Atrial Fibrillation in Africa-An Underreported and Unrecognized Risk Factor for Stroke

Jacobs, Maartje S; van Hulst, Marinus; Adeoye, Abiodun M; Tieleman, Robert G; Postma, Maarten J; Owolabi, Mayowa O

Published in:
Global heart

DOI:
10.1016/j.gheart.2019.04.003

Publication date:
2019

Atrial Fibrillation in Africa—An Under-Reported and Unrecognized Risk Factor for Stroke

A Systematic Review

Maartje S. Jacobs*,†,‡, Marinus van Hulst*,‡, Abiodun M. Adeoye§,‖, Robert G. Tieleman¶,#, Maarten J. Postma†,‡,**, Mayowa O. Owolabi§,‖

Groningen, the Netherlands; and Ibadan, Nigeria

ABSTRACT

Over three-quarters of deaths from cardiovascular disease and diabetes occur in low- and middle-income countries, which include many African countries. Global studies showed that the prevalence of the cardiac arrhythmia atrial fibrillation (AF) appeared to be lower in Africa. A systematic search of PubMed and African Journals Online was conducted to determine the prevalence of AF and associated stroke risk factors in Africa and to quantify the need for screening. The publications search yielded a total of 840 articles of which 41 were included. AF was often not identified as the disease of primary interest with its own risks. Data on prevalence in the general population was scarce. The prevalence of stroke risk factors showed a large variation between studies, as well as within clustered subpopulations. AF in Africa is under-reported in published reports. The study types and populations are highly heterogeneous, making it difficult to draw a definitive conclusion on AF prevalence.

Noncommunicable diseases cause more than one-half of the total burden of disease in Sub-Saharan Africa (SSA) [1-4]. Cardiovascular diseases constitute a major part of this burden. Strokes and heart attacks are by far the most common cause of cardiovascular death [1,5,6]. For prevention of these conditions, a total-risk approach is recommended by the World Health Organization (WHO) with integrated management of hypertension, diabetes, high cholesterol, and other cardiovascular risk factors. WHO identified counselling and multidrug therapy for people with a high risk of developing heart attacks and stroke as being among the best-buy interventions [7]. Interestingly, targeting of cardiac arrhythmias such as atrial fibrillation (AF) is not mentioned in any of the best-buy strategies, although it is an established risk factor for stroke. AF increases the risk of stroke about 5-fold and it is associated with a 1.5- to 2.0-fold increase in all-cause mortality [8]. A global increase of 42.8% in AF-related deaths has been seen from 2006 to 2016, though a proportion may be attributable to an increased likelihood of reporting AF or atrial flutter as an underlying cause of death [9]. The disease has a high prevalence that can go up to at least 10% in people age 80 years and over in high-income countries [10,11]. The prevalence of AF is not clear in low- and middle-income countries (LMIC), including countries in Africa. It is uncertain if the low incidence and prevalence reported for the African region is due to poor surveillance, under-reporting, or genetic predisposition [12]. Underestimation could have resulted from poor access to health care and weak or nonexistent surveillance systems. We therefore conducted a systematic review of published reports to determine the prevalence of AF and associated stroke risk factors in Africa and to assess the need for appropriate screening and stroke prevention strategies.

METHODS

Search Strategy

We searched the PubMed database, which includes MEDLINE, for articles published between January 1, 2000, and April 15, 2018, on the epidemiology of AF in Africa. An additional search was performed in the African Journals Online (AJOL) database within the period January 1, 2000 (inserted as "1st of January 2004" as the earliest available date to choose) up to April 15, 2018 [13]. For the initial identification of published studies, we used the following search terms: "atrial fibrillation," "stroke," and "anticoagulation" as Medical Subject Headings, or MeSH, terms. Details of the search are outlined in the Online Appendix.

After the initial search phase in the databases, the secondary inclusion criterion was the term "atrial fibrillation" in the abstract combined with a number that could be the number of people with AF (n or %), the number of AF episodes, or prevalence and/or incidence of AF. If there was no indication for an incidence and/or prevalence number in the abstract, but it did contain the term "atrial fibrillation," the full text would be screened to see whether a number was included in the full-text manuscript. Articles that included the words "atrial fibrillation" in the abstract but did not provide any insight into incidence and/or prevalence were excluded. Articles were only included if

Dr. Tieleman reports receiving grants and personal fees from Boehringer Ingelheim; personal fees from Bayer; and personal fees from Pfizer/ Bristol Meyer Squibb, all outside the submitted work. Dr. Postma reports receiving grants and honoraria from pharmaceutical companies developing, producing and marketing anticoagulants including Bayer, Boehringer Ingelheim, and Bristol-Myers Squibb, all outside the submitted work; and holding stocks in Ingress Health and Pharmacoeconomics Advice Groningen (PAG Ltd). Dr. Jacobs is an employee of Sanofi; the work presented here is not related to this employment. All other authors report no relationships that could be construed as a conflict of interest.

Dr. Owolabi is supported by the SIREN grant no. U54 HG007479 from the National Institutes of Health.

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.gheart.2019.04.003.

From the *Department of Clinical Pharmacy and Toxicology, Martini Hospital, Groningen, the Netherlands; †University of Groningen, Groningen Research Institute of Pharmacy, Groningen, the Netherlands; ‡Department of Health Sciences, University of Groningen, University Medical Center, Groningen, the Netherlands; §Department of Medicine, College of Medicine, University of Ibadan and University College Hospital, Ibadan, Nigeria; ‖Center for Genomics and Precision Medicine, College of Medicine, University of Ibadan, Ibadan, Nigeria; ¶Department of Cardiology, Martini Hospital, Groningen, the Netherlands; #Department of Cardiology, University

Medical Center, University of Groningen, Groningen, the Netherlands; and the **Department of Economics, Econometrics, and Finance, Faculty of Economics and Business, University of Groningen, Groningen, the Netherlands. Correspondence: M. S. Jacobs (m.s.jacobs@rug.nl).

GLOBAL HEART

VOL. 14, NO. 3, 2019
ISSN 2211-8160/$36.00.
https://doi.org/10.1016/j.gheart.2019.04.003

the research described the African population living in Africa, the data were original (no duplicate publication), the full text was available, and the article was available in English. International articles were excluded if they did not provide country- and/or region-specific numbers for African countries [14]. All the articles were initially screened by 1 reviewer.

