IJC Heart & Vasculature 34 (2021) 100787

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: www.journals.elsevier.com/ijc-heart-and-vasculature

Novel model-based point scoring system for predicting stroke risk in atrial fibrillation patients: Results from a nationwide cohort study with validation

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ARTICLE INFO

Article history:
Received 17 March 2021
Accepted 15 April 2021

Keywords:
Atrial fibrillation
Catheter ablation
Scoring system
Stroke

ABSTRACT

Background: The stroke risk scoring system for atrial fibrillation (AF) patients can vary considerably based on patients' status while receiving ablation. This study aimed to demonstrate a novel scoring system for stroke risk stratification based on the status of catheter ablation.
Methods: First, 787 patients with AF undergoing ablation were matched according to age, sex, and underlying diseases with the same number of patients not undergoing ablation using the propensity-score (PS)-matched cohort. Multivariate Cox model-derived coefficients were used to construct a simple point-based clinical model using the PS-matched cohort. Thereafter, the novel model (AF-CA-Stroke score) was validated in a nationwide AF cohort.
Results: The AF-CA-Stroke score was calculated based on age (point = 5), ablation status (point = 4), prior history of stroke (point = 4), chronic kidney disease (point = 2), diabetes mellitus (point = 1), and congestive heart failure (point = 1). Risk function to predict the 1-, 5-, 10-year absolute stroke risks was reported. The estimated area under the receive operating characteristic curve of the AF-CA-Stroke score in the PS-matched cohort was 0.845 (95% confidence interval: 0.824–0.865) to predict long-term stroke. A validation study showed that discrimination abilities in the AF-CA-Stroke scores were significantly higher than those in the $CHADS_2/CHA_2DS_2$-VASc scores. The best cut-off value of the AF-CA-Stroke score to predict future strokes was ≥ 5.
Conclusions: This novel model-based point scoring system effectively identifies stroke risk using clinical factors and AF ablation status of patients with AF. Various age stratifications and AF ablation should be considered in AF management.

1. Introduction

Atrial fibrillation (AF) is a common arrhythmia that increases the risk of stroke and mortality in adults [1,2]. The stroke risk in AF patients varies greatly (ranging from 1% to 15% per year), and depends on several demographic and clinical factors [3]. Effective risk stratification of stroke is a cornerstone for AF management [4]. Pharmacologic therapies for AF management includes rate control, rhythm control, and thromboembolic prevention [5]. However, the long-term efficacy of rate control and rhythm control may be limited on reducing stroke risk based on the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study [6]. Catheter ablation has become an alternative therapy for AF. As compared with rhythm control therapy, catheter ablation was associated with reduced subsequent AF episodes [7]. A prior study using the Taiwan National Health Insurance database (NHIRD) demonstrated that AF catheter ablation was associated with lower stroke risk [8]. A recent

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https://doi.org/10.1016/j.ijcha.2021.100787
2352-9067/

meta-analysis (analyzing one randomized clinical trial - the Catheter Ablation Versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation [CABANA] and other eight large matched population studies) exhibited reduced stroke risk in AF patients with catheter ablation than medical therapy [9].

Currently, the $CHADS_2$ and CHA_2DS_2-VASc scores as the conventional scoring systems are commonly used to identify stroke risk and determine antithrombotic therapies in patients with AF [10,11]. Prior studies suggested that AF patients with $CHADS_2$ score of "0" or CHA_2DS_2-VASc score of "0–1" could be used to stratify truly low stroke risk in AF patients undergoing catheter ablation [12–14]. However, the stroke risk scoring systems for AF patients can vary considerably based on the status while receiving the AF ablation and was not considered in conventional scoring systems. This study aimed to demonstrate a scoring system for stroke risk stratification using the conventional risk factors plus the status of catheter ablation, as compared with the conventional scoring systems.

2. Methods

2.1. Study design and study population

This study included a propensity-score (PS) matched cohort (Cohort 1) and a validation AF cohort (Cohort 2). Participants with prior AF ablation or aged < 18 years before the baseline were excluded from this study. This study was approved by the Institutional Review Board (IRB Number: 201305044W and 2017-09-013BCF) of the Taipei Veterans General Hospital (TVGH) in accordance with the Good Clinical Practice Guidelines.

2.2. Propensity-score matched Cohort (Cohort 1)

In Cohort 1, AF patients receiving catheter ablation for pulmonary vein isolation from 2003 to 2012 based on the TVGH AF ablation dataset were studied to construct a novel scoring system. TVGH AF ablation dataset recruited patients based on the consensus for performing AF catheter ablation, including: (1) AF types, AF history, and left atrial size; (2) the severity of underlying cardiovascular diseases; (3) history of pharmacologic therapies; and (4) the patients' will and the physicians' judgment [15].

Comparison cohort of the non-ablation group was derived by randomly selecting 10,000 patients with AF without ablation in 2003 from the NHIRD. In order to minimize the impact of higher stroke risk due to imbalanced distributions between patients with AF without/with ablation in Cohort 1, for AF patients undergoing ablation were age- sex-, underlying disease-matched to the same number of patients with AF without ablation (Fig. 1).

2.3. Validation AF Cohort (Cohort 2)

Cohort 2 was a nationwide cohort generating from the NHIRD in 2003. In Cohort 2, a total of 147,225 patients with AF aged over 17 years as the validation AF cohort were identified; among them, 1,897 drug refractory patients with AF with catheter ablation of pulmonary ablation were confirmed according to procedure code of AF catheter ablation (Cohort 2; Fig. 1). The newly constructed scoring system constructed in Cohort 1 was validated using Cohort 2.

