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Stratification of the risk of thromboembolic complications according to CHA_2DS_2–VASc and CHA_2DS_2–VA scores in patients with atrial fibrillation receiving non–vitamin K antagonist oral anticoagulants

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Aim. To compare the performance of the CHA_2DS_2-VASc and the simplified CHA_2DS_2-VA scores in predicting 1-year thromboembolic events among patients with atrial fibrillation (AF) treated with non-vitamin K antagonist oral anticoagulants (NOACs).
Material and methods. In this single-centre observational cohort study, we followed 212 consecutive patients (median age 76 years, 53.5% female) with non-valvular AF receiving NOAC therapy for 12 months. Baseline clinical characteristics and thromboembolic risk scores were recorded. The primary outcome was thromboembolic events, defined as a composite of ischemic stroke, transient ischemic attack, or systemic embolism. Discriminative performance of the CHA_2DS_2-VASc and CHA_2DS_2-VA scores was assessed using receiver operating characteristic analysis and compared with the DeLong test. Cox proportional hazards regression was used to identify predictors of thromboembolic events.
Results. During follow-up, 33 patients (15.6%) experienced thromboembolic events. The median CHA_2DS_2-VASc score was 5 (IQR 4-6) and the median CHA_2DS_2-VA score was 4 (IQR 3-5). Event rates increased progressively across higher strata of both scores. The area under the receiver operating characteristic curve was 0.640 for CHA_2DS_2-VASc and 0.637 for CHA_2DS_2-VA, with no significant difference between the two scores (p=0.966). Using a cut-off value of ≥4, CHA_2DS_2-VASc yielded a sensitivity of 93.9% and specificity of 24.6%, while CHA_2DS_2-VA yielded a sensitivity of 90.9% and specificity of 30.2%. In multivariable analysis including individual score components, impaired renal function (estimated glomerular filtration rate <60 mL/min/1.73 m²) was the only independent predictor of thromboembolic events (hazard ratio 2.36, 95% confidence interval 1.11-5.02; p=0.026).
Conclusion. In anticoagulated patients with AF, the CHA_2DS_2-VASc and CHA_2DS_2-VA scores demonstrated modest and comparable discrimination for 1-year thromboembolic events. A higher score threshold (≥4) identified patients with increased residual risk, while impaired renal function was the only independent predictor of events.

Keywords: CHA_2DS_2-VA, CHA_2DS_2-VASc, oral anticoagulant therapy, thromboembolic complications, atrial fibrillation, NOACs, ischemic stroke, renal dysfunction.

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Стратификация риска тромбоэмболических осложнений по шкалам CHA_2DS_2–VASc и CHA_2DS_2–VA у пациентов с фибрилляцией предсердий, получающих прямые оральные антикоагулянты, не являющиеся антагонистами витамина K

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Цель. Сравнить прогностическую эффективность шкал CHA_2DS_2-VASc и упрощённой шкалы CHA_2DS_2-VA в прогнозировании тромбоэмболических событий в течение 1 года у пациентов с фибрилляцией предсердий (ФП), получающих прямые оральные антикоагулянты (ПОАК), не являющиеся антагонистами витамина К.
Материал и методы. В одноцентровое наблюдательное когортное исследование в течение 12 мес. последовательно включены 212 пациентов (медиана возраста 76 лет, 53,5% женщин) с неклапанной ФП, получавших терапию ПОАК. Были зарегистрированы исходные клинические характеристики и показатели тромбоэмболического риска. Первичной конечной точкой являлись тромбоэмболические события, определяемые как комбинированный показатель, включавший ишемический инсульт, транзиторную ишемическую атаку или системную эмболию. Дискриминационная способность шкал CHA_2DS_2-VASc и CHA_2DS_2-VA оценивалась с помощью анализа ROC-кривых с последующим сравнением по тесту Делонга. Для выявления предикторов тромбоэмболических событий применялась регрессия пропорциональных рисков Кокса.
Результаты. В течение периода наблюдения у 33 пациентов (15,6%) были зарегистрированы тромбоэмболические события. Медиана баллов по шкале CHA_2DS_2-VASc составила 5 (межквартильный размах (МКР) 4-6), по шкале CHA_2DS_2-VA – 4 (МКР 3-5). Частота событий последовательно возрастала с увеличением значений обеих шкал. Площадь под ROC-кривой составила 0,640 для CHA_2DS_2-VASc и 0,637 для CHA_2DS_2-VA, без статистически значимых различий между шкалами (p=0,966). При пороговом значении ≥4 шкала CHA_2DS_2-VASc характеризовалась чувствительностью 93,9% и специфичностью 24,6%, тогда как для CHA_2DS_2-VA чувствительность составила 90,9%, а специфичность – 30,2%. При многофакторном анализе с включением отдельных

