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Burden of atrial fibrillation among adults with heart failure in sub-Saharan Africa: a systematic review and meta-analysis

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ABSTRACT

Objectives This study aimed to estimate the prevalence of atrial fibrillation (AF) in adults with heart failure (HF) and summarise the all-cause mortality ratio among adult patients with coexisting HF and AF in sub-Saharan Africa (SSA).

Setting This was a systematic review and meta-analysis of cross-sectional and cohort studies with primary data on the prevalence and incidence of AF among patients with HF and the all-cause mortality ratio among patients with HF and AF in SSA. We combined text words and MeSH terms to search MEDLINE, PubMed and Global Health Library through Ovid SP, African Journals Online and African Index Medicus from database inception to 10 November 2021. Random-effects meta-analysis was used to estimate pooled prevalence.

Primary outcome measures The prevalence and incidence of AF among patients with HF, and the all-cause mortality ratio among patients with HF and AF.

Results Twenty-seven of the 1902 records retrieved from database searches were included in the review, totalling 9987 patients with HF. The pooled prevalence of AF among patients with HF was 15.6% (95% CI 12.0% to 19.6%). At six months, the all-cause mortality was 18.4% (95% CI 13.1% to 23.6%) in a multinational registry and 67.7% (95% CI 51.1% to 74.3%) in one study in Tanzania. The one-year mortality was 48.6% (95% CI 32.5% to 64.7%) in a study in the Democratic Republic of Congo. We did not find any study reporting the incidence of AF in HF.

Conclusion AF is common among patients with HF in SSA, and patients with AF and HF have poor survival. There is an urgent need for large-scale population-based prospective data to reliably estimate the prevalence, incidence and risk of mortality of AF among HF patients in SSA to better understand the burden of AF in patients with HF in the region.

PROSPERO registration number CRD42018087564.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study used a systematic approach to summarise prevalence of atrial fibrillation (AF) among heart failure (HF) patients in sub-Saharan Africa.
⇒ Limited country-level estimates prevents the generalisability of the study's findings.
⇒ The certainty of evidence on mortality in AF and HF was limited by a small sample size.

INTRODUCTION

Heart failure (HF) is a global public health problem estimated to affect about 26 million people worldwide.[1] The global prevalence of HF has been on the rise owing to improvements in life expectancy, the management of acute heart conditions and the rising prevalence of cardiovascular disease risk factors, such as hypertension, obesity and diabetes mellitus.[1 2] HF disproportionately affects low-income and middle-income countries, especially those in sub-Saharan Africa (SSA), where it is associated with high economic costs, poor quality of life, high readmission rates and high in-hospital and 1-year mortality rates.[3 4] For example, about 35% of patients discharged for acute HF will be readmitted within 30 days.[5] This is important in the African context, where about 90% of the cost of management of HF is borne by the patient and their immediate families.[3] In addition, the in-hospital mortality of HF in SSA ranges from 15% to 35%, with 1-year mortality of up to 58%.[3] The 1-year mortality rate from HF is highest in Africa compared with other regions such as Southeast Asia, Middle East and South America.[6]

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide.[7] In 2017, there were 37.6 million individuals with AF, including 3.1 million new cases.[7] AF is associated with a higher risk of stroke and systemic embolism, HF and mortality.[8] AF is associated with poorer outcomes among patients with HF, and is estimated to affect about 16%–21% of patients with HF in SSA.[9–12] In addition, AF accelerates the natural history

of HF and is associated with more frequent admissions, longer hospital stays and increased mortality in patients with HF.[9 13–15]

Data on the burden of AF in patients with HF in SSA have not been systematically summarised. Hence, this systematic review and meta-analysis sought to estimate the prevalence of AF in adults with HF and summarise the all-cause mortality ratio among adult patients with coexisting HF and AF in SSA.

METHODS

The review protocol was published.[16] This study is reported following the 2020 Preferred Reporting Items for Systematic Reviews and Meta-analyses.[17]

Literature search

We searched MEDLINE, Excerpta Medica Database (Embase) and Global Health Library through Ovid SP, African Journals Online and African Index Medicus from database inception to 10 November 2021 with no language restrictions. The search strategy combined text words and medical subject headings related to AF and HF, and a validated geographical filter for SSA[18] (online supplemental tables 1–5). We handsearched the reference list of eligible full-text articles to obtain additional data.

