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Original Article

One-year clinical outcome of patients with nonvalvular atrial fibrillation: Insights from KERALA-AF registry☆

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ABSTRACT

Background: We report patient characteristics, treatment pattern and one-year clinical outcome of nonvalvular atrial fibrillation (NVAF) from Kerala, India. This cohort forms part of Kerala Atrial Fibrillation (KERALA-AF) registry which is an ongoing large prospective study.
Methods: KERALA-AF registry collected data of adults with previously or newly diagnosed atrial fibrillation (AF) during April 2016 to April 2017. A total of 3421 patients were recruited from 53 hospitals across Kerala state. We analysed one-year follow-up outcome of 2507 patients with NVAF.
Results: Mean age at recruitment was 67.2 years (range 18–98) and 54.8% were males. Main co-morbidities were hypertension (61.2%), hyperlipidaemia (46.2%) and diabetes mellitus (37.2%). Major

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Nonvalvular atrial fibrillation
Stroke

co-existing diseases were chronic kidney disease (42.1%), coronary artery disease (41.6%), and chronic heart failure (26.4%). Mean CHA_2DS_2-VASc score was 3.18 (SD ± 1.7) and HAS-BLED score, 1.84 (SD ± 1.3). At baseline, use of oral anticoagulants (OAC) was 38.6% and antiplatelets 32.7%. On one-month follow-up use of OAC increased to 65.8% and antiplatelets to 48.3%. One-year all-cause mortality was 16.48 and hospitalization 20.65 per 100 person years. The main causes of death were cardiovascular (75.0%), stroke (13.1%) and others (11.9%). The major causes of hospitalizations were acute coronary syndrome (35.0%), followed by arrhythmia (29.5%) and heart failure (8.4%).

Conclusions: Despite high risk profile of patients in this registry, use of OAC was suboptimal, whereas antiplatelets were used in nearly half of patients. A relatively high rate of annual mortality and hospitalization was observed in patients with NVAF in Kerala AF Registry.

1. Introduction

Atrial fibrillation (AF) is the common cardiac arrhythmia seen in clinical practice, associated with high morbidity and mortality.[1] AF is becoming a major public health problem worldwide,[2] leading to increased health care resource utilization with its impact on global health budget.[3,4] Epidemiological data on AF is available mainly from North America, Europe and Far East.[5–9] Significant difference exists between developed and developing countries on aetiology, co-morbid conditions, treatment preferences, mortality and morbidity due to AF.[10,11] Even though effective therapies have evolved in the last 4 decades and newer drugs were introduced for stroke prevention in AF patients in the last 7–8 years, there is wide variability in adherence to guideline recommended treatment in different regions of the world.

Limited information is available on clinical epidemiology, management and outcome of AF patients from south Asia, particularly from India.[10] In this manuscript, we provide patient characteristics, risk factors, treatment pattern and one-year clinical outcome of NVAF patients who were prospectively recruited from 53 hospitals located in both rural and urban areas of Kerala state.

2. Methods

KERALA-AF registry is an ongoing large prospective cohort registry of AF patients from Kerala. A total of 3421 AF patients were enrolled during the year 2016–17. Patients with transient AF due to causes like acute myocardial infarction, infection, alcohol intoxication, metabolic abnormalities, post-operative cases and critically ill patients with life expectancy less than 30 days were excluded. Each patient was enrolled in the registry after examination by the cardiologist(s) of participating centres from either in-patient or out-patient services. Majority of patients were from out-patient service. Detailed methodology and the baseline findings of the study is published elsewhere.[12] Medical history, physical examination, New York Heart Association (NYHA) status and laboratory investigations including echocardiography were done at baseline. Patients were classified into AF with valvular heart disease (AFVHD) and nonvalvular AF (NVAF).[13,14] AFVHD is defined as those cases associated with mitral stenosis, prosthetic valve implantation and mitral valve repair. Findings from clinical examination, chest X-ray and echocardiography were utilized to make diagnosis of valvular heart disease. There were 914 AFVHD patients and 2507 NVAF patients enrolled. Follow up was done at one-month, six months and at one-year. One-month follow-up was exclusively clinic visit and six month and one-year visits were either clinic visit or telephonic contact. Among the total 2507 patients, we could follow up 97.4% at one month, 88.9% at six month and 84.1% at one-year (Fig. 1).

