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Atrial fibrillation among adults with heart failure in sub-Saharan Africa — prevalence, incidence and all-cause mortality: a systematic review and meta-analysis protocol

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ABSTRACT

Introduction Heart failure (HF) remains a major non-communicable disease in sub-Saharan Africa (SSA) associated with high rates of readmission, mortality and loss of economic productivity as it affects mostly young and economically active adults. Atrial fibrillation (AFib) is a major determinant of mortality among patients with HF in SSA. Meanwhile, the use of anti-arrhythmic medications in the region remains unacceptably low. This review aims to evaluate the prevalence and incidence of AFib in adult patients with HF in SSA, and the all-cause mortality rate among patients with HF and AFib.

Methods and analysis The Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols 2015 statement was used to prepare this protocol. All eligible studies from database inception to December, 31 2018 in MEDLINE, Embase, Google Scholar, Web of science and Africa-specific databases (AFROLIB, African Index Medicus and African Journals Online) will be included without language restrictions. The process of study screening, selection, data extraction and assessment of risk of bias will be conducted independently by two reviewers. Disagreements will be arbitrated by a third reviewer. Study-specific estimates will be pooled using random-effect meta-analysis and summary measures obtained will be presented in forest plots. The χ^2 test on Cochrane's Q and the I^2 statistics will be used to assess and quantify heterogeneity, respectively. The Egger's test and funnel plots will be used to assess publication bias.

Ethics and dissemination Since our review will be based on already published data, an ethical approval is not required. The findings of this review will be presented in conferences and peer-reviewed journals and shared on social media such as Researchgate, Facebook, WhatsApp and Twitter.

PROSPERO registration number CRD42018087564.

Strengths and limitations of this study

- This will be the first systematic review and meta-analysis to evaluate the prevalence and incidence of atrial fibrillation (AFib) among heart failure (HF) patients in sub-Saharan Africa (SSA), and the mortality rate of HF patients with AFib in the same population.
- Our largely sensitive search strategy is anticipated to capture the maximum number of studies on the subject in SSA.
- Robust statistical methods will be used to summarise data on the selected primary outcomes.
- Due to the possibility of missing patients with asymptomatic and brief episodes of AFib by individual studies, this review might underestimate the incidence and/or prevalence of AFib among African patients with HF. On the other hand, there is a probability of overestimating the prevalence of AFib in HF as cross-sectional studies do not permit to know which pathology (AFib or HF) started first.
- Heterogeneity in study-specific estimates of the prevalence, incidence and mortality of AFib across studies is a possible limitation to the study.

INTRODUCTION

The rapid transition in disease epidemiology from communicable to chronic non-communicable diseases (NCDs) in sub-Saharan Africa (SSA) has been particularly linked to the increasing prevalence of cardiovascular risk factors such as hypertension, diabetes, obesity and dyslipidaemia, and poor dietary and sedentary lifestyles owing to the breeze of westernisation and urbanisation.[1–3] Cardiovascular disease (CVD) is the leading cause of death globally and is said to overtake the Human Immunideficiency Virus as the top killer in SSA in the next two decades.[4]

Heart failure (HF) is a major public health threat in SSA. It is the leading cause of admission into cardiology units and is associated with longer duration of hospital stay, high rates of readmissions and mortality, and a huge economic burden.[5 6] On the other hand,

atrial fibrillation (AFib) remains the most common cardiac arrhythmia globally, and its prevalence in Africa is expected to rise due to increasing prevalence of risk factors such as rheumatic heart disease, hypertension, diabetes, obesity, cardiopathy and ageing population.[1 7 8] It is associated with a high risk of thromboembolic events, especially stroke, morbidity and mortality.[8] About 16%–20% of HF patients in SSA are diagnosed with AFib.[9–11] Patients with HF in SSA are particularly prone to AFib and its complications due to the significant contributions of hypertension, cardiomyopathy and rheumatic valvular disease in the development of HF in the region.[5] In addition to being a complication of HF, AFib can be the aetiology of HF through the development of atrial cardiomyopathy.[12–14] AFib is a major decompensating factor and predictor of mortality among HF patients in SSA[5] and elsewhere.[15 16] In fact, HF patients with AFib are 1.3–3.4 times at risk of death compared to their counterparts without AFib.[6 9] Atrial fibrillation is associated with more than 25% of all-cause mortality among patients with HF in SSA.[11] Moreover, HF patients with AFib are at risk of higher readmissions rates, longer hospital stay and mortality compared with those without AFib.[15 16] Meanwhile, the integration of anticoagulants and antiarrhythmic drugs such as beta-blockers and digoxin in the treatment of HF in SSA remains unacceptably low.[5] This is aggravated by the unavailability of these drugs in the local pharmacies.[17]