компонентов шкал нарушение функции почек (расчётная скорость клубочковой фильтрации <60 мл/мин/1,73 м²) оказалось единственным независимым предиктором тромбоэмболических событий (отношение рисков 2,36; 95% доверительный интервал 1,11-5,02; p=0,026).
Заключение. У пациентов с ФП, получающих ПОАК, шкалы CHA_2DS_2-VASc и CHA_2DS_2-VA продемонстрировали умеренную и сопоставимую дискриминационную способность в прогнозировании тромбоэмболических событий в течение 1 года. Более высокий порог шкалы (≥4) позволил выявить пациентов с повышенным остаточным риском, тогда как нарушение функции почек являлось единственным независимым предиктором неблагоприятных событий.

Ключевые слова: CHA_2DS_2-VA, CHA_2DS_2-VASc, пероральная антикоагулянтная терапия, тромбоэмболические осложнения, фибрилляция предсердий, ПОАК, ишемический инсульт, нарушение функции почек.

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Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with substantially increased risks of ischemic stroke, systemic embolism, major bleeding, and all-cause mortality [1]. The introduction of non-vitamin K antagonist oral anticoagulants (NOACs) has transformed the management of AF by providing effective stroke prevention with improved safety and convenience compared with vitamin K antagonists. Contemporary AF management therefore emphasizes broad access to NOAC therapy in eligible patients, alongside individualized assessment of thromboembolic and bleeding risk [2].

Bedside clinical risk scores remain central to thromboembolic risk stratification in AF. The CHA_2DS_2-VASc score, comprising congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke or transient ischemic attack (TIA) (2 points), vascular disease, age 65-74 years, and female sex, has been widely adopted to guide anticoagulation decisions and inform guideline recommendations [2]. However, the inclusion of female sex as an independent risk factor has been increasingly debated. Accumulating evidence suggests that female sex acts predominantly as an age-dependent risk modifier rather than a stand-alone determinant of stroke risk, raising concerns that CHA_2DS_2-VASc may overestimate thromboembolic risk in younger women without additional comorbidities [3-5]. To address this issue, the simplified CHA_2DS_2-VA score, which excludes female sex, has been proposed and endorsed as an alternative risk stratification tool in recent guidelines [2].

Both CHA_2DS_2-VASc and CHA_2DS_2-VA were originally derived and validated in cohorts largely treated with vitamin K antagonists [6-8]. Whether these scores retain comparable predictive performance in contemporary populations treated with NOACs remains an important clinical question. Moreover, as anticoagulation has become widely implemented, the role of these scores may extend beyond treatment initiation to the identification of patients with residual thromboembolic risk despite anticoagulation. We therefore aimed to evaluate and compare the performance of CHA_2DS_2-VASc and CHA_2DS_2-VA scores in predicting 1-year systemic thromboembolic events among patients with AF treated with NOACs.

Methods

Study Design and Population

This was a single-centre observational cohort study conducted at People's Hospital 115, Ho Chi Minh City, Vietnam. We included consecutive adult patients (aged ≥18 years) with non-valvular AF who received NOACs between December 2023 and June 2025. AF was documented by electrocardiography prior to enrolment. Patients treated before the initiation of the prospective registry were identified retrospectively from hospital medical records, whereas those treated thereafter were enrolled and followed prospectively according to a predefined protocol. Exclusion criteria were the presence of mechanical prosthetic heart valves, moderate-to-severe mitral stenosis, acute coronary syndrome or cardiac surgery within the preceding three months, and incomplete follow-up data. The study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Pham Ngoc Thach University of Medicine (approval number 1212/TĐHYKPNT-HĐĐĐ; November 12, 2024). Informed consent was obtained from all participants.

Data Collection

Baseline demographic characteristics, cardiovascular comorbidities, laboratory parameters, and echocardiographic findings were collected at the time of NOAC initiation from electronic medical records. Thromboembolic risk was assessed using both the CHA_2DS_2-VASc and CHA_2DS_2-VA scores. For the CHA_2DS_2-VASc score, one point was assigned for age 65-74 years, hypertension, diabetes mellitus, history of heart failure, vascular disease (myocardial infarction/peripheral arterial disease), and

female sex, and two points for age ≥75 years and prior stroke or TIA. The CHA_2DS_2-VA score was calculated by excluding female sex from the CHA_2DS_2-VASc score.