Details of co-morbidities and co-existing diseases were assessed. Treatment details collected included drugs used for rate/rhythm control as well as for stroke prevention. Stroke and bleeding risk of patients were assessed using CHA_2DS_2-VASc and HAS-BLED score.[15,16] If death occurred, cause of death was noted. Additionally, data on clinical events such as stroke, transient ischemic attack (TIA), arrhythmia, systemic embolism other than stroke, gastro-intestinal (GI) bleed, intra cranial (IC) bleed and minor bleed were collected. Details of causes of hospitalization were also noted. Estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 was taken as chronic kidney disease (CKD).[17]

The study was conducted according to the ethical guidelines of Indian Council of Medical Research (ICMR) and conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Informed written consent was taken from each participant and the study was approved by the ethics committees of the collaborating institutions. This study was supported by the Cardiological Society of India, Kerala Chapter (CSI–K).

Continuous variables were reported as mean ± SD and/or median and interquartile range (IQR). Categorical variables were reported as percentages. Univariate analyses were applied to both continuous and categorical variables. A p-value of <0.05 was considered as statistically significant. Data was entered using Epi Data Entry 3.1 version software[18] and analysed using R software[19] and Microsoft Excel package.

3. Results

3.1. Baseline characteristics

The mean age of study patients was 67.2 years (SD ± 13) (range: 18–98) and 54.8% were males. The mean CHA_2DS_2-VASc score was 3.2 (SD ± 1.7) and HAS-BLED score was 1.8 (SD ± 1.2). Most prevalent co-morbidities were hypertension (61.2%), followed by hyperlipidaemia (46.2%) and diabetes mellitus (DM) (37.2%). Major co-existing diseases were CKD (42.1%), coronary artery disease (CAD) (41.6%), and chronic heart failure (CHF) (26.4%). Paroxysmal, persistent and permanent AF were present in 45.6%, 14.9% and 39.4% of patients respectively. Baseline characteristics including NYHA classes were presented in Table 1. DM, Hyperlipidaemia and CAD were significantly higher in males and thyroid disease was more in females.

3.2. Treatment pattern

3.2.1. Rate and rhythm control drugs

Strategy of rate control was used in 72.8% and rhythm control in 27.2% of patients. Betablocker was the most commonly used rate/rhythm control drug (47.9%), followed by Digoxin (24.8%) and

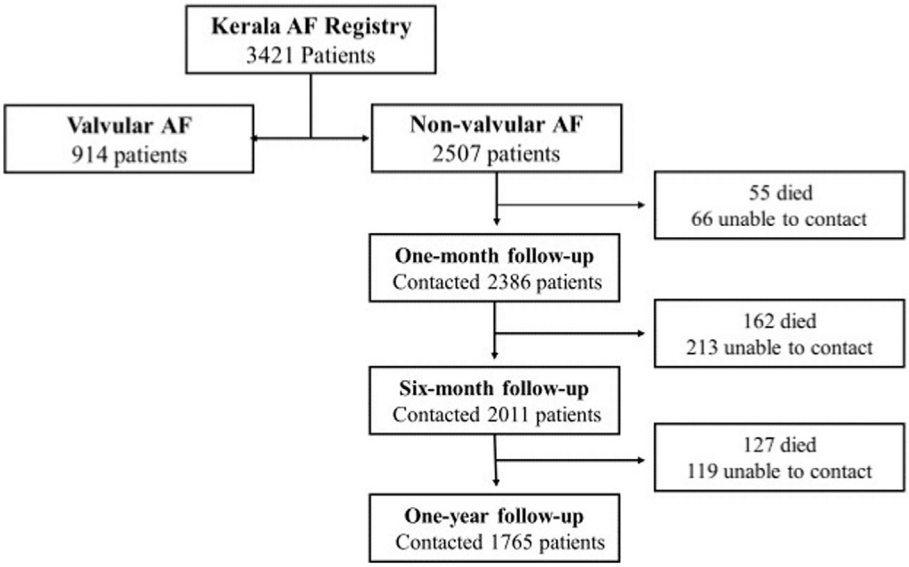

Fig. 1. Kerala AF Registry NVAF patient's follow-up

Table 1
Baseline characteristics of NVAF patients by sex.

