International Journal of Cardiology 280 (2019) 84–88

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Age-and-sex stratified prevalence of atrial fibrillation in rural Western India: Results of SMART-India, a population-based screening study

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ARTICLE INFO

Article history:
Received 12 October 2018
Received in revised form 14 November 2018
Accepted 4 December 2018
Available online 6 December 2018

Keywords:
Atrial fibrillation
India
Epidemiology
ECG screening
Mobile technology

ABSTRACT

Background: Early detection of Atrial Fibrillation (AF) is a public health priority across the globe because AF-related strokes are preventable. Despite an ongoing stroke epidemic in India, a public health strategy for AF screening and treatment is missing because the epidemiology of AF in India remains poorly defined.
Methods: This population-based study used mobile technology to derive age and sex-stratified AF prevalence by screening 7 participants in each of six age and sex strata (age 40–55, 56–65, 65+, and male and female) from 50 villages (2100 participants). A health worker from each village used a handheld digital electrocardiogram (iECG) device (Kardia) to screen for AF on 3 separate days, and administered a questionnaire. All abnormal (AF or unclassified) iECGs were reviewed by the Indian cardiologist and AF determination confirmed by a US-based cardiac electrophysiologist.
Results: Of the 2100 individuals enrolled, iECGs were collected from 2074 participants (98.8%) and 1947 (92.7%) participants responded to the questionnaire. AF was identified in 33 participants (1.6%), two-thirds on the first iECG. AF prevalence was higher among males (2.3% vs 1.0%, $p = 0.03$) and in older people (0.6%, 0.9%, 2.1%, 5.6%; $p < 0.01$).
Conclusions: The prevalence of AF observed in our population-based sample is comparable to rates found in studies from North America and Western Europe and increases similarly with age. AF screening using village health workers in rural India is feasible and presents an opportunity for a strategy to address the stroke epidemic in India through primary prevention.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide [1]. This disorder increases the risk of stroke 5-fold and is associated with one third of strokes [2,3]. Risk factors for AF include increasing age, hypertension, diabetes mellitus, myocardial infarction, smoking, and alcohol consumption [4]. AF is a progressive disease; early intermittent episodes often advance to more persistent episodes and eventually a permanent state of arrhythmia [5]. AF episodes can be asymptomatic or minimally symptomatic, leading to delays in diagnosis and treatment. Numerous studies have found that stroke is the first clinical symptom of AF in more than a quarter of newly diagnosed cases of AF [6,7]. Treatment of AF with oral anti-coagulants (OAC) reduces stroke by 64% and mortality by 27% [2,8,9]. Therefore, programs that identify AF earlier may play a critical role in the primary prevention strategy for stroke. However, the promise of systematic or opportunistic AF screening has not been realized, particularly in low and middle-income countries such as India, where there is a growing epidemic of cardiovascular diseases and stroke [1,10,11].

The literature suggests that AF prevalence is highest in North America, Western Europe, and Oceania [12–15]. Systematic reviews of AF epidemiology in South America, Africa, and South and East Asia identified 96 studies, 62 of them from China, Japan, or South Korea [15,16]. Only four Indian studies were included in the two reviews, and they reported the prevalence of AF in India to be <0.5% [17–20]. However, these studies suffer from selection bias, and included only a small proportion

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https://doi.org/10.1016/j.ijcard.2018.12.016
0167-5273/

over age 65, raising concerns regarding the validity of the findings. Furthermore, all studies performed screening for AF at a single time-point. This approach enhances feasibility, but may miss cases of paroxysmal AF. By contrast, in a previous pilot study, we screened 353 Indian adults aged 50 years or older at their homes for five consecutive days [21]. We found a markedly higher prevalence of AF (5.1%) among screened individuals but our limited sample size did not meet the inclusion criteria for the systematic review of sample size of ≥750 [16].

The present study used a technology-assisted, community-based AF screening strategy to determine the prevalence of AF among adults over the age of 45 years, with a further breakdown according to predefined age- and sex-strata. We hypothesized that the prevalence of AF observed among middle-aged and older adults from Gujarat, India would be comparable to the prevalence of AF observed in adults from North America, Western Europe, and Oceania, and that prevalence would increase with advancing age, as it does in other ethnic groups.