Renal function was assessed using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [9]. Chronic kidney disease (CKD) was defined by evidence of renal impairment or a sustained reduction in estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m² for a minimum duration of three months, in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 recommendations [9, 10]. Hypertension was identified based on a prior clinical diagnosis recorded in the medical history or the ongoing use of antihypertensive medications [11]. Diabetes mellitus was defined by established diagnostic criteria, including fasting plasma glucose ≥126 mg/dL, glycated hemoglobin (HbA1c) ≥6,5%, or treatment with glucose-lowering agents [12]. Details of oral anticoagulant therapy, including the specific NOAC prescribed (dabigatran, rivaroxaban, apixaban) and the administered dose, were extracted from medical records. Dose selection and adjustment were assessed according to the approved prescribing information for each agent, taking into account renal function, age, body weight, and serum creatinine levels. On this basis, NOAC regimens were categorized as on-label when consistent with product recommendations, or off-label when deviating from the approved dosing criteria.

Outcomes

The primary outcome was the occurrence of thromboembolic events within 12 months, defined as a composite of ischemic stroke, TIA, or systemic embolism. Ischemic stroke was defined as the acute onset of a focal neurological deficit consistent with cerebral ischemia and confirmed by computed tomography or magnetic resonance imaging. Outcome events were identified through scheduled outpatient visits, review of hospital records, and structured telephone interviews conducted at 1, 3, 6, and 12 months. Complete follow-up was achieved for all patients.

Statistical analysis

Continuous variables were presented as means with standard deviations or medians (Me) with interquartile ranges (IQR), and categorical variables as counts and percentages. Between-group comparisons were performed using Student's *t*-test or Mann–Whitney *U* test for continuous variables and χ^2 or Fisher's exact test for categorical variables, as appropriate. Kaplan–Meier curves were generated to illustrate event-free survival. The discriminative performance of CHA_2DS_2-VASc and CHA_2DS_2-VA for thromboembolic events was assessed by receiver operating characteristic (ROC) curves and quantified using the area under the curve (AUC). Comparisons between scores were made using the DeLong test. Cox proportional hazards models were applied to explore associations between baseline variables and outcomes. Variables with $p < 0.2$ in univariate analysis were considered for multivariate models. Because the individual risk factor components of CHA_2DS_2-VASc and CHA_2DS_2-VA were included in the multivariate analysis, the composite scores themselves were not entered simultaneously to avoid multicollinearity. A two-sided p-value <0.05 was considered statistically significant. All analyses were performed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics

In total, 212 patients with AF on NOACs were enrolled. The median age was 76 years (IQR 67-84), and 53.5% were female. A total of 33 patients (15.6%) experienced thromboembolic events during follow-up.

Compared with those without events, affected patients were older, had a higher prevalence of vascular disease (66.7% vs. 43.6%, p=0.022) and prior stroke/TIA (51.5% vs. 29.6%, p=0.025), and lower eGFR (56.9 vs. 70 mL/min/1.73 m², p=0.006).

With respect to anticoagulant treatment, rivaroxaban was the predominant NOAC used, followed by apixaban and dabigatran. The majority of patients were treated according to approved dosing recommendations, and no significant differences were observed between patients with and without thromboembolic events in terms of NOAC type or the proportion of on-label dosing.

The median CHA_2DS_2-VASc and CHA_2DS_2-VA scores were also higher in the event group (6 vs. 5, p=0.01; and 5 vs. 4, p=0.011, respectively) (Table 1).

The cumulative incidence of thromboembolic events increased progressively with higher CHA_2DS_2-VASc and CHA_2DS_2-VA scores (Figure 1). Event rates ranged from 7.7% at a CHA_2DS_2-VASc score of 2 to 35.7% at a score of 8, and from 4.5% at a CHA_2DS_2-VA score of 2 to 100% at a score of 8, indicating a stepwise gradient of risk across categories.

ROC curve analysis showed AUC of 0.640 (95% confidence interval [CI], 0.541-0.739; p=0.011) for CHA_2DS_2-VASc and 0.637 (95% CI, 0.539-0.734; p=0.013) for CHA_2DS_2-VA, with no statistically significant difference between the two scores (p=0.966 by DeLong test). Using a threshold of ≥4, CHA_2DS_2-VASc yielded a sensitivity of 93.9% and specificity of 24.6%, whereas CHA_2DS_2-VA yielded a sensitivity of 90.9% and specificity of 30.2%.