Data Extraction

The following data, if available, was extracted from the included publications: country/location; study design; type of population; population size; proportion of female subjects, average age (mean or median); estimates of AF prevalence and/or incidence; method of diagnosis; type of AF (paroxysmal, persistent, permanent); $CHADS_2$ (Congestive Heart Failure History, Hypertension History, Age ≥75 Years, Diabetes Mellitus History, Previous Stroke or Transient Ischemic Attack Symptoms) or CHA_2DS_2-VASc (Congestive Heart Failure of Left Ventricular Dysfunction, Hypertension, Age ≥75 [doubled], Diabetes, Thromboembolism or Stroke History [doubled], Vascular Disease, Age 65 to 74 Years, and Sex Category) score; HAS-BLED (Hypertension, Abnormal Renal or Liver Function, Stroke History, Bleeding History, Labile International Normalized Ratio, Elderly (Age >65), Drugs or Alcohol) score; presence of stroke risk factors including diabetes, hypertension, stroke history vascular disease, heart failure, and age ≥75 years old; anticoagulant and/or antiplatelet drug use in AF patients. The stroke risk factors included were based on the items included in the CHA_2DS_2-VASc score [15].

If specific numbers for the AF cohort were not available, we reported the information available for the whole population. Study country was the country where patient recruitment took place. The study types were coarsely classified as a retrospective cohort study, prospective cohort study, or a case-control study.

Quality Assessment

Study quality was assessed using the checklist of Downs and Black [16]. This checklist is appropriate for both randomized and nonrandomized studies. The checklist item on power (item 27) was not taken into account; the maximum achievable score was therefore 27. Score ranges were given an overall quality level to qualify the available evidence included in the review: excellent (26 to 27); good (20 to 25); fair (15 to 19); and poor (≤14).

RESULTS

The systematic search identified 776 eligible articles from PubMed and 52 articles through the AJOL search. Two articles were indexed in both PubMed and AJOL. Of the identified articles, 115 were excluded because a full text was not available or the article was not in English. A total of 699 abstracts were screened and after exclusion of all articles that did not meet the predefined inclusion criteria, 41 original articles remained. The results are summarized in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart (Fig. 1).

Quality Assessment

Overall, 14 studies had the quality score "poor," 26 studies were scored "fair," and only 2 were scored "good." Low scores were partially due to the exploratory, nonrandomized nature of the studies. Study quality assessment results with a detailed summary of subscores for the questionnaire items can be found in Online Table 1.

AF Prevalence

The studies identified mainly focused on different patient subgroups and only 3 of the included articles described a population that would be representative for the general population. The results are summarized in Table 1 [17-57]. AF prevalence in the older, general population was 0.30% to 0.70% [17-19]. The study of Dewhurst et al. [17] in a rural area calculated a crude prevalence of 0.67% and an age-adjusted prevalence of 0.64%. Prevalence was different between men (0.31%) and women (0.96%). Also, prevalence increased with age from 0.46% in people age 70 to 74 years up to 1.3% to those age 85 years and older [17]. The age limit for the prevalence number of 0.30% was 50 years and over, and for the higher prevalence of 0.70%, the age limit was 70 years and over [17,18]. In patients with known cardiovascular disease presenting at the hospital, the prevalence varied from 3.8% to 59.0% [20-30]. Patient inclusion for these studies on patients with cardiovascular disease was mainly carried out at a hospital and also described patients that were previously diagnosed with AF. The most frequently used method for AF diagnosis confirmation was a 12-lead electrocardiogram. In heart failure patients, the prevalence was higher and ranged from 15.7% up to 34.0% [31-35]. Four of the studies on heart failure patients were hospital-based and 1 included outpatients [32]. Patients who (recently) underwent cardiac surgery had an AF prevalence of 4.0% to 17.0% [36-40]. Stroke patients, which include patients who had an acute stroke or had a history of stroke, had an AF prevalence of 1.5% to 17.6% [41-47]. Patients with rheumatic heart disease (RHD), had a prevalence of 13.9% to 44.5% [27,48-52]. Patients with RHD represented a more heterogeneous population, including children as well as adults, and with 2 studies also including outpatient data [48,52]. Studies in anticoagulation clinics showed that 25.1% to 65.0% of the patients were using oral anticoagulation for nonvalvular AF as the indication [53-57].

Several studies had information on the type of AF, which is generally categorized as paroxysmal, persistent, or permanent [21,23,24,27,36,44]. Persistent AF was the most found type of AF, ranging from 21.2% to 81.0%. Permanent AF was seen in 5.0% to 58.8% of the patients, and paroxysmal AF accounted for 11.8% to 32.1% of the AF cases (see Table 2) [17-57].

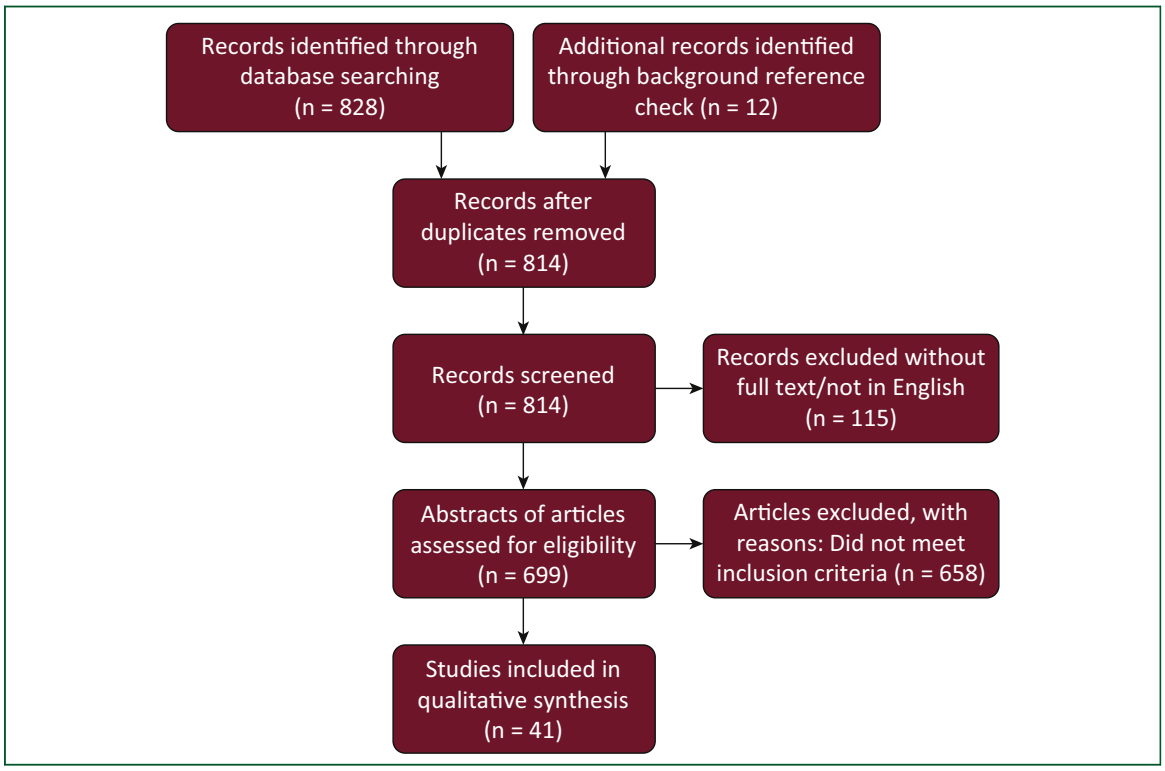

FIGURE 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow chart of systematic review article screening and reasons for exclusion.