2. Methods

Complete details of the design and protocol for Smartphone Monitoring for Atrial fibrillation in Real-Time - India (SMART-India) study have been previously published [22]. This study protocol underwent two independent reviews for ethical consideration, with an institutional review board in U.S. (IRB # H00008089) and a human research ethics committee in India (#701516016). Relevant details for the analyses presented in this manuscript are presented below.

SMART-India is a cross-sectional study designed to screen for previously undetected AF among Indian adults living in the rural region of Anand district, Gujarat, India. The SMART-India study was conducted by an Indo-US collaboration of two academic institutions. The Indian institution operates a tertiary care medical center in the Anand district and oversees a community extension program that has recruited a female village health worker (VHW) from each of 60 of its surrounding villages. These VHWs conducted an initial census in their respective villages in 2015, which constituted our primary study base for the SMART-India study. Six of the 60 villages were randomly selected for the pilot study and thus were excluded from the present study. Four of the remaining 54 villages were randomly selected for a trial run of the SMART-India protocols to train research coordinators and identify potential complications.

A list of village residents belonging to one of six strata based on the combination of age (40–55, 56–65, and 65+) and sex (male and female) was created based on the census list. Detailed sample size calculations for this study are described elsewhere but a sample size of 1823 was necessary to estimate overall AF prevalence with 1% error assuming the a priori prevalence of AF to be 5% based on the pilot study; similarly, a minimum of 300 participants in each stratum was needed to estimate the prevalence with 2% error [21,22]. Therefore, residents of villages were approached for participation in the study until seven participants in each stratum from each village were enrolled, totaling 2100 participants from 50 villages. Only four participants with a previous diagnosis of AF were identified by this strategy, and all four refused to participate in this study.

After signing an informed consent, study participants were screened for AF using a FDA-approved, single-lead iECG device (Kardia, Alivecor) for a 30 s recording as recommended by the consensus document endorsed by four major international bodies with expertise in heart rhythm [23]. Participants were screened using the Kardia Mobile device three times over a five-day period [24]. On the first screening day, the trained research coordinators administered a standardized questionnaire in the local language that was adapted to the cultural context using cognitive response testing [22]. The questionnaire collected information about screened individuals' sociodemographic characteristics, healthcare usage, lifestyle habits, current or past medical conditions, and current medication usage. The training phase of SMART-India study took place over the course of four months (August, 2016 to November, 2016). The AF screening phase was completed over a 12-month period between December, 2016 and December, 2017.

The study cardiologist in India reviewed all iECGs deemed by the automated Kardia algorithm to represent "possible AF" or "unclassified." To be considered to have AF, the participant had to have at least one single-lead iECG deemed to represent AF by the Indian cardiologist and confirmed by a US-based cardiac electrophysiologist. Additionally, two US physicians reviewed a random subset of 250 iECG deemed as "Normal" by automated Kardia algorithm and did not find any AF rhythm.

Descriptive statistical analyses were performed to describe the distribution of participant characteristics and AF screening results across different age strata. Statistical significance of the associations with age categories was assessed using Cuzick's test for trend across ordered categories [25]. All statistical analyses were performed in STATA MP 15.1.

3. Results

A total of 8473 residents of 50 villages were identified from village census as potentially eligible based on age and sex criteria. Of these, a random sample of 2313 (27.3%) were approached, enabling us to reach the requisite sample size of 2100 participants (response rate of 90.8%) (e-Table 1). Of the 2100 participants enrolled in the SMART-India study, 26 were never screened for technical reasons; among those screened, 127 did not complete the study questionnaire (Fig. 1).

Of the 2074 participants who were screened, most (1670, 80.5%) were screened three times for AF and 300 (14.5%) were screened twice. Based on the Kardia's automated algorithm, 88 (4.2%) participants had a screen diagnosis of "possible AF". After clinical adjudication of the iECG tracing, 32 individuals were confirmed to have AF. One participant whose heart rhythm was deemed "unclassified" by the automated algorithm was classified as AF after clinical adjudication, yielding an overall AF prevalence of 1.6% (n = 33). Two-thirds (22) of those identified as having AF were identified during the first screening, an additional six on second screening, while the rest on the third screening (Table 1).