In univariate analysis, age, prior stroke, vascular disease, impaired renal function, and both CHA_2DS_2-VASc and CHA_2DS_2-VA scores were significantly associated with thromboembolic events (Table 2). In multivariate analysis including clinical covariates, only reduced renal function (eGFR <60 mL/min/1.73 m²) remained independently predictive (HR 2.36, 95% CI 1.11-5.02, p=0.026).

Kaplan–Meier survival analysis demonstrated a significantly higher cumulative incidence of thromboembolic events in patients with CHA_2DS_2-VASc ≥4 compared

Table 1. Baseline characteristics of study population according to thromboembolic events

Variable	With events (n=33)	Without events (n=179)	p-value
Age, Me (IQR), years	80 (73.5–87)	76 (66–83)	**0.017**
· Age <65 years, n (%)	5 (15.2)	38 (21.2)	0.146
· Age 65-74 years, n (%)	4 (12.1)	43 (17.9)	
· Age ≥75 years, n (%)	24 (72.7)	98 (54.7)	
Female, n (%)	19 (57.6)	94 (52.5)	0.705
Comorbidities (components of CHA_2DS_2-VASc/CHA_2DS_2-VA), n (%)			
· Hypertension	32 (97)	174 (97.2)	1.0
· Diabetes mellitus	14 (42.4)	66 (36.9)	0.562
· History of heart failure	21 (63.6)	134 (74.9)	0.202
· Vascular disease	22 (66.7)	78 (43.6)	**0.022**
· Previous stroke/TIA	17 (51.5)	53 (29.6)	**0.025**
CKD, n (%)	19 (57.6)	60 (33.5)	**0.011**
Anemia, n (%)	13 (40.6)	54 (33.5)	0.542
Hemoglobin (g/dL)	12.8 (10.5–14.8)	13 (11.8–14.6)	0.564
eGFR, mL/min/1.73 m², Me (IQR)	56.9 (43.1–72)	70 (52.6–85.2)	**0.006**
eGFR <60 mL/min/1.73 m², n (%)	21 (63.6)	55 (34.2)	**0.003**
LVEF, %, Me (IQR)	60 (48–70)	60 (47–67)	0.439
LAD, mm, Me (IQR)	38 (32–42.5)	40(32.7–42)	0.960
LA enlargement, n (%)	14 (42.4)	73 (42.9)	1.0
Antiplatelet drugs use, n (%)	3 (9.1)	19 (10.9)	1.0
NOAC use, n (%)			
· Dabigatran	2 (6.1)	15 (8.4)	0.322
· Rivaroxaban	24 (72.7)	143 (79.9)	
· Apixaban	7 (21.2)	21 (11.1)	
NOAC dosing, n (%)			
· On-label dose (per SmPC)	23 (69.7)	108 (60.3)	0.309
· Off-label dose	10 (30.3)	71 (39.7)	
CHA_2DS_2-VASc score, Me (IQR)	6 (4–7)	5 (4–6)	**0.01**
CHA_2DS_2-VA score, Me (IQR)	5 (4–6)	4 (3–5)	**0.011**

CKD – chronic kidney disease, eGFR – estimated glomerular filtration rate, IQR – interquartile range; LA – left atrium, LAD – left atrial diameter, LVEF – left ventricular ejection fraction, Me – median, NOAC – non-vitamin K antagonist oral anticoagulant, SmPC – summary of product characteristics, TIA – transient ischemic attack

