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Clinical characteristics and prognosis of patients admitted for heart failure: A 5-year retrospective study of African patients

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ABSTRACT

Background: Mortality associated with heart failure (HF) remains high. There are limited clinical data on mortality among HF patients from African populations. We examined the clinical characteristics, long-term outcomes, and prognostic factors of African HF patients with preserved, mid-range or reduced left ventricular ejection fraction (LVEF).

Methods and results: We conducted a retrospective longitudinal cohort study of individuals aged ≥18 years discharged from first HF admission between January 1, 2009 and December 31, 2013 from the Cardiac Clinic, Directorate of Medicine of the Komfo Anokye Teaching Hospital, Ghana. A total of 1488 patients diagnosed of HF were included in the analysis. Of these, 345 patients (23.2%) had reduced LVEF (LVEF < 40%) [HFrEF], 265(17.8%) with mid-range LVEF (40% ≥ LVEF < 50%) [HFmEF] and 878 (59.0%) had preserved LVEF (LVEF ≥ 50%) [HFpEF]. Kaplan–Meier curves and log-rank test demonstrated better prognosis for HFpEF compared to HFrEF and HFmEF patients. An adjusted Cox analysis showed a significantly lower risk of mortality for HFpEF (hazard ratio (HR); 0.74; 95% confidence interval (CI) 0.57–0.94) $p = 0.015$). Multivariate analyses showed that age, higher New York Heart Association (NYHA) functional class, lower LVEF, chronic kidney disease, atrial fibrillation, anemia, diabetes mellitus and absence of statin and aldosterone antagonist treatment were independent predictors of mortality in HF. Although, prognostic factors varied across the three groups, age was a common predictor of mortality in HFpEF and HFmEF.

Conclusions: This study identified the clinical characteristics, long-term mortality and prognostic factors of African HF patients with reduced, mid-range and preserved ejection fractions in a clinical setting.

1. Introduction

Heart failure (HF) is a complex clinical syndrome which has become a major public health problem associated with high morbidity and mortality [1,2]. The incidence and prevalence of HF continue to rise due to an ageing population, improved health care and survival of patients with chronic cardiovascular diseases such as hypertension and ischemic heart disease [3,4]. Despite advances in treatment in recent decades, HF mortality is still high [5,6] and this could be attributed to the advanced age of patients and associated comorbidities [7].

It is estimated that about half of patients presenting with clinical HF have an ejection fraction of >50% [1,8–11], an entity termed as HF with preserved ejection fraction (HFpEF) which is attributable to diastolic dysfunction [12,13]. Several studies have shown that patients with HFpEF are likely to be elderly, women, have a history of hypertension and less likely to have prior myocardial infarction compared to HF patients with reduced ejection fraction (HFrEF) [1,9,14,15]. Patients with HFpEF have shown better survival compared to HFrEF in a number of studies [9,14,16–22] whereas others [4,23,24] have not demonstrated any difference in outcomes between the two groups. Thus, it appears unclear whether HFpEF patients have better prognosis than those with HFrEF. The results of previous outcome studies of the two groups of HF patients have been conflicting, and the estimates of rates of rehospitalization and mortality

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vary widely, since they are derived from heterogeneous populations with different inclusion criteria [8,14,25–28].

Racial and ethnic differences have been shown to play an important role in patient characteristics, treatment, hospitalization rates and prognoses for HF [29–33]. Black patients particularly African Americans compared with other racial groups are at increased risk for development of HF [30–32]. In addition, HF occurs at much younger age in blacks and are associated with higher prevalence of cardiovascular risk factors particularly hypertension and diabetes mellitus but lower frequency of coronary artery disease [34]. Among African Americans, the prevalence of HFpEF may be higher than estimates in the general population [32]; however reports of survival outcomes have been mixed [29,33,35]. Although little is known about clinical characteristics, treatments and outcomes of HF among Sub-Saharan Africans [34,36,37], poor prognosis has been reported [37–39] and predictors of long-term mortality outcomes have hitherto not been well studied. This present study evaluates the clinical characteristics and long-term outcomes of patients with HF and HF cohorts with preserved ejection fraction compared to those with reduced ejection fraction in predominantly black African population.