Baseline Characteristics		Male (N = 1375) n (%)	Female (N = 1132) n (%)	Total (N = 2507) n (%)	P value
Age (in years)	Median (IQR)	68(60–76)	69 (60–76)	68(60–76)	0.57
	Mean (SD)	67.0(13.0)	67.3 (13.0)	67.2 (13.0)	0.59
CHA_2DS_2-VASc score (Mean ± SD)		2.82 ± 1.68	3.61 ± 1.71	3.18 ± 1.74	<0.05
HAS-BLED score (mean ± SD)		1.88 ± 1.29	1.79 ± 1.27	1.84 ± 1.29	0.059
Risk factors					
Hypertension		839(61.0)	695(61.4)	1534(61.2)	0.869
Diabetes mellitus		540(39.3)	392(34.6)	932(37.2)	<0.001
Dyslipidemia		665(48.4)	494(43.6)	1159(46.2)	<0.001
Co-existing diseases					
Stroke/TIA or Systemic Embolism		188(13.7)	165(14.6)	353(14.1)	0.526
Coronary Artery Disease		693(50.4)	351(31.0)	1044(41.6)	<0.001
Chronic Heart Failure		376(27.3)	286(25.3)	662(26.4)	0.237
Chronic Liver Disease		33(2.4)	20(1.8)	53(2.1)	0.329
Respiratory Disease		312 (22.7)	223(19.7)	535(21.3)	0.038
Thyroid Disease		193(14.0)	251(22.2)	444(17.7)	<0.001
Chronic Kidney Disease		541 (51.3)	513 (48.7)	1054 (42.1)	0.073
NYHA					
Class I & II		1139(82.8)	934(82.5)	2073(82.6)	0.710
Class III & IV		232(16.9)	198(17.5)	430(17.2)	
AF Classification					
Paroxysmal AF		645(47.6)	500(44.2)	1145(45.6)	0.116
Persistent AF		213(15.5)	161(14.2)	374(14.9)	
Permanent AF		516(37.5)	471(41.6)	987(39.4)	

Amiodarone (16.7%) and other anti-arrhythmic drugs (10.6%). At the time of entry into the study, 14 patients had a history of catheter ablation, 115 had pacemaker implantation, three had surgery for AF, eleven had implantable cardioverter defibrillator (ICD) and six had left atrial (LA) appendage occlusion.

3.2.2. Oral anticoagulants (OACs)

The most commonly used OAC was Vitamin K Antagonists (VKA) 58.2% . Patients receiving OAC showed an increase from 38.6% at the time of recruitment to 65.8% at one-month follow-up, and the use of NOAC increased from 2.7% to 7.6%. Among 2064 (82.3%) patients who had CHA_2DS_2-VASc score ≥ 2, the use of OAC was 39.2% which was increased to 67.8% at one-month follow-up. Patients with CHA_2DS_2-VASc score of ≤1 also received OAC at baseline (37.9%), which was increased to 55.7% at one-month follow-up (Figs. 2 and 3). Although 58.2% of patients were receiving VKA, International Normalised Ratio (INR) monitoring and dose adjustments were inadequate. Among those who were on VKA treatment 51.0% were aware of their INR values at one-month and 58.6% at six month and 77.3% at one-year.

3.2.3. Antiplatelets

At baseline, 32.7% of patients were receiving antiplatelets which increased to 48.3% on one-month follow-up (Fig. 2). Among patients with CHA_2DS_2-VASc score ≥2, 33.2% of patients were treated with antiplatelets which increased to 49.1% at one-month follow-up. In 23.0% of patients with CHA_2DS_2-VASc score of ≤1 and 39.4% of CHA_2DS_2-VASc score ≥4 were on antiplatelets at baseline. Both groups showed an increase in the use of antiplatelets on one-month follow up, 36.1% and 57.1% respectively (Figs. 3 and 4).