Sociodemographic characteristics, cardiovascular risk factors, and physiologic measures of the 1947 participants who were screened for AF and responded to the questionnaire are described in Table 1. Just over half of the participants screened and completing questionnaires were female, only 343 (18)% had completed high-school, and most of the participants belonged to the households with a per capita income of <25 cents per day. Hypertension (335, 18.6%) and diabetes (144, 8.0%) were the two most common conditions that were self-reported by the participants. Advanced age was associated with lower education, higher household income, visiting a healthcare provider in the previous year, and a greater burden of comorbid cardiovascular conditions and risk factors. Older participants were also more likely to be on medications and had higher blood pressure measured at the time of AF screening (Fig. 2).

Older participants were more likely to complete all three screenings ($p = 0.01$) (e-Table 2) and were more likely to have AF ($p < 0.01$) (Fig. 3). Less than 1% of the participants under the age of 65 had AF, whereas 3.2% of participants >65 years of age had AF ($p < 0.01$). Men were more likely to screen positive than women, particularly among older participants; the prevalence of AF among men 65 and older was 2-fold higher than the prevalence among women in the same age group ($p < 0.01$). The highest prevalence of AF (7.2%) was observed among males over the age of 75. Of the 31 participants who screened positive for AF and responded to the questionnaires, 17 (54.9%) had a CHADS-VASc score of ≥2 based on self-report. By comparison, 595 (33.7%) of the 1765 participants who did not screen positive for AF had a CHADS-VASc score of 2 or higher ($p = 0.01$). None of the participants who screened positive for AF reported existing use of aspirin or oral anticoagulants.

4. Discussion

In this population-based AF screening study including >2000 Indian adults randomly selected from a census of villagers to derive age- and sex-stratified prevalence, we found 33 (1.6%) with previously undiagnosed AF. The prevalence observed in our study is three times more than previously reported in India and is comparable to rates found in

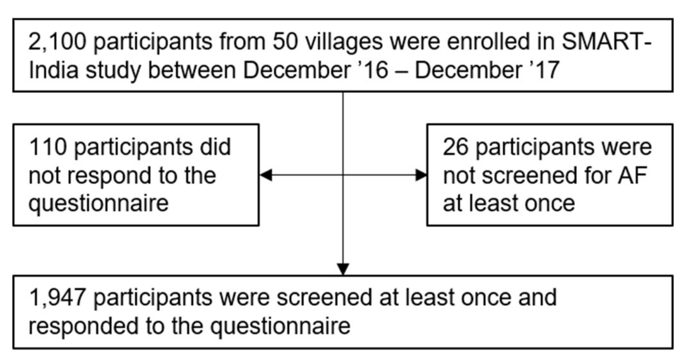

Fig. 1. Flowchart of SMART-India study participants who were screened for AF and responded to the questionnaire.

Table 1
The distribution of sociodemographic characteristics, lifestyle habits, and health history across different age groups among the participants of the SMART-India study.

