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$CHADS_2$ and CHA_2DS_2-VASc Scores in the Prediction of Clinical Outcomes in Patients With Atrial Fibrillation After Catheter Ablation

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Objectives This study aimed to evaluate whether $CHADS_2$ and CHA_2DS_2-VASc scores are useful for risk stratification in patients after catheter ablation of atrial fibrillation (AF).

Background AF is associated with increased risk of cardiovascular events. However, limited data are available on the predictors of adverse events in patients with AF after catheter ablation.

Methods A total of 565 patients with AF who underwent catheter ablation were enrolled in the study. The clinical endpoint was occurrence of thromboembolic events (ischemic stroke, transient ischemic attack, peripheral embolism, or pulmonary embolisms) or death during follow-up after catheter ablation.

Results During a follow-up of 39.2 ± 22.6 months, 27 patients (4.8%) experienced adverse events. Both the $CHADS_2$ and CHA_2DS_2-VASc scores were useful predictors of events in separate multivariate models. The areas under the receiver-operator characteristic curves based on the $CHADS_2$ and CHA_2DS_2-VASc scores in predicting events were 0.785 and 0.830, respectively. Although the difference did not reach statistical significance ($p = 0.116$), the CHA_2DS_2-VASc score could be used to further stratify the patients with $CHADS_2$ scores of 0 or 1 into 2 groups with different event rates (7.1% vs. 1.1%, $p = 0.003$) at a cutoff value of 2.

Conclusions The $CHADS_2$ and CHA_2DS_2-VASc scores are useful predictors of adverse events after catheter ablation of AF. (J Am Coll Cardiol 2011;58:2380–5) © 2011 by the American College of Cardiology Foundation

Atrial fibrillation (AF) is a common arrhythmia that represents an independent risk factor for strokes and is associated with marked morbidity and mortality (1). Recently, a newly developed scoring system, the CHA_2DS_2-VASc score, which extends the $CHADS_2$ scheme by considering additional stroke risk factors, was recommended to guide antithrombotic therapy in patients with AF (2,3). However, these 2 scoring systems were developed and validated in AF patients who did not receive catheter ablations. This study aimed to investigate whether the $CHADS_2$ or CHA_2DS_2-VASc score is useful for predicting thromboembolic events and mortality after catheter ablation for AF.

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Methods

A total of 565 consecutive patients with symptomatic drug-refractory AF who received radiofrequency catheter ablation were enrolled in the study. The $CHADS_2$ score was calculated for each patient (4). The CHA_2DS_2-VASc score was calculated for every patient based on a point system in which 2 points were assigned for a history of stroke or transient ischemic attack (TIA) or age ≥75 years. One point was assigned for age between 65 and 74 years; history of hypertension, diabetes, recent cardiac failure, and

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Table 1 Baseline Characteristics of the Patients With and Without Adverse Events

Variable	With Events (n = 27)	Without Events (n = 538)	p Value
Age, yrs	67.8 ± 12.7	53.5 ± 12.0	<0.001
Age ≥65 yrs	59.3%	17.8%	<0.001
Age ≥75 yrs	40.7%	3.0%	<0.001
Male	77.8%	72.3%	0.534
Medical history			
Hypertension	74.1%	45.0%	0.003
Diabetes mellitus	25.9%	11.9%	0.065
Congestive heart failure	33.3%	6.5%	<0.001
Coronary artery disease	66.7%	27.1%	<0.001
Previous stroke/TIA	25.9%	4.1%	<0.001
Previous vascular disease	7.4%	1.1%	0.052
Long-term use of warfarin	7.4%	3.2%	0.216
Left atrial diameter, mm	45.5 ± 11.8	39.1 ± 6.7	<0.001
LVEF, %	52.7 ± 11.0	58.9 ± 7.7	0.008
AF type (paroxysmal AF)	48.1%	79.4%	<0.001
Recurrence rate after ablations	59.3%	28.1%	<0.001
$CHADS_2$ score	2 (1–3)	1 (0–1)	<0.001
CHA_2DS_2-VASc score	3 (2–4)	1 (0–2)	<0.001

Values are mean ± SD, %, or median (interquartile range).
AF = atrial fibrillation; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.

vascular disease (myocardial infarction, complex aortic plaque, or peripheral artery disease); and female sex (2).

Catheter ablation of AF and anticoagulant strategy. Before catheter ablation, every patient underwent transesophageal echocardiography to confirm the absence of a left atrial thrombus. Details of ablation procedures are provided in the Online Appendix.

Before catheter ablation, the use of oral anticoagulation therapy with an adjusted dose of warfarin was based on the patients' $CHADS_2$ scores. Warfarin was intended to be prescribed for patients whose $CHADS_2$ scores were ≥2 to maintain the international normalized ratio (INR) of the prothrombin time between 2 and 3 (3). After catheter ablation, warfarin was continued for 3 months for patients who were already receiving warfarin treatment before ablation. After 3 months, discontinuation of warfarin was generally not considered for patients with $CHADS_2$ scores of ≥2. However, if patients remained symptom free, and there was no evidence of AF recurrences, replacement of warfarin with