Study selection

We included cross-sectional and cohort studies conducted in SSA that reported the prevalence and incidence of AF among patients with HF, all-cause mortality ratio among patients with HF and AF, or provided sufficient data to compute these estimates. We excluded reviews, editorials, studies with fewer than 30 participants and studies conducted in persons aged <15 years. In addition, we only included the study with the most recent, comprehensive and largest sample size for published studies that used data from the same cohort of participants (duplicate data).

Records retrieved from database searches were exported to EndNote V.X9 to remove duplicates and then uploaded to Rayyan QCRI for title and abstract screening. Three authors (CMM, SJNP and LPS) independently screened the citations based on titles and abstract and assessed the full texts of selected records for final inclusion in the review. Disagreement between authors during the study inclusion process was resolved through consensus or arbitration by a fourth author (VNA).

Data extraction, management and risk of bias assessment

Four authors (VNA, CMM, SJNP and LPS) used a predesigned Google Form to independently abstract data on: the surname of the first author, year of publication, country of study, study setting, study design, sampling method, timing of data collection, mean or median age of study participants, percentage of male participants, percentage of participants on beta-blockers, sample size, percentage of participants in New York Heart Association (NYHA) stage III or IV, method of diagnosis of AF, method of diagnosis of HF and the duration of follow-up for cohort studies. For multinational studies, data were extracted by the individual country of the study where possible.

For the outcome of prevalence and incidence of AF in HF, data were also extracted on the number of prevalent AF cases, the number of new AF cases if reported by the study, and the number of participants with HF. Where the authors reported the proportion or percentage rather than number of patients with AF, we multiplied this proportion or percentage by the number of HF patients to obtain the number of participants with AF.

For all-cause mortality ratio among patients with AF and HF, we extracted data on the number of participants with HF and AF and the number of deaths from any cause.

Risk of bias assessment

Two reviewers (CMM and SJNP) independently assessed the risk of bias in the included studies. An adapted version of the risk of bias assessment tool developed by Hoy *et al*[16 19] was used to assess the risk of bias in studies reporting on the prevalence of AF in HF. In addition, we modified the original version of the Newcastle-Ottawa Scale[20] to evaluate the risk of bias in studies that reported all-cause mortality in patients with HF and AF.

Data analysis and synthesis

All analyses were conducted with the 'meta' package of R version 4.1.2 (The R Foundation for Statistical Computing, Vienna, Austria). To estimate the prevalence of AF among participants with HF, we performed an inverse-variance weighted random-effects meta-analysis of proportions after stabilising the variance using the Freeman-Tukey double-arcsine transformation.[21] The degree of heterogeneity across studies was assessed using the Cochrane's Q χ^2 test and quantified using the I^2 statistic.[22] I^2 values below 30%, 30%–49%, 50%–70% and over 70% were considered to represent low, moderate, substantial and considerable degree of heterogeneity, respectively.[22] A p<0.05 on the Cochrane's Q χ^2 test indicated significant heterogeneity between studies. We used the Baujat plot to inspect for influential studies on the pooled summary effect.

We conducted subgroup analyses using random-effects meta-analysis without assuming a common between-study variance to investigate the sources of heterogeneity by region, study design, timing of data collection, method of AF diagnosis, risk of bias, age of participants and percentage of participants in NYHA stage III or IV. The Q test was used to investigate moderation effects across subgroups. A p<0.1 for test of subgroup difference was used as the threshold for statistical significance.[22] Where appropriate, studies were merged into meaningful categories to minimise loss of power during subgroup analyses. Where a lone category could not be merged into other categories, this was excluded from the subgroup analysis.

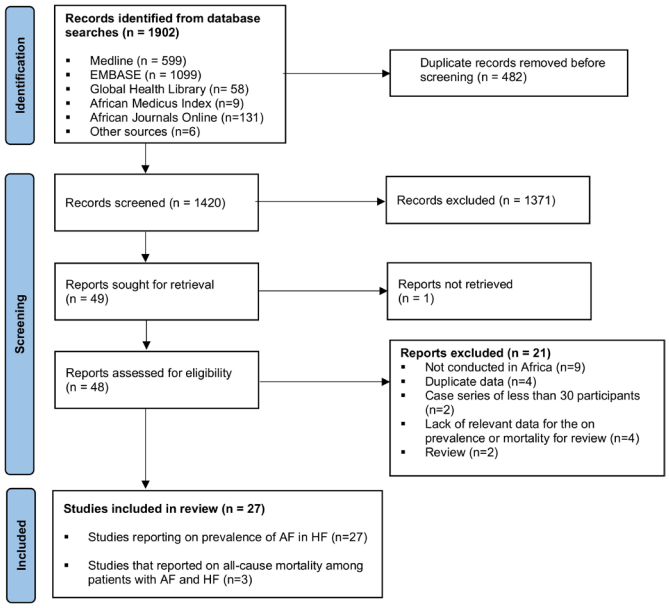

Figure 1 PRISMA flow diagram for inclusion of articles in the meta-analysis. AF, atrial fibrillation; HF, heart failure; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses .

Funnel plot was used to investigate small-study effect, and plot asymmetry was suggestive of small-study effect. Egger's regression test was used to test for publication bias. A p<0.1 from Egger's test was considered statistically significant. A sensitivity analysis was conducted to assess the impact of excluding influential studies on the overall summary prevalence.

Mortality ratio was defined as the proportion of participants with AF and HF who died from any cause within a given follow-up time. Due to the small number of studies reporting on all-cause mortality ratio among patients with AF and HF, this outcome was summarised narratively.

Patient and public involvement

Patients or the public were not directly involved in this study.

RESULTS

Study selection and characteristics

From 1902 records retrieved through database searches, 27 were eligible for inclusion in the review[9 11 23–47] (figure 1 and online supplemental table 6). The included studies provided 30 data points on the prevalence of AF in HF (data from the multinational study by Karaye *et al*[47] were disaggregated by the country of study). Only three studies[9 34 44] provided data on mortality among patients with AF and HF, and none reported on the incidence of AF in HF.

All included studies were published from 1995 to 2021 (table 1). The majority (n=23, 76.7%) of studies were published after 2010, and all were hospital-based. Most studies were cohort studies (n=24, 80%), conducted in West Africa (n=11, 36.7%), used a non-probabilistic sampling method (n=24, 80%) and diagnosed AF using 12-lead ECG (n=23, 76.7%).

Table 1 Characteristics of studies included in the meta-analysis

Characteristics	N=30
Year of publication	
Range	1995–2021
1995–2010	7 (23.3%)
After 2010	23 (76.7%)
Subregion	
Central	6 (20.0%)
East	6 (20.0%)
South	6 (20.0%)
West	11 (36.7)
Multinational registry	1 (3.3%)
Study design	
Cohort	24 (80.0%)
Cross-sectional	6 (20.0%)
Study setting	
Hospital-based	30 (100.0%)
Population-based	0 (0.0%)
Sampling method	
Non-probabilistic	24 (80.0%)
Not reported	6 (20.0%)
Participants in NYHA III or IV (%)	
Below 50	8 (26.7%)
50–80	9 (30.0%)
Over 80	6 (20.0%)
Not reported	7 (23.3%)
Atrial fibrillation diagnostic procedure	
12-lead ECG	19 (63.3%)
Holter ECG	2 (6.7%)
Medical history	1 (3.3%)
Not reported	4 (13.3%)
Risk of bias	
Low	19 (63.3%)
Moderate	11 (36.7)

NYHA, New York Heart Association.

Prevalence of AF in patients with HF

A total of 9987 patients with HF were included in the meta-analysis. Almost three-quarters of the studies reporting on the prevalence of AF in HF had a low risk of bias (table 1 and online supplemental table 7). The pooled prevalence of AF in HF was 15.6% (95% CI 12.0% to 19.6%), with considerable heterogeneity between studies (I^2=96.0%, p<0.00001) (figure 2). Table 2 and online supplemental figures 1–9 summarise the results of the subgroup analysis. The prevalence of AF in HF was significantly higher