2.4. Ascertainment of baseline Data

The NHIRD was provided by the Health and Welfare Data Science Center, Taipei, Taiwan. The NHIRD includes records of outpatient visits, hospital admissions, prescriptions, and disease diagnoses for > 99% of the 23 million population. All patient information was anonymized, and the requirement for written informed consent from patients was officially waived. All participants in the ablation group provided written informed consent. The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) coding system was used for identifying

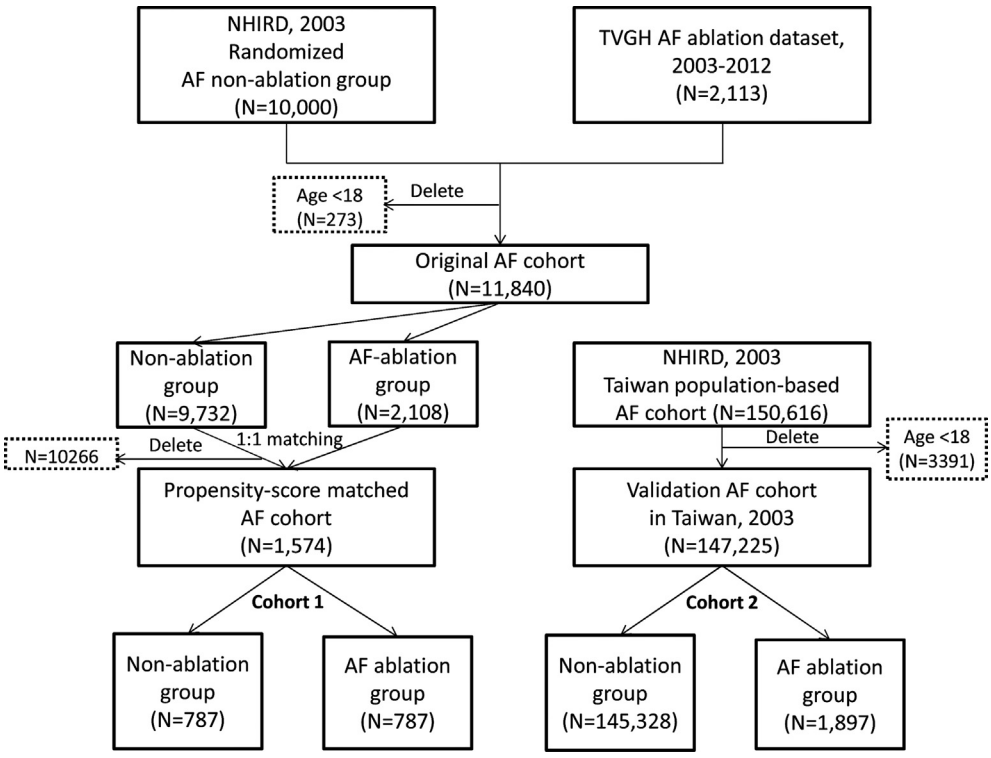

Fig. 1. Study flow chart (AF: atrial fibrillation; NHIRD: Taiwan National Health Insurance database; TVGH: Taipei Veterans General Hospital).

Table 1
Basic characteristics and estimated coefficient.

Risk factors	Mean or proportion (%)	Hazard ratio (95% confidence interval)	P-value
Included in the novel system			
Age, +1 year	54.5 years	1.05 (1.04–1.07)	<0.001
AF, no catheter ablation	50%	4.64 (3.24–6.64)	<0.001
Prior history of stroke	6.0%	6.89 (5.07–9.36)	<0.001
Chronic kidney disease	0.9%	4.54 (2.14–9.65)	<0.001
Diabetes mellitus	7.4%	1.55 (1.01–2.36)	0.04
Congestive heart failure	6.4%	1.58 (1.01–2.47)	0.048
Excluded from the novel system			
Hypertension	36.8%	0.80 (0.60–1.06)	0.12
Prior acute coronary syndromes	2.5%	0.35 (0.09–1.41)	0.14
Vascular disease	2.7%	0.48 (0.15–1.51)	0.21
Hyperlipidemia	12.6%	0.76 (0.49–1.19)	0.23
Thyroid diseases	3.4%	0.69 (0.31–1.56)	0.38
Valvular diseases	4.1%	1.25 (0.68–2.29)	0.47
Chronic obstructive disease	3.0%	1.23 (0.61–2.49)	0.57
Female	30%	1.01 (0.77–1.32)	0.97

the disease diagnoses (details for ascertainment of baseline data, $CHADS_2$/ CHA_2DS_2-VASc scoring systems were summarized in the Data in Brief). The diagnoses were confirmed only if the patient had at least one incidence of hospitalization or at least three consecutive outpatient visits with the above listed diseases to improve the accuracy of coding (refer to the Data in Brief). The diagnostic accuracy of AF (ICD-9-CM: 427.31) using this definition in NHIRD has been validated previously [16]. For Cohort 2, the status of receiving AF ablation or not was based on: (1) an AF diagnosis of ICD-9-CM code: 427.31; (2) a procedural code of AF catheter ablation; and (3) a procedural code for *trans*-septal puncture [8]. Medications were identified using the codes based on the Anatomical Therapeutic Chemical (ATC) Classification System.

2.5. Follow-up strategy and outcome confirmation

This study evaluated the rates of stroke (ICD-9-CM: 430–438) using the NHIRD database. The accuracy of identifying ischemic stroke using the NHIRD was approximately 94% [17]. Participants were followed until the occurrence of first stroke event or at the end of 2015. Deaths were recorded to the Death Registry and followed until the end of 2016.

2.6. Statistical analysis

Continuous variables are presented as mean ± standard deviation, whereas categorical variables are presented as proportion. For Cohort 1, the AF ablation group was 1:1 matched in the PS regarding age, sex, hypertension, chronic kidney disease, and chronic obstructive pulmonary disease with a 0.15 caliper width to patients with AF without ablation.