Stroke Risk Factors

The prevalence and presence of stroke risk factors were deducted from patients' characteristics tables of the included studies. The prevalence of stroke risk factors showed a large variation between studies but also within clustered subpopulations. Studies describing a population with known cardiovascular disease—AF or any other type of cardiovascular disease—included the most comprehensive information on stroke risk factors. Stroke history and the proportion of patients age 75 years and over were the factors that were least reported. The proportion of patients age 75 years and over was the least reported (nonmodifiable) factor, reported in only 4 studies, and in general <30% of the patients were age ≥75 years.

Hypertension was the most frequently reported stroke risk factor, with prevalence at least around 60% to 70% for all studies. Prevalence seemed higher in the stroke subpopulation with a range of 31.0% to 93.8%, and it was lowest in RHD patients ranging from 5.2% to 53.3%. Diabetes prevalence ranged from as low as 8% in AF patients without valvular disease in Kenya up to 80.0% in coronary artery bypass surgery patients [27,39]. The definition of vascular disease varied between studies ranging from 6.0% up to 52.2% in post—cardiac surgery patients in South Africa [38]. Some studies only used a history of myocardial infarction, and other studies did not include a definition for vascular disease. Stroke history was reported in less than one-half of the included studies. For the subpopulation of stroke patients, the stroke history was scored prior to the admission. Overall, the reported stroke history showed a large variation ranging between 1.3% and 40.0% for the nonstroke patient subpopulation. Heart failure was present in 16.6% up to 60.3% of the population when excluding the subpopulation with known heart failure.

Indication for Stroke Prevention, Anticoagulant Use, and Aspirin Use

Only 9 studies mentioned the $CHADS_2$ or CHA_2DS_2-VASc score. The reported $CHADS_2$ scores ranged from 1.5 to 2.4 and CHA_2DS_2-VASc scores ranged from 3.1 up to 3.9. The use of oral anticoagulation (OAC) and/or aspirin was reported in 10 studies, excluding the studies that focused on international normalized ratio (INR) clinics. All studies conducted in INR clinics described warfarin as the OAC being used [53-57]. Anticoagulants use showed a wide variation from7.0% up to 81.2% of the patients, which included AF and non-AF patients. Aspirin was used in 14.0% to 94.1% of the patients. AF was the indication for OAC use in 25.1% to 65.0% of the patients that visited an INR clinic. Only 2 studies reported OAC and aspirin use for patients with a $CHADS_2$ score of 2 or higher, OAC use

TABLE 1. Study characteristics of included articles describing AF prevalence in Africa

Author(s) Ref. #	Year	Study Type	Country	Population	Patients (n)	Female (%)	Age*	AF (%)
General population								
Dewhurst et al. [17]	2012	Prospective cohort study	Tanzania	People age 70 yrs and over in a rural African community	2,232	56.3	77.8	0.70
Koopman et al. [18]	2014	Prospective cohort study	Ghana	Individuals age 50 yrs and over in a rural area	924	48.1	*66.0*	0.30
Gray et al. [19]	2016	Prospective cohort study	Tanzania	People age 70 yrs and over	2,232	56.3	77.8	0.60
Patients with known cardiovascular disease								
Nqayana et al. [20]	2008	Retrospective cohort study	South Africa	Patients with cardiac disease in pregnancy	95	100.0	—	9.5
Ntep-Gweth et al. [21]	2010	Prospective cohort study	Cameroon	Patients >18 yrs with AF documented on an ECG during the index visit	172	56.4	65.8	100.0
Sliwa et al. [22]	2010	Prospective cohort study	South Africa	Patients presenting to the cardiology unit (Heart of Soweto study)	5,328	61.0	58.8	4.6
Shavadia et al. [23]	2013	Retrospective cohort study	Kenya	Patients with discharge diagnosis of either AF or atrial flutter	162	44.0	67.0	59.0
Jardine et al. [24]	2014	Prospective cohort study	South Africa	Patients with confirmed AF drawn from the private insured sector	302	40.1	67.0	100.0†
Gamra et al. [25]	2014	Cross-sectional observational study	Algeria, Egypt, Morocco, Tunisia	Patients with a history of AF documented by ECG	1,680‡	61.1	64.2	100.0
Akpa and Ofori [26]	2015	Retrospective cohort study	Nigeria	All patients referred to the cardiology unit or seen in the cardiac clinic with ECG evidence of AF	228	42.6	59.8	29.8
Bloomfield et al. [27]	2015	Prospective cohort study	Kenya	Patients age 18 yrs and over with AF based on ruling out significant valvular heart disease	298	53.0	68.0	24.0
Ajayi et al. [28]	2016	Prospective cohort study	Nigeria	Patients with an ECG at the hospital	1,462	67.4§	67.3	3.8
Yameogo et al. [29]	2016	Retrospective cohort study	Burkina Faso	Patients at the cardiology department with nonvalvular heart disease	970	44.6	65.5	7.0
Temu et al. [30]	2017	Prospective cohort study	Kenya	AF patients in a teaching/referral hospital: both nvAF as well as vAF	146	55.0	69.4	47.3
Patients with HF								
Stewart et al. [31]	2008	Prospective cohort study	South Africa	De novo presentation of patients with HF and related cardiomyopathies	844	57.0	55.3	53.0
Magaña-Serrano et al. [32]	2011	Prospective cohort study	Tunisia, Algeria	Patients with HF and preserved ejection fraction	648	47.0	63.0	34.0
Damasceno A [33]	2012	Prospective cohort study	Cameroon, Ethiopia, Kenya, Mozambique, Nigeria, Senegal, South Africa, Sudan	Patients admitted to the hospital with diagnosed acute HF	1,006	50.8	52.3	18.3