2. Methods

We conducted a retrospective longitudinal cohort study of newly diagnosed HF aged ≥18 years who were hospitalized for HF between January 1, 2009 and December 31, 2013. Heart failure was diagnosed, using the modified Framingham criteria for the diagnosis of HF [40,41]. Major criteria included: paroxysmal nocturnal dyspnoea, raised jugular venous pressure, clinical cardiomegaly, basal crepitations, S3 gallop, clinical acute pulmonary oedema, and pulmonary upper lobe blood diversion or pulmonary oedema on chest X-ray. Minor criteria included: tachycardia, orthopnoea, exertional dyspnoea, nocturnal cough, hepatomegaly, pleural effusion, and diuretic use. HF was diagnosed if the patient had two major and one minor or one major and two minor criteria. Patients were eligible for the study if they were discharged from first hospitalization for HF. The first hospitalization for HF was considered index admission. The follow-up commenced from the date of discharge from index admission to time of mortality from all-cause, cardiovascular, worsening HF mortality, loss to follow up or the end of study.

2.1. Study location

The study was conducted at the Komfo Anokye Teaching Hospital (KATH). KATH is a 1200-bed tertiary health centre located in Kumasi, which is the regional capital of the Ashanti region of Ghana. The Ashanti region has a population of about 4 million and the geographical location, road network of the country and commercial nature of the regional capital city, Kumasi make the hospital accessible to all the regions that share its border and beyond. Thus KATH receives referrals from many hospitals across the country. The Cardiac Clinic, Directorate of Medicine of KATH is the only tertiary facility which serves patients from the northern half of Ghana. Approximately 85% of patients who seek health care at KATH subscribe to the National Health Insurance Scheme (NHIS). The NHIS is a nationwide insurance scheme which was introduced in 2004 to cater for the healthcare needs of all Ghanaians.

The study was approved by the Committee on Human Research, Publications and Ethics of Kwame Nkrumah University of Science and Technology, Ghana and the Monash University Human Research Ethics Committee, Australia. A patient's informed consent was not required.

2.2. Data collection

Information was collected about demographics, medical history, clinical characteristics and laboratory tests of the study population through review of information contained in hospital medical records from the Cardiac Clinic, Directorate of Medicine, KATH. Data for the study were extracted from medical records of HF patients from the Cardiac Clinic. Complete patient data for review contain medical records linked with corresponding insurance claim records from the pharmacy department and NHIS units in the hospital for the study duration. The medical and claims' records are manually kept in the hospital. The NHIS requires that diagnosis, procedures and medication prescribed are linked with the Ghana Diagnosis-Related Group (G-DRG) codes. The G-DRG codes consist of the patient disease condition or procedure and age group linked with the International Statistical Classification of Diseases and Related Health Problems—Tenth Revision (ICD-10) coded diagnosis. Information collected from the medical records were vital signs (heart rate and blood pressure), diagnosis, comorbidities (anemia, prior angina pectoris, atrial fibrillation, hypertension, diabetes mellitus, prior myocardial infarction, chronic obstructive pulmonary disease, dilated cardiomyopathy, coronary artery disease, chronic kidney disease, chronic liver disease and history of stroke), laboratory investigations and results (low density lipoprotein cholesterol [LDL-C] and high density lipoprotein cholesterol [HDL-C]), chest X-ray reports, echocardiogram, electrocardiogram and procedures conducted on patients, prescribed medications (angiotensin converting enzyme inhibitors [ACE inhibitors], angiotensin receptor blockers [ARBs], calcium channel antagonists, beta-blockers, diuretics, statins, aldosterone antagonist, digoxin, oral anticoagulant and nitrates) and cost covered at discharge from index admission or follow-up clinic visit. The medical records contain demographic profile and medical and drug history of patients. The demographic data include age, sex, height, weight, marital status and highest level of education of patients. Also included in the data, are dates of index admission and readmissions, dates of discharge from readmissions, dates of follow-up clinic visits as well as death dates if the patient died. The insurance claim records cover patients' date of birth, age, sex, NHIS unique number, admission date, date of discharge or death, diagnosis according to G-DRG codes, procedures conducted on patients, generic name, dosage and quantity of drugs dispensed and cost covered under the scheme. A combination of both direct and indirect identifiers—NHIS unique number, admission date, discharge date, patient sex, and patient age or date of birth—were used to link medical and claim records. Trained clinical researchers extracted the data from patients' records and disagreements were resolved by consensus or by consulting a physician when necessary. The cause of death was ascertained from medical records, autopsy report and claim records.