Cox proportional hazard models were used to evaluate stroke risk with hazard ratio (HR) with 95% confidence interval (CI). This study examined the incremental predictive values of adding these variables into the multivariate Cox model-derived coefficients to construct a simple point-based clinical model using Cohort 1. The final risk factors in the multivariate model were selected from the univariate model using a significance level of 0.1. The categorization point model was constructed according to clinical covariates in Cohort 1 by applying the methods of the Framingham study risk score functions [18,19] (see details in the Data in Brief). Finally, to adjust for the over-optimism in model fitting, the novel model (AF-CA-Stroke score) was validated using Cohort 2. The initial clinical model included age (years), sex, receiving AF ablation or not, congestive heart failure, hypertension, diabetes mellitus, prior stroke, vascular diseases, acute coronary diseases, chronic kidney disease, chronic obstructive pulmonary disease, valvular heart diseases, hyperlipidemia, and thyroid diseases. The "point" of stroke risk assessment of < 1% at 1 year was set to be "low risk", 1–5% at 1 year was set to be "moderate risk", and > 5% at 1 year was set to be "high risk".

We compared the performance of the novel AF-CA-Stroke score model with the $CHADS_2$/CHA_2DS_2-VASc scoring systems. The integrated discrimination abilities of area under receive operating characteristic curve (AUC), integrated discrimination improvement (IDI) and category-free net reclassification improvement (NRI) were assessed to compare among all models [20,21]. The best cut-of-value predicting the incident stroke events was calculated using the Youden index of the AUC (sensitivity + specificity −1). The Kaplan–Meier method was used to compare the stroke-free survival rate in different score groups. All statistical analyses were performed using the SAS software version 9.4 (SAS Institute, Inc., Cary, NC, USA). Statistical significance was set at two-tailed $P < 0.05$.

3. Results

3.1. Propensity-score matched Cohort (Cohort 1)

A total of 11,840 patients with AF were identified in the original cohort, including 2,108 patients in the TVGH AF ablation dataset

Table 2
Clinical point-based scoring system.

Clinical risk factors	Estimated coefficient ($Beta_{risk\ factor}$)	$W_{i\text{-}j}$-$W_{i\text{-}ref}$	$Beta_{risk\ factor}$ * ($W_{i\text{-}j}$-$W_{i\text{-}ref}$)	Risk points
Age, +1 year	$Beta_{age\text{-}1}$ = 0.052			$Beta_{age\text{-}10}$ = 0.52
<35 (reference)		0	0	0
35–44		12.5	0.65	1
45–54		22.5	1.18	2
55–64		32.5	1.70	3
65–74		42.5	2.22	4
≥75		52.5	2.74	5
AF, no catheter ablation	1.90	1	1.90	4
Prior history of stroke	2.07	1	2.07	4
Chronic kidney disease	0.94	1	0.94	2
Diabetes mellitus	0.55	1	0.55	1
Congestive heart failure	0.49	1	0.49	1

($W_{i\text{-}j}$-$W_{i\text{-}ref}$) represents the difference between each value of risk factor and its reference value;
Risk points = $Beta_{risk\ factor}$*($W_{i\text{-}j}$-$W_{i\text{-}ref}$)/$Beta_{age\text{-}10}$.

and 9,732 patients without ablation (see Fig. 1 and **Table S1** in the Data in Brief). After PS-matching, a total of 1,574 patients were studied for constructing a model-based scoring system. The baseline characteristics of Cohort 1 (mean age: 54.5 years, 30% of them were women) are summarized in Table 1 and **Table S2** in the Data in Brief. This study identified 237 stroke events (25.5% in the non-ablation group and 4.6% in the AF ablation group) during a mean follow-up duration of 7.8 ± 3.4 years.

Significant risk factors in the multivariate Cox regression model are summarized in Table 1. The new "AF-CA-Stroke" score to estimate stroke risks in patients with AF was developed according to the survival function at 1, 5, 10 years. Depending on the 1-year increment of baseline beta coefficient change in age, up to 5 points were assigned for the following age groups: <35 years: 0, 35–44 years: 1, 45–54 years: 2, 55–64 years: 3, 65–74 years: 4, and ≥ 75 years: 5 points (Table 2). The AF-CA-Stroke scoring system includes other important clinical risk factors, such as ablation status (point = 4), prior history of stroke (point = 4), chronic kidney disease (point = 2), diabetes mellitus (point = 1), and congestive heart failure (point = 1) (Table 2). The absolute risk function that predicts the 1-, 5-, 10-year stroke rates by calculating the AF-CA-Stroke scores and 1-year stroke rates of the $CHADS_2$ and CHA_2DS_2-VASc scores are summarized in Fig. 2 **and** Table 3.

Because information regarding the AF subtypes, AF recurrences, methods of AF ablation were not available in the NHIRD study (AF types were available only in AF ablation group in Cohort 1). Hence, we used AF-related admissions as the surrogate of AF recurrences. The AF-related admission rates were 55.4% vs. 34.2% in the non-ablation vs. ablation groups in Cohort 1 (P < 0.001; **Table S2** in the Data in Brief). In the sub-analysis of this study using the TVGH AF ablation dataset in Cohort 1, when adjusting for multi-variate risk factors of age, sex, risk scores (including: various status of underlying diseases), and anti-coagulant uses (warfarin and non-vitamin K antagonist oral anticoagulants [NOAC]), AF-related admissions in AF ablation group did not significantly affect the incident stroke risk: HR = 5.39 (95% CI: 0.57–50.8), P = 0.14. In the ablation group, AF patients with persistent AF (15.2%; **Table S2** in the Data in Brief) were not associated with increased stroke risk in this study: HR = 1.47 (95% CI: 0.72–3.00), P = 0.29. In addition, the uses of warfarin (HR = 0.69, 95% CI: 0.13–3.64, P = 0.66) and NOAC (HR = 0.73, 95% CI: 0.15–3.66, P = 0.70) were not associated with increased future stroke risk.