Makubi et al. [34]	2014	Prospective cohort study	Tanzania	Patients age 18 yrs and over with HF attending a cardiovascular center	427	51.0	55.0	15.7
Ogah et al. [35]	2015	Prospective cohort study	Cameroon, Ethiopia, Kenya, Mozambique, Nigeria, Senegal, South Africa, Sudan, Uganda	Patients with HF from cardiology units	1,006	50.8	52.4	18.4
Patients undergoing/who underwent cardiac surgery								
Lorgat et al. [36]	2012	Prospective cohort study	South Africa	Patients who underwent robotically assisted catheter ablation therapy in a hospital	95	25.0	59.4	100.0[†]
Mazibuko et al. [37]	2012	Retrospective cohort study	South Africa	Pregnant patients with a prosthetic valve prostheses referred to a tertiary hospital	61	100.0	24.0	13.1
Mansoor [38]	2014	Retrospective cohort study	South Africa	Post—cardiac surgery patients	997	44.1	51.9	5.9
Abdel-Salam and Nammas [39]	2016	Prospective cohort study	Egypt	Patients scheduled for CABG with/without valve surgery	740	30.5	56.5	10.4
Bun et al. [40]	2016	Prospective cohort study	Morocco	Patients scheduled for radiofrequency catheter ablation or pacemaker implantation	75	29.3	67.8	4.0
Chtaou et al. [41]	2016	Retrospective cohort study	Morocco	All patients treated with rt-PA at a stroke unit	52	50.5	63.0	17.0
Stroke patients								
Alkali et al. [42]	2013	Prospective cohort study	Nigeria	Patients presenting with acute stroke	272	38.2	55.1	9.2
Walker et al. [43]	2014	Case-control study	Tanzania, Hai	Incident stroke cases, age/sex-matched control subjects	93	46.2	68.2	6.5
Walker et al. [43]	2014	Case-control study	Tanzania, Dar-es-Salaam	Incident stroke cases, age/sex-matched control subjects	39	38.5	61.1	7.7
Germain et al. [44]	2015	Retrospective cohort study	Burkina Faso	Hospitalized patients at the cardiology and neurology departments with ischemic stroke	391	62.3[§]	63.3	17.6
Gomes et al. [45]	2015	Case-crossover study	Mozambique	Patients admitted to the hospital for newly occurring ischemic and hemorrhagic stroke	593	47.5	58.8	5.6
Adeoye et al. [46]	2017	Prospective cohort study	Nigeria, Ghana	Acute stroke patients who had a 12-lead ECG recording within first 24 h of admission	890	58.3	58.3	4.2
Lekoubou et al. [47]	2017	Retrospective cohort study	Cameroon	Stroke patients that were admitted to the hospital	1,678	50.2	*62.0*	1.5
Patients with RHD								
Sliwa et al. [48]	2010	Prospective cohort study	South Africa	De novo cases of RHD presenting to the cardiology unit	344	68.0	*43.0*	34.0
Okello et al. [49]	2013	Prospective cohort study	Uganda	Patients with newly diagnosed RHD	309	63.5	*30.0*	13.9

(continued)

TABLE 1. Continued

Author(s) Ref. #	Year	Study Type	Country	Population	Patients (n)	Female (%)	Age*	AF (%)
Zhang et al. [50]	2013	Prospective cohort study	Uganda	Patients with newly diagnosed RHD	130	71.0	*33.0*	13.9
Bloomfield et al. [27]	2015	Prospective cohort study	Kenya	Patients age 18 yrs and over with nvAF and vAF	298	78.0	38.0	24.0
Zühlke et al. [51]	2016	Prospective cohort study	LIC: Ethiopia, Kenya, Malawi, Rwanda, Uganda, and Zambia	Patients with symptomatic RHD visiting the hospital	1,110	65.8	*24.0*	18.2
Zühlke et al. [51]	2016	Prospective cohort study	UMIC: Namibia and South Africa	Patients with symptomatic RHD visiting the hospital	863	71.3	*39.0*	27.5
Okello et al. [52]	2017	Prospective cohort study	Uganda	Patient ages 5—60 yrs with established RHD	449	66.8	*31.4*	20.3
Patients visiting an INR clinic								
Njovane et al. [53]	2013	Retrospective cohort study	South Africa	Patients using warfarin that attended a primary health care clinic	111	—	—	44.5
Anakwue et al. [54]	2014	Retrospective cohort study	Nigeria	Patients that utilized anticoagulation services in a university hospital	26	53.4	53.8	30.8
Sonuga et al. [55]	2016	Retrospective cohort study	South Africa	Patients attending the INR clinic	136	56.6	*64.0*	65.0
Schapkaitz and Sithole [56]	2017	Prospective cohort study	South Africa	Patients attending the anticoagulation clinic	147	57.8	56.8	36.1
Ebrahim et al. [57]	2018	Retrospective cohort study	South Africa	Patient visiting the INR clinic	363	65.6	*55.0*	25.1

AF, atrial fibrillation; CABG, coronary artery bypass graft; ECG, electrocardiography; HF, heart failure; INR, international normalized ratio; LIC, low-income country; nvAF, nonvascular atrial fibrillation; RHD, rheumatic heart disease; rt-PA, recombinant tissue plasminogen activator; UMIC, upper-middle-income country; vAF, valvular atrial fibrillation.

*_Italics_ indicate median age.

†Prevalence is 100% because the nominator and denominator were the same due to preselection of AF patients and no numbers of the larger sample population were given.

‡Also includes patient from Lebanon, numbers not differentiated for African countries.

§Average for AF subcohort.

