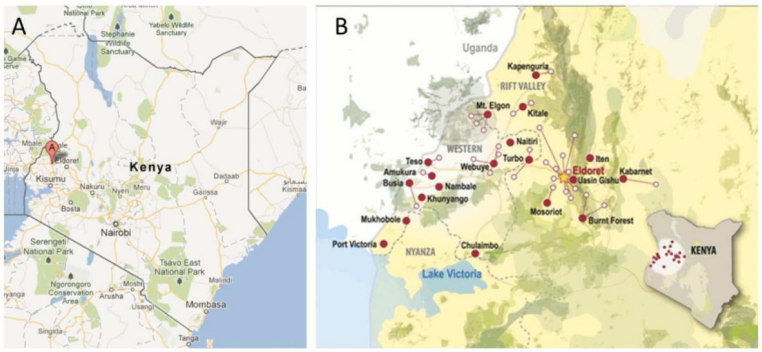

Figure 1. Map of the study catchment area

(A) Kenya. (B) Academic Model Providing Access to Healthcare (AMPATH) catchment area in western Kenya. This study was carried out in Eldoret (red type).

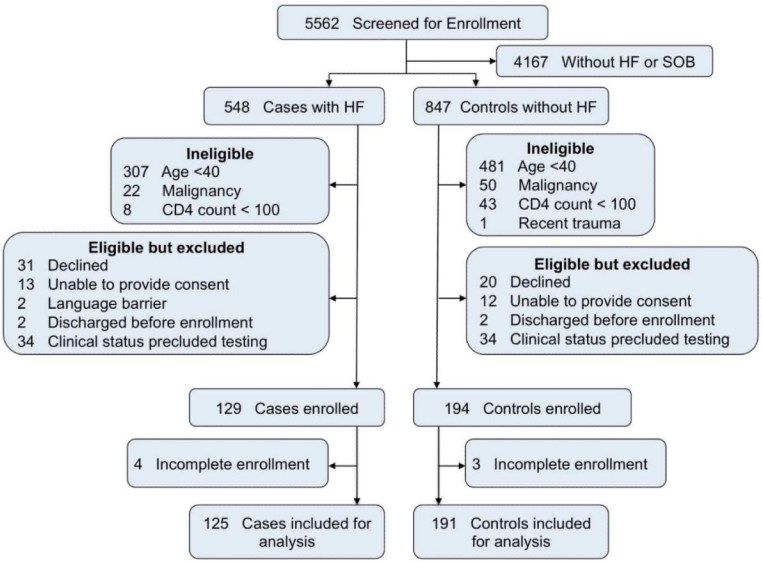

Figure 2. Screening and enrollment diagram

HF, heart failure; SOB, shortness of breath.

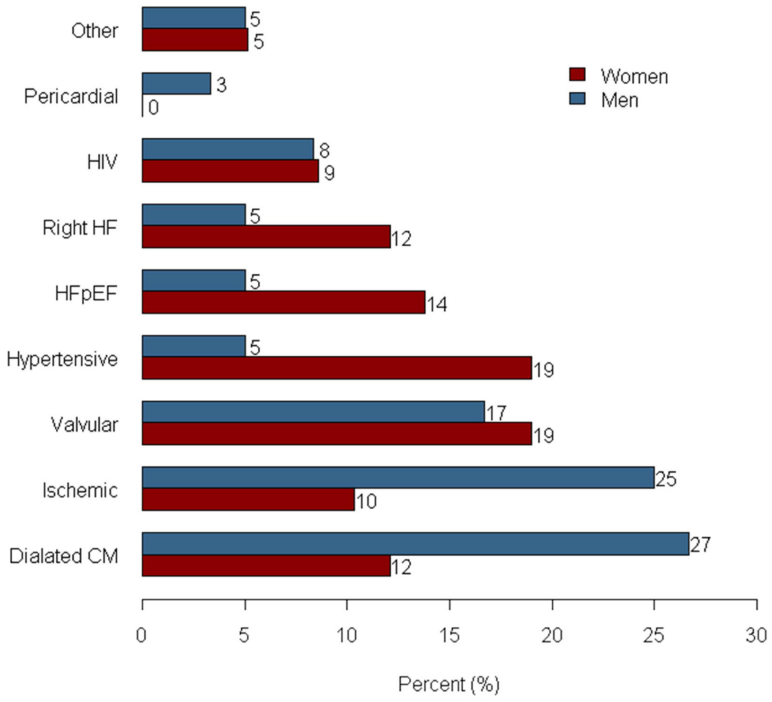

Figure 3. Percentage of causes of HF (n=118) in western Kenya by sex

CM, cardiomyopathy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HIV, human immunodeficiency virus.