3.2. Validation AF Cohort (Cohort 2)

In Cohort 2, a total of 1,897 (1.3%) patients with AF underwent catheter ablation (**Table S3** in the Data in Brief). A total of 46,863 stroke events were identified from the total of 147,225 patients with AF (32.1% in non-ablation group and 14.5% in AF ablation group) during a mean follow-up of 5.1 ± 3.2 years. Fig. 2**C** demonstrates the trends of stroke rates of estimated 1-year rates (%) and observed rates (per 100 person-years). The validation study showed that discrimination abilities of category-free NRI (NRI: 0.251, P < 0.001) were significantly higher and the absolute IDI (IDI: 0.01, P = 0.79) was similar in the AF-CA-Stroke score as compared with the CHA_2DS_2-VASc score system (**Table S4 and S6** in the Data in Brief). The discrimination ability of AF-CA-Stroke score in terms of AUCs for predicting the 1-, 5-, 10-year incident stroke risks was significantly higher than that of conventional score systems in both Cohorts 1 and 2 (all P < 0.001; Fig. 3). The estimated AUCs using the AF-CA-Stroke score was 0.845 (95% confidence interval [CI]: 0.824–0.865) in Cohort 1 and 0.649 (95% CI: 0.646–0.652) in Cohort 2 (Fig. 3 **and Table S4** in the Data in Brief**)**. Youden indices indicated that the best cut-off-values predicting the incident stroke event were ≥ 5, ≥1, and ≥ 3 in the AF-CA-Stroke, $CHADS_2$, and CHA_2DS_2-VASc scoring systems, respectively (Table 3).

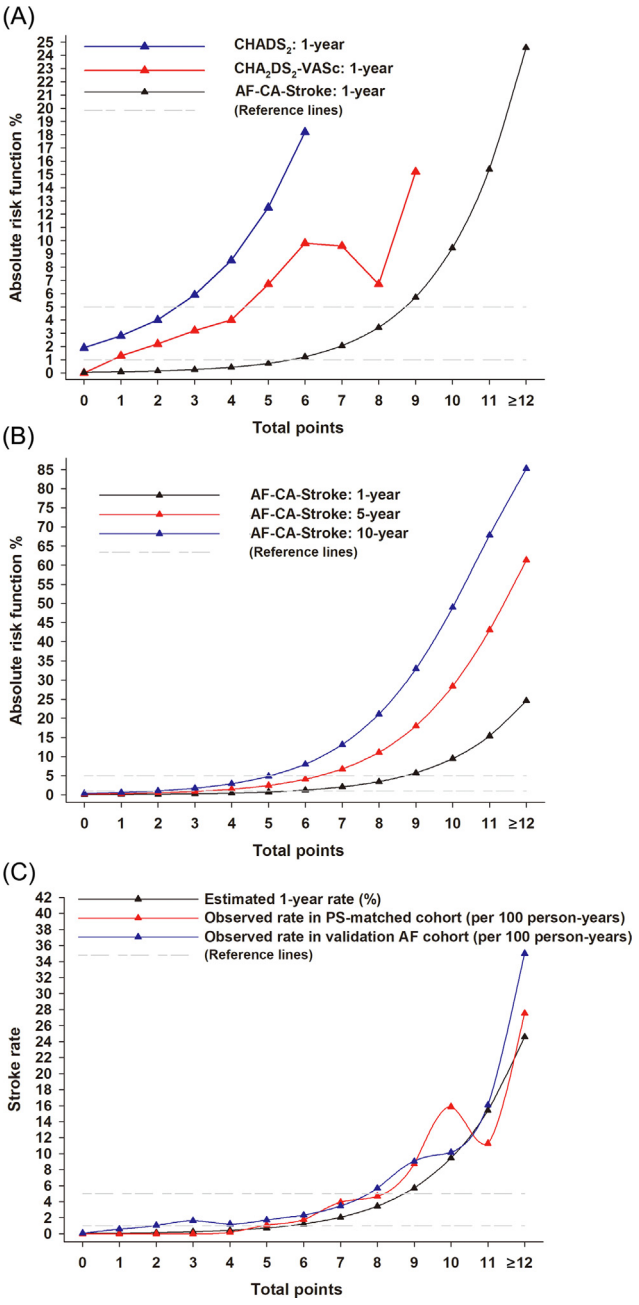

Fig. 2. Risk functions of: (A) the comparisons of estimated 1-year risks among various scoring systems depending on the total points, (B) estimated 1-, 5-, 10-year risks of the AF-CA-Stroke score, and (C) comparisons between estimated 1-year rate and observed stroke rate (per 100 person-years) of the AF-CA-Stroke score in Cohort 1 and Cohort 2.

3.3. Distributions among various scoring systems and incident stroke risks

Fig. 4 summarizes the score distributions and stroke events among various soring systems with and without ablation. The average AF-CA-Stroke scores in the ablation group were similar between Cohorts 1 and 2 (Fig. 4**A & 4D**). In the Cox proportional hazard model, subgroup analysis on various AF-CA-Stroke scores showed that scores of ≥ 5 had significantly higher risk of future stroke (P for trend < 0.001; **Figure S1** in the Data in Brief). Based

on the risk assessment of stroke at 1 year, patients with total points of AF-CA-Stroke scores between 0 and 4 were identified as low stroke risk, 5–8 points as moderate stroke risk, and > 8 points as high stroke risk. **Figure S2** in the Data in Brief shows the results of survival analyses based on various score groups categorized by the AF-CA-Stroke scores. In addition, one increment of the AF-CA-Stroke score contributed to 37% increased stroke risk in patients with AF (HR: 1.37, 95% CI: 1.36–1.38; P < 0.001) (in the non-ablation group, HR: 1.38, 95% CI: 1.37–1.39; and in the AF-ablation group, HR: 1.64, 95% CI: 1.55–1.75).

Table 4 summarizes accurate stroke rates during the 1-, 5-, 10-year follow-up periods based on risk groups of scoring systems and ablation status in Cohorts 1 and 2. For all patients with AF, 0.1%, 0.2%, and 0.4% incident strokes occurred during 1-, 5-, 10-year follow-up periods in Cohort 1, and 1.9%, 5.0%, and 6.7% incident strokes occurred during 1-, 5-, 10-year follow-up periods in Cohort 2, respectively, as identified by AF-CA-Stroke scores of < 5 (low risk). In contrast, 1.9%, 6.0%, and 10% incident strokes occurred during 1-, 5-, 10-year follow-up periods in Cohort 1, and 5.9%, 14.4%, and 18.4% during 1-, 5-, 10-year follow-up periods in Cohort 2, respectively, based on CHA_2DS_2-VASc scores of < 2 (low risk).