TABLE 2. Stroke risk factors in patients with AF in Africa

Author [Ref. #]	Year	AF Type: Paroxysmal; Persistent; Permanent	$CHADS_2$* or CHA_2DS_2-VASc	HAS-BLED	Population						OAC Use in AF Patients (%)	Aspirin Use in AF Patients (%)
					Diabetes (%)	HT (%)	Stroke History (%)	Vascular Disease (%)	HF (%)	Age ≥75 yrs (%)		
General population												
Dewhurst et al. [17]	2012	—	—	—	—	—	—	—	—	60.7	—	—
Koopman et al. [18]	2014	—	—	—	—	24.2	1.2†	—	—	—	—	—
Gray et al. [19]	2016	—	—	—	—	73.2	2.9	—	—	—	—	—
Patients with known cardiovascular disease												
Nqayana et al. [20]	2008	—	—	—	—	—	—	13.7†	—	—	—	—
Ntep-Gweth et al. [21]	2010	22.7; 21.5; 55.8	*1.9 ± 1.1*	—	10.5	64.5	17.4	6.4	58.1	27.3	30.8	58.7
Sliwa et al. [22]	2010	—	*1.5 ± 0.9*	—	—	60.0‡	—	6.5‡	56.0‡	—	50.0§	50.0§
Shavadia et al. [23]	2013	—	64.7% ≥2	—	33.0	68.0		19.0	38.0	—	79.8‖	17.8‖
Jardine et al. [24]	2014	32.1; 21.2; 46.7	3.08	—	15.6	65.9	—	26.8	32.5	—	75.2	39.4
Gamra et al. [25]	2014	27.9; 21.6; 50.5	—	—	22.7	54.7	—	19.1	16.6	—	52.5‖	21.9‖
Akpa and Ofori [26]	2015	—	*39.7% $CHADS_2$ =1*	—	—	58.8‡	—	—	—	—	8.8	94.1¶
Bloomfield et al. [27]	2015	—	—	—	8.0	67.0	25.0	—	—	—	—	—
Ajayi et al. [28]	2016	—	*2.38*	—	18.2‡	87.3‡	40.0‡	—	36.3‡	—	—	—
Yameogo et al. [29]	2016	11.8; —; 58.8	3.9 ± 1.6	3.5 ± 1.5		—	—	—	60.3‡	26.0	35.3	76.5
Temu et al. [30]	2017	—	*2.2*		8.7	72.5	26.1	—	49.0	—	81.2	—
Patients with heart failure												
Stewart et al. [31]	2008	—	—	—	—	—	—	—	100.0	—	—	—
Magaña-Serrano et al. [32]	2011	—	—	—	42.0	76.0	5.0	50.0	100.0	—	—	—
Damasceno et al. [33]	2012	—	—	—	11.4	55.5	—	—	100.0	—	7.0	35.0
Makubi et al. [34]	2014	—	—	—	45.0	—	3.7	9.0	100.0	—	—	—
Ogah et al. [35]	2015	—	—	—	11.4	55.5	2.5	9.4	100.0	—	—	—
Patients undergoing/who underwent cardiac surgery												
Lorgat et al. [36]	2012	14.0; 81.0; 5.0	—	—	9.0	52.0	24.0#	—	—	—	—	—
Mazibuko et al. [37]	2012	—	—	—	—	—	—	—	—	—	—	—
Mansoor [38]	2014	—	—	—	40.7‡	59.3‡	—	52.2	—	—	—	—
Abdel-Salam and Nammas [39]	2016	—	—	—	80.0	66.8	—	—	—	—	—	—
Bun et al. [40]	2016	—	—	—	—	—	—	—	—	—	—	—
Chtaou et al. [41]	2016	—	—	—	12.0	31.0	10.0	6.0	—	—	—	—
Stroke patients												
Alkali et al. [42]	2013	—	—	—	25.6	83.7	—	—	—	—	—	—
Walker et al. [43]	2014	—	—	—	—	—	—	—	—	—	—	—
Walker et al. [43]	2014	—	—	—	—	—	—	—	—	—	—	—
Germain et al. [44]	2015	13.0; 52.1; 34.8	4.72	39.1% ≥ 3	21.7‡	85.5‡	100‡	7.2‡	20.3‡	18.8‡	79.7	14.0
Gomes et al. [45]	2015	—	—	—	13.4	86.2	18.9	—	—	—	—	—
Adeoye et al. [46]	2017	—	—	—	32.9	93.8	—	—	—	—	—	—
Lekoubou et al. [47]	2017	—	—	—	12.8	67.9	14.5	—	—	—	—	—
Patients with rheumatic heart disease												
Sliwa et al. [48]	2010	—	—	—	—	—	—	—	18.0	—	—	—
Okello et al. [49]	2013	—	—	—	—	32.7	1.3	—	46.9**	—	—	—
Zhang et al. [50]	2013	—	—	—	—	53.3	—	—	45.9**	—	—	—

(continued)

TABLE 2. Continued

Author [Ref. #]	Year	AF Type: Paroxysmal; Persistent; Permanent	$CHADS_2$* or CHA_2DS_2-VASc	HAS-BLED	Population						OAC Use in AF Patients (%)	Aspirin Use in AF Patients (%)
					Diabetes (%)	HT (%)	Stroke History (%)	Vascular Disease (%)	HF (%)	Age ≥75 yrs (%)		
Bloomfield et al. [27]	2015	—	—	—	1.0	27.0	23.0	—	—	—	—	—
Zühlke et al. [51]	2016	—	—	—	—	5.2	—	43.5	—	—	—	—
Zühlke et al. [51]	2016	—	—	—	—	14.5	—	25.8	—	—	—	—
Okello et al. [52]	2017	—	—	—	—		—		—	—	—	—
Patients visiting an INR clinic												
Njovane et al. [53]	2013	—	—	—	16.2	60.1	—	—	—	—	100.0	—
Anakwue et al. [54]	2014	—	—	—	—	—	—	—	—	—	100.0	—
Sonuga et al. [55]	2016	—	—	—	27.2	69.9	12.5	25.7	—	—	100.0	—
Schapkaitz and Sithole [56]	2017	—	—	—	—	—	—	—	—	—	100.0	—
Ebrahim et al. [57]	2018	—	—	—	—	—	—	—	—	—	100.0	—

$CHADS_2$, Congestive Heart Failure, Hypertension, Age ≥75, Diabetes, Stroke or Transient Ischemic Symptoms; CHA_2DS_2-VASc, Congestive Heart Failure of Left Ventricular Dysfunction, Hypertension, Age ≥75, Diabetes, Thromboembolism or Stroke History, Vascular Disease, Age 65 to 74 Years, and Sex Category; HAS-BLED, Hypertension, Abnormal Renal or Liver Function, Stroke History, Bleeding History, Labile International Normalized Ratio, Elderly (Age > 65), Drugs or Alcohol; HT, hypertension; INR, international normalized ratio; OAC, oral anticoagulation.

*$CHADS_2$ scores are *italic*.

†Only myocardial infarction scored.

‡Percentages for the AF subcohort.

§Fifty percent used an anticoagulant or aspirin.

‖In patients with $CHADS_2$ ≥2.

¶Ten percent of these patients also used warfarin.

#Ischemic heart disease.

**Pulmonary hypertension.

was 52.5% to 79.8% and aspirin use was 17.8% to 21.9% in these patients [23,25]. Patients with known AF had a mean OAC use between 8.8% and 81.2% and aspirin use ranging from 17.8% up to 94.1% [21-27,29,30].

DISCUSSION

AF is under-reported in published reports from the African region. None of the included studies identify the extent of asymptomatic AF, which is crucial information to determine the overall prevalence and incidence. Underdiagnosis is most probably high and studies that focus on AF screening are lacking. This information is essential to determining the true AF burden and related severe consequences such as stroke. The study types and study populations are highly heterogeneous, making it difficult to draw definitive conclusions on AF prevalence in African populations. The focus of published studies seems to be on AF as a risk factor in other comorbid disease such as stroke, heart failure, or cardiovascular disease in general. AF is often not identified as the disease of primary interest with its own risks and complications. Data on prevalence in the general population was scarce; numbers that approached generalizable prevalence numbers ranged from 0.30% to 0.70% in patients ages 50 or 70 years and over, respectively. Remarkably, none of the studies included in this systematic review were used in the GBD (Global Burden of Disease) 2010 study [12]. The GBD estimates for AF seem not to be representative of the true AF burden in SSA and it is most likely an underestimation because studies with higher estimates and studies describing asymptomatic AF were not taken into account. This also illustrates that evidence on AF in this region is difficult to identify, even with a systematic approach, and search strategies need to be more tailored to the region. Based on published data, prevalence of AF in Africa seems low when compared with in the Western population where prevalence is at least 5.5% in people age 65 years and over [10,58]. AF patients in Africa are in general younger than AF patients in high-income countries [59]. Stroke also tends to occur at an earlier age in the African population when compared with age of occurrence in high-income countries [42-47]. Reasons for an earlier presentation of the disease and its complications are not clear, though it seems that stroke type patterns are different for Africans.