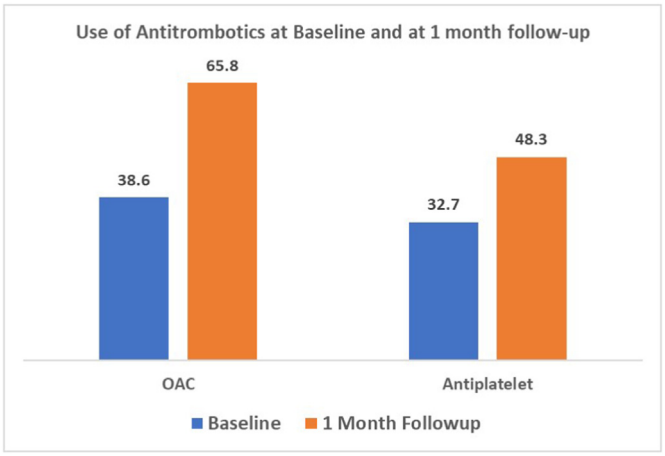

Fig. 2. Use of antithrombotics at baseline and at 1 month follow-up

3.2.4. One-year clinical outcome: death and hospitalizations

During one-year follow-up, all-cause mortality of 16.48/100 person years was observed. Cardiac death was 12.36/100 person years. Majority of death were cardiac (75.0%), followed by stroke (13.1%) and others (11.9%). Nearly half of the deaths (49%) were for patients with paroxysmal AF followed by permanent AF (35%) and persistent AF (16%).

Among the total 431 patients (20.65/100 person years) who required hospitalization, majority were due to acute coronary syndrome (ACS), followed by arrhythmia and heart failure (Table 2).

4. Discussion

KERALA-AF Registry is the largest and comprehensive study on AF from India. NVAF constituted the major portion of patients in this cohort unlike the earlier studies from India which reported high prevalence of rheumatic valvular heart disease.[20,21] The mean age of patients (67.2 years) in this study was similar to the mean age of Indian cohort (65.8 years) of GARFIELD-AF registry.[22] Prevalence of risk factors and co-existing diseases were relatively higher. CAD and risk factors like DM, hyperlipidaemia were higher than the average reported in the Indian as well as non-Indian patients of GLORIA-AF[23] and GARFIELD-AF[24] registries (TATable 3). Prevalence of hypertension, in this cohort was similar to what was reported in many other AF registries.[9,22,23] CKD was found to be high (42.1%) in our study. A relatively higher prevalence of these life style diseases and cardiovascular risk factors observed in this registry might be a reflection of higher prevalence in general population of Kerala. The influence of coronary risk factors, like DM, hyperlipidaemia and hypertension on the observed higher incidence of ACS in this study requires further evaluation.

The mean CHA_2DS_2-VASc score of patients in this registry was similar to what was reported in the European cohort of GLORIA-AF, GARFIELD-AF and EORP-AF registries and higher than the Indian cohort of GARFIELD-AF registry. The use of OAC at baseline (38.6%) was much lower than what was reported in EORP-AF registry (78.7%). Among patients with CHA_2DS_2-VASc score $\geq$2, those who were not receiving OAC at baseline was 60.8% as compared to 31.9% in the GARFIELD-AF registry. HAS-BLED score in general has not been considered for selection of anti-thrombotic drugs in this cohort. It was observed that OAC usage in patients with HAS_BLED score $\geq$3, and $\leq$2 were not significantly different, 68.1% and 63.5% respectively. Neither the bleeding risk nor the associated co-morbidities do not seem to have influenced the use of OACs. Low OAC use reflected its inadequate usage for stroke prevention in NVAF patients in Kerala. Even though the commonly used OAC was VKAs in this registry, its use was suboptimal because of unsatisfactory INR monitoring, dose adjustments and lack of compliance to therapy.

