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Internal Medicine Section

Clinical Outcomes in Non Valvular Atrial Fibrillation Patients Receiving Oral Anticoagulation Therapy using CHA_2DS_2-VASc and HAS-BLED Scores: A Cohort Study from Western Gujarat, India

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ABSTRACT

Introduction: Non Valvular Atrial Fibrillation (NVAF) is one of the most common sustained arrhythmias. The Congestive heart failure, Hypertension, Age, Diabetes, Stroke/TIA (or Thrombembolism), Vascular disease, Age, Sex category (for CHA_2DS_2-VASc) score, which includes Congestive heart failure, Hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65-74 and Sex category (female), as well as the Hypertension, Abnormal Renal/Liver function, Stroke, Bleeding history or predisposition, Labile International Normalised Ratio (INR), Elderly, Drugs/alcohol concomitantly (for HAS-BLED)-comprising Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly and Drugs/alcohol concomitantly-assists in assessing bleeding risk. However, the outcomes of NVAF have remained underreported in Gujarat, western India.

Aim: To characterise thromboembolic and bleeding risks using the CHA_2DS_2-VASc and HAS-BLED scores among NVAF patients receiving oral anticoagulation therapy.

Materials and Methods: This ambidirectional cohort study (retrospective and prospective) was conducted over an 11-year period (January 2014 - December 2024) at the Bhanubhai and Madhuben Patel Cardiac Centre, Shree Krishna Hospital and Medical Research Centre, Karamsad, Gujarat, India, a tertiary care hospital in a rural setting. The study evaluated NVAF cases based on age, sex, co-morbidities, anticoagulation therapy {Vitamin K Antagonists (VKA) or Novel Oral Anticoagulants (NOAC)} and clinical outcomes, including stroke and bleeding events. HAS-BLED scores, treatment strategies and clinical outcomes were compared across CHA_2DS_2-VASc risk groups (low ≤3, intermediate 4-5 and high ≥6). Statistical analysis was performed using statistical software Statistical Analysis System (SAS) Viya (SAS Institute Inc., NC, USA). Comparisons of risk groups used the Mann-Whitney U test, Chi-square/Fisher's-exact test and Kruskal-Wallis test as appropriate. The Cochrane-Armitage trend test evaluated anticoagulant use patterns. A p-value <0.05 was considered statistically significant.

Results: Among 347 NVAF patients, CHA_2DS_2-VASc scores were significantly higher in females (p<0.0001), indicating greater thromboembolic risk. Hypertension, diabetes mellitus, ischaemic heart disease, prior stroke, chronic kidney disease and heart failure were strongly associated with risk groups (p<0.0001). High-risk patients were older (median 80 vs. 61 years, p<0.0001) and had higher HAS-BLED scores (p<0.0001). NOACs were more frequently prescribed to high-risk patients than VKAs (p<0.0001), with combination antithrombotic therapy being more common among NOAC users (p=0.001). Major bleeding events, including ischaemic and haemorrhagic strokes, were significantly more frequent in high-risk patients (p<0.0001), while mortality was highest in the intermediate-risk group (25.0%, p<0.0001).

Conclusion: The present study observed sex-based differences in CHA_2DS_2-VASc scores and their association with thromboembolic risk. Higher scores were associated with advanced age, multiple co-morbidities, increased bleeding risk and the use of NOACs. Adverse clinical outcomes, including major bleeding, were more frequent in higher-risk groups, indicating the need for personalised anticoagulation therapy based on the patient's bleeding and thromboembolic risk.

Keywords: Haemorrhage risk, Risk assessment, Stroke prevention, Thromboembolism

INTRODUCTION

Atrial Fibrillation (AF) is the most common significant arrhythmia, increasing the risk of ischaemic stroke by five-fold and accounting for 15% of strokes [1]. It worsens quality of life, functional status and cardiac performance [2], while also increasing healthcare expenditures and mortality rates [3]. The incidence of AF rises with age [4] and often progresses from intermittent to permanent AF [5]. Many cases are asymptomatic, which can delay diagnosis; over 25% of newly detected AF cases present initially as stroke [6]. AF affects 0.5% to 5.5% of the global population [7-10], while the prevalence in India ranges from 0.1% to 1.6% [11,12].

