Characteristics and 12-month outcome of patients with atrial fibrillation at a tertiary hospital in Botswana

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Abstract

Background: Atrial fibrillation (AF) is the commonest sustained cardiac arrhythmia associated with high morbidity and mortality rates. Notwithstanding the scale of the problem, there are sparse data on the characteristics and outcomes of both valvular and non-valvular AF patients in sub-Saharan Africa (SSA).

Objective: This study aimed at describing the clinical features and outcome of AF patients at a tertiary hospital in Botswana.

Methods: This prospective study was carried out in the Princess Marina Hospital in Gaborone, Botswana between August 2016 and July 2018. We consecutively enrolled 138 (97.8% black Africans) adult patients with electrocardiographically documented AF. Their baseline clinical and biomedical data were documented, and each patient was followed up for 12 months. The primary study outcome was 12-month all-cause mortality.

Results: The mean [standard deviation (SD)] age of enrolled patients was 66.7 (17.2) years, and 63.8% were females. Common co-morbidities were hypertension (59.4%), rheumatic heart disease (37.7%) and heart failure (35.5%). Stroke/transient ischaemic attack (TIA) (21.7%) and obesity (34.8%) were also prevalent. Compared to patients with non-valvular AF, those with valvular AF were more likely to be female (82 vs 55%, p = 0.003), younger (60 vs 75 years, p < 0.001), on anticoagulation (88.6 vs 66%, p = 0.005), or have a dilated left atrium (5.3 vs 4.5 cm, p < 0.001). They were also less likely to present with hypertension (33 vs 72%, p < 0.001), stroke/TIA (nine vs 27%, p < 0.017), chronic kidney disease (five vs 20%, p < 0.02), or history of cigarette smoking (two vs 13%, p = 0.049) than non-valvular AF patients. The mean (SD) CHA2DS2-VASc score in non-valvular AF patients was 3.6 (1.5), and the median HAS-BLED score was 2.0 [interquartile range (IQR) 1.0–3.0]. During the 12-month follow up, 20 (14.5%) patients died. Despite differences in baseline characteristics, there was no difference in mortality rate in patients with valvular compared to those with non-valvular AF (13.8 vs 15.9%; p = 0.746).

Conclusion: In this study, hypertension, rheumatic heart disease and heart failure were the most prevalent co-morbidities. AF presented in young people and conferred high mortality rates in both valvular and non-valvular AF patients. Prevention and optimal management of AF and associated co-morbidities are of critical importance.

Atrial fibrillation (AF) is the most frequent sustained cardiac arrhythmia of public health importance. The prevalence of AF has been lower in Africa than in the developed world. The burden of AF in sub-Saharan Africa has, however, been increasing over the past few decades. This trend may partly be explained by the population ageing and an increasing burden of chronic non-communicable diseases of lifestyle that predispose to AF, such as obesity, smoking, hypertension, diabetes and cardiovascular diseases. Unfortunately, these diseases tend to occur earlier in life among Africans compared to Caucasians. Their presence dramatically magnifies the risk of AF, particularly non-valvular AF. As a result, patients with non-valvular AF in Africa tend to be younger than patients in other regions. Due to the high burden of rheumatic heart disease, patients with valvular AF in SSA also tend to be younger than those from developed countries where age-related degenerative valvular diseases predominate.

Given that AF is not a benign disease, AF-related morbidity and mortality pose another challenge to the young population in SSA countries where infectious diseases are a burden. The disease is associated with an approximately five-fold increased risk for stroke, a two-fold increased risk for heart failure, and two-fold increased risk for mortality. Despite the extent of the problem, there are sparse data on the characteristics and

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outcomes of both valvular and non-valvular AF patients in SSA. This information is critical for the identification of patients needing priority attention to minimise dire consequences. This study aimed at evaluating the characteristics and outcomes of patients with valvular and non-valvular AF at a tertiary hospital in Botswana.

**Methods**

This prospective study was conducted in the medical in- and out-patient departments at Princess Marina Hospital (PMH) in Gaborone between 1 August 2016 and 31 July 2018. PMH is a tertiary referral and university teaching hospital that not only serves patients from the city but also patients from around the country.

We sought ethical approval for this study from the University of Botswana, Ministry of Health and Princess Marina ethical review committees. The study was conducted as per the principles of the Declaration of Helsinki. Written informed consent was obtained from all study participants.

The study enrolled consecutive patients aged 18 years and older, with a documented diagnosis of AF on an electrocardiogram (ECG), who presented to the medical wards and clinics. Data were collected through patient interviews, a review of electronic medical records, and physical and echocardiographic examinations. The presence of hypertension, ischaemic heart disease, valvular heart disease, heart failure, diabetes mellitus, stroke and transient ischaemic attack (TIA), and hyper/hypothyroidism was determined in all the patients. A history of smoking, alcohol consumption, antihypertensive and anti-diabetic medication use, and previous cardiac surgery was also determined.