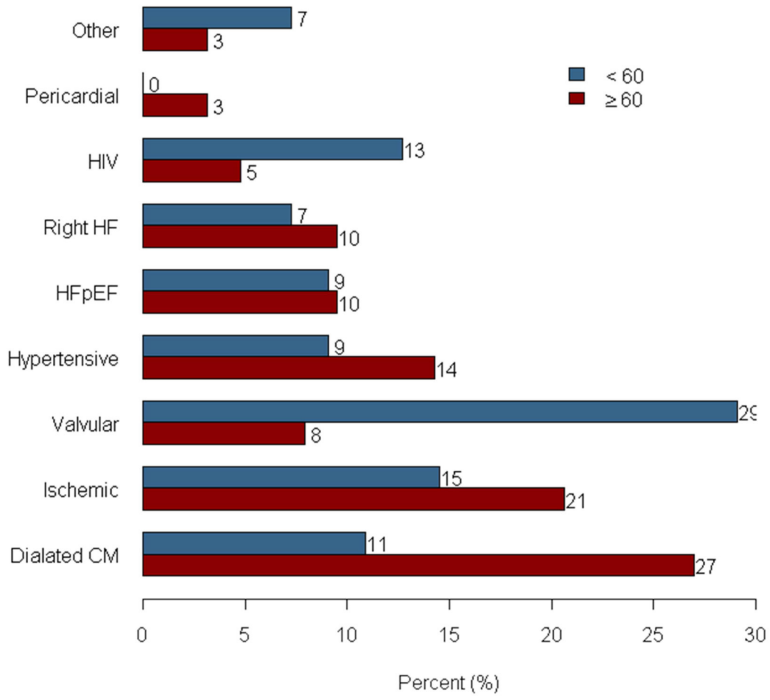

Figure 4. Percentage of causes of HF (n=118) in western Kenya by age category
Abbreviations as in Figure 3.

Table 1

Criteria for primary probably cause of heart failure

Study Definition	Criteria
LV systolic dysfunction	LVEF ≤45%
LV diastolic dysfunction	Based on mitral valve inflow velocities, left atrial size, and mitral annulus tissue Doppler velocities according to recommendations from the American Society of Echocardiography
Idiopathic dilated cardiomyopathy	(1) LVEF ≤45% and LV end diastolic dimension >55 mm
	(2) Absence of myocardial ischemic/infarct pattern on ECG
Ischemic cardiomyopathy	(1) LVEF ≤45%
	(2) WMSI ≥1.8 or myocardial ischemic/infarct pattern on ECG
Hypertensive HF	(1) LVEF ≤45% or LV septal wall dimension >1.3 cm or diastolic dysfunction grade ≥2
	(2) Systolic blood pressure >180 mmHg or diastolic blood pressure >100 mmHg
HFpEF	(1) LVEF >50%
	(2) Diastolic dysfunction grade ≥2
Valvular HF	(1) LVEF ≤45%
	(2) Presence of rheumatic or degenerative valvular disease
Right HF	(1) LVEF >40%
	(2) Elevated jugular venous pressure or maximum inferior vena cava size >2.1 cm or <50% reduction in inferior vena cava size with inspiration
	(3) Greater than moderate tricuspid regurgitation or peak pulmonary arterial pressure >35 mmHg or signs of venous congestions
	(4) Absence of rheumatic heart disease
	(5) Diastolic dysfunction grade <3
Hypertrophic cardiomyopathy	(1) LV septal or posterior wall dimension >1.5 cm
	(2) Diastolic dysfunction grade ≥2 or moderate/severe mitral regurgitation or aortic outflow gradient ≥30 mmHg
Endomyocardial fibrosis	(1) LVEF ≤45%
	(2) Typical intraventricular thrombus or endomyocardial thickening present
HIV-associated HF	(1) LVEF ≤45%
	(2) HIV positive
	(3) Absence of other identifiable cause
Other causes	HF due to congenital heart defects, endocrine disorders, and pericardial disease