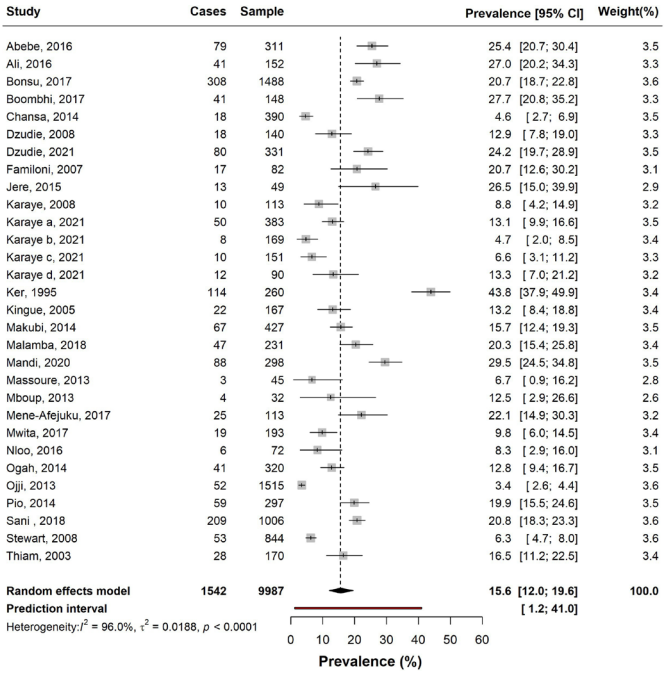

Figure 2 Pooled prevalence of atrial fibrillation in patients with heart failure. The grey squares and the horizontal bars are the study-specific prevalence and 95% CIs. Each study-specific estimate is weighted by the inverse of the variance using random-effect meta-analysis. The centre and the horizontal edges of the black diamond are the pooled summary prevalence and 95% CI.

in studies with retrospective data collection compared with those with prospective data collection (p=0.0147) and in studies with no reported method for AF diagnosis compared with those with recommended methods for AF diagnosis (12-lead or Holter ECG, p=0.0035) (table 2 and online supplemental figures 3 and 4). In addition, the prevalence of AF in HF was significantly higher in studies where the mean age of the participants was 60 years and over compared with studies with younger participants (p=0.0132) (table 2 and online supplemental figure 5). There was no evidence of moderation of the pooled prevalence by region, study design, the severity of HF in study participants (based on the NYHA classification), sample size, risk of bias and percentage of males included in each study (table 2 and online supplemental figures 1,2, 6-9).

There was no evidence of publication bias (P_{Egger}=0.2593) (online supplemental figure 10). In sensitivity analysis, the studies by Ojji *et al*[42] and Ker and Myburgh[32] were identified to significantly influence the pooled summary estimate (online supplemental figure 11). However, excluding these studies and re-estimating the pooled prevalence of AF in HF did not substantially change the results (pooled prevalence=15.4% (95% CI 12.6% to 18.5%), (online supplemental figure 12).

All-cause mortality among patients with AF and HF

Three studies reported on all-cause mortality among patients with AF and HF (table 3).[9 34 44] Two of the studies were prospective cohort studies, while one was a retrospective cohort study. The mean ages of the participants ranged from 52.3 to 56.0 years and 79%–80% of the participants were in NYHA stage III or IV. Two studies had low risk of bias (online supplemental table 8).

At six months, the all-cause mortality was 18.4% (95% CI 13.1% to 23.6%) in a multinational registry and 67.7% (95% CI 51.1% to 74.3%) in a study in Tanzania. All-cause mortality at one year was 48.6% (95% CI 32.5% to 64.7%) in a study in DR Congo (table 3).

DISCUSSION

This review sought to estimate the prevalence and incidence of AF among patients with HF and all-cause mortality among patients with AF and HF in SSA. The pooled prevalence of AF in HF was 15.6%, and varied by the timing of data collection, methods of AF diagnosis and mean age of the study participants. Moreover, the all-cause mortality ratio was 18.4%–67.7% after six months of follow-up and approximately 49% after one year. We did not find any study reporting on the incidence of AF among patients with HF.

The pooled prevalence of AF in HF in this study was lower than reports from North and South America, Europe and East Asia.[48–52] The prevalence of AF among HF patients in the ADHERE (USA), EHFS II (Europe) HF and China-HF registries were 31.0, 39.0 and 24.4%, respectively.[48] In addition, in a 20-year population-based cohort of 88 416 patients with incident HF in the UK, about 39% had AF.[53] In contrast, the pooled prevalence of AF in this study was similar to studies from North Africa and the Middle East, except in Egypt where the prevalence was higher.[49 54] This difference in prevalence could be explained, in part, by variations in age distributions and the prevalence of coronary heart disease in patients with HF across populations.[3 48 53] Older age, subclinical atherosclerosis and ischaemic heart disease have been associated with a higher risk of AF.[55 56] We found a higher prevalence of AF in HF among studies where the mean age of participants was at least 60 years and over compared with those with younger participants. The lower prevalence of AF in HF could also be explained by a lack of adequate testing in SSA, as ECG, inpatient telemetry and Holter monitors are largely absent in the region.