The INTERSTROKE (Global and Regional Effects of Potentially Modifiable Risk Factors Associated With Acute Stroke in 32 Countries) study [60] showed that the

prevalence of ischemic stroke was lower and the prevalence of hemorrhagic stroke was higher in Africa and other LMIC than in high-income countries. In a SIREN (Stroke investigative research and educational network) study [61], a case-control study carried out in Ghana and Nigeria that aimed to identify and characterize stroke risk factors in SSA, 68% of the cases had ischemic stroke. However, this SIREN study [61] did not include data on AF as an individual factor and was only included in the combined risk factor "cardiac disease," which had an odds ratio of 2.21 (99% confidence interval: 1.38 to 3.54) for ischemic stroke.

A genetic component could play an important role in global and regional differences. The INTERSTROKE study [60] looked at global and regional effects of risk factors associated with acute stroke. AF was a significant predictor for ischemic stroke in Africa (odds ratio: 4.59; 99% confidence interval: 3.66 to 5.75; n = 1,364), and this effect was comparable in Western countries [60]. The population attributable risk of AF in stroke was lower in Africa than in the Western countries: 7.9% versus 17.1% [60]. The ORBIT-AF (Outcomes Registry for Better Informed Treatment for Atrial Fibrillation) study [62] found no difference in outcomes associated with AF, which included stroke, systemic embolism, transient ischemic attack, and various types of hospitalizations. Studies included in this review that described subpopulations of stroke patients showed an AF prevalence ranging from 1.5% to 17.6%, which was much lower than expected based on the knowledge that 20% to 30% of all strokes are due to AF [8].

The higher prevalence of RHD in African countries introduces an increase in complications related to AF, already at a young age [63]. Valvular heart disease can be associated with an increased thromboembolic risk, which probably also adds to the stroke risk in AF patients [64]. In the studies included in this systematic review, we found AF prevalence ranging from 13.9% up to 44.5% in the subpopulations describing RHD. The REMEDY (Global Rheumatic Heart Disease Registry) study [51], a large prospective registry in 12 African countries, India, and Yemen found AF as a comorbidity in 18.2% of the patients for the low-income countries (Ethiopia, Kenya, Malawi, Rwanda, Uganda, and Zambia), 22.6% for the LMIC (Egypt, India, Mozambique, Nigeria, Sudan, and Yemen), and 27.5% in the upper-middle-income countries (South Africa and Namibia).

Anticoagulant use in the populations studied was low and so was access to surgical interventions, especially in SSA. The included studies suggest that stroke prevention strategies in AF are suboptimal. WHO recommends aspirin as the drug of choice to reduce heart attacks and strokes in LMIC. It is understandable to choose a drug therapy that is affordable in these regions; however, this also implies that we would accept to provide suboptimal therapy. Analyses comparing the use of aspirin to OAC have shown that antiplatelet therapy is around 40.0% to 50.0% less effective in reducing the stroke burden in nonvalvular AF patients, though treatment benefit from vitamin K OAC is highly dependent on the time in therapeutic range [65,66]. Nonvitamin K antagonist OAC do not require routine monitoring and could therefore be a good alternative to vitamin K OAC therapy, with due consideration of prices that in all probability will drop the next couple of years because of expiring patents and also with possible inclusion on WHO's essential drug list.

AF is not mentioned as a target for stroke prevention in any of the global actions plans or best-buy strategies of WHO. The World Heart Federation has published a very useful roadmap for nonvalvular AF in LMIC. One of the potential solutions includes optimization of AF detection, for example with a screening program by nonphysician health workers [67]. Screening for AF as a target for stroke prevention can be a cost-effective strategy depending on how the screening is arranged, the prevalence of AF and also the initiation of an appropriate stroke prevention strategy [68-77]. Opportunistic screening for AF is recommended in patients ≥65 years of age and systematic electrocardiogram screening may be considered to detect AF in patients age >75 years or those at high stroke risk according to the European Society of Cardiology guideline and the American Heart Association [8,78]. Systematic screening would be a good approach to determine the true prevalence of AF in the general population in Africa. In a low-resource region, it is very plausible that underdiagnosis is keeping the AF prevalence estimates artificially low. When taking into account that AF patients seem to be younger in Africa, one should consider screening at an earlier age to determine in which subpopulation this intervention would be most beneficial. Research has to be carried out to unravel racial differences in AF prevalence as well as consequential stroke severity and mortality. More attention needs to be paid to diagnosis and timely detection of AF in Africa. A broader prevention approach that also focuses on conditions predisposing to AF such as hypertension, heart failure, valvular heart disease, diabetes mellitus, and obesity should be the future practice.

CONCLUSIONS

AF is under-reported in published reports from the African region. Prevalence of AF seems lower and patients are generally younger compared with numbers found in high-income countries. Reasons for the earlier presentation of the disease and its complications are not clear. Numbers found most likely represent an underestimate because access to health care, use of routine monitoring electrocardiography, and patient surveillance is less common in Africa. Screening for AF would be an important approach to determine the true prevalence in the general population and to identify asymptomatic AF patients at risk for stroke.

REFERENCES

1. World Health Organization. Global Status Report on Noncommunicable Disease. Geneva, Switzerland: World Health Organization, 2014.