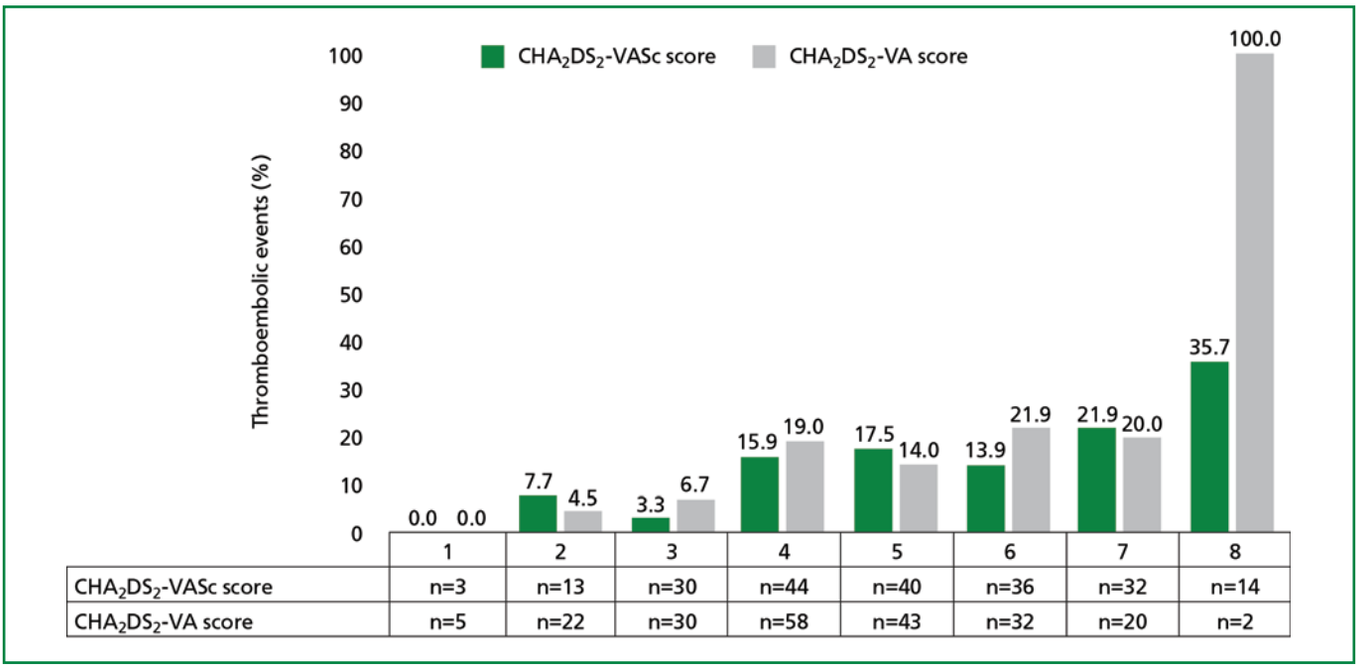
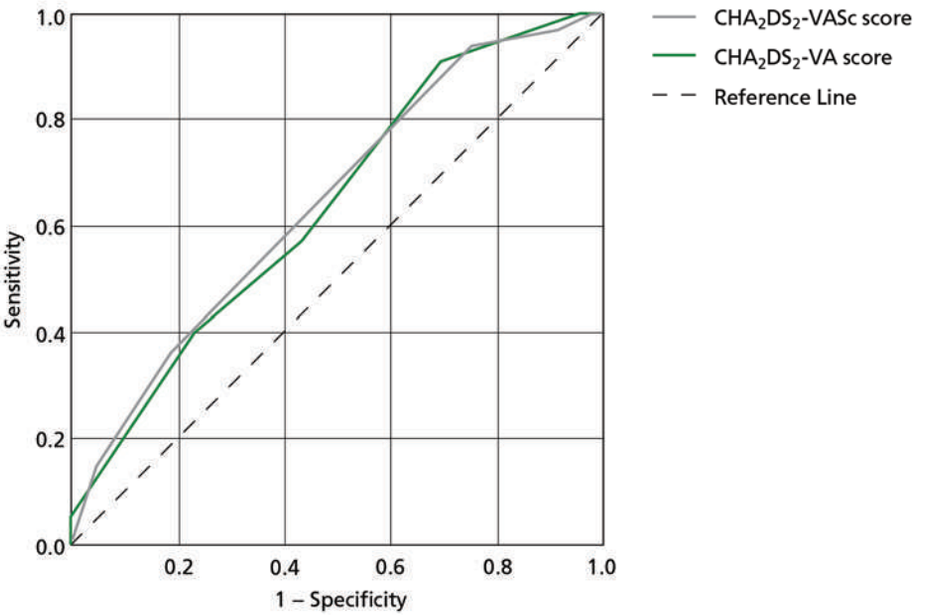


Figure 1. Distribution of thromboembolic events across CHA_2DS_2-VASc and CHA_2DS_2-VA strata.