The $CHADS_2$ and CHA_2DS_2-VASc (Congestive heart failure, Hypertension, Age ≥75 years (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65-74 years and Sex category (female)} scores are validated tools for evaluating thromboembolic risk factors in assessing stroke risk in NVAF patients. The CHA_2DS_2-VASc score assigns 1 point each for congestive heart failure, hypertension, diabetes, vascular disease and age between 65 and 74 years, with an additional point for female sex. The higher the CHA_2DS_2-VASc score, the greater the risk of stroke and thromboembolism in patients with NVAF. The CHA_2DS_2-VASc score allocates 2 points to individuals aged 75 years or older or those with an increased risk of stroke, such as a history of previous stroke or Transient Ischaemic Attack (TIA), thus making it widely accepted in clinical practice [13,14].

The HAS-BLED score calculates the risk of major bleeding, providing clinicians with an opportunity to balance interventions between stroke prevention and bleeding complications. These globally

accepted scores serve as a guide for the optimal utilisation of oral anticoagulants among NVAF patients [13,15-18].

In rural India, the application of the CHA_2DS_2-VASc and HAS-BLED scores remains a challenge. This includes addressing the young population and the higher incidences of undiagnosed hypertension and rheumatic heart disease, as well as socio-economic challenges such as low literacy, irregular treatment follow-ups and an inability to afford the cost of medical care [19,20]. The limited healthcare infrastructure poses challenges to safe and effective anticoagulation management. For example, monitoring the labile International Normalised Ratio (INR) for VKAs and NOACs is resource-intensive, which many patients cannot afford [21,22]. Lifestyle factors (such as diet, smoking or chewing tobacco and alcohol consumption), as well as prevalent co-morbidities like malnutrition and poorly treated diabetes, may affect therapeutic adherence and the predictive accuracy of these scoring systems [22].

There is limited research on the use of CHA_2DS_2-VASc and HAS-BLED scores in the rural Indian population, highlighting the lack of evidence-based management strategies for NVAF [23]. The performance of these scoring systems in the current study can help strengthen the evidence for their use in regional stroke control and bleeding risk management protocols. The present study provides insights into the prognostic value of CHA_2DS_2-VASc and HAS-BLED scores for localised anticoagulation strategies in low-resource settings.

The aim of the present study was to characterise thromboembolic and bleeding risks using the CHA_2DS_2-VASc and HAS-BLED scores among NVAF patients receiving oral anticoagulation therapy at a tertiary care hospital in rural Western Gujarat, India. The study objectives included: 1) describing patient demographics and clinical characteristics by CHA_2DS_2-VASc score risk groups (low ≤3, intermediate 4–5 and high ≥6); 2) examining associations between CHA_2DS_2-VASc score risk groups and clinical outcomes such as ischaemic stroke, haemorrhagic stroke, systemic embolism and other major bleeding events; and 3) examining the use of different oral anticoagulation treatments (VKAs versus NOACs), as well as patient mortality and hospitalisation among CHA_2DS_2-VASc risk groups. Through these objectives, the present study contributes valuable information on real-life management approaches to anticoagulation therapy in low-resource settings in rural Western Gujarat, India.

The present study is part of a larger research project evaluating clinical outcomes in NVAF patients. While both studies originate from the same patient cohort, there is no duplication of data presentation or outcome reporting. Each manuscript addresses distinct research objectives: the current study focuses on risk stratification using CHA_2DS_2-VASc and HAS-BLED scores, while the other assesses the comparative effectiveness of different oral anticoagulant regimens. Measures have been taken to avoid data redundancy and ensure scientific clarity.

MATERIALS AND METHODS

This ambidirectional cohort study (retrospective and prospective) was conducted over an 11-year period (January 2014 - December 2024) at the Bhanubhai and Madhuben Patel Cardiac Centre, Shree Krishna Hospital and Medical Research Centre, Karamsad, Gujarat, India, a tertiary care hospital in a rural setting. Ethical approval was obtained from the Institutional Ethics Committee, with initial approval granted on 28 September 2022 (IEC/BU/140/Faculty/03/222/2022), which included a waiver for patient consent (IEC/BU/140/Faculty/03/46/2023). Final approval for publication prior to manuscript submission was granted under IEC/BU/2025/Ex.25/74/2025.