The overall use of NOAC among KERALA-AF Registry patients (7.6%) was low, similar to what was reported in Indian Heart Rhythm Society-Atrial Fibrillation (IHRS-AF) registry (4%).[25] In GLORIA-AF Registry, the use of NOAC varied among patients recruited from different countries ranging from 20% in Asia to 52% in North America. Although NOAC is the preferred drug for stroke prevention in AF as per guideline recommendations,[26,27] the cost considerations and wide difference in prescription practices among physicians might contribute to lower use of NOACs in Kerala.

Use of antiplatelets was 48.3% (single antiplatelet therapy (35.1%) and dual antiplatelet (13.2%) which was high when

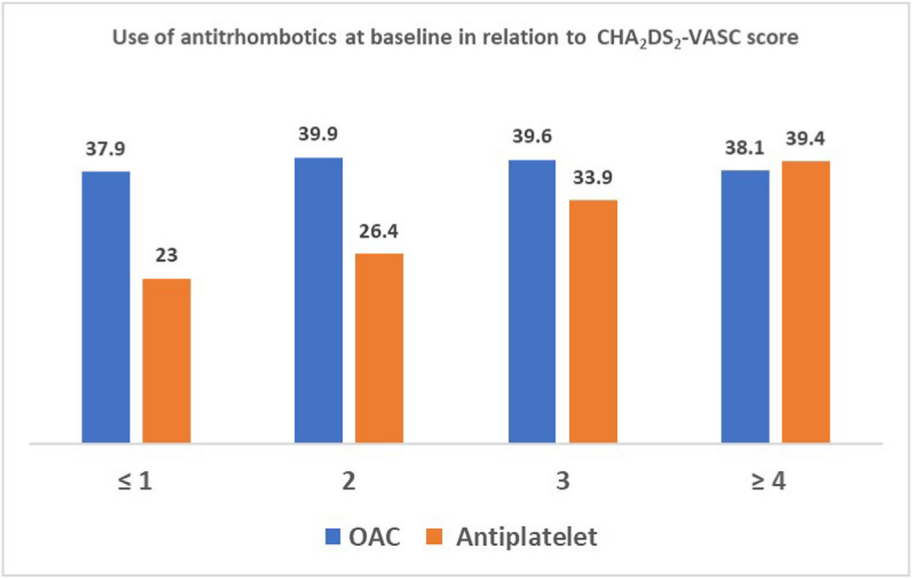

Fig. 3. Use of antithrombotics at baseline in relation to CHA_2DS_2-VASC score

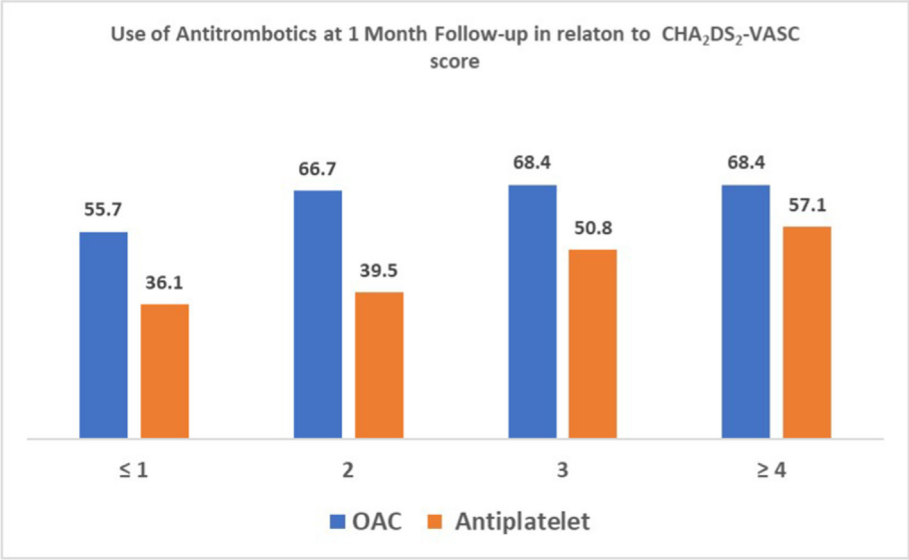

Fig. 4. Use of antithrombotics at 1 month follow-up in relation to CHA_2DS_2-VASC score

Table 2
Death and non-fatal Hospitalization at each time point within one-year.