This systematic review and meta-analysis will focus on AFib as a complication of HF. Therefore, it seeks to summarise data on the prevalence and incidence of AFib in adults with HF in SSA, and all-cause mortality of patients with HF and AFib in the same population. The result of this study will go a long way to inform healthcare professionals and policy-makers on the burden of AFib among HF patients in SSA so that adequate measures can be implemented to curb the morbidity and mortality associated with AFib among patients with HF in the region.

OBJECTIVE

To estimate the prevalence and incidence of AFib among adult patients with HF in SSA, and the mortality rate of patients with HF and AFib in the same population.

REVIEW QUESTIONS

1. What is the prevalence of AFib among patients with HF in SSA?
2. What is the incidence of AFib among patients with HF in SSA?
3. What is the proportion of all-cause mortality rate among HF patients with AFib in SSA?

METHODS AND ANALYSIS

Criteria for considering studies for the review

Inclusion criteria

1. Observational studies reporting on the prevalence (cross-sectional and cohort studies), incidence (cohort and randomised controlled trials) of AFib in patients with heart failure and all-cause mortality rates (cross-sectional, cohort and randomised controlled trials) among patients with HF and AFib in SSA.
2. Age limit: participants must be at least 15 years of age.
3. For duplicate studies: we shall include only the most recent and comprehensive study with the largest sample.
4. Publication date: from database inception to December, 31 2018.

Exclusion criteria

We shall exclude

1. Letters to the editor, editorials, commentaries, review articles and case series with fewer than 30 participants.
2. Studies conducted in participants with an initial diagnosis of AFib without HF.
3. Studies with incomplete data that could not be recovered even after a reasonable request from the corresponding author of the study.

Information sources

Search strategy for identifying relevant studies

MEDLINE, Embase, Google Scholar, Web of science and Africa-specific databases (AFROLIB, African Index Medicus and African Journals Online) will be searched from the inception date of each database to December 31, 2018 for relevant abstracts with information on the prevalence and/or incidence of AFib in HF, and/or mortality rate among HF patients with AFib in SSA. Medical subject headings and key text words like 'atrial fibrillation' and 'heart failure' will be used to build the search strategy. A validated search filter[18] will be used to increase the geographical precision of our search. Table 1 depicts the main strategy for MEDLINE. This strategy will be adapted to suit other databases.

The full texts of eligible abstracts will be retrieved and assessed for final inclusion in this review. Database searches will be supplemented by scrutinising the reference lists of eligible articles and relevant reviews for additional studies. In case the full text of an article cannot be retrieved online, the corresponding authors will be contacted via their emails or other social platforms like Researchgate and a fortnightly reminder will be scheduled. If no response is received after eight reminder emails or before the end of the data extraction process, the study will be automatically excluded.

Study records

Data management

Titles and abstracts retrieved from database searches will initially be imported to the software EndNote V.7.4 for removal of duplicates. The unduplicated titles and abstracts will then be uploaded to Rayyan QCRI,[19] a mobile and web-based application that facilitates collaboration between authors involved in study screening and selection for final inclusion in a systematic review. The process of study selection will