Risk factors		Total	Age group: N (column %)				
			40–55	56–65	66–75	75+	p[b]
N		1947	643 (33.0)	647 (33.2)	461 (23.7)	196 (10.1)	–
Female		1016 (52.2)	350 (54.46)	334 (51.9)	234 (50.4)	98 (49.8)	0.14
Education	None	249 (12.8)	59 (9.2)	86 (13.4)	74 (16.0)	30 (15.2)	<0.01
	Up to 6th grade	297 (15.3)	83 (12.9)	84 (13.1)	82 (17.7)	48 (24.4)	
	7–10th grade	1056 (54.2)	345 (53.7)	365 (56.8)	244 (52.6)	102 (51.8)	
	12+ grade	345 (17.7)	156 (24.3)	108 (16.8)	64 (13.8)	17 (8.6)	
Caste	General	1560 (80.2)	510 (79.3)	516 (80.3)	376 (81.0)	158 (80.2)	0.55
	Other backwards caste	138 (7.1)	42 (6.5)	49 (7.6)	37 (8.0)	10 (5.1)	
	Scheduled caste or tribe	249 (12.8)	91 (14.2)	78 (12.1)	51 (11.0)	29 (14.8)	
Per-capita income[a]	<0.25	1306 (67.5)	433 (67.5)	455 (70.9)	304 (65.8)	114 (59.7)	0.04
	$0.25 < $0.75	230 (11.9)	76 (11.9)	68 (10.6)	61 (13.2)	25 (13.1)	
	$0.75 < $1.25	220 (11.4)	77 (12.0)	70 (10.9)	51 (11.0)	22 (11.5)	
	$1.25 or more	180 (9.3)	55 (8.6)	49 (7.6)	46 (10.0)	301 (15.7)	
Health behavior	Smoking	78 (4.0)	25 (3.9)	21 (3.3)	23 (5.0)	9 (4.6)	0.29
	Nonsmoking tobacco	132 (6.8)	53 (8.2)	36 (5.6)	30 (6.5)	13 (6.6)	0.38
	Alcohol	30 (1.5)	9 (1.4)	12 (1.9)	4 (0.9)	5 (2.5)	0.75
HC visit in last year		599 (31.0)	12 (18.9)	205 (32.1)	187 (40.5)	87 (44.2)	<0.01
Medical history	HTN	336 (18.7)	65 (11.1)	106 (17.9)	107 (24.6)	58 (32.0)	<0.01
	Diabetes	145 (8.1)	37 (6.3)	45 (7.6)	41 (9.5)	22 (12.2)	<0.01
	Hypercholesterolemia	36 (2.0)	9 (1.5)	10 (1.7)	12 (2.9)	5 (2.9)	0.10
	Heart valve disease	43 (2.4)	6 (1.0)	14 (2.3)	15 (3.5)	8 (4.6)	<0.01
	Coronary artery disease	4 (0.2)	3 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	0.08
	COPD/chronic lung disease	103 (5.7)	14 (2.4)	27 (4.5)	41 (9.6)	21 (11.7)	<0.01
	Previous MI	45 (2.5)	4 (0.7)	12 (2.0)	20 (4.7)	9 (4.9)	<0.01
	Heart failure	6 (0.3)	0 (0.0)	3 (0.5)	1 (0.2)	2 (1.1)	0.07
	Previous stroke or TIA	21 (1.2)	4 (0.75)	6 (1.0)	9 (2.1)	2 (1.1)	0.13
Self-reported Rx	HTN	107 (5.5)	12 (1.9)	25 (3.9)	43 (9.3)	29 (14.8)	<0.01
	Diabetes	30 (1.5)	6 (0.9)	6 (0.9)	11 (2.4)	7 (3.6)	<0.01
	Oral anticoagulation	14 (0.4)	0 (0.0)	5 (0.8)	7 (0.6)	2 (1.0)	0.01

HC: healthcare; HTN: hypertension; MI: Myocardial Infarction; TIA: transient ischemic attack; Rx: medication.
[a] Calculated from self-reported monthly household income by accounting for household numbers, 30 days per month, and currency conversion rate of 60 Indian Rupees to 1 US Dollar.
[b] Cuzick's test for trend across ordered categories of age.

studies from North America and Western Europe [12,15–20,26]. Our approach to use census data to randomly select participants reduces the likelihood of selection bias observed in other studies from India and may contribute to the difference in results [22]. Additionally, we conducted three separate iECG screenings over a five-day period: had we used only a single reading, the prevalence would have been 1.1%, which is still higher than previous reports from India. Our findings suggests that India may be facing a comparable public health burden of AF as observed in western, high-income countries and a public health program to increase AF awareness, identification, and management may help India in addressing its stroke epidemic.

In Europe and US, robust epidemiological data have led researchers and clinicians to begin exploring the benefits of opportunistic and systematic AF screening to reduce stroke risk. India is uniquely positioned to pursue a similar path because of its nationwide program, the National Program for Prevention and Control of Cancer, Diabetes, CVD and Stroke (NPCDCS). Under the NPCDCS, state governments receive earmarked resources to establish programs through their primary and secondary