We observed a higher six-month and one-year mortality ratio among patients with AF and HF than reports from high-income countries, including Canada and Romania.[57 58] The high mortality in our study could be due to the higher proportion of patients in advanced HF compared with the studies from high-income countries. In addition, the high mortality ratio in this study could reflect limited availability, accessibility and affordability of good quality care. Advanced therapies such as mechanical circulatory support and left ventricular assistive devices for patients with advanced HF are limited in SSA.[3] Advanced therapies such as cardiac resynchronisation, pacing and ablation for rate and rhythm control for AF, and mechanical circulatory supports and left ventricular

Table 2 Prevalence of atrial fibrillation in heart failure by various subgroups

Subgroups	No of studies	Cases of AF	Sample size	Prevalence (95% CI)	I² (%)	P for subgroup difference
Subregion*						0.8961
Central	6	214	1089	17.7 (12.7 to 23.4)	80.8	
East	6	212	1176	15.5 (9.5 to 22.6)	85.8	
South	6	225	1905	13.5 (4.5 to 26.2)	97.7	
West	11	682	4811	15.6 (9.6 to 22.8)	97.1	
Study design						0.7347
Cross-sectional	6	148	819	16.6 (10.7 to 23.3)	81.0	
Cohort	24	1394	9168	15.4 (11.4 to 19.9)	96.7	
Timing of data collection†						**0.0147**
Prospective/cross-sectional	23	913	7242	13.5 (9.9 to 17.7)	95.3	
Retrospective	7	629	2745	22.9 (16.7 to 29.9)	92.5	
Method of AF diagnosis						**0.0035**
12-lead or Holter ECG	23	1009	7443	14.1 (10.1 to 18.8)	96.3	
Not reported	6	514	2351	22.7 (19.5 to 26.1)	56.8	
Risk of bias						0.3025
Low	19	829	6559	14.2 (10.1 to 18.9)	95.8	
Moderate	11	713	3428	18.1 (12.6 to 24.4)	94.1	
Mean age, years‡						**0.0132**
Below 55	14	613	5080	12.4 (7.9 to 17.8)	96.2	
55–59.9	8	338	2414	15.1 (9.5 to 21.8)	93.8	
60 and over	6	572	2372	25.5 (18.2 to 33.6)	91.6	
Participants in NYHA III or IV (%)‡						0.1601
Below 50	8	615	4738	14.3 (7.2 to 23.3)	98.1	
50–80	9	413	2654	12.3 (8.6 to 16.5)	88.0	
Over 80	6	197	986	19.5 (13.3 to 26.6)	83.5	
Sample size						0.6415
Below 150	10	149	884	15.6 (11.0 to 20.7)	72.8	
150–300	10	436	2088	18.0 (11.3 to 25.8)	94.8	
Over 300	10	957	7015	13.6 (8.3 to 20.0)	98.0	
Male percentage (%)‡						0.6220
Below 50	16	1135	7535	15.8 (10.6 to 21.8)	97.6	
50 and over	11	313	2021	13.9 (9.6 to 18.9)	88.4	

*The study by Sani *et al*[44] was excluded from the analysis as this was a multinational study and the prevalence of AF in heart failure could not be disaggregated into the individual countries where the study was conducted in.
†The study by Mwita *et al*[39] was excluded as this was the only study that reported on physician-diagnosed AF.
‡Studies with missing data were excluded.
AF, Atrial fibrillation; NYHA, New York Heart Association.

assistive devices for patients with advanced HF are limited in SSA.[3] Observational evidence suggests that AF is associated with a higher risk of mortality among patients with HF. Makubi *et al* observed that AF was associated with a threefold higher risk of mortality among patients with HF in Tanzania.[9] In addition, Sani *et al* also reported a 61% higher risk of mortality among HF patients with valvular AF than those without AF, even though the authors found no evidence of an association of non-valvular AF with mortality.[44] In a meta-analysis of about 61 000 cases of AF, 150 000 patients with HF and 40 000 deaths, AF was associated with a 17% higher risk of death.[59]

AF in HF is associated with faster progression of HF in affected patients.[60] AF could significantly worsen premature mortality in HF patients, especially in SSA, where HF patients are mostly young adults. However, whether AF in HF is associated with increased risk of mortality and how much of this association is due to confounding

Table 3 Characteristics of studies reporting on mortality among patients with AF and HF