In Cohort 2 (Fig. 4**D-4F**, Table 4), a total of 33.4% patients with AF ablation with CHA_2DS_2-VASc scores of ≥ 2 were identified. However, 18.1% of patients with AF ablation were identified as AF-CA-Stroke scores of ≥ 5. For the AF ablation group, 2.5%, 18.3%, and 66.7% of patients developed incident strokes within 1 year in the low-, moderate-, high-risk groups according to AF-CA-Stroke scores, respectively (Table 4). Conversely, 2.3%, 9.7%, and 64.3% of patients developed incident strokes within 1 year in the low-, moderate-, high-risk groups according to CHA_2DS_2-VASc scores, respectively.

4. Discussions

4.1. Primary findings

This study developed a novel model-based point scoring system (AF-CA-Stroke score) to predict incident stroke events in patients with AF based on six clinical variables using a matched AF cohort. Risk functions to predict the 1-, 5-, 10-year estimated stroke risks were reported. The accurate stroke trends in both PS-matched and AF validation cohorts were nearly matched to the 1-year estimated risk function according to AF-CA-Stroke scores were demonstrated. The AF-CA-Stroke score had significantly higher decimation abilities in predicting 1-year, 5-year, and 10-year incident stroke events than conventional score systems.

4.2. Effects of various age groups and comorbidities on stroke risks

Evidences revealed that the incidence of AF increased with aging, which also led to worse prognosis, incident stroke events, and higher mortality in patients with AF [22]. Most developed countries have accepted the age of 65 years as a definition of elderly. Ages 60 and 65 years are often used, despite its arbitrary nature. Currently, the $CHADS_2$ system includes age ≥ 75 years as 1 point [10], the CHA_2DS_2-VASc set age ≥ 65 years as 1 point and ≥ 75 years as 2 points in predicting future stroke risk in patients with AF [10]. However, to identify the risk of stroke in patients with AF, aging and incident comorbidities are generally a complex issue, and previous studies had difficulties in discussing this issue. A meta-analysis concluded that age as a criterion in patients with AF shall not be simply considered based on gender or age stratifications of ≥ 65/≥75 years [23]. Age and comorbidities mutually impact the stroke risks in patients with AF [4,24,25]. Taipei Group described that a younger age of > 50 years had an increased stroke risk even without comorbidity based on the NHIRD analysis in Taiwan, and stroke risks vary based on the status of comorbidities in various age groups [25,26]. In the current study, the model-based scoring system depending on the baseline beta coefficient changes in age was constructed, with up to 5 points being assigned to the age groups, and a total of > 12 points were established in our novel AF-CA-Stroke scoring system. This newly developed AF-CA-Stroke score can provide more flexibility in predicting long-term stroke risks in patients with AF in various age groups and conditions regardless of gender.

4.3. Managing stroke risks in patients with AF and the impact of catheter ablation

Several stroke prediction models have been developed and validated by previous studies [10,11,27–29]. For the management of stroke risks in patients with AF, both European and American guidelines recommend to use $CHADS_2$ and CHA_2DS_2-VASc scoring systems to determine an optimal strategy of stroke prevention [10,11]. Chao, TF, et al. demonstrated that AF patients in Asian with CHA_2DS_2-VASc score of 0 had a truly low stoke risk than $CHADS_2$

Table 3
Total points and absolute risk functions for various scoring systems.

AF-CA-Stroke				$CHADS_2$		CHA_2DS_2-VASc	
Total points	1-year estimated risk (%)	5-year estimated risk (%)	10-year estimated risk (%)	Total points	1-year estimated risk (%)	Total points	1-year estimated risk (%)
0	0.05%	0.18%	0.36%	**0**	1.90%	**0**	0.00%
1	0.09%	0.30%	0.61%	**1***	2.80%	**1**	1.30%
2	0.15%	0.51%	1.02%	**2**	4.00%	**2**	2.20%
3	0.26%	0.86%	1.72%	**3**	5.90%	**3***	3.20%
4	0.43%	1.44%	2.88%	**4**	8.50%	**4**	4.00%
5*	0.72%	2.42%	4.82%	**5**	12.5%	**5**	6.70%
6	1.22%	4.05%	7.99%	**6**	18.2%	**6**	9.80%
7	2.05%	6.73%	13.1%			**7**	9.60%
8	3.43%	11.1%	21.1%			**8**	6.70%
9	5.71%	18.0%	32.9%			**9**	15.2%
10	9.44%	28.4%	49.0%				
11	15.2%	43.1%	67.9%				
≥12	≥24.6%	≥61.3%	≥85.3%				

*Best cut-of-value predicting incident stroke event by calculating the Youden index of the area under receive operating characteristic curve: Sensitivity + Specificity −1.
$CHADS_2$: congestive heart failure (1 point), hypertension (1 point), age ≥ 75 years (1 point), diabetes mellitus (1 point), stroke (2 points);
CHA_2DS_2-VASc: congestive heart failure (1 point), hypertension (1 point), age ≥ 65 years (1 point), age ≥ 75 years (2 points), diabetes mellitus (1 point), stroke (2 points), vascular diseases (1 point), female (1 point);
AF-CA-Stroke: refer to Table 2.