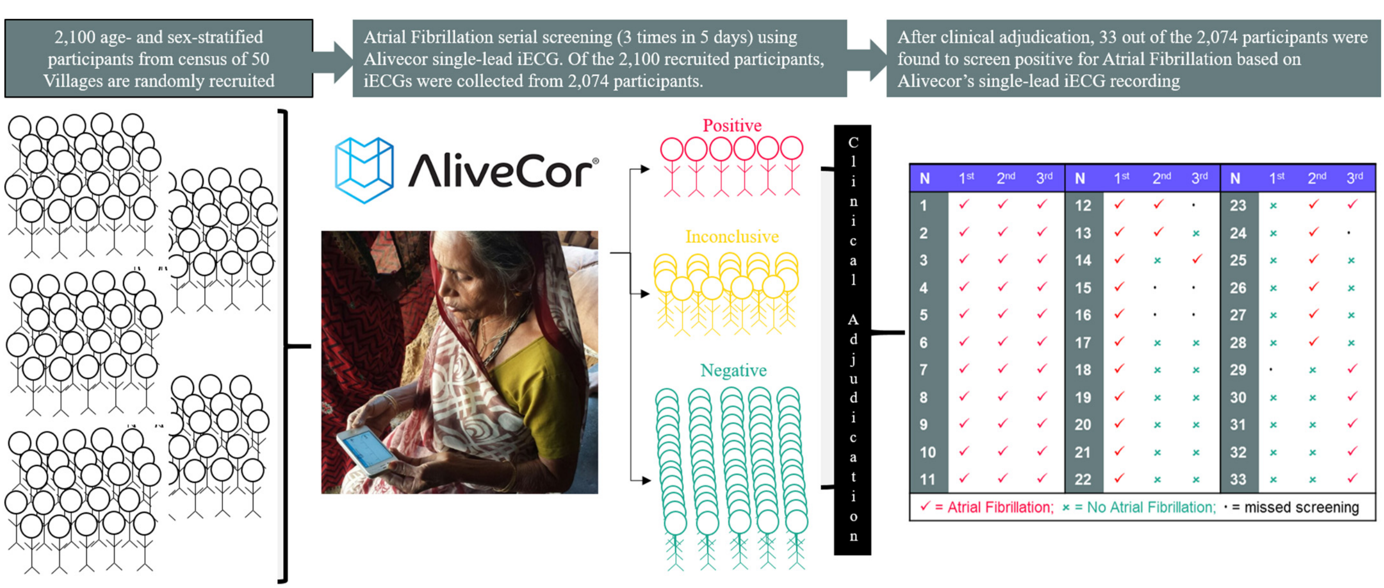

Fig. 2. An overview of SMART-India screening study and results to derive prevalence of Atrial Fibrillation among residents of rural Anand district in Gujarat, India.

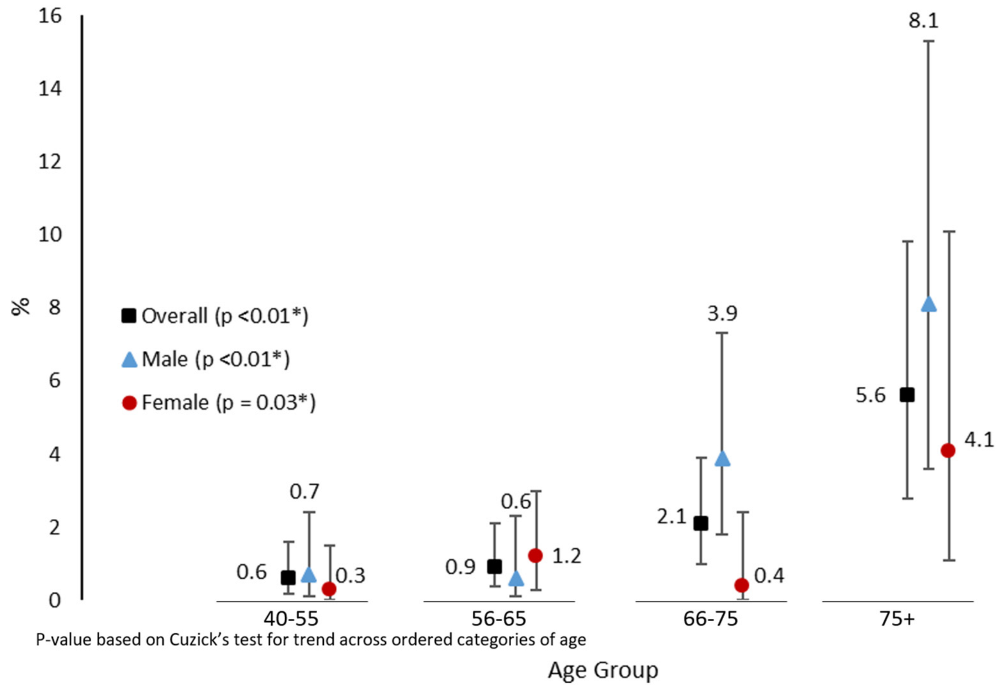

Fig. 3. Age and sex stratified prevalence of Atrial Fibrillation among the participants of the SMART-India study.

health centers that i) generate disease awareness and promote healthy lifestyle, ii) screen and detect diseases in early stages, iii) diagnose diseases affordably, timely, and accurately, iv) provide affordable treatment, and v) rehabilitate patients who experience adverse outcomes.