Table 1 Search strategy for PubMed

SN	Search items
1.	'Heart failure' [Mesh] OR 'Cardiac failure' [tiab] OR 'Cardiac insufficiency' [tiab] OR 'heart failure' [tiab]
2.	'Atrial fibrillation' [Mesh] OR 'Atrial fibrillation' [tiab]
3.	**#1 AND #2**
4.	benin/or burkina faso/or cape verde/or cote d'ivoire/or gambia/or ghana/or guinea/or guinea-bissau/or liberia/or mali/or mauritania/or nigeria/or senegal/or sierra leone/or togo/or ((africa*adj2 west* or benin* or burkina fas* or cape verd* or cabo verd* or ivory coast or cote d'ivoire* or gambia* or ghana* or (guinea* not pig*) or bissau or liberia* or (mali not fowl) or malian or mauritania* or nigeria* or senegal* or sierra leon* or togo*).mp. or (Lagos or Accra or Abidjan or Dakar or Abobo or Abuja or Freetown or Ouagadougou or Conakry or Lome or Bamako or Cotonou or Kumasi or Monrovia or Ibadan or Kano or Port harcourt or Benin City or Porto Novo or Niamey or Yamoussoukro or Banjul or Timbuktu or Djenne or Abomeyu or Zaria or Tamale or Jos or Cape Coast or Maidugul or Aba or Gao or Calabar or Warri or Maiduguri or Bobo Dioulasso or Parakou or Djougou or Bohicon or Sekondi Takoradi or Sunyani or Obuasi or Teshie or Tema or Sikasso or Kalabankoro or Nouakchott or Dakhlet Nouadhibou or Benin City or Port Harcourt or Ilorin or Kaduna or Enugu or Ikorodu or Onitsha or Bauchi or Akure or Abeokuta or Sokoto or Bouake or Makeni or Kaduan or Sosgbo or Osogbo or Gombe or Ilesa or Badagry or makurdi or Sagamu or Iseyin or obbomosho or Awka or Ado Ekiti or Nsukka or Ikeja or Katsina or Okene or Lafia or Minna or Ondo city or Umuahia or Calabar or Yola or Pikine or Touba or Thies Nones or Saint Louis or Kolak or Ziguinch or (San Pedro not (Spain or Mexico or Argentina or California or United States or Italy)) or Bandama or Daloa or Owerri or Kandi or Ifi or Dakar or Ogbomosho or Divo or Korhogo)).ti,ab or Exp africa, central/or ((africa adj2 central) or angola or cameroon* or chad.mp. or tchad.mp. or congo* or DRC or equatorial guinea* or gabon* or Sao Tome or Principe or Luanda or lobito or kuito or huambo or Malanje or Douala or Yaounde or Bamenda or Garoua of Bafoussam or Nganoundere or Maroua or Kouosseri or Buena or Kumba or N'Djamena or Moundou or Bangui or Bimbo or Brazzaville or Point Noire or Kinshasa or Lubumbashi or Leopoldville or Elizabethville or Mbuji Mayi or Bakwanga or Bukavu or Costermansville or Kananga or Luluabourg or Kisangani or Stanleyville or Tshikapa or Koalwezi or Likasi or Jadotville or Goma or Kikwit or Uvira or Bunia or Mbandaka or Coquilhatville or Matadi or Butembo or Kabinda or Mwene Ditu or Isiro or Paulis or Boma or Kindu or Bata or Malabo or Libreville).ti,ab or Exp Africa, Eastern/or ((east* adj2 africa*) or British Indian Ocean Territory or Burundi* or Comoros or Djibouti* or Eritrea* or Ethiopia* or Kenya* or Madagascar or Malawi or Mauritius or Mayotte or Mozambique or Reunion OR Rwanda* or Seychelles or Somalia* or Sudan* or Tanzania* or Uganda* or Zambia or Zimbabwe or Crozet Islands or Iles Crozet or Scattered Islands or Iles Eparses or Mwanza or Zanzibar or Eldoret or Morogoro or Hargeysa or Berbera or Nyeri or Mbeya or Machakos or Marka or Tabora or Iringa or Gondar or Meru or Geita or Musoma or Mtwara or Songea or Kigoma or Dese or Mek'ele or Bahir Dar or Jimma or Sinyanga or Korogwe or Nairobi or “Dar es Salaam” or Mombasa or Addis Ababa or Kampala or Kigali or Mogadishu or Dodomoa or Bujumbura or Nakuru or Anananarivo or Kisumu or Maputo or Asmara or Lusaka or Harare or Port Louis or Arusha or kitale or lilongwe or malindi or machakos or hargeisa or Bulawayo or Ruiru or Lamu or Kire Dawa or Kikuyu or naivasha or mwanza or tanga or nanyuki or voi or garissa or lodwar of kakamega or maralal or kitui or webuye or Axum or Nyahururu or Jinja or Kismayo or Namanga or Mumias or Moshi or Moroni or Lokichogio or Hola or Rwenzori Mountains or Lake Victoria or Puntland* or (Adiharush or Ali-Addeh or Alinjugur or Buramino or Dadaab or Dagahaley or Dollo Ado or Fugnido or Hagadera or Hilaweyn or Ifo or Kakuma or Kambioos or Kayaka II or Kobe or Kyangwali Nakivale or Nyarugusu or Wad Sherife or Bokolmanyo or Melkadida or Rwamanja) adj5 (camp or refug*)).ti,ab or angola/or botswana/or lesotho/or malawi/or mozambique/or namibia/or south africa/or swaziland/or zambia/or zimbabwe/or ((africa* adj2 south*) or angola* or botswana* or lesotho* or malawi* or mozambiq* or namibia* or swaziland or zambia* or zimbabwe or Zulu or Tsonga or Xhosa or Swazi or Ndebele or Tswana or Sotho or Shona people or BaLunda or Mbundu or Ovimbundu or Chaga or Sukuma or Pretoria or Cape Town or Johannesburg or Durban or Port Elizabeth or Bloemfontein or Windhoek or Maseru or Pietermaritz or (Kimberley not Australia) or Nespruit or Soweto or Polokwane or Limpopo or Rustenburg or Mahikeng or Oudtshroom or Stellenbosch or Paarl or Gaborone or Luanda or Cabinda or Huambo or Lubango or Kuit or Malanje or Lobito or Lilongwe or Blantyre or Mzuzu or Maputo or Matola or Beira or Nampula or Chimoio or Nacala or Quelimane or Lusaka or Kitwe or Ndola or Kabwe or Copperbelt Harare or Bulawayo or Chitungwiza or Mutare or Masvingo or Monashonaland or Manicaland).ti,ab.
5.	**#3 AND #4**
6.	Publication date limits: from database inception to December 31, 2018 with no language restrictions