2.3. End point assessment

The outcomes of interest are time to all-cause, cardiovascular and worsening HF mortality. Time of death was assessed as date of death recorded in medical and claims' records if patient died.

2.4. Censoring

Patients who did not experience any of the study end points or outcomes before the end of study or loss to follow-up were censored. The censoring dates were defined as (a) end of study period or (b) date on which the patient's data were no longer available.

2.5. Statistical analysis

The demographic and risk profile of the study population were characterized using descriptive statistics. All parameters analyzed were taken at discharge from index admission and at follow-up clinic visit. We used chi-squared tests to compare categorical variables and Student's *t*-test to investigate the relationship in continuous variables between two groups. Differences in time to death between groups were analyzed by Kaplan-Meier estimation and compared using a two-sided log-rank test. Cox proportional hazard approach was used to model time to all-cause, cardiovascular and worsening HF deaths while controlling for the effects of key baseline and follow-up variables on outcomes to estimate hazard ratios and corresponding 95% confidence intervals. We constructed univariate Cox proportional hazard models for each predictor variables. Multivariate Cox proportional hazard models were then constructed on the overall study population and for predefined groups to estimate the hazard ratios and associated confidence intervals to identify factors or variables that independently predict death in HF. In each of the multivariate Cox models, variables that were significant in univariate models as well as those which did not show any statistical significance but have been shown from literature to predict outcomes among patients with HF were included. Further, backward variable elimination, with an elimination criterion of a $p > 0.05$, was used to create a parsimonious model for predicting death. We checked for the effects of interactions and further ensured that proportional hazard assumptions in each model were not violated. The study sample was stratified by the ejection fraction variable into HF with reduced ejection fraction (LVEF < 40%) [HFrEF], HF with mid-range ejection fraction (40% ≥ LVEF > 50%) [HFmEF] and HF with preserved ejection fraction (LVEF ≥ 50) [HFpEF]. We constructed separate multivariate Cox models with same variables and approaches described above to identify predictors of death in HFrEF, HFmEF and HFpEF. Statistical analysis was performed with R statistical software version 3.2.4 (R foundation for Statistical Computing, Vienna, Austria). A two sided *p*-value of <0.05 was considered to indicate statistical significance.

3. Results

3.1. Study population

Data from a total of 2058 patients were screened and abstracted for the study as patients admitted, discharged or seen for HF at the Cardiac Clinic of the Komfo Anokye Teaching Hospital between January1, 2009 and December 31, 2013. Of these, 570 did not meet the predefined inclusion criteria and were excluded from the study. For purposes of the present investigation, we excluded; 76 (3.7%) patients aged <18 years, 117 (5.7%) who died during the index admission, 129 (6.3%) with severe valvular heart disease requiring surgery, 154 (7.5%) with incomplete data at baseline and follow-up and 94 (4.6%) without ejection fraction data from the analysis. The remaining 1488 patients met the predefined criteria of index admission for HF at age ≥ 18 years and had ejection fraction data during the study period. Of these patients, 345(23.2%) had HFrEF (LVEF < 40%), 265 (17.8%) with HFmEF (40% ≥ LVEF > 50%) and 878 (59.0%) had HFpEF (EF ≥ 50%).

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