Awareness about AF in India is disproportionately low in the context of the country's epidemiologic transition from communicable to noncommunicable diseases [27]. Most of our understanding of AF in India is based on patient registries, which are important to inform clinical strategy for management of AF but cannot quantify the public health importance of the disease [27,28]. Therefore, our study provides valuable information about AF epidemiology and its association with increasing age to justify AF screening as a reasonable approach to the ongoing stroke epidemic.

A recent white paper published by an international collaboration of >100 experts from 31 countries reported that screen-detected AF is likely not a benign condition and carries sufficient additional risk of stroke to justify initiation of oral anticoagulation therapy to prevent stroke [6]. When one considers the high burden of thromboembolic strokes observed among Indian adults and the significant barriers to conventional clinical care in many parts of India, AF screening using mobile health devices and automated AF detection algorithms represents an attractive and scalable option [10,29–31]. In our study, we found an increasing prevalence of AF and stroke risk factors with age, mirroring trends observed in studies conducted in other countries. The prevalence of AF triples among adults older than 65 in our study compared to those aged 40–65 years. Therefore, focusing AF screening among those over 65 or 75 years of age would be an efficient, scalable approach, with sufficient yield to justify identification of undiagnosed AF that would likely benefit from treatment.

India has long championed the VHW model to support its national maternal and child health programs and has endorsed a similar model to combat the growing epidemic of non-communicable diseases through the NPCDCS [32]. VHWs were shown in our study to be ideally suited to screen for AF and would be the logical pathway to facilitate longer-term management of newly detected AF, including monitoring medication adherence or laboratory INR testing when oral anticoagulation is initiated.

Findings from our study also has important implications for understanding AF epidemiology beyond India. Low and middle-income countries are facing a rise in the incidence of lifestyle related cardiovascular disease, and many do not have the adequate healthcare system to surveil and manage this growing epidemic [1,14,33]. The SMART-India study illustrates the opportunity for international collaborations to leverage advances in mobile technology to overcome resource shortcomings and constitute an effective public health program.

Our study has several strengths, including its scope and integration into an existing community-based cardiovascular surveillance effort. However, there are some limitations. Our findings are based on a single-lead iECG recording collected using a FDA-approved device, whereas the gold-standard for the diagnosis of AF has usually been thought to be a 12-lead ECG. However, our approach was consistent with recommendations enumerated in the most recent concensus document endorsed by four major international entities for heart rhythm societies [23]. Although clinical adjudication of single-lead iECG is widely accepted as a screening and clinical decision-making strategy, we do not present results of further cardiovascular evaluation of participants in this manuscript because clinical follow-ups are ongoing. This lack of more detailed clinical evaluation and follow-up which was beyond the scope of this study limits our ability to present the outcomes of AF detection including rates of OAC prescription, OAC adherence, or stroke/bleeding rates among screen-positive participants.

In conclusion, results from the SMART-India study disrupt the conventional wisdom about the epidemiology of AF in India by demonstrating a three-fold higher rate of AF than has been previously reported, most of which had not previously diagnosed. Furthermore, our finding that older Indians suffer AF at rates similar to populations in North America, Europe, and Oceania underscores the need for more studies to better understand AF and its related consequences within the context of the complex healthcare system in India. We also present a roadmap for VHW-driven, community-based targeted AF screening programs that can help identify patients with AF who are at high risk for experiencing adverse event, and a potential route to facilitate commencement and monitoring of thromboprophylaxis to prevent AF-related cardio-embolic stroke.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.12.016.

Funding

This study was supported by 2016 University of Massachusetts Medical School Office of Global Health Pilot Project Award through institutional CTSA grant (UL1-TR001453). AS received support from the National Center for Advancing Translational Sciences (TL1-TR001454) and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (1F30HD091975-01A1). JJA received support from the National Institute on Minority Health and Health Disparities (P60-MD006912-05). DDMM's time was supported by 1R15HL121761, R01HL126911, R01HL137734, R01HL137794, R01HL13660 from the National Heart, Lung, and Blood Institute.