be guided by a tool developed a priori based on the eligibility criteria.

Study screening

Two reviewers (CMM and FLT) will independently screen the titles and abstracts retrieved from the searches. Discrepancies in the screening of abstracts will be resolved through discussion and consensus. If disagreement persists, a third reviewer (VNA) will be consulted for arbitration. Two reviewers (CMM and FLT) will then download and independently screen the full texts of selected records for final inclusion. Discrepancies and disagreements will be handled as mentioned above.

Data items and extraction

Using a pre-established Google data abstraction form, two reviewers (CMM and SNP) will independently extract data (online) depending on the outcomes of interest: prevalence, incidence and all-cause mortality rates of AFib among patients with HF in SSA. Generally, data will be extracted on: the surname of the first author and year of study publication; the country in which the study was conducted; the region (western, central, southern and eastern); study setting (hospital- vs community-based); study design (cross-sectional, cohort, case-control or randomised controlled trials); sampling method (random, consecutive or exhaustive); data collection (prospective or retrospective); male proportion; mean or median age in years; age range in years; proportion of anticoagulant use; proportion of beta-blocker use and sample size. Additional data will be extracted on (1) the characteristics of HF such as the mean or median duration of HF in years, causes of HF (like hypertensive heart

disease, cardiomyopathy, rheumatic heart disease or ischaemic heart disease) and severity of HF (according to the New York Heart Association [NYHA] classification and left ventricular ejection fraction [EF] on echocardiography) and (2) the characteristics of AFib: mean or median duration since diagnosis in years, type of AFib (paroxysmal, persistent or permanent) and proportion of participants on any anticoagulation therapy.

In addition to the aforementioned data items to be extracted, we shall extract data on the number of AFib cases in patients with HF. To determine the incidence of AFib in HF patients, data will be extracted on the number of new cases of AFib among patients with HF. Finally, data will be extracted on the mean or median duration of follow-up, the number of death due to any cause among patients with HF, and the number of deaths due to any cause among HF patients with AFib in order to determine proportion of all-cause mortality among HF patients with AFib.