Inclusion and Exclusion criteria: Patients aged 18 years or older with a confirmed diagnosis of NVAF, based on clinical, electrocardiographic and echocardiographic findings and who received oral anticoagulation therapy (either VKAs or NOACs), were included in the study. Patients were excluded if they: 1) had an indication for anticoagulation therapy unrelated to NVAF, such as pulmonary embolism, deep vein thrombosis, or prosthetic metallic valves; 2) had End-Stage Renal Disease (ESRD) requiring dialysis; 3) had valvular atrial fibrillation or rheumatic heart disease; 4) had incomplete or missing medical records; or 5) had a co-existing arrhythmia requiring distinct management strategies.

Sample size calculation: For sample size calculation, Winpepi, Version 11.65 was used and a minimum sample size of 347 NVAF patients was determined to achieve 80% power while allowing for a 5% alpha (Type 1 error).

Study Procedure

The data collected for NVAF patients included baseline demographic and clinical parameters such as age, sex, co-morbid conditions and treatments for NVAF and existing co-morbidities. The CHA_2DS_2-VASc scores assessed thromboembolic risk, whereas the HAS-BLED scores assessed the risk of bleeding based on several factors, including hypertension, renal/liver function and prior bleeding episodes. Published studies have validated these scores [24-27] and they will further guide anticoagulation treatment. For analytical purposes, CHA_2DS_2-VASc scores were stratified into three categories: low risk (≤3), intermediate risk (4-5) and high risk (≥6). These risk categories were developed in close consultation with the senior cardiology team at this study hospital, reflecting locally adapted thresholds that align with routine clinical practice to enhance risk communication and management decision-making. It is important to note that these categories do not represent guideline-based thresholds for initiating anticoagulation therapy.

Body Mass Index (BMI) was calculated and classified as underweight (<18.5 kg/m^2), normal (18.5-22.9 kg/m^2), overweight (23–24.9 kg/m^2) and obese (≥25 kg/m^2) according to Asian Indian guidelines [28]. Data on anticoagulation treatment included the use of VKAs or NOACs, while clinical outcomes were categorised into primary and secondary outcomes. Primary outcomes encompassed ischaemic and haemorrhagic strokes, as well as major bleeding events leading to hospitalisation. Secondary outcomes included minor bleeding events and mortality (both all-cause and cardiovascular).

A total of 347 NVAF patients identified from hospital electronic records met the study criteria during 2014-2024. The clinical events and outcome data were obtained from medical files and hospital electronic health records, as well as through follow-up telephone conversations with patients.

STATISTICAL ANALYSIS

Baseline characteristics were analysed using mean (±standard deviation) or median (interquartile range/min-max) for continuous variables and frequencies (percentages) for categorical variables. The Kolmogorov-Smirnov test assessed the normality of continuous variables (CHA_2DS_2-VASc and HAS-BLED scores and age). Comparisons across CHA_2DS_2-VASc risk groups were performed using the Mann-Whitney U test for non normally distributed continuous or ordinal count variables and the Chi-square or Fisher's-exact test for categorical variables. The Cochrane-Armitage trend test assessed patterns in anticoagulant use across risk categories, while the Kruskal-Wallis test compared mean age and HAS-BLED scores across CHA_2DS_2-VASc groups. A p-value of <0.05 was considered statistically significant. Data collection and management were conducted using Microsoft Excel 2016 and statistical analyses were performed using statistical software SAS Viya (SAS Institute Inc., NC, USA).

RESULTS

A total of 347 NVAF patients met the study's inclusion criteria, comprising 171 male (49.3%) and 176 female (50.7%). The Kolmogorov-Smirnov test indicated that CHA2DS2-VASc scores (p<0.01), HAS-BLED scores (p<0.01) and patient age (p<0.01) were not normally distributed in the study population. The presents the distribution of CHA2DS2-VASc scores by sex, revealing differences in risk profiles between male and female is presented in [Table/Fig-1].