Conflicts of interest

BF reports prior fees and advisory board honoraria from Bayer Pharma AG, Boehringer Ingelheim, and BMS/Pfizer but for the past year has removed himself from pharmaceutical advisory boards and receives speaker fees only for accredited educational meetings. Current investigator-initiated grant from BMS-Pfizer for a study part funded by Heart Foundation of Australia, NSW CVRN grant. DDM has received research grant funding from Bristol-Myers Squibb, Pfizer, Samsung, Philips Healthcare, Biotronik, has received consultancy fees from Bristol-Myers Squibb, Pfizer, Flexcon, Boston Biomedical Associates, and has inventor equity in Mobile Sense Technologies, Inc. (CT).

Acknowledgements

AS had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, including and especially any adverse effects. AS performed the analyses and prepared the first draft of the manuscript. SK, NF, SS, HP, SR, ST, SN, BF, JA, and DDM contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript.

We are thankful to Kandarp Talati and Foundation for Diffusion of Innovations for providing logistical support with the screening protocol. We also want to acknowledge Vikas Parmar, Arun Parmar, Nita Macchi, and Dhaval Patel for their tireless efforts in coordinating the screening efforts with the VHWs.

References

[1] A. Alonso, L.G.S. Bengtson, A rising tide: the global epidemic of atrial fibrillation, Circulation 129 (2013) 829–830.

[2] C.T. January, F.L.S. Wann, F. Joseph, S. Alpert, F.H. Calkins, F.J. C, et al., 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary, J. Am. Coll. Cardiol. 64 (2014) 2246–2280.

[3] L. Friberg, M. Rosenqvist, A. Lindgren, A. Terént, B. Norrving, K. Asplund, High prevalence of atrial fibrillation among patients with ischemic stroke, Stroke 45 (2014) 2599–2605.

[4] E.J. Benjamin, D. Levy, S.M. Vaziri, R.B. D'Agostino, A.J. Belanger, P.A. Wolf, Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study, JAMA 271 (1994) 840–844.

[5] D.G. Wyse, I.C. Van Gelder, P.T. Ellinor, A.S. Go, J.M. Kalman, S.M. Narayan, et al., Lone atrial fibrillation: does it exist? J. Am. Coll. Cardiol. 63 (2014) 1715–1723.

[6] B. Freedman, J. Camm, H. Calkins, J.S. Healey, M. Rosenqvist, J. Wang, et al., Screening for atrial fibrillation, Circulation 135 (2017).

[7] A. Kishore, A. Vail, A. Majid, J. Dawson, K.R. Lees, P.J. Tyrrell, et al., Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: a systematic review and meta-analysis, Stroke 45 (2014) 520–526.

[8] B. Freedman, T.S. Potpara, G.Y.H. Lip, Stroke prevention in atrial fibrillation, Lancet 388 (2016) 806–817.

[9] R.G. Hart, L.A. Pearce, M.I. Aguilar, Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation, Ann. Intern. Med. 146 (2007) 857–867.

[10] D. Prabhakaran, P. Jeemon, A. Roy, Cardiovascular diseases in India: current epidemiology and future directions, Circulation 133 (2016) 1605–1620.

[11] A. Gunarathne, J.V. Patel, B. Gammon, P.S. Gill, E.A. Hughes, G.Y. Lip, Ischemic stroke in South Asians: a review of the epidemiology, pathophysiology, and ethnicity-related clinical features, Stroke 40 (2009) e415–e423.

[12] S.S. Chugh, R. Havmoeller, K. Narayanan, D. Singh, M. Rienstra, E.J. Benjamin, et al., Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study, Circulation 129 (2014) 837–847.

[13] T.S. Potpara, D.A. Lane, Diving to the foot of an iceberg: the SEARCH for undiagnosed atrial fibrillation, Thromb. Haemost. 112 (2014) 1–3.

[14] F. Rahman, G.F. Kwan, E.J. Benjamin, Global epidemiology of atrial fibrillation, Nat. Rev. Cardiol. 11 (2014) 639–654.

[15] G.Y.H. Lip, C.M. Brechin, D.A. Lane, The global burden of atrial fibrillation and stroke: a systematic review of the epidemiology of atrial fibrillation in regions outside North America and Europe, Chest 142 (2012) 1489–1498.

[16] Y. Bai, Y.-L. Wang, A. Shantsila, G.Y.H. Lip, The global burden of atrial fibrillation and stroke: a systematic review of the clinical epidemiology of atrial fibrillation in Asia, Chest 152 (2017) 810–820.