For multinational studies, data on the outcome of interest will be disaggregated according to the countries in which the study was conducted. Otherwise, these studies will be presented as a single study and the countries where the study was conducted in will be highlighted. The extracted data will be cross-checked at least once by two authors (LNA and VNA) for consistency and obvious errors.

A duplicate of the online data abstraction form will be created for both authors who will be responsible for data extraction (CMM and SNP), while the consistency of the extracted data will be monitored online by a third author (LNA) who will conduct the statistical analysis. Disagreements among authors will be resolved through consensus.

Assessment of methodological quality and risk of bias

Two reviewers (CMM and SNP) will independently assess the included full texts for bias. The risk of bias and quality of included studies reporting on prevalence and incidence measures will be assessed using the risk of bias tool for prevalence studies proposed by Hoy *et al*,[20] adapted for the purpose of this study (online supplementary file 1). Also, the Quality In Prognosis Studies (QUIPS) tool (see online supplementary file 2)[21] will be used to evaluate the risk of bias or quality of studies reporting on the mortality rate among HF patients with AFib. Disagreements during this process will be arbitrated by a single reviewer (CD).

Data synthesis and analysis

The author, LNA, will conduct the statistical analysis. The *'meta'* package of the statistical software R (V.3.3.3, The R Foundation for statistical computing, Vienna, Austria) will be used to analyse the extracted data. Study-specific prevalence, incidence and mortality estimates will be recalculated using crude numerators and denominators from the individual studies. Using the Freeman-Tukey arc-sine transformation, the variance of study-specific estimates will be stabilised before pooling with random effect meta-analysis model.[22] Heterogeneity across studies will be assessed and quantified using the Cochrane's Q and I^2 statistics, respectively.[23] Low, medium and substantial heterogeneity will be represented by I^2 values of 25%, 50% and 75%, respectively.[24] A subgroup analysis using the following variables will be performed in case of substantial heterogeneity: region (western, central, southern and eastern); study type (hospital- vs community-based); study design; study area (urban, rural or both); random sampling (yes vs no); data collection (prospective vs retrospective); gender (male vs female); age group (below vs at or above the median age); cause of HF (valvular vs non-valvular); severity of HF (NYHA stage I and II vs III and IV; and EF <35% vs >35%); type of AFib (paroxysmal, persistent or permanent); proportion of anticoagulants and beta-blocker use (as continuous variables) and study quality.

Estimates of the prevalence, incidence and all-cause mortality rates will be pooled according to the SSA region and compared using the Q-test on analysis of variance. Publication bias will be assessed with the aid of a symmetry of forest and funnel plots and Egger's test.[25] A p value below 10% on Egger's test will be considered statistically significant.

Presentation and reporting of results

This review will be published in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[26] With the aid of a flow diagram, the process of study screening, selection, final inclusion and reasons for study exclusion will be demonstrated. Where necessary, summary tables and forest plots will be used to display quantitative data. The risk of bias for all the included studies will be presented using narrative summaries and tables.

The prevalence and incidence of AFib among HF patients, and the mortality rate of HF patients with AFib will be reported according to the SSA region (western, eastern, southern and central), cause of HF (valvular vs non-valvular), HF severity (NYHA stage I and II versus III and IV; and EF <35% vs >35%) and study type (hospital- vs community-based).

Protocol amendments

We do not plan to modify the present protocol. However, any modification will be succinctly described in the final review.

Patient and public involvement

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

Ethics and dissemination

Since the review is based on already published data, an ethical approval is not required. The findings of this review will be presented in conferences and peer-reviewed journals and shared on social media such as ResearchGate, Facebook, WhatsApp and Twitter.

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Contributors VNA conceived the study. VNA LNA and JJN: designed the study protocol. VNA drafted the initial manuscript. LNA, FLT CMM, SNP, CD and JJN critically revised the protocol for methodological and intellectual content. All authors read and approved the final version of the manuscript prior to submission. VNA is the guarantor of the review.

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