Score	Male (n=171) n (%)	Female (n=176) n (%)	Total (N=347) N (%)
2	69 (40.4)	0	69 (19.9)
3	44 (25.7)	107 (60.8)	151 (43.5)
4	24 (14.0)	27 (15.3)	51 (14.7)
5	20 (11.7)	21 (11.9)	41 (11.8)
6	12 (7.0)	14 (8.0)	26 (7.5)
7	2 (1.2)	6 (3.4)	8 (2.3)
9	0	1 (0.6)	1 (0.3)

[Table/Fig-1]: CHA_2DS_2-VASc scores by patients' sex.

Among the 171 male participants, 113 (66.1%) had a CHA2DS2-VASc score of 3 or lower, indicating relatively low thromboembolic risk. In contrast, all 176 female participants had CHA_2DS_2-VASc scores of 3 or higher, reflecting a higher thromboembolic risk.

The CHA_2DS_2-VASc risk groups were significantly associated with patient demographics and co-morbidities is shown in [Table/Fig-2]. There was a notable difference in risk group distribution by sex (p=0.01) and strong associations with hypertension, diabetes, ischaemic heart disease and other conditions (p<0.0001). Additionally, median age and BMI varied significantly across risk groups, with older patients and those with lower BMI being more likely to fall into higher risk categories. Furthermore, the median HAS-BLED score was significantly higher in the high-risk group, indicating a greater bleeding risk among these patients.

The use of oral anticoagulants among patients in the intermediate and high CHA_2DS_2-VASc risk groups is summarised in [Table/Fig-3]. Over half of the patients were treated with NOACs, while the rest received VKAs. A significant association was observed between CHA_2DS_2-VASc risk groups and the type of anticoagulant prescribed (p<0.0001), with lower-risk patients more frequently receiving anticoagulation. Additionally, medications for managing co-morbidities were prescribed and showed significant variation across different risk groups.

A significant difference in the distribution of CHA_2DS_2-VASc scores between patients treated with NOACs (median: 4; Interquartile Ranges (IQR): 3, 5; Wilcoxon (rank sum) mean score: 204.3) and

Demographic and clinical characteristics	Total (N=347)	CHA2 -DS2 - VASc risk group* Low (<=3) (n=220)	Intermediate (4-5) (n=92)	High (≥6) (n=35)	p-value†
Gender, n (%)					
Male	171 (49.3)	113 (51.4)	44 (47.8)	14 (40.0)	0.01
Female	176 (50.7)	107 (48.6)	48 (52.2)	21 (60.0)	
Age (years)					
Median (minimum-maximum)	69 (24-94)	61 (24-94)	76.5 (48-91)	80 (63-90)	<0.0001‡
95% CI upper limit, lower limit	64.4, 67.6	58.0, 61.8	73.5, 77.4	76.3, 81.1	
Body Mass Index (BMI) (in kilograms per meters squared (kg/m_2)), n (%)					
Underweight (less 18.5)	191 (55.0)	128 (58.2)	43 (46.7)	20 (57.1)	<0.0001
Normal (18.5 to less 23)	125 (36.0)	75 (34.1)	38 (41.3)	12 (34.3)	
Overweight (23 to less than 25)	14 (4.0)	10 (4.6)	4 (4.4)	0 (0)	
Obese (25 and higher)	17 (4.9)	7 (3.2)	7 (7.6)	3 (8.6)	
Co-morbidities§, n (%)					
Hypertension	200 (57.6)	86 (39.1)	80 (87.0)	34 (97.1)	<0.0001
Diabetes mellitus	101 (29.1)	33 (15.0)	48 (52.2)	20 (57.1)	<0.0001
Ischaemic heart disease	65 (19.6)	23 (11.8)	32 (34.8)	10 (28.6)	<0.0001
Rheumatic heart disease	70 (20.2)	65 (29.6)	5 (5.4)	0 (0)	<0.0001
Congestive heart failure	20 (5.8)	9 (4.1)	9 (9.8)	2 (5.7)	0.001
Prior ischemic stroke/transient ischemic attack	95 (27.4)	38 (17.3)	33 (35.9)	24 (68.6)	<0.0001
Prior intracranial haemorrhage	3 (0.9)	1 (0.5)	2 (2.2)	0 (0)	0.13
Venous thromboembolism	2 (0.6)	1 (0.5)	0 (0)	1 (2.9)	0.01
Chronic kidney disease	29 (8.4)	12 (5.5)	11 (12.0)	6 (17.1)	<0.0001
Liver failure	1 (0.3)	1 (0.5)	0 (0)	0 (0)	0.04
Cancer	8 (2.3)	6 (2.7)	1 (1.1)	1 (2.9)	0.01
HAS-BLED score					
Median (minimum- maximum)	2 (0-8)	2 (0-5)	2 (1-5)	3 (2-8)	<0.0001‡
95% CI upper limit, lower limit	2.3, 2.5	2.0-2.3	2.4-2.9	3.0-3.7	