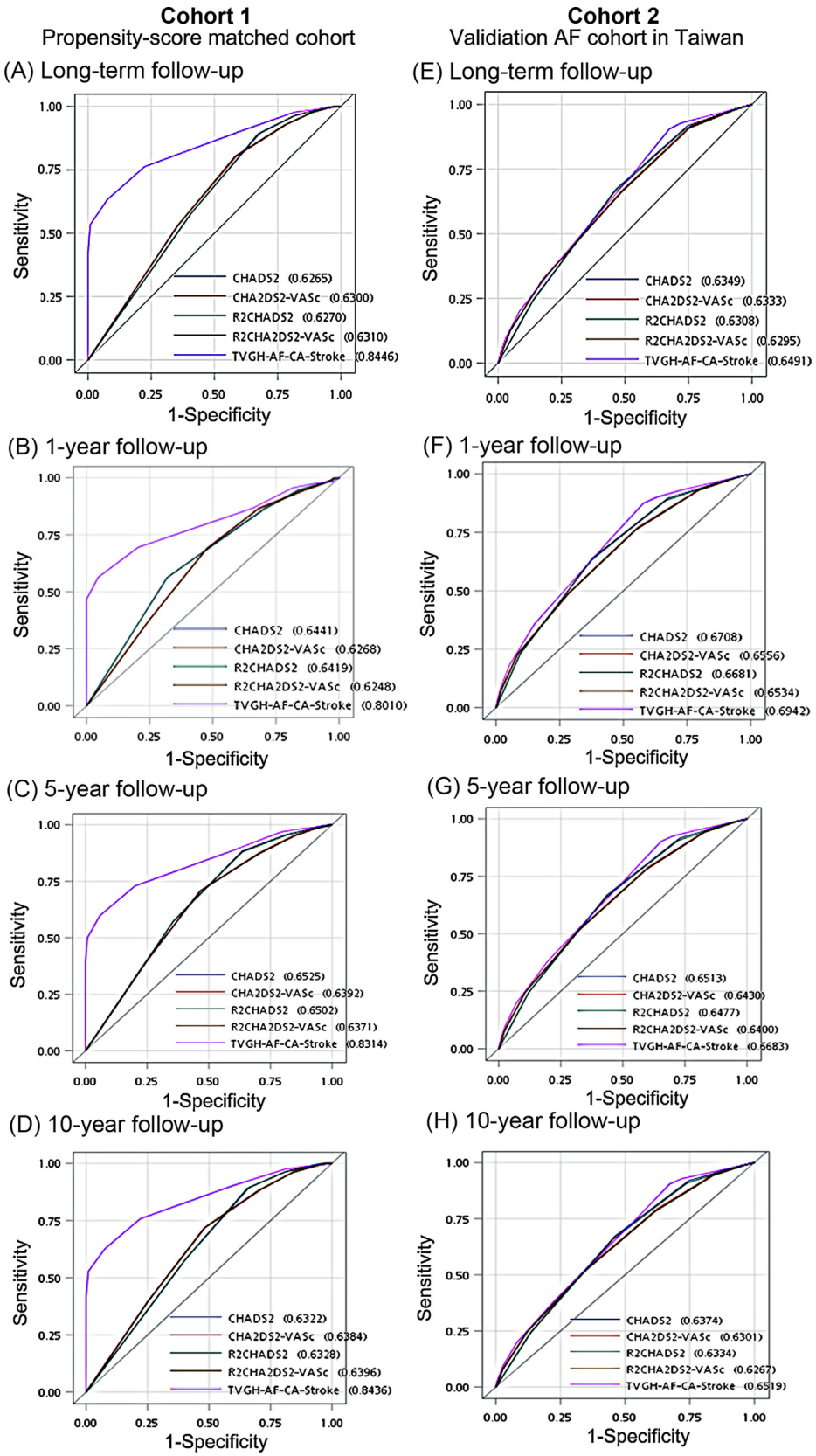

Fig. 3. Discrimination abilities of area under receive operating characteristic curves (ROC) for the propensity-score matched cohort (Cohort 1) during (A) long-term, (B) 1-year, (C) 5-year, and (D) 10-year follow-up ($P < 0.001$ when AF-CA-Stroke score compares with other all scores); and for the validation AF cohort (Cohort 2) during (E) long-term, (F) 1-year, (G) 5-year, and (H) 10-year follow-up ($P < 0.001$ when AF-CA-Stroke score compares with other all scores).