2. Di Cesare M, Khang Y, Asaria P, et al., for the Lancet NCD Action Group. Inequalities in non-communicable diseases and effective responses. Lancet 2013;381:585–97.
3. World Health Organization. Global Health Estimates 2014 Summary Tables. Geneva, Switzerland: World Health Organization, 2014.
4. Institute for Health Metrics and Evaluation. Global Burden of Disease (GDB) Compare. Available at: https://vizhub.healthdata.org/gbd-compare/. Accessed July 3, 2018.
5. World Health Organization. Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000—2016. Geneva, Switzerland: World Health Organization, 2018.
6. Moran A, Forouzanfar M, Sampson U, Chugh S, Feigin V, Mensah G. The epidemiology of cardiovascular diseases in sub-Saharan Africa: the Global Burden of Diseases, Injuries and Risk Factors 2010 Study. Prog Cardiovasc Dis 2013;56:234–9.
7. World Health Organization, World Economic Forum. From Burden to "Best Buys": Reducing the Economic Impact of NCDs in Low- and Middle-Income Countries. Geneva, Switzerland: World Health Organization, 2011.
8. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37:2893–962.
9. Vos T, Abajobir AA, Abate KH, et al., for the GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990—2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017; 260:1211–59.
10. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation: analysis and implications. Arch Intern Med 1995;155:469–73.
11. Friberg L, Bergfeldt L. Atrial fibrillation prevalence revisited. J Intern Med 2013;274:461–8.
12. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation 2014;129:837–47.
13. African Journals Online. Available at: https://www.ajol.info/index.php/index/search. Accessed June 28, 2018.
14. The World Bank. Countries and Regions; Sub-Saharan Africa. Available at: https://data.worldbank.org/region/sub-saharan-africa?view=chart. Accessed June 26, 2018.
15. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on Atrial Fibrillation. Chest 2010;137:263–72.
16. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998;52:377–84.
17. Dewhurst MJ, Adams PC, Gray WK, et al. Strikingly low prevalence of atrial fibrillation in elderly Tanzanians. J Am Geriatr Soc 2012;60: 1135–40.
18. Koopman JJ, van Bodegom D, Westendorp RG, Jukema JW. Scarcity of atrial fibrillation in a traditional African population: a community-based study. BMC Cardiovasc Disord 2014;14:87.
19. Gray WK, Dewhurst F, Dewhurst MJ, et al. Rates and predictors of three-year mortality in older people in rural Tanzania. Arch Gerontol Geriatr 2016;62:36–42.
20. Nqayana T, Moodley J, Naidoo DP. Cardiac disease in pregnancy. Cardiovasc J Afr 2008;19:145–51.
21. Ntep-Gweth M, Zimmermann M, Meiltz A, et al. Atrial fibrillation in Africa: clinical characteristics, prognosis, and adherence to guidelines in Cameroon. Europace 2010;12:482–7.
22. Sliwa K, Carrington MJ, Klug E, et al. Predisposing factors and incidence of newly diagnosed atrial fibrillation in an urban African community: insights from the Heart of Soweto Study. Heart 2010;96:1878–82.
23. Shavadia J, Yonga G, Mwanzi S, Jinah A, Moriasi A, Otieno H. Clinical characteristics and outcomes of atrial fibrillation and flutter at the Aga Khan University Hospital, Nairobi. Cardiovasc J Afr 2013;24:6–9.
24. Jardine RM, Fine J, Obel IW. A survey on the treatment of atrial fibrillation in South Africa. S Afr Med J 2014;104:623–7.
25. Gamra H, Murin J, Chiang CE, Naditch-Brule L, Brette S, Steg PG. Use of antithrombotics in atrial fibrillation in Africa, Europe, Asia and South America: insights from the International Realise AF Survey. Arch Cardiovasc Dis 2014;107:77–87.
26. Akpa M, Ofori S. Atrial fibrillation: an analysis of etiology and management pattern in a tertiary hospital in Port-Harcourt, southern Nigeria. Res J Health Sci 2015;3:303–9.
27. Bloomfield GS, Temu TM, Akwanalo CO, Chen PS, Emonyi W, Heckbert SR. Genetic mutations in African patients with atrial fibrillation: rationale and design of the Study of Genetics of Atrial Fibrillation in an African Population (SIGNAL). Am Heart J 2015;170:455–464.e5.
28. Ajayi E, Adeyeye V, Adeoti A. Clinical and echocardiographic profile of patients with atrial fibrillation in Nigeria. J Health Sci 2016;6:37–42.
29. Yameogo AR, Kologo JK, Mandi G, et al. Use of vitamins K antagonists in non-valvular atrial fibrillation thromboembolic risk prevention in Burkina Faso. Pan Afr Med J 2016;24:108.
30. Temu TM, Lane KA, Shen C, et al. Clinical characteristics and 12-month outcomes of patients with valvular and non-valvular atrial fibrillation in Kenya. PLoS One 2017;12:e0185204.
31. Stewart S, Wilkinson D, Hansen C, et al. Predominance of heart failure in the Heart of Soweto Study cohort: emerging challenges for urban African communities. Circulation 2008;118:2360–7.
32. Magana-Serrano JA, Almahmeed W, Gomez E, et al., for the I PREFER Investigators. Prevalence of heart failure with preserved ejection fraction in Latin American, Middle Eastern, and North African Regions in the I PREFER study (Identification of Patients With Heart Failure and PREserved Systolic Function: an epidemiological regional study). Am J Cardiol 2011;108:1289–96.
33. Damasceno A, Mayosi BM, Sani M, et al. The causes, treatment, and outcome of acute heart failure in 1006 Africans from 9 countries. Arch Intern Med 2012;172:1386–94.
34. Makubi A, Hage C, Lwakatare J, et al. Contemporary aetiology, clinical characteristics and prognosis of adults with heart failure observed in a tertiary hospital in Tanzania: the prospective Tanzania Heart Failure (TaHeF) study. Heart 2014;100:1235–41.
35. Ogah OS, Davison BA, Sliwa K, et al. Gender differences in clinical characteristics and outcome of acute heart failure in sub-Saharan Africa: results of the THESUS-HF study. Clin Res Cardiol 2015;104:481–90.
36. Lorgat F, Pudney E, van Deventer H, Chitsaz S. Robotically controlled ablation for atrial fibrillation: the first real-world experience in Africa with the Hansen robotic system. Cardiovasc J Afr 2012;23:274–80.
37. Mazibuko B, Ramnarain H, Moodley J. An audit of pregnant women with prosthetic heart valves at a tertiary hospital in South Africa: a five-year experience. Cardiovasc J Afr 2012;23:216–21.
38. Mansoor E. De novo atrial fibrillation post cardiac surgery: the Durban experience. Cardiovasc J Afr 2014;25:282–7.
39. Abdel-Salam Z, Nammas W. Atrial fibrillation after coronary artery bypass surgery: Can ivabradine reduce its occurrence? J Cardiovasc Electrophysiol 2016;27:670–6.
40. Bun SS, Latcu DG, Errahmouni A, et al. Pacemakers implantation and radiofrequency catheter ablation procedures during medical missions in Morocco: an 8-year experience. Europace 2016;18:1038–42.
41. Chtaou N, Rachdi L, Midaoui AE, Souirti Z, Wahlgren N, Belahsen MF. Intravenous thrombolysis with rt-PA in stroke: experience of the Moroccan stroke unit. Pan Afr Med J 2016;24:207.
42. Alkali NH, Bwala SA, Akano AO, Osi-Ogbu O, Alabi P, Ayeni OA. Stroke risk factors, subtypes, and 30-day case fatality in Abuja, Nigeria. Niger Med J 2013;54:129–35.
43. Walker RW, Dewhurst M, Gray WK, et al. Electrocardiographic assessment of coronary artery disease and stroke risk factors in rural and urban Tanzania: a case-control study. J Stroke Cerebrovasc Dis 2014;23:315–20.
44. Germain M, André S, Aristide Y, Georges M, Temoua N. Nonvalvular atrial fibrillation related ischaemic stroke at the Teaching Hospital of Yalgado Ouédraogo, Burkina Faso. J Vasc Med Sur 2015;3:171.
45. Gomes J, Damasceno A, Carrilho C, et al. Triggering of stroke by ambient temperature variation: a case-crossover study in Maputo, Mozambique. Clin Neurol Neurosurg 2015;129:72–7.