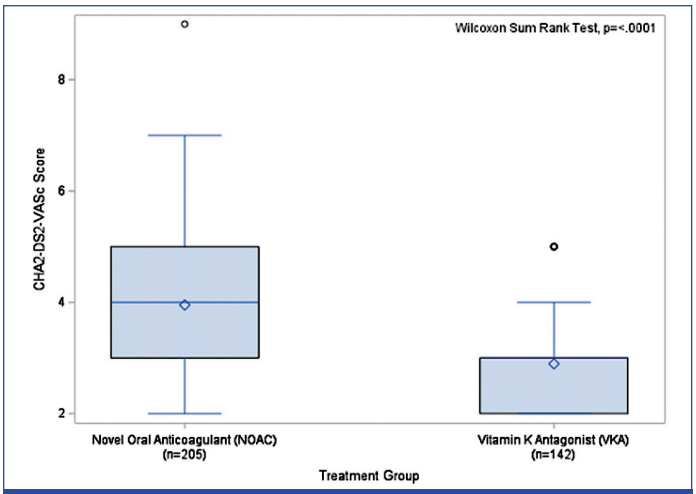
[Table/Fig-2]: CHA_2DS_2-VASc* risk group by patients' demographic and baseline clinical characteristics.
*CHA_2DS_2-VASc Scores: Low (3 or less), Intermediate (4-5), and High (6 or higher); Note: CI: Confidence Interval; †Fisher's-exact test p-value. ‡Kruskal-Wallis test p-value; §Co-morbidities are not mutually exclusive. A patient can have more than one co-existing health condition

Variables	Total (N=347)	CHA2 -DS2 - VASc risk group† Low (<3) (n=220)	Intermediate (4-5) (n=92)	High (≥6) (n=35)	p-value‡
Treatment group, n (%)					
NOACs*	205 (59.1)	100 (45.5)	70 (76.1)	35 (100.0)	<0.0001‡‡
Vitamin K Antagonists (VKA) **	142 (40.9)	120 (54.5)	22 (23.9)	0 (0)	
Medications, n (%)					
Angiotensin-Converting Enzyme (ACE) inhibitors	36 (10.4)	29 (13.2)	5 (5.4)	2 (5.7)	0.004

Angiotensin receptor blockers	44 (12.7)	28 (12.7)	11 (12.0)	5 (14.3)	0.03
Acetylsalicylic Acid (ASA) drug	179 (51.6)	112 (50.9)	38 (41.3)	29 (82.9)	<0.0001
Clopidogrel	66 (19.0)	39 (17.7)	19 (20.7)	8 (22.9)	0.01
Proton pump inhibitors	192 (55.3)	127 (57.7)	43 (46.7)	22 (62.9)	0.002
Alpha blockers	36 (10.4)	24 (10.9)	7 (7.6)	5 (14.3)	0.02
Beta blockers	243 (70.0)	153 (69.6)	64 (69.6)	26 (74.3)	0.01
Calcium channel blockers	89 (25.6)	53 (24.1)	26 (28.3)	10 (28.6)	0.01
Amiodarone	56 (16.1)	44 (20.0)	7 (7.6)	5 (14.3)	0.001
Digoxin	80 (23.1)	67 (30.5)	13 (14.1)	0 (0)	<0.0001
Diuretic	182 (52.4)	123 (55.9)	47 (51.1)	12 (34.3)	0.001
Statin	189 (54.5)	108 (49.1)	56 (60.9)	25 (71.4)	0.0002
Antidiabetic	71 (20.5)	40 (18.2)	23 (25.0)	8 (22.9)	0.008