Clinical Events	1 Month (N = 2441)	1–6 Months (N = 2173)	6–12 months (N = 1892)	Cumulative 1 Year (/100 person years)
All cause Death	**55**	**162**	**127**	**344 (16.48)**
Cardiac	45	118	95	258 (12.36)
Stroke	6	18	21	45 (2.16)
Others	4	26	11	41 (1.96)
Non-fatal Hospitalization (n (%))	**101**	**161**	**169**	**431 (20.65)**
Stroke	11	11	17	39 (1.87)
Transient Ischemic Attack	0	6	6	12 (0.57)
Arrhythmia	21	39	67	127 (6.08)
Acute Coronary Syndrome	28	71	52	151 (7.23)
Heart Failure	27	18	17	62 (3.02)
Systemic Embolism other than stroke	0	4	2	6 (0.28)
Gastro intestinal bleed	7	5	4	16 (0.77)
Intracranial Bleed	1	1	0	2 (0.09)
Minor Bleed	6	6	3	15 (0.72)

compared to other studies conducted worldwide.[9,22,23] GLORIA-AF Registry reported antiplatelet usage as 6.0% in European, 14% in North American and 25% in Asian cohorts. Other Indian studies have also shown high usage of antiplatelets among the population with highest risk of stroke. In the Indian cohort of the Realise-AF Registry,[20] 58% received only antiplatelet therapy for prevention of stroke. In IHRS-AF Registry, 30% of patients received only antiplatelet as stroke prevention treatment. The higher prevalence of CAD in this cohort might have contributed to the increased use of antiplatelets.

5. Outcome

One-year mortality per 100 person years was 16.48 in KERALA-AF Registry, which was 7.8 for Indian cohort of GARFIELD-AF Registry and 4.3 in Global GARFIELD-AF Registry. IHRS- AF registry reported an annual all cause death of (6.5%). RELY-AF Registry[28] reported 11% death in one-year in patients presenting to emergency department with AF in 47 countries with marked difference between participant countries with 20% in Africa, 17% in South America and 10% in North America, Europe and Australia.[29] In KERALA-AF Registry, majority (75%) of death were due to cardiac causes, similar to what was observed in the Indian cohort of GARFIELD-AF Registry. The rate of hospitalization was 20.65/100 person years and majority were due to cardiac causes. This is relatively higher than previously reported rate of hospitalizations in other registries from India, including IHRS-AF Registry. The increased rate of cardiac death and hospitalization due to ACS is probably indicative of a greater extent of CAD. A detailed evaluation of multimorbidity among these patients is required to clarify this issue.

5.1. Limitations

The registry data will not reflect the true incidence or prevalence of NVAF in the population since this is a hospital-based study. For VKA treated patients, other than the three time point INR values, we do not have enough data to comment on INR monitoring and dose adjustments.

6. Conclusion

High propensity of risk factors like hypertension, hyperlipidaemia, diabetes mellitus, and co-existing diseases like CAD, CKD has been observed among NVAF patients in Kerala AF Registry. Despite high stroke risk, a good proportion of patients were not receiving OAC whereas nearly half were treated with antiplatelets. Though most commonly used anticoagulant was VKAs, INR

Table 3
Risk factors and co-morbidities of published NVAF registries.