We measured blood pressure, pulse rate, height and weight in all participants. Patients’ weight (to the nearest kg) and height (to the nearest 1 cm) were measured on individuals in light clothing without shoes. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m²), and participants with a BMI of ≥ 30 kg/m² were classified as obese.11 We conducted three blood pressure measurements after 10 minutes of rest, and the mean of the three measurements was recorded. Hypertension was diagnosed if blood pressure was ≥ 140/90 mm Hg or if the subject was receiving antihypertensive medication.12 Diabetes was defined as a prior documented diagnosis of diabetes in patients’ medical records or the use of insulin or oral hypoglycaemic agents.

A diagnosis of heart failure was reached based on a previously documented diagnosis or diagnosed at enrolment, based on the European Society of Cardiology criteria.13 Patients’ serum creatinine, urea, alanine aminotransferase, aspartate aminotransferase and thyroid function test results were also recorded. The risk for stroke among patients with non-valvular AF was stratified by using the CHA 2DS 2-V ASc score.14 The HAS-BLED score was used to assess the risk of bleeding among patients who qualified for anticoagulation.14,15

Two-dimensional, motion mode (M-mode) and Doppler transthoracic echocardiography were performed to assess cardiac structure and function. Assessment of dimensions, systolic and diastolic function of the ventricles, valvular function, rheumatic heart disease and pulmonary hypertension was done using standard guidelines.16-20 Patients with heart failure (HF) were classified into those with preserved ejection fraction (HFpEF) when left ventricular ejection fraction (LVEF) was ≥ 50%, mid-range ejection (HFmrEF) when the LVEF was 40–49%, and reduced ejection fraction (HFrEF) when LVEF was < 40%.20

Valvular AF was defined as AF that occurred in the presence of mechanical prosthetic heart valves or moderate-to-severe rheumatic mitral stenosis. Non-valvular AF was referred to as AF that occurred in the absence of mechanical prosthetic heart valves and the absence of moderate-to-severe rheumatic mitral stenosis.21,22

The primary outcome of interest was 12-month all-cause mortality. We obtained this information by telephone calls to participants or their relatives or from the patients’ electronic medical records.

**Statistical analysis**

There was no pre-calculation of the sample size. The study enrolled consecutive patients who presented to the medical wards and clinics between 1 August 2016 and 31 July 2018. All statistical analyses were conducted using Stata (version 13, Stata Corp, College Station, Texas, USA). Continuous variables were summarised using the mean (SD), and categorical variables were expressed in percentages. Comparisons of data between valvular and non-valvular AF patients were conducted using Pearson’s chi-squared analysis or Fisher’s exact test for categorical variables, and unpaired Student’s t-test for continuous variables. All-cause mortality was assessed as the number of patients who died during the 12-month follow-up period, divided by the total number of participants. A p-value less than 0.05 was considered statistically significant.

**Results**

Of the 138 patients who were enrolled, the majority (97.8%) were of black African origin. Follow-up data were available in all participants. Table 1 shows the baseline characteristics of patients at enrolment. The mean (SD) age of the patients was 66.7 (17.2) years and 63.8% of patients were female. Hypertension (59.4%), rheumatic heart disease (37.7%) and heart failure (35.5%) were frequent among participants. Patients with rheumatic heart disease had moderate-to-severe mitral regurgitation (35, 67.3%), moderate-to-severe mitral stenosis (20, 38.4%), moderate-to-severe aortic regurgitation (four, 7.7%), or moderate-to-severe aortic stenosis (two, 3.8%). Twenty-five (18.1%) patients had mechanical heart valves, the majority (92%) being mitral valve prostheses.

Chronic kidney disease (15.2%), cigarette smoking (9.4%), diabetes mellitus (8%) and alcohol consumption (5.1%) were uncommon. None of the participants had hyper- or hypothyroidism. Overall, the mean (SD) heart rate was 83.9 (24.9) beats/minutes. The left atrial diameters were enlarged to a mean (SD) value of 4.8 (1.0) cm and pulmonary hypertension was diagnosed in 37% of the patients. The mean (SD) LVEF was 52.8 (17.7) and about a quarter (26.8%) of the patients had HFrEF, and 13.0% presented with HFmrEF (50%).