ECG, electrocardiogram; EF, ejection fraction; LV, left ventricular; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; WMSI, wall motion score index

Table 2

General characteristics of HF cases and controls

Characteristic	Total (n=316)	Case (n=125)	Control (n=191)
Age, yrs (SD)	60 (13)	61 (13)	58 (12) *
Male, %	49	49	49
Socioeconomic status category, %			
0	53	52	53
1	21	18	23
2	15	14	15
3	7	8	6
4	3	6	2
5	1	2	1
Farmer, %	41	42	39
Urban residence, %	25	25	25
Past medical history, %			
Stroke	4	5	4
Thyroid disease	2	3	1
Asthma	18	12	22 *
Angina	38	45	34
Atrial fibrillation	10	18	5 **
Tuberculosis	15	12	17
Malaria	93	93	94
NYHA class, %			
1	12	11	12
2	37	28	43
3	34	41	29
4	18	20	16
Heart rate, beats per minute (SD)	86 (20)	87 (22)	85 (18)
Systolic BP, mmHg (SD)	129 (29)	130 (27)	129 (30)
Diastolic BP, mmHg (SD)	79 (17)	81 (18)	78 (15)
Peripheral edema, %	48	69	34 **
S3 gallop, %	25	45	12 **
eGFR <60 mL/min/1.73m^2, %	15	22	10 **
Hemoglobin, g/dL (SD)	13.4 (3)	13.3 (3)	13.5 (3)
HIV positive, %	16	14	17
Heavy alcohol intake, %	16	16	16

BP, blood pressure; eGFR, estimated glomerular filtration rate; HF, heart failure; NYHA, New York Heart Association; SD, standard deviation.

Continuous variables presented as mean (SD). All comparisons adjust for age and sex.

*p<0.05

**p<0.01

Table 3

Clinical, physical and laboratory-based cardiovascular risk factors among cases and controls

Risk factor	Total (n=316)	Case (n=125)	Control (n=191)	Odds ratio* (95% CI)
Clinical risk factors				
Past medical history, %				
Treatment for hypertension	53	68	44†	2.55 (1.57–4.14)†
Diabetes	11	11	11	0.98 (0.47–2.04)
Current/former smoker, %	37	39	35	1.18 (0.71–1.99)
Family history of early MI, %	6	6	6	0.88 (0.27–2.82)
Physically active, %	32	27	35	0.80 (0.48–1.35)
Physically measured risk factors				
Overweight/obese‡, %	34	38	32	1.39 (0.85–2.27)
Waist-hip ratio (SD)	0.9 (0.1)	0.9 (0.1)	0.9(0.1)	1.06 (0.76–1.49)
Ankle-brachial index <0.9, %	37	46	31	1.99 (1.19–3.32)†
Laboratory-based risk factors				
C-reactive protein >75th percentile§, %	24	22	25	0.88 (0.50–1.56)
LDL, mg/dL (SD)	99 (49)	91 (45)	104 (50)	0.94 (0.9–1.0)‖
HDL, mg/dL (SD)	36 (16)	32 (14)	39 (17)	0.67 (0.6–0.8)†
Apo A1, g/L (SD)	1.2 (0.4)	1.1 (0.3)	1.3 (0.4)	0.18 (0.09–0.35)†
Apo B ≥0.9, g/L, %	32	28	34	0.79 (0.47–1.33)
Lp(a), g/L (SD)	0.60 (0.6)	0.53 (0.5)	0.64 (0.6)	0.69 (0.43–1.10)
Total cholesterol, mg/dL (SD)	164 (57)	152 (56)	173 (56)	0.93 (0.89–0.97)†
Triglycerides, mg/dL (SD)	131 (68)	115 (47)	141 (77)	0.94 (0.9–0.98)‖
Metabolic syndrome, %	42	50	38	1.66 (1.04–2.65)‖
Hemoglobin A1c, % (SD)	6.4 (1.4)	6.4 (1.2)	6.4 (1.4)	0.99 (0.83–1.18)

Overweight/obesity defined as body mass index ≥ 25 kg/m^2. Waist-hip ratio calculated as waist circumference/hip circumference.

CI, confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Lp(a), lipoprotein (a); MI, myocardial infarction; SD, standard deviation.

*OR for LDL, HDL, total cholesterol, and triglycerides is per 10 units higher. OR for sedentary time is per 1 hour longer. OR for waist-hip ratio is per 0.1 unit higher. All models adjusted for age and sex.