Table 2. Cox regression analysis for thromboembolic events

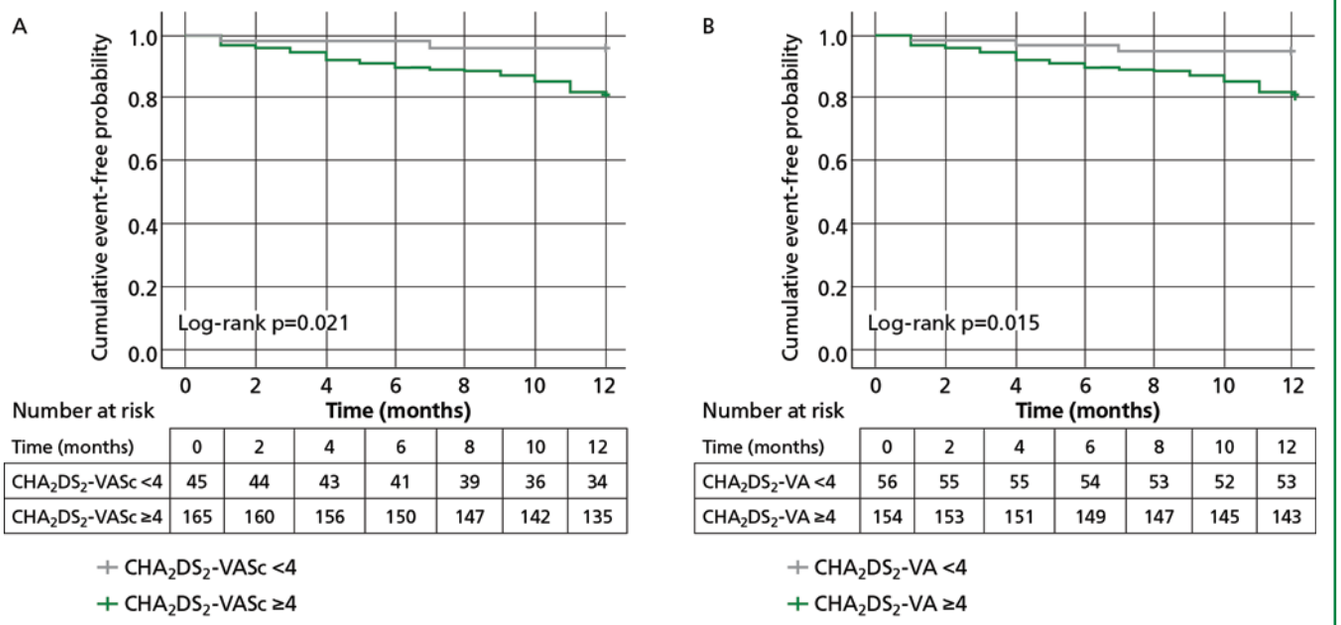
Variable	Univariate analysis	p-value	Multivariate analysis	p-value
	HR (95% CI)		HR (95% CI)	
Age (per year)	1.035 (1.002-1.070)	**0.04**	1.019 (0.983-1.056)	0.307
Female sex	1.21 (0.61-2.42)	0.584	–	–
Hypertension	1.00 (0.14-7.32)	1.000	–	–
Diabetes mellitus	1.28 (0.64-2.56)	0.481	–	–
History of heart failure	0.62 (0.30-1.25)	0.182	–	–
Prior stroke/TIA	2.28 (1.15-4.52)	**0.018**	1.85 (0.89-3.83)	0.097
Previous vascular disease	2.43 (1.18-5.01)	**0.016**	1.85 (0.86-3.98)	0.116
eGFR <60 mL/min/1.73 m²	2.99 (1.47-6.07)	**0.002**	2.36 (1.11-5.02)	**0.026**
Antiplatelet drugs use	0.85 (0.26-12.75)	0.792	–	–
NOAC on-label dose	1.46 (0.69-3.07)	0.317	–	–
CHA_2DS_2-VASc (per point)	1.33 (1.07-1.64)	**0.009**	–	–
CHA_2DS_2-VASc ≥4 vs. <4	4.56 (1.09-19.05)	**0.038**	–	–
CHA_2DS_2-VA (per point)	1.38 (1.09-1.74)	**0.007**	–	–
CHA_2DS_2-VA ≥4 vs. <4	3.89 (1.19-19.05)	**0.025**	–	–

CI – confidence interval, eGFR – estimated glomerular filtration rate, HR – hazard ratio, NOAC – non-vitamin K antagonist oral anticoagulant, TIA – transient ischemic attack
Because the risk factor components of CHA_2DS_2-VASc and CHA_2DS_2-VA were entered into the multivariate model, the composite scores themselves were not simultaneously included to avoid collinearity



The area under the curve (AUC) was 0.640 (95% CI 0.541-0.739) for CHA_2DS_2-VASc and 0.637 (95% CI 0.539-0.734) for CHA_2DS_2-VA, with no significant difference between the two scores (DeLong test p=0.966). The dashed diagonal line represents the reference line (AUC=0.5)

Figure 2. Receiver operating characteristic (ROC) curves of the CHA_2DS_2-VASc and CHA_2DS_2-VA scores for prediction of 1-year thromboembolic events.