The mean (SD) CHA 2DS 2-V ASc score for patients with non-valvular AF was 3.6 (1.5), with the majority (89.4%) scoring ≥ 2. The median HAS-BLED score for patients was 2.0 (IQR 1.0–3.0), with 58.1% scoring ≤ 2. For non-valvular
AF with CHA2DS2-VASC scores ≥ 2, 73.8% of patients were prescribed anticoagulation therapy [66.7% warfarin and 7.1% novel oral anticoagulants (NOACs)]. Anticoagulant therapy was not prescribed in 26.2% of patients with CHA2DS2-VASC scores ≥ 2. Beta-blockers (70.3%) and digoxin (37.3%) were the only prescribed rate-controlling medications. Amiodarone,
calcium channel blockers and electrical cardioversion were not documented among our participants. Angiotensin converting enzyme (ACE) inhibitors, furosemide and spironolactone were also frequently used.

Results in Table 2 compare the clinical and biomedical data from patients with valvular and non-valvular AF. Compared to patients with non-valvular AF, patients with valvular AF were significantly younger ($p < 0.001$) and more likely to be female ($p = 0.003$). They were less likely to have hypertension ($p < 0.001$), chronic kidney disease ($p < 0.02$) and a previous stroke/TIA ($p < 0.017$). Participants with valvular AF had significantly larger left atrial diameter ($p < 0.001$) than the non-valvular AF patients.

Patients’ median aspartate aminotransferase (AST) ($p = 0.006$) and alanine aminotransferase (ALT) ($p = 0.009$) levels were higher than those with non-valvular AF. Other laboratory data, including haemoglobin, were comparable between the two groups. Those with valvular AF had a significantly lower HAS-BLED score ($p < 0.001$) than the non-valvular AF patients. An anticoagulation prescription was significantly more frequent in patients with valvular AF than the non-valvular AF patients ($p = 0.005$). Few patients with non-valvular AF were on a non-vitamin K antagonist (NOAC). The prescriptions of other medications were comparable between the two groups.

There was a total of 20 (14.5%) deaths during the 12-month follow-up period. There were 13 (13.8%) and seven (15.9%) deaths in patients with valvular and non-valvular AF, respectively ($p = 0.746$).

Discussion

Only a few studies have been done on AF in SSA, despite its growing public health importance. This study describes the characteristics and outcomes of patients with AF in a developing SSA country.

Hypertension, heart failure and rheumatic heart disease (RHD) were the most common underlying diseases for AF in our relatively young cohort. We also identified a low prevalence of diabetes mellitus, cigarette smoking, alcohol consumption and chronic kidney disease among patients. There was a baseline difference in age and burden of cardiovascular disease in patients with valvular AF and those with non-valvular AF. However, despite these differences, death rates (all-cause mortality) were comparable between the two groups. The overall mortality rate during the 12-month follow-up period was high (14.5%).

Consistent with previous reports from SSA, our cohort was younger (67 years) than patients in developed countries, where most cases are recorded around the eighth decade of life. A shorter life expectancy in SSA and differences in the epidemiology of diseases associated with AF in developed and developing countries partly explain this age difference. The main risk factors of AF in SSA (RHD, hypertension and heart failure) tend to present at a younger age and in a more severe form than in developed countries.

The finding of female predominance in the present study is consistent with previous results in South Africa and Cameroon. This pattern is likely explained by gender-based differences in potential underlying diseases (particularly RHD). Although there is no apparent gender predilection for acute rheumatic fever, RHD tends to be more common in females than males. Also, there is a two-fold increased risk for AF in women with valvular heart disease compared to their male counterparts. Consequently, the proportion of female patients among our valvular AF patients was significantly higher compared to patients with non-valvular AF.

In the present study, RHD was found in more than a third (37.7%) of participants. This is not surprising as RHD is much more common in patients with AF in Africa than in the developed world. In the global Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) AF registry that enrolled patients presenting with AF to emergency departments, RHD was present in only 2.2% of North American patients compared to 21.5% in Africa. Likewise, the proportion of African patients with RHD in South Africa and Cameroon was reported as 21 and 25.6%, respectively. Although the exact reasons for the higher frequency of RHD in our cohort than in other African settings are unclear, one may be that there is variation in the overall burden of RHD across African countries. About a third (32%) of our cohort was found to have moderate-to-severe mitral stenosis or prosthetic heart valve AF and was classified as having valvular AF. As a consequence of the higher prevalence of RHD, valvular AF patients were significantly younger and more likely to be female than those with non-valvular AF. This finding has clinical implications, as the presence of AF in the reproductive years may be associated with worse pregnancy outcomes.

We found a high burden of hypertension and heart failure among our participants, consistent with previous AF studies worldwide. Unfortunately, these diseases are likely to remain undiagnosed or poorly controlled in Africa compared to developed countries. Early detection and control of hypertension have the potential to reduce the occurrence and progression of AF in SSA. In contrast to reports from developed countries, diabetes and coronary artery diseases were infrequent in our cohort, as in other African studies. Likewise, in the RE-LY AF registry, the prevalence of diabetes and coronary artery diseases were the lowest among Africans compared to other regions of the world. With the increasing burden of non-communicable diseases in SSA, the contribution of diabetes and coronary artery disease to the overall prevalence of AF in this region is likely to rise.