†p<0.01

‡Defined as body mass index ≥25 kg/m^2.

§Log-transformed. 75th percentile corresponds to 30 mg/L.

‖p<0.05

Table 4

Markers of atherosclerosis among congestive heart failure cases and controls*

Marker	Total (n=316)	Case (n=125)	Control (n=191)	Odds ratio (95% CI)
WMSI >1.8, %[a]	31	54	15	7.00 (3.95–12.39)[b]
Ankle-brachial index <0.9, %[b]	37	46	31	1.99 (1.19–3.32)†
Ischemic/infarct pattern on ECG, %[c]	24	35	17	2.68 (1.53–4.68)†
Total number of markers, %[d]				
0	36	13	53	Reference
1	39	42	37	4.65 (2.26–9.56)†
2	21	36	10	15.06 (6.35–35.68)†
3	4	9	1	61.01 (6.96–535.21)†

CI, confidence interval; ECG, electrocardiogram; WMSI, wall motion score index.

*adjusted for age and gender

†p<0.01

‡p<0.05

[a]N=290,

[b]N=270,

[c]N=292,

[d]N=246

Table 5

Selected ECG, echocardiographic, clinical, and medication use patterns of HF according to cause of HF (n=118)

Characteristic	CMP (n=23)	Ischemic (n=21)	Valvular (n=21)	HTN (n=14)	HFpEF (n=11)	Right HF (n=10)	HIV (n=10)	Other* (n=8)
Atrial fibrillation, %	19	14	47	0	0	22	0	0
LBBB, %	22	5	0	7	0	10	0	12
Heart rate, bpm (SD)	99 (26)	87 (21)	84 (18)	75 (19)	83 (23)	75 (17)	96 (18)	78 (14)
LVEF, % (SD)	23 (10)	23 (10)	45 (15)	37 (17)	61 (13)	50 (8)	37 (14)	44 (18)
LVIDs, cm (SD)	5.5 (0.8)	5.1 (0.9)	3.7 (1.0)	4.0 (1.0)	2.7 (0.7)	2.9 (0.8)	4.1 (1.4)	4.0 (0.8)
LVIDd, cm (SD)	6.1 (0.8)	5.6 (0.9)	4.9 (1.2)	5.0 (0.6)	4.1 (0.7)	3.8 (0.9)	5.1 (1.1)	5.1 (0.3)
IVSd, cm (SD)	1.0 (0.2)	1.0 (0.3)	1.2 (0.4)	1.3 (0.2)	1.2 (0.2)	1.3 (0.4)	1.0 (0.2)	1.3 (0.6)
LA volume, cm^3 (SD)	11 (6)	9 (4)	15 (11)	8 (3)	6 (3)	7 (4)	8 (4)	9 (3)
RVSP, mmHg (SD)	50 (12)	43 (15)	54 (17)	53 (28)	38 (16)	75 (28)	48 (14)	63 (13)
Smoking, %	43	43	52	14	45	30	40	38
Angina, %	35	38	57	50	45	70	30	50
NYHA ≥3, %	68	67	67	69	27	56	60	50
Ankle-brachial index (SD)	0.89 (0.1)	0.90 (0.2)	0.89 (0.2)	0.91 (0.2)	0.81 (0.2)	1.0 (0.1)	1.0 (0.2)	1.0 (0.3)
Heavy/hazardous drinking, %	13	24	24	7	27	0	10	25
Medication use								
Diuretic, %	86	85	76	100	82	90	67	100
Digoxin, %	23	11	43	23	9	30	29	14
ACEi, %	55	65	29	62	55	70	50	43
ARB, %	9	11	5	15	18	20	12	0
Beta-blocker, %	45	42	14	31	18	40	25	25
Antiplatelet, %	27	30	43	15	27	10	12	14

ACEi; angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CMP, dilated cardiomyopathy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HIV, human immunodeficiency virus; HTN, hypertension; IVSd, interventricular septum dimension in diastole; LA, left atrial; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; LVIDd, left ventricular internal dimension during diastole; LVIDs, left ventricular internal dimension in systole; NYHA, New York Heart Association; RVSP, right ventricular systolic pressure.

*Other includes hypertrophic cardiomyopathy, pericardial disease, thyroid disease, and unknown etiology.