	KERALA-AF Registry (NVAF) (N = 2507)	GARFIELD Registry (NVAF)			GLORIA-AF (NVAF)		
		India (n = 1388)	All (N = 52,014)	Asia (n = 3071)	Europe (n = 7108)	N. America (n = 3403)	All (N = 15,092)
Age (mean/median)	67(±13)	65.8(±12.2)	69.7(±11.5)	68.0(IQR 60–76)	73.0 (IQR 66–79)	71.0(IQR 64–79)	70.5 (IQR 64–78)
Age ≥ 75	30.0	26.3	37.2	28.5	44.3	39.6	39.1
Female (%)	45.2	40.1	43.8	43.5	46.7	44.8	45.5
Hypertension (%)	61.2	68.5	76.3	69.4	73.4	80.5	74.6
Diabetes mellitus (%)	37.2	36.2	22.2	20.2	21.2	27.1	23.1
Hyperlipidemia (%)	46.2	13.6	41.6	26.7	36.5	61.3	39.9
Stroke/TIA (%)	14.1	9.1	11.4	13.0	15.6	12.4	14.2
Coronary Artery Disease (%)	41.6	28.1	21.6	21.9	16.4	27.0	20.3
Chronic Heart Failure (%)	26.4	15.5	20.6	27.3	23.4	19.7	24.2
Chronic Kidney Disease (%)	42.1	5.2	10.3	–	–	–	17.3
CHA_2DS_2-VASc score (mean/median)	3.2(±1.74)	2.9 (±1.5)	3.2 (±1.6)	3(2–4)	3 (2–4)	3 (2–4)	3.2
HASBLED (mean or Median)	1.8(±1.3)	1.5(±0.9)	1.4(±0.9)	1.0(IQR 1–2)	1.0(IQR 1–2)	1.0(IQR 1–2)	1.0(IQR 1–2)
Paroxysmal AF (%)	45.6	16.4	25.2	58.1	46.8	65.8	53.4
Persistent AF (%)	14.9	8.5	15.6	35.4	38.9	29.6	35.5
Permanent AF (%)	39.4	10.4	13.2	5.9	14.3	4.6	11.1
OAC (%)	65.8	35.5	80.0	55.2	90.1	78.3	79.9
NOAC (%)	7.6	6	47.7	25.5	52.4	52.1	47.6
VKA (%)	58.2	29.5	32.3	31.9	37.8	26.2	32.3
Antiplatelet (%)	48.3	43.3	12.3	25.8	6.0	14.0	12.1
No Antithrombotic agents (%)	16.0	21.4	7.6	16.9	3.8	7.5	7.8
All cause death/100 person years	16.48	7.8	4.34	–	–	–	–

monitoring and dose adjustment was suboptimal. A comparatively higher rate of annual mortality and hospitalization was observed. The study brings out high-risk characteristics of patients, higher annual mortality and hospitalization, inadequacies of treatment and need for improvement in the care of NVAF patients.

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Declaration of competing interest

None to declare.

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References

1. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation*. 1998 Sep 8;98(10):946–952.
2. Morillo CA, Banerjee A, Perel P, Wood D, Jouven X. Atrial fibrillation: the current epidemic. *Journal of geriatric cardiology: JGC*. 2017 Mar;14(3):195.
3. Stewart S, Murphy N, Walker A, McGuire A, McMurray JJ. Cost of an emerging epidemic: an economic analysis of atrial fibrillation in the UK. *Heart*. 2004 Mar 1;90(3):286–292.
4. Blomstrom Lundqvist C, Lip GY, Kirchhof P. What are the costs of atrial fibrillation? *Europace*. 2011 May 1;13(suppl_2):9–12.
5. Krahn AD, Manfreda J, Tate RB, Mathewson FA, Cuddy TE. The natural history of atrial fibrillation: incidence, risk factors, and prognosis in the Manitoba Follow-Up Study. *Am J Med*. 1995 May 1;98(5):476–484.
6. Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. *Am J Cardiol*. 1998 Oct 16;82(7):2N–9N.
7. Zubaid M, Rashed WA, Alsheikh-Ali AA, et al. Gulf survey of atrial fibrillation events (Gulf SAFE) design and baseline characteristics of patients with atrial fibrillation in the arab middle East. *Circulation: Cardiovascular Quality and Outcome*. 2011 Jul;4(4):477–482.
8. Nieuwlaat R, Capucci A, Camm AJ, et al. Atrial fibrillation management: a prospective survey in ESC member countries: the Euro Heart Survey on Atrial Fibrillation. *Eur Heart J*. 2005 Nov 1;26(22):2422–2434.
9. Lip GY, Laroche C, Dan GA, et al. A prospective survey in European Society of Cardiology member countries of atrial fibrillation management: baseline results of EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry. *Europace*. 2014 Mar 1;16(3):308–319.
10. Lip GY, Brechin CM, Lane DA. 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*. 2012 Dec 1;142(6):1489–1498.
11. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. *Circulation*. 2014 Feb 25;129(8):837–847.
12. Gopalan BC, Namboodiri N, Abdullakutty J, et al. Kerala Atrial Fibrillation Registry: a prospective observational study on clinical characteristics, treatment pattern and outcome of atrial fibrillation in Kerala, India, cohort profile. *BMJ open*. 2019 Jul 1;9(7), e025901.
13. Fauchier L, Philippart R, Clementy N, et al. How to define valvular atrial fibrillation? *Archives of cardiovascular diseases*. 2015 Oct 1;108(10):530–539.
14. Martins RP, Galand V, Colette E, et al. Defining nonvalvular atrial fibrillation: a quest for clarification. *Am Heart J*. 2016 Aug 1;178:161–167.
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 Feb 1;137(2):263–272.
16. Pisters R, Lane DA, Nieuwlaat R, De Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest*. 2010 Nov 1;138(5):1093–1100.
17. Thomas C, Thomas L. Renal failure—measuring the glomerular filtration rate. *Deutsches Ärzteblatt International*. 2009 Dec;106(51–52):849.
18. Lauritsen JM, Bruus ME. *A Comprehensive Tool for Validated Entry and Documentation of Data*. Odense Denmark: The EpiData Association; 2003, 2004.
19. Team RCR. A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org/.