[17] S.S.S. Kaushal, D.J.J. DasGupta, B.S.S. Prashar, A.K.K. Bhardwaj, Electrocardiographic manifestations of healthy residents of a tribal Himalayan village, J. Assoc. Physicians India 43 (1995) 15–16.

[18] D.K. Saggu, G. Sundar, S.G. Nair, V.C. Bhargava, K. Lalukota, S. Chennapragada, et al., Prevalence of atrial fibrillation in an urban population in India: the Nagpur pilot study, Heart Asia 8 (2016) 56–59.

[19] P. Hingorani, M. Natekar, S. Deshmukh, D.R. Karnad, S. Kothari, D. Narula, et al., Morphological abnormalities in baseline ECGs in healthy normal volunteers participating in phase I studies, Indian J. Med. Res. 135 (2012) 322–330.

[20] A. Kalra, Y. Pokharel, R.S. Hira, S. Risch, V. Vicera, Q. Li, et al., Cardiovascular disease performance measures in the outpatient setting in India: insights from the American College of Cardiology's PINNACLE India Quality Improvement Program (PIQIP), J. Am. Heart Assoc. 4 (2015) e001910.

[21] A. Soni, A. Earon, A. Handorf, N. Fahey, K. Talati, J. Bostrom, et al., High burden of unrecognized atrial fibrillation in rural India: an innovative community-based cross-sectional screening program, JMIR Public Heal. Surveill. 2 (2016), e159.

[22] A. Soni, S. Karna, H. Patel, N. Fahey, S. Raithatha, A. Handorf, et al., Study protocol for smartphone monitoring for atrial fibrillation in real-time in India (SMART-India): a community-based screening and referral programme, BMJ Open 7 (2017), e017668.

[23] G.H. Mairesse, P. Moran, I.C. Van Gelder, C. Elsner, M. Rosenqvist, J. Mant, et al., Screening for atrial fibrillation: a European Heart Rhythm Association (EHRA) consensus document endorsed by the Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología (SOLAECE), Europace 19 (2017) 1589–1623.

[24] J. Lau, N. Lowres, L. Neubeck, D.B. Brieger, R.W. Sy, C. Galloway, et al., Validation of an iphone ECG application suitable for community screening for silent atrial fibrillation: a novel way to prevent stroke, Circulation 126 (2012).

[25] J. Cuzick, A Wilcoxon-type test for trend, Stat. Med. 4 (1985) 87–90.

[26] N. Lowres, L. Neubeck, J. Redfern, S. Ben Freedman, Screening to identify unknown atrial fibrillation: a systematic review, Thromb. Haemost. 110 (2013) 213–222.

[27] R. Deore, A. Vora, Epidemiology and risk factor for atrial fibrillation in India, J. Prev. Cardiol. 3 (2014) 505–507.

[28] A. Vora, A. Kapoor, M. Nair, Y. Lokhandwala, C. Narsimhan, A.G. Ravikishore, et al., Clinical presentation, management, and outcomes in the Indian Heart Rhythm Society-Atrial Fibrillation (IHRS-AF) registry, Indian Heart J. 69 (2017) 43–47.

[29] J.D. Pandian, G. Singh, P. Kaur, R. Bansal, B.S. Paul, M. Singla, et al., Incidence, short-term outcome, and spatial distribution of stroke patients in Ludhiana, India, Neurology 86 (2016) 425–433.

[30] J.D. Pandian, P. Sudhan, Stroke epidemiology and stroke care services in India, J. Stroke 15 (2013) 128–134.

[31] E.L. O'Keefe, J.J. DiNicolantonio, H. Patil, J.H. Helzberg, C.J. Lavie, Lifestyle choices fuel epidemics of diabetes and cardiovascular disease among Asian Indians, Prog. Cardiovasc. Dis. 58 (2016) 505–513.

[32] A. Soni, S. Masoud, Z. Bhutta, National programs and policies to address child malnutrition in India: challenges and opportunities, Handb. Famine, Starvation, Nutr. Deprivation, Springer International Publishing, Cham 2018, pp. 1–24.

[33] S.S. Chugh, G.A. Roth, R.F. Gillum, G.A. Mensah, Global burden of atrial fibrillation in developed and developing nations, Glob. Heart 9 (2014) 113–119.