[Table/Fig-3]: CHA_2DS_2-VASc risk stratification by treatment group and other medications.
*NOACs: Non vitamin K Antagonist aka Novel Oral Anticoagulants in this study include Dabigatran, Rivaroxaban, and Apixaban; **VKAs in this study include Acitrom (coumarin derivative) and Warfarin; †CHA_2DS_2-VASc Scores: Low (3 or less), Intermediate (4-5) and High (6 or higher); ‡P-value: Fisher's-exact test. ‡‡p-value for treatment groups (NOAC and VKA): Cochrane-Armitage trend test; §Medications are not mutually exclusive. A patient can have more than one prescribed medication for a co-existing health condition

those receiving VKAs (median: 3; IQR: 2, 3; Wilcoxon mean score: 130.2) is illustrated in [Table/Fig-4]. Patients prescribed NOACs tended to have higher thromboembolic risk compared to those on VKAs. This finding highlights a treatment preference for NOACs in patients with elevated risk profiles. The statistical significance (Wilcoxon Sum Rank Test Z=-7.1199, p<0.0001) indicates that this difference is unlikely to be due to chance.



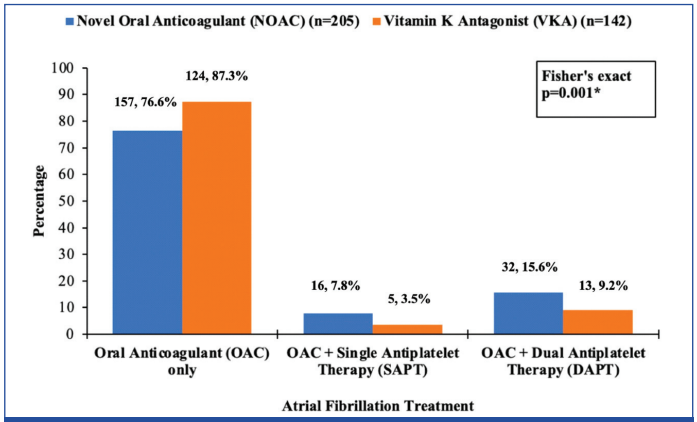
[Table/Fig-4]: CHA_2DS_2-VASc scores obtained by the treatment group for Non Valvular Atrial Fibrillation (NVAF).
*NOAC: Novel Oral Anticoagulants; VKAs: Vitamin K Antagonists; †Wilcoxon Rank Sum Test p-value

The antithrombotic treatment strategies used for NVAF patients is presented in [Table/Fig-5]. Treatment patterns significantly differed between NOAC and VKA users (p=0.001), with the majority in both groups receiving only oral anticoagulants. Combination therapies involving antiplatelets were less common overall but slightly more frequent among NOAC users. This suggests a tendency to pair NOACs with additional antithrombotic agents in patients with more complex risk profiles.

The clinical outcomes stratified by CHA2DS2-VASc risk groups is outlined in [Table/Fig-6]. Adverse events were significantly more frequent in the high-risk group, while hospitalisations were unexpectedly more common in the low- and intermediate-risk groups. Major and minor bleeding events occurred at a higher rate among patients in the high-risk group, indicating a link between thromboembolic risks and bleeding complications. Interestingly, mortality was highest in the intermediate-risk group, suggesting that clinical outcomes may not follow a strictly linear pattern across risk categories.

DISCUSSION

The present cohort study evaluated clinical outcomes based on CHA_2DS_2-VASc and HAS-BLED scores among NVAF patients in rural western India. Female exhibited a higher thromboembolic



[Table/Fig-5]: Antithrombotic treatment strategies for Non Valvular Atrial Fibrillation (NVAF) patients in this study.

risk. Advanced age and the presence of co-morbidities such as hypertension, diabetes, ischaemic heart disease, chronic kidney disease, prior stroke, heart failure, cancer and venous thromboembolism were associated with higher CHA_2DS_2-VASc scores. NOACs for anticoagulation were more frequently prescribed to patients in the CHA_2DS_2-VASc high-risk group (scores ≥6). Major bleeding events were more prevalent in the CHA_2DS_2-VASc high-risk groups. Despite receiving antithrombotic therapy, mortality was highest among NVAF patients in the CHA_2DS_2-VASc intermediate-risk group (scores 4-5).