20. Narasimhan C, Verma JS, Kishore AR, et al. Cardiovascular risk profile and management of atrial fibrillation in India: real world data from RealiseAF survey. *Indian Heart J*. 2016 Sep 1;68(5):663–670.
21. Chiang CE, Naditch-Brûlé L, Murin J, et al. Distribution and risk profile of paroxysmal, persistent, and permanent atrial fibrillation in routine clinical practice: insight from the real-life global survey evaluating patients with atrial fibrillation international registry. *Circulation: Arrhythmia and Electrophysiology*. 2012 Aug;5(4):632–639.
22. Sawhney JP, Kothiwale VA, Bisne V, et al. Risk profiles and one-year outcome of patients with newly diagnosed atrial fibrillation in India: insights from the GARFIELD-AF Registry. *Indian Heart J*. 2018 Nov 1;70(6):828–835.
23. Huisman MV, Rothman KJ, Paquette M, et al. The changing landscape for stroke prevention in AF: findings from the GLORIA-AF registry phase 2. *J Am Coll Cardiol*. 2017 Feb 13;69(7):777–785.
24. Bassand JP, Accetta G, Camm AJ, et al. Two-year outcome of patients with newly diagnosed atrial fibrillation: results from GARFIELD-AF. *Eur Heart J*. 2016 Oct 7;37(38):2882–2889.
25. Vora A, Kapoor A, Nair M, et al. Clinical presentation, management, and outcome in the Indian heart rhythm society-atrial fibrillation (IHRS-AF) registry. *Indian Heart J*. 2017 Jan 1;69(1):43–47.
26. Kirchhof P, Benussi S, Kotecha D, et al. ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur J Cardio Thorac Surg*. 2016;50(5):1–88, 2016 Nov 1.
27. January CT, Wann LS, Calkins H, et al. AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American college of cardiology/American heart association task force on clinical practice guidelines and the heart rhythm society. *J Am Coll Cardiol*. 2019;74(1):104–132, 2019 Jul 1.
28. Oldgren J, Healey JS, Ezekowitz M, et al. Variations in cause and management of atrial fibrillation in a prospective registry of 15 400 emergency department patients in 46 countries: the RE-LY Atrial Fibrillation Registry. *Circulation*. 2014 Apr 15;129(15):1568–1576.
29. Healey JS, Oldgren J, Ezekowitz M, et al. Occurrence of death and stroke in patients in 47 countries 1 year after presenting with atrial fibrillation: a cohort study. *Lancet*. 2016 Sep 17;388:1161–1169, 10050.