Comparable to previous studies in Africa, our patients with non-valvular AF were more likely to have hypertension than those with valvular AF. Also, chronic kidney disease, obesity and cigarette smoking were more frequent in this group. The presence of these co-morbidities is known to adversely affect survival in individuals with AF. The observed higher burden of co-morbidities in non-valvular AF patients compared to valvular AF may in part be explained by the older age of participants in this group. This burden of co-morbidities partly reflects in high thromboembolic risk (mean CHA2DS2-VASc 3.6), comparable to the risk previously reported in the European GARFIELD study (mean CHA2DS2-VASc 3.3). As previous studies in Africa have stratified patients’ thromboembolic risk using CHADS3 scores, it was difficult to compare our findings to other SSA countries. Using the CHADS3 score, AF patients in SSA have consistently been reported to have low thromboembolic risk.

Similar to the data obtained previously in Kenya, a significant proportion of our patients had a history of stroke/TIA. The
burden of stroke/TIA in our AF cohort was, however, higher than seen in previous reports from other countries in SSA.\textsuperscript{7,24,25} Although the majority of patients with stroke/TIA were those with non-valvular AF, the burden of stroke/TIA (9.3%) in the young cohort with valvular AF was still higher than what was previously reported in South Africa (2.4%). The reason for this disparity is unclear but may lead to speculation about variation in thromboembolic risks across communities.

The majority of our patients with non-valvular AF had CHA\textsubscript{2}.DS-VASc scores $\geq 2$ and required oral anticoagulation to prevent stroke. A higher proportion of our AF patients were on warfarin anticoagulation compared to other reports across the globe.\textsuperscript{7} Although NOACs are indicated as an alternative to warfarin for non-valvular AF, these drugs were prescribed in only 4.4% of these patients. Availability of these drugs in public health facilities in Botswana (and possibly in other SSA countries) is limited by their high cost and probably the absence of antidotes. The drugs remain an option for only a select group of individuals in private health facilities. For the same cost-related reasons, beta-blockers and digoxin were the only prescribed rate-controlling medications. Similar observations were made in Cameroon where digoxin and beta-blockers were the main anti-arrhythmic drugs used.\textsuperscript{26}

In the present study, the overall mortality rate at 12 months (14.5%) was higher than previously reported in a similar study in Kenya (10%).\textsuperscript{26} It was much higher than the 24-month mortality rate (3.8%) observed in a large European study.\textsuperscript{27} A much higher 12-month mortality rate (29.5%) has, however, been reported in an African study.\textsuperscript{28}

The reasons for the higher mortality rates in our cohort and other SSA countries than in Europe may include variation in the study settings, management and control of co-morbidities, quality of anticoagulation control, and in the treatment of AF.\textsuperscript{7} The present study was conducted in a tertiary hospital where complex and very ill cases are more likely to be referred, and hence the high mortality rate. Although the use of oral anticoagulants was high in our patients, a recent report from Botswana showed suboptimal anticoagulation control among patients on anticoagulation.\textsuperscript{29} The high burden of RHD among our patients could also have contributed to an increased risk of mortality in our cohort, as this subgroup of AF patients is known to have high mortality rates.

Our study had some limitations. It was conducted in a tertiary hospital, limiting the generalisability of the findings to other settings in the country where facilities and expertise are limited. A selection bias is possible as patients in a tertiary healthcare facility are more likely to be more ill than those who are managed at primary or secondary level healthcare facilities. This may have, in part, contributed to the high mortality rate observed in the present study. The size of the sample and the duration of follow up did not allow for the assessment of the determinants of mortality among our patients.

Although we demonstrated a high use of anticoagulation, we have insufficient data to comment on whether the mortality rate of AF patients was altered by the level of anticoagulation control, as suggested by others. However, a recent study has reported poor anticoagulation control in the same setting.\textsuperscript{30} Therefore, we believe that despite the high prescription of anticoagulation, poor anticoagulation control may have had some influence on the observed high mortality rate. Data on the causes of death were difficult to ascertain, as some patients died outside the hospital and autopsies were not performed. We therefore reported on all-cause mortality in our patients.

### Conclusion

AF is a common arrhythmia that presents in patients with hypertension, RHD and heart failure in our setting. The disease presents in young people and confers a high mortality rate that is comparable to other SSA countries. In light of the high death rate associated with AF in our young cohort, additional research is needed to address the prevention and optimal management of AF and associated co-morbidities.

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### References