In recent years, several studies have evaluated clinical outcomes in NVAF patients using the CHA_2DS_2-VASc and HAS-BLED scores, including studies conducted in India [29-31]. The Kerala-AF registry study in the southern region of India (involving 53 hospitals from 2016-2017) highlighted sex differences in baseline clinical characteristics, treatment and outcomes for patients with atrial fibrillation [32]. Calvert P et al., found that among male patients with atrial fibrillation, ischaemic heart disease, smoking and alcohol use were more common, whereas females were more likely to suffer from valvular atrial fibrillation [32]. Despite higher CHA_2DS_2-VASc scores, one-fourth of the patients did not receive anticoagulation therapy, thus confirming the considerable gap between published evidence and optimal management. The Kerala-AF study showed no significant differences between male and female in Major Adverse Cardiovascular Events (MACE) outcomes, but minor bleeding events were more common in male [32].

Bahuleyan CG et al., found that oral anticoagulants were sub-optimally utilised, with only 38.6% of patients at baseline receiving the drugs in the Kerala-AF study. The most commonly prescribed oral anticoagulant was VKA (58.2%) [33]. Both studies affirm the need to address the underutilisation of anticoagulation therapy and emphasise the complicated management of thromboembolic and bleeding risks in atrial fibrillation patients.

Clinical outcomes	Total (N=347)	CHA2 -DS2 - VASc risk group*			p-value†
		Low (<3) (n=220)	Intermediate (4-5) (n=92)	High (≥6) (n=35)	
Any adverse event, n (%)	60 (17.3)	26 (11.8)	23 (25.0)	11 (31.4)	<0.0001
Any hospitalisations, n (%)	181 (52.2)	113 (51.4)	55 (59.8)	13 (37.1)	0.0001
Major bleeding, n (%)‡					
Haemorrhagic stroke	5 (1.4)	2 (0.9)	2 (2.2)	1 (2.9)	0.001
Ischemic stroke	25 (7.2)	11 (5.0)	9 (9.8)	5 (14.3)	<0.0001
Subdural/epidural bleeding	4 (1.2)	1 (0.5)	2 (2.2)	1 (2.9)	00.0004
Minor bleeding, n (%)‡					
Gastrointestinal bleeding	8 (2.3)	4 (1.8)	3 (3.3)	1 (2.9)	0.0002
Anal fissure bleeding	2 (0.6)	1 (0.5)	0 (0)	1 (2.9)	0.0002
Contusion	21 (6.1)	13 (5.9)	5 (5.4)	3 (8.6)	0.0003
Easy bruising	3 (0.9)	1 (0.5)	1 (1.1)	1 (2.9)	0.0001
Gingival bleeding	1 (0.3)	1 (0.5)	0 (0)	0 (0)	0.001
Haematuria	3 (0.9)	3 (1.4)	0 (0)	0 (0)	0.09
Other minor bleeding	47 (13.5)	29 (13.2)	14 (15.2)	4 (11.4)	0.03
Patient status at the end of study, n (%)					
Death	104 (30.0)	59 (26.8)	37 (40.2)	8 (22.9)	<0.0001
Alive	183 (52.7)	129 (58.6)	40 (43.5)	14 (40.0)	
Loss to follow-up	60 (17.3)	32 (14.6)	15 (16.3)	13 (37.1)	

[Table/Fig-6]: CHA_2DS_2-VASc risk group by clinical outcomes.
*CHA_2DS_2-VASc Scores: low (3 or less), intermediate (4-5), and high (6 or higher); †Fisher's-exact test p-value; ‡Major and minor bleeding events are not mutually exclusive, respectively. The same patient can have more than one major or minor bleeding event

The multicentre Global Anticoagulant Registry in the FIELD–Atrial Fibrillation (GARFIELD-AF) study spanned 35 countries, including India and showed a high prevalence of co-morbidities among NVAF patients, which aligns with the findings of the present study. However, in the GARFIELD-AF study, VKAs were used in combination with antiplatelets for stroke prevention, while NOACs were prescribed to patients with high HAS-BLED scores [34]. In contrast, NOACs were prescribed more frequently across all thromboembolic risk groups in the present study, with 19% of patients receiving combination therapy with antiplatelets. This difference is driven by distinct anticoagulation strategies and clinical decision-making.