Number at risk

Time (months)	0	2	4	6	8	10	12
CHA_2DS_2-VASc <4	45	44	43	41	39	36	34
CHA_2DS_2-VASc ≥4	165	160	156	150	147	142	135

Number at risk

Time (months)	0	2	4	6	8	10	12
CHA_2DS_2-VA <4	56	55	55	54	53	52	53
CHA_2DS_2-VA ≥4	154	153	151	149	147	145	143

Panel A shows the cumulative incidence of thromboembolic events stratified by CHA_2DS_2-VASc score (<4 vs ≥4).
Panel B shows the cumulative incidence of thromboembolic events stratified by CHA_2DS_2-VA score (<4 vs ≥4)

Figure 3. Kaplan–Meier curves for thromboembolic events.

with those with scores <4 (log-rank p=0.021), and similarly for CHA_2DS_2-VA ≥4 versus <4 (log-rank p=0.015) (Figure 3).

Discussion

In this single-centre observational cohort of patients with AF treated with NOACs, both the CHA_2DS_2-VASc and CHA_2DS_2-VA scores demonstrated modest but statistically significant discrimination for 1-year thromboembolic events, with no meaningful difference in predictive performance between the two tools. Thromboembolic risk increased progressively across higher score strata, and patients classified as high risk (score ≥4) by either score experienced a significantly higher cumulative incidence of events during follow-up. When individual risk components were evaluated simultaneously, impaired renal function emerged as the only independent predictor of thromboembolic events.

Our findings should be interpreted in the context of evolving evidence regarding the prognostic role of female sex in AF. In the nationwide FinACAF study, which included over 140,000 anticoagulant-naïve patients with incident AF between 2007 and 2018, the predictive value of female sex declined substantially over time [13]. During the early study period, when women exhibited higher AF-related stroke risk, the CHA_2DS_2-VASc score outperformed the CHA_2DS_2-VA score. However, as sex-related differences in stroke risk attenuated, the performance gap narrowed, and by 2017-2018 the CHA_2DS_2-VA score demonstrated marginal but statistically significant advantages in net reclassification and discrimination metrics. In this context, the near-identical discriminative performance of CHA_2DS_2-VASc and CHA_2DS_2-VA observed in our contemporary NOAC-treated cohort is consistent with the temporal trends reported in FinACAF. Our results support the concept that, in modern clinical practice where sex-related differences in AF-associated thromboembolic risk are minimal, exclusion of female sex from the risk score does not compromise predictive accuracy.

Several registry-based and modelling studies have explored whether more complex, integrated risk models can improve thromboembolic risk prediction beyond the CHA_2DS_2-VASc score. The GARFIELD-AF risk tool, developed from a large prospective international registry using multivariable modelling techniques, represents one of the most comprehensive efforts in this field. In its derivation and external validation cohorts, the GARFIELD-AF model demonstrated superior discrimination for ischemic stroke/systemic embolism compared with CHA_2DS_2-VASc, with AUCs of approximately 0.68-0.69 versus 0.64-0.66, respectively [14]. Notably, the absolute improvement in discrimination for stroke outcomes was modest, despite the substantially greater complexity of the model and inclusion of treatment-related variables. These findings are highly informative when interpreting the performance of simpler clinical scores. The AUC values observed in our

study for both CHA_2DS_2-VASc and CHA_2DS_2-VA (approximately 0.64) are consistent with those reported for CHA_2DS_2-VASc in large international registries, including GARFIELD-AF. Even with advanced modelling approaches, the discriminative ability for thromboembolic events in AF appears to plateau below 0.70, highlighting the intrinsic challenges of stroke prediction in this population [14, 15]. In this context, the near-identical performance of CHA_2DS_2-VA and CHA_2DS_2-VASc in our contemporary NOAC-treated cohort suggests that exclusion of female sex does not result in a clinically meaningful loss of predictive information. While integrated models such as GARFIELD-AF may offer incremental gains in selected settings, particularly for mortality prediction or in low-risk patients, the simplicity, transparency, and bedside applicability of CHA_2DS_2-VA and CHA_2DS_2-VASc remain important strengths for routine clinical use.