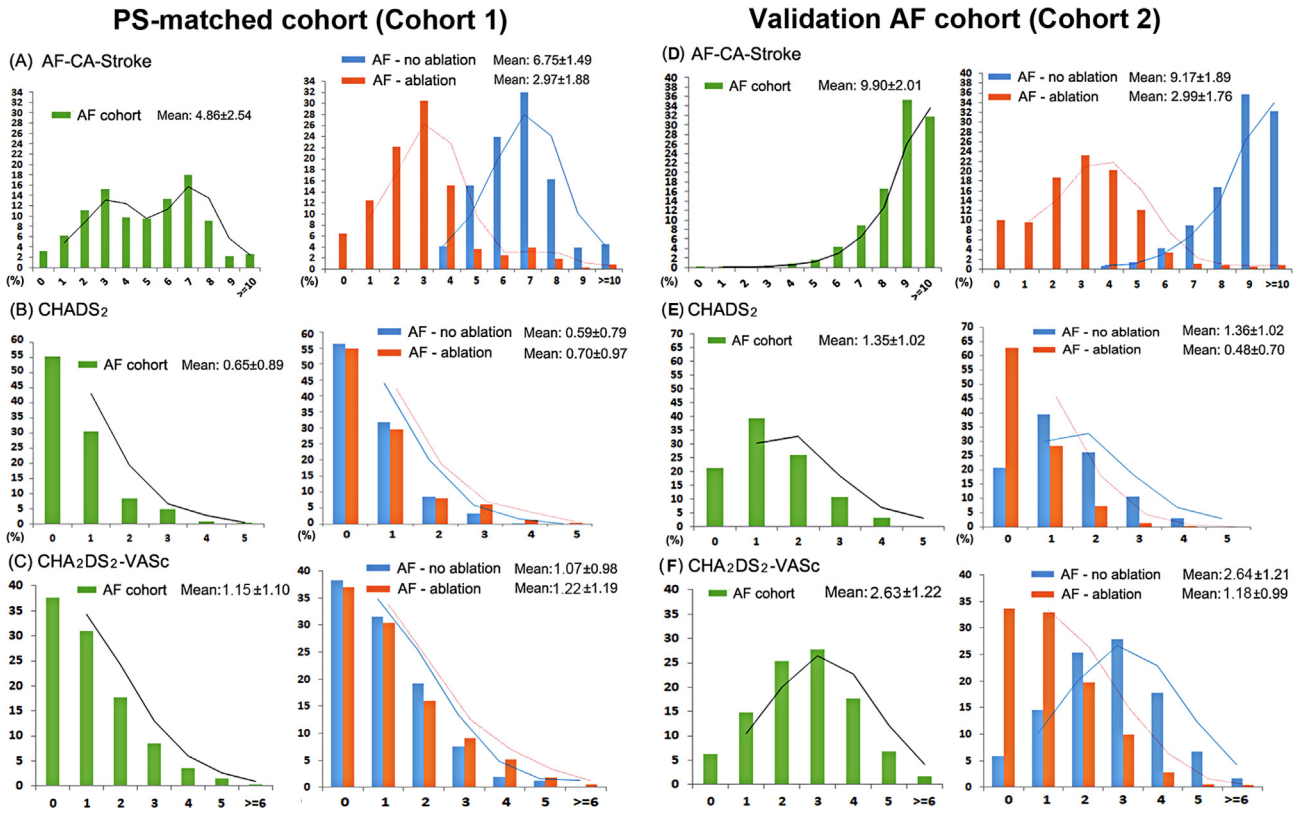

Fig. 4. Distributions among various soring systems and AF groups in the propensity-score (PS) matched cohort, for the scoring systems of (A) AF-CA-Stroke, (B) $CHADS_2$, and (C) CHA_2DS_2-VASc; and in the validation AF cohort in Taiwan, for the scoring systems of (D) AF-CA-Stroke, (E) $CHADS_2$, and (F) CHA_2DS_2-VASc. Trend line: moving average of stroke rate by every 2-unit score.

score, and CHA_2DS_2-VASc score might be used for stroke risk stratification in Asians as with Caucasians [29]. Previous studies suggested that patients with AF ablation with $CHADS_2$ score of "0" or CHA_2DS_2-VASc score of < 2 were indeed classified as low stroke risk [13], especially in patients with AF ablation [12,14].

In the era of catheter ablation, several observational studies in different countries have reported that AF ablation was an effective therapy in AF patients at various ages with multiple co-morbidities [30,31]. In AF patients receiving ablation, they had significantly decreased risks of stroke, AF-related complications, and mortality than AF patients receiving antiarrhythmic drugs but without AF ablation [32,33]. In the largest randomized (CABANA) trial for comparing the effects between antiarrhythmic drugs and AF ablation by using intention-to-treat analysis, AF ablation did not significantly reduce stroke risks in AF ablation group [34]. The reason of non-significant ablation effect on reducing stroke risk could be the crossovers between antiarrhythmic drugs and AF ablation during follow-up, which may affect the final outcomes.

This study firstly showed that the status of receiving AF ablation is a significant factor in the new scoring system with equivalent scores of 4 points in the risk stratification of the future stroke risk. Second, when assessing the risk of stroke after an ablation in low-risk patients based on AF-CA-Stroke scores, 19.5% in Cohort 1 and 15.3% in Cohort 2 were classified as moderate-to-high-risk group based on CHA_2DS_2-VASc scores, but classified as a low-risk group based on AF-CA-Stroke scores. The long-term outcome in terms of cardiovascular risk was confirmed (Table 4). In Cohort 1, the 1-year stroke rate was 0% for patients with AF ablation in the low-risk group according to AF-CA-Stroke and CHA_2DS_2-VASc score; whereas in Cohort 2, the 1-year stroke rates were 2.3–2.5% based on AF-CA-Stroke and CHA_2DS_2-VASc scores. That is, both AF-CA-Stroke and CHA_2DS_2-VASc scores can be used for assessing low stroke risk in AF patients in Asia. Based on the AF-CA-Stroke score, around 80–85% patients may take benefits form AF ablation procedures with lower stroke risks, and they may not be necessary to receive oral anticoagulants after receiving successful AF ablations (however, only around 65% AF patients were grouped as low risk group based on the CHA_2DS_2-VASc scores in this study). We suggest that long-term anticoagulants may be discontinued in around 80% of patients with AF ablation based on AF-CA-Stroke scores, irrespective of the recurrence state of ablation.

4.4. Limitations

This were several limitations in this study. First, the diagnoses were based on ICD-9-CM codes, which were established by the physicians and re-confirmed by a certified coding specialist, we could not exclude the possibility of miscoding. Second, information regarding the AF subtypes, AF recurrences, methods of AF ablation were not available in this study. Whether the above-mentioned status might affect the stroke outcome remains unclear. However, in the sub-analysis of this study using the TVGH AF ablation dataset in Cohort 1 (AF types were available only in AF ablation group in Cohort 1), AF patients with persistent AF were not associated with increased stroke risk. And we used AF-related admissions as the surrogate of AF recurrences, AF-related admissions in AF ablation group did not significantly affect the incident stroke risk. Third, the uses of medications such as anti-coagulation and anti-arrhythmic drugs may affect the stroke outcomes. However, due to this study was a cohort study, medication uses varied among patients. Besides, the study aim was to demonstrate a scoring system using the conventional risk factors plus the status of catheter

Table 4
Stroke rates during various follow-up periods based on risk groups and ablation status in Cohort 1 and Cohort 2.