The HAS-BLED score and CHA_2DS_2-VASc scores are correlated and equally important when making decisions regarding thromboembolic prophylaxis. In the present study, HAS-BLED scores were highest among NVAF patients in the CHA_2DS_2-VASc high-risk group (scores ≥6). These findings were consistent with those from the Jordan Atrial Fibrillation (JoFib) multicentre registry study. In the JoFib study, Jarrah MI et al., observed concordance between HAS-BLED and CHA_2DS_2-VASc scores and concluded that patients with high HAS-BLED scores receive anticoagulation therapy based on their CHA_2DS_2-VASc scores for risk stratification [35]. Similar to the JoFib registry study, Poli D et al., concluded that stroke stratification scores based on HAS-BLED or HAS-BED alone are adequate for treatment decisions [36]. In the present study, treatment decisions were based on stroke and bleeding risk scores, as well as in the context of real-world clinical outcomes such as hospitalisations, healthcare access and treatment availability.

Overall, these findings highlight key differences in stroke risk assessment and anticoagulation treatment patterns between NOAC and VKA users. The higher CHA_2DS_2-VASc scores in patients using NOACs suggest that these anticoagulants are preferred for individuals at greater thromboembolic risk, which is in alignment with recent expert panel recommendations for the use of NOACs in India [37]. Additionally, the increased use of combination therapies among NOAC users may indicate a more tailored approach to stroke prevention in high-risk patients. The findings of the present study provide perspective on navigating high-risk NVAF cases in rural areas, where access to advanced anticoagulation therapy, INR monitoring for the effectiveness of anticoagulation medications and regular follow-up may be limited. This underscores the importance of appropriate risk-stratification tools in guiding effective therapeutic decisions, as well as the need for individualised anticoagulation strategies adapted to patient-specific risk profiles to improve outcomes in resource-constrained rural settings.

The present rural study holds significant relevance, as it is the first of its kind from the western region of India, incorporating an outcome evaluation of NVAF patients using CHA_2DS_2-VASc and HAS-BLED scores. However, there are a few limitations.

Limitation(s)

This was a single hospital-based study and it may not fully reflect variations in patient characteristics and NVAF management found across different regions in India. Therefore, the present study does not reflect the true incidence or prevalence of NVAF in the western region of India and the findings are not generalisable to other cohorts in India or globally. Due to the observational nature of the present study, there was no randomisation of patients to any particular treatment group. This limited the ability to control for potential confounding factors that may differ between treatment and risk groups. Patients lost to follow-up may have had different exposures and clinical outcomes than those retained in the study. Loss to follow-up and incomplete data on outcomes may have introduced selection and information biases, resulting in an overestimation or underestimation of associations between patient and clinical characteristics (including treatment) and thromboembolic or bleeding risk. Despite these limitations, the findings of the present study provide valuable insight into real-life anticoagulation strategies in a rural Indian context.

CONCLUSION(S)

The present eleven-year cohort study from rural western India demonstrated that higher CHA_2DS_2-VASc scores in NVAF patients were associated with increased bleeding risk, higher HAS-BLED scores and greater use of NOACs. Female exhibited consistently higher thromboembolic risk than male and mortality was highest in the intermediate-risk group despite anticoagulation. These findings highlight the critical need for individualised risk stratification using

CHA_2DS_2-VASc and HAS-BLED scores to guide safe and effective anticoagulation therapy, especially in resource-constrained rural healthcare settings. Future research can mitigate some of these limitations through appropriate steps in study design, conduct, and data analysis. This could include: 1) accounting for potential confounding factors during patient recruitment; 2) conducting multicentre studies in a variety of healthcare settings across India or globally; 3) increasing sample sizes; 4) employing more robust electronic health records and patient registries to improve data completeness and reduce the impact of loss to follow-up; and 5) performing sensitivity analyses to adjust for any remaining biases. Establishing patient registries could improve data completeness and lessen the impact of loss to follow-up.

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