Our findings are highly consistent with those reported from the GLORIA-AF Registry, a large contemporary, prospective cohort in which CHA_2DS_2-VA and CHA_2DS_2-VASc demonstrated similar and modest discrimination for thromboembolic events, with AUC values in the range of 0.63-0.66 [16]. The close agreement between the AUCs observed in GLORIA-AF and those in our study supports the external validity of our results and underscores the intrinsic limitations of clinical risk scores for predicting thromboembolism in the modern era of widespread anticoagulation. Importantly, while the GLORIA-AF analysis focused primarily on comparative discrimination metrics (AUC, IDI, and NRI) and the interaction between sex, age, and oral anticoagulant use, it did not address optimal score thresholds for identifying residual thromboembolic risk. In contrast, our study extends the existing literature by exploring clinically relevant cut-off values using ROC analysis in a fully anticoagulated cohort. We found that a threshold of ≥4 for both CHA_2DS_2-VASc and CHA_2DS_2-VA provided very high sensitivity (>90%) but low specificity, highlighting their utility as screening tools for identifying patients at increased residual risk rather than for ruling out future events.

Beyond clinical risk scores, impaired renal function emerged as the only independent predictor of thromboembolic events in our multivariable analysis. CKD is a well-recognized determinant of adverse outcomes in AF, reflecting a complex interplay of systemic inflammation, endothelial dysfunction, prothrombotic state, and altered pharmacokinetics of anticoagulant therapy [17]. Prior studies have consistently demonstrated the prognostic importance of renal dysfunction beyond traditional CHA_2DS_2-VASc components. In the Taiwan Stroke Registry, advanced renal dysfunction was independently associated with recurrent stroke, mortality, and poor functional outcomes in patients with embolic stroke of undetermined source, and incorporation of renal impairment into the CHA_2DS_2-VASc score significantly improved risk reclassification as assessed by IDI and NRI metrics [18]. Similarly, in high cardiovascular risk populations, the R^2 – CHA_2DS_2-VASc – score, which explicitly incorporates renal function, showed improved discrimination for all-cause mortality compared with CHA_2DS_2-VASc alone, with an absolute increase in AUC of approximately 0.05 [19]. Nevertheless, these improvements in discrimination have generally been modest and context-dependent, varying according to population characteristics and clinical endpoints. Despite the strong and consistent association between renal dysfunction and adverse outcomes, the incremental gains achieved by simple score modification have not been sufficient to support widespread adoption of renal-augmented scores in routine practice [17]. Our findings reinforce the concept that renal impairment conveys prognostic information not fully captured by traditional clinical scores and may be better addressed through multivariable or composite prediction models. Notably, in a previously published analysis from the same cohort focusing on age-stratified outcomes in very elderly patients with AF receiving NOACs, impaired renal function similarly emerged as a key determinant of adverse cardiovascular events, whereas chronological age was not independently predictive after multivariable adjustment [20]. Together, these observations underscore renal dysfunction as a major contributor to residual risk in anticoagulated patients with AF.

Our findings have three practical messages. First, in a contemporary NOAC-treated AF population, the simplified CHA_2DS_2-VA performs comparably to CHA_2DS_2-VASc for 1-year thromboembolic prediction and may avoid over-classification of low-risk women, echoing results from large national and registry datasets. Second, more complex risk engines such as GARFIELD-AF or biomarker-based scores (e.g., ABC-stroke ([age, biomarkers, including N-terminal pro-B-type natriuretic peptide and high-sensitivity cardiac troponin, and clinical history of prior stroke/TIA) can offer modestly improved discrimination and deserve consideration in research and selected clinical scenarios [14, 21]. Third, renal dysfunction identifies patients at higher residual risk despite anticoagulation and should prompt closer monitoring and consideration of integrated risk assessment beyond the traditional clinical score.

Study limitations

Several limitations should be acknowledged. This was a single-centre observational study with a relatively small sample size, which limited statistical power for subgroup analyses and reduced the precision of estimates, particularly at extreme score ranges. The number of thromboembolic events was modest, and optimal cut-off values were derived from internal ROC analyses without external validation, which may restrict their generalizability. Follow-up was limited to one year, and the study population consisted exclusively of Asian patients, potentially limiting applicability to other ethnic groups. In addition, the present analysis focused on thromboembolic outcomes and did not assess bleeding risk or net clinical benefit. Finally, residual confounding cannot be excluded given the observational study design.

Conclusion

In NOAC-treated patients with AF, the CHA_2DS_2-VA and CHA_2DS_2-VASc scores showed modest and comparable discrimination for 1-year thromboembolic events. A higher score threshold (≥4) identified patients with increased residual risk, suggesting a potential role for these scores in risk stratification beyond anticoagulation initiation. Renal dysfunction was the only independent predictor of thromboembolism, highlighting the need for additional risk assessment beyond traditional clinical scores.

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