46. Adeoye AM, Ogah OS, Ovbiagele B, et al., for the SIREN Team as part of the H3Africa Consortium. Prevalence and prognostic features of ECG abnormalities in acute stroke: findings from the SIREN Study among Africans. Glob Heart 2017;12:99–105.
47. Lekoubou A, Nkoke C, Dzudie A, Kengne AP. Recurrent stroke and early mortality in an urban medical unit in Cameroon. J Stroke Cerebrovasc Dis 2017;26:1689–94.
48. Sliwa K, Carrington M, Mayosi BM, Zigiriadis E, Mvungi R, Stewart S. Incidence and characteristics of newly diagnosed rheumatic heart disease in urban African adults: insights from the heart of Soweto study. Eur Heart J 2010;31:719–27.
49. Okello E, Wanzhu Z, Musoke C, et al. Cardiovascular complications in newly diagnosed rheumatic heart disease patients at Mulago Hospital, Uganda. Cardiovasc J Afr 2013;24:80–5.
50. Zhang W, Mondo C, Okello E, et al. Presenting features of newly diagnosed rheumatic heart disease patients in Mulago Hospital: a pilot study. Cardiovasc J Afr 2013;24:28–33.
51. Zuhlke L, Karthikeyan G, Engel ME, et al. Clinical outcomes in 3343 children and adults with rheumatic heart disease from 14 low- and middle-income countries: two-year follow-up of the Global Rheumatic Heart Disease Registry (the REMEDY Study). Circulation 2016;134:1456–66.
52. Okello E, Longenecker CT, Beaton A, Kamya MR, Lwabi P. Rheumatic heart disease in Uganda: predictors of morbidity and mortality one year after presentation. BMC Cardiovasc Disord 2017;17:20.
53. Njovane XW, Fasinu PS, Rosenkranz B. Comparative evaluation of warfarin utilisation in two primary healthcare clinics in the Cape Town area. Cardiovasc J Afr 2013;24:19–23.
54. Anakwue R, Ocheni S, Madu A. Utilization of oral anticoagulation in a teaching hospital in Nigeria. Ann Med Health Sci Res 2014;4(Suppl 3):S286–90.
55. Sonuga BO, Hellenberg DA, Cupido CS, Jaeger C. Profile and anticoagulation outcomes of patients on warfarin therapy in an urban hospital in Cape Town, South Africa. Afr J Prim Health Care Fam Med 2016;8:e1–8.
56. Schapkaitz E, Sithole J. Predictors of warfarin dose requirements in South African patients attending an anticoagulation clinic. J Vasc Nurs 2017;35:27–30.
57. Ebrahim I, Bryer A, Cohen K, Mouton J, Msemburi W, Blockman M. Poor anticoagulation control in patients taking warfarin at a tertiary and district-level prothrombin clinic in Cape Town, South Africa. S Afr Med J 2018;108:490–4.
58. Heeringa J, van der Kuip DA, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J 2006;27:949–53.
59. Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. Eur Heart J 2012;33:1500–10.
60. O'Donnell MJ, Chin SL, Rangarajan S, et al., for the INTERSTROKE Investigators. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. Lancet 2016;388:761–75.
61. Owolabi MO, Sarfo F, Akinyemi R, et al., for the SIREN Team as part of H3Africa Consortium. Dominant modifiable risk factors for stroke in Ghana and Nigeria (SIREN): a case-control study. Lancet Glob Health 2018;6:e436–46.
62. Golwala H, Jackson LR 2nd, Simon DN, et al., for the ORBIT-AF Registry. Racial/ethnic differences in atrial fibrillation symptoms, treatment patterns, and outcomes: insights from Outcomes Registry for Better Informed Treatment for Atrial Fibrillation Registry. Am Heart J 2016;174:29–36.
63. Mayosi BM, Gamra H, Dangou JM, Kasonde J. Rheumatic heart disease in Africa: the Mosi-o-Tunya call to action. Lancet Glob Health 2014;2:e438–9.
64. Halperin JL, Hart RG. Atrial fibrillation and stroke: new ideas, persisting dilemmas. Stroke 1988;19:937–41.
65. van Walraven C, Hart RG, Singer DE, et al. Oral anticoagulants vs aspirin in nonvalvular atrial fibrillation: an individual patient meta-analysis. JAMA 2002;288:2441–8.
66. Connolly SJ, Pogue J, Eikelboom J, et al., for the ACTIVE W Investigators. Benefit of oral anticoagulant over antiplatelet therapy in atrial fibrillation depends on the quality of international normalized ratio control achieved by centers and countries as measured by time in therapeutic range. Circulation 2008;118:2029–37.
67. Murphy A, Banerjee A, Breithardt G, et al. The World Heart Federation Roadmap for Nonvalvular Atrial Fibrillation. Glob Heart 2017;12:273–84.
68. Jacobs MS, Kaasenbrood F, Postma MJ, van Hulst M, Tieleman RG. Cost-effectiveness of screening for atrial fibrillation in primary care with a handheld, single-lead electrocardiogram device in the Netherlands. Europace 2018;20:12–8.
69. Welton NJ, McAleenan A, Thom HH, et al. Screening strategies for atrial fibrillation: a systematic review and cost-effectiveness analysis. Health Technol Assess 2017;21:1–236.
70. Moran PS, Flattery MJ, Teljeur C, Ryan M, Smith SM. Effectiveness of systematic screening for the detection of atrial fibrillation. Cochrane Database Syst Rev 2013;4:CD009586.
71. Simpson E, Stevenson M, Scope A, Poku E, Minton J, Evans P. Echocardiography in newly diagnosed atrial fibrillation patients: a systematic review and economic evaluation. Health Technol Assess 2013;17:1–263, v—vi.
72. Aronsson M, Svennberg E, Rosenqvist M, et al. Cost-effectiveness of mass screening for untreated atrial fibrillation using intermittent ECG recording. Europace 2015;17:1023–9.
73. Bury G, Swan D, Cullen W, et al. Screening for atrial fibrillation in general practice: a national, cross-sectional study of an innovative technology. Int J Cardiol 2015;178:247–52.
74. Fitzmaurice DA, Hobbs FD, Jowett S, et al. Screening versus routine practice in detection of atrial fibrillation in patients aged 65 or over: cluster randomised controlled trial. BMJ 2007;335:383.
75. Levin LA, Husberg M, Sobocinski PD, et al. A cost-effectiveness analysis of screening for silent atrial fibrillation after ischaemic stroke. Europace 2015;17:207–14.
76. Maeda K, Shimbo T, Fukui T. Cost-effectiveness of a community-based screening programme for chronic atrial fibrillation in Japan. J Med Screen 2004;11:97–102.
77. Rhys GC, Azhar MF, Foster A. Screening for atrial fibrillation in patients aged 65 years or over attending annual flu vaccination clinics at a single general practice. Qual Prim Care 2013;21:131–40.
78. Meschia JF, Bushnell C, Boden-Albala B, et al., American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Functional Genomics and Translational Biology, Council on Hypertension. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2014;45:3754–832.