Surname of first author	Year	Country of study	Study design	Sampling method	Timing of data collection	Median age, year	Participants in NYHA III and IV (%)	Method of diagnosis of AF	Participants with AF and HF (n)	Deaths (n)	Mortality ratio (%) (95% CI)	Follow-up (months)
Makubi *et al*[9]	2014	Tanzania	Cohort	Non-probabilistic	Prospective	55	79	12-lead ECG	67	42	67.7 (51.1 to 74.3)	6
Malamba *et al*[34]	2018	DRC	Cohort	Non-probabilistic	Retrospective	56	NR	12-lead ECG	37	18	48.6 (32.5 to 64.7)	12
Sani *et al*[44]	2018	Multinational registry*	Cohort	Non-probabilistic	Prospective	52.3	80	12-lead ECG	207	38	18.4 (13.1 to 23.6)	6

*Study countries included: Sudan; Cameroon; South Africa; Nigeria; Ethiopia; Kenya; Uganda; Senegal; Mozambique.
AF, atrial Fibrillation; DRC, Democratic Republic of Congo; HF, heart failure; n, frequency; NYHA, New York Heart Association.

and reverse causation remains uncertain. Two large-scale randomised controlled trials showed no evidence of rhythm control in reducing mortality among patients with AF and HF.[61 62] Nevertheless, these trials were limited by their ability to maintain sinus rhythm in the intervention group, reducing the power of the analyses. Consequently, although contemporary evidence suggests that rhythm control might have some benefit in reducing the risk of mortality in patients with AF and HF,[63] robust evidence is lacking on whether AF increases mortality risk in patients with HF or is rather a marker of advanced HF.

The findings from this study have implications for improving research on AF among patients with HF in SSA to inform local guidelines for managing patients with HF. Efforts are needed to generate reliable evidence on the incidence, subtypes and prognosis of AF in HF patients in the region. In addition, collaborative efforts are warranted to assess the efficacy and safety of interventions to reduce the risk of mortality among patients with AF and HF in SSA.

We made minor amendments to the methods of the initial protocol to improve transparency, reliability and interpretation of the results.[16] Instead of the proposed Quality In Prognosis Studies tool, the Newcastle-Ottawa Scale was used to assess the risk of bias in studies reporting on all-cause mortality among patients with AF and HF because we found it relatively easier to use and interpret. In addition, the Newcastle-Ottawa tool can easily be adapted to assess the risk of bias in descriptive cohort studies. Furthermore, data on the type of AF, valvular or non-valvular causes of HF, ejection fraction and percentage of participants on anticoagulants were not reported as data on the variables were missing in over 50% of the included studies.

This study had some limitations that are worth highlighting. The geographical coverage of studies included in this review was limited. Although all four SSA subregions were represented, the individual studies were from a limited number of countries, with about a third of all the studies conducted in West Africa. In addition, all studies were hospital-based and included patients with more advanced HF. This may have overestimated the prevalence of AF in HF and all-cause mortality in patients with AF and HF. Furthermore, the retrospective nature of some studies is likely to have given the authors limited control over the quality of data collected, leading to biased estimates of the prevalence of AF in HF or mortality in patients with AF and HF. We found that studies that collected data retrospectively had a higher pooled prevalence of AF in HF compared with prospective studies. This review highlights limited capacity in diagnosing AF cases among patients with HF in SSA as only two of the studies included in this review used Holter ECG for diagnosis. Even though 12-lead ECG is widely accepted to confirm the diagnosis of AF,[1] it only provides a snapshot of the electrical activity of the heart. Consequently, the standard 12-lead ECG is more likely to miss cases of paroxysmal AF, contrary to ambulatory ECG, which monitors cardiac

electrical activity for sustained periods.[64] Finally, only three studies reported on mortality among patients with AF and HF. Hence, our estimates on all-cause mortality should be interpreted with caution. However, this study provides comprehensive and contemporary evidence on the burden of AF among HF patients in SSA.

CONCLUSION

AF was common among patients with HF in SSA, and patients with AF and HF appear to have poor survival. There is an urgent need for large-scale population-based prospective data to reliably estimate the prevalence, incidence and risk of mortality in patients with AF and HF in SSA to better understand the burden of these conditions in SSA. Such evidence would be crucial for policies and context-specific guidelines aimed at improving the survival of patients with HF in SSA.

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Contributors VNA conceived the study. VNA, LNA, MDC and JJN designed the protocol. VNA conducted the literature search. VNA, CMM, SJNP and LPS selected the studies and extracted the relevant information. VNA synthesised the data. VNA wrote the first draft of the paper. TTFL, LNA, MDC, AD and JJN critically revised successive drafts of the paper. All authors approved the final version of the manuscript. VNA is the guarantor of the review.

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