All patients	**AF-CA-Stroke score**				**CHA_2DS_2-VASc**			
	Scores: 0–4	**Scores: 5–8**	**Scores: >8**	**All**	**Scores: 0–1**	**Scores: 2–4**	**Scores: >4**	**All**
PS-matched cohort (Cohort 1)	**N = 716 (45.5%)**	**N = 783 (49.7%)**	**N = 75 (4.8%)**	**N = 1574**	**N = 1080 (68.7%)**	**N = 465 (29.5%)**	**N = 29 (1.8%)**	**N = 1574**
1-year stroke	0.1%	4.7%	10.7%	2.8%	1.9%	4.5%	6.9%	2.8%
5-year stroke	0.2%	14.2%	38.7%	8.9%	6.0%	14.2%	31.0%	8.9%
10-year stroke	0.4%	22.7%	56.0%	14.2%	10.0%	21.5%	51.7%	14.2%
Validation cohort (Cohort 2)	**N = 2525 (1.7%)**	**N = 45931 (31.2%)**	**N = 98769 (67.1%)**	**N = 147225**	**N = 30871 (21.0%)**	**N = 104015 (70.6%)**	**N = 12339 (8.4%)**	**N = 147225**
1-year stroke	1.9%	7.0%	18.3%	14.5%	5.9%	14.7%	34.4%	14.5%
5-year stroke	5.0%	17.3%	33.2%	27.8%	14.4%	28.5%	55.1%	27.8%
10-year stroke	6.7%	21.8%	36.6%	31.5%	18.4%	32.2%	58.4%	31.5%
AF – no ablation	**AF-CA-Stroke score**				**CHA_2DS_2-VASc**			
	Scores: 0–4	**Scores: 5–8**	**Scores: >8**	**All**	**Scores: 0–1**	**Scores: 2–4**	**Scores: >4**	**All**
PS-matched cohort (Cohort 1)	**N = 33 (4.2%)**	**N = 688 (87.4%)**	**N = 66 (8.4%)**	**N = 787**	**N = 550 (69.9%)**	**N = 227 (28.8%)**	**N = 10 (1.3%)**	**N = 787**
1-year stroke	1.0%	4.3%	10.6%	4.6%	3.8%	6.6%	0.0%	4.6%
5-year stroke	4.1%	13.7%	37.9%	15.1%	11.8%	22.5%	30.0%	15.1%
10-year stroke	8.6%	21.7%	51.5%	23.8%	19.6%	32.6%	50.0%	23.8%
Validation cohort (Cohort 2)	**N = 972 (0.7%)**	**N = 45599 (31.3%)**	**N = 98757 (68.0%)**	**N = 145328**	**N = 29607 (20.4%)**	**N = 103396 (71.1%)**	**N = 12325 (8.5%)**	**N = 145328**
1-year stroke	1.0%	6.9%	18.3%	14.6%	6.1%	14.7%	34.3%	14.6%
5-year stroke	2.6%	17.2%	33.2%	28.0%	14.7%	28.5%	55.1%	28.0%
10-year stroke	3.7%	21.7%	36.6%	31.7%	18.8%	32.2%	58.4%	31.7%
AF – ablation	**AF-CA-Stroke score**				**CHA_2DS_2-VASc**			
	Scores: 0–4	**Scores: 5–8**	**Scores: >8**	**All**	**Scores: 0–1**	**Scores: 2–4**	**Scores: >4**	**All**
PS-matched cohort (Cohort 1)	**N = 683 (86.8%)**	**N = 95 (12.1%)**	**N = 9 (1.1%)**	**N = 787**	**N = 530 (67.3%)**	**N = 238 (30.3%)**	**N = 19 (2.4%)**	**N = 787**
1-year stroke	0.0%	7.4%	22.2%	1.0%	0.0%	2.5%	10.5%	1.0%
5-year stroke	0.0%	18.1%	44.4%	2.7%	0.0%	6.3%	31.6%	2.7%
10-year stroke	0.0%	29.7%	88.9%	4.6%	0.0%	10.9%	52.6%	4.6%
Validation cohort (Cohort 2)	**N = 1553 (81.9%)**	**N = 332 (17.5%)**	**N = 12 (0.6%)**	**N = 1897**	**N = 1264 (66.6%)**	**N = 619 (32.7%)**	**N = 14 (0.7%)**	**N = 1897**
1-year stroke	2.5%	18.3%	66.7%	5.2%	2.3%	9.7%	64.3%	5.2%
5-year stroke	6.5%	29.1%	75.0%	11.5%	6.1%	21.2%	78.6%	11.5%
10-year stroke	8.6%	31.4%	75.0%	14.4%	8.7%	24.6%	78.6%	14.4%

AF: atrial fibrillation; PS: propensity-score.

ablation for stroke management, as a result, we did not consider the effects of medication uses for constructing the scoring system. Finally, changes in therapy may occur over time due to changed status of ablation, underlying diseases, and age, the AF-CA-Stroke score shall be re-assessed annually. Because of lacking data on the comparisons between the novel and conventional scoring systems, it is difficult to conclude that the new scoring system might generate when applied to other populations. However, we provided 1-year, 5-year, and 10-year outcomes using a nationwide cohort with validation to support our study findings.

The large number of population-based AF cohort and the long-term follow-up were the advantages of our study in constructing a clinical model-based scoring system. The status of AF ablation in the PS-match cohort was provided by a medical center in Taiwan, and then, the cohort was linked to the NHIRD, regardless ablation outcomes of the study patients. The ablation strategy and the outcome may be different among centers; nevertheless, we still exhibited good discrimination ability for risk stratifications of stroke in patients with AF as calculated using the new scores.

5. Conclusion

A newly constructed clinical model-based point scoring system is useful in identifying risk stratifications of stroke in patients with AF using clinical factors, including various age stratifications and catheter ablation status. These clinical factors shall be considered as risk stratification for stroke prevention.

Funding

This work was supported by the Ministry of Science and Technology of Taiwan (MOST 109-2314-B-010-058-MY2); Grant of the Taipei Veterans General Hospital (V109D48-001-MY2-2, C19-027); Research Foundation of Cardiovascular Medicine (109-02-012); and Szu-Yuan Research Foundation of Internal Medicine (No. 110001).[1]

Declaration of Competing Interest

None of the authors have any conflicts of interest or financial relationships related to the study.

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[1] **Acknowledgement:** We appreciate the Health and Welfare Data Science Center, Taipei, Taiwan for providing the Taiwan's National Health Insurance database and Death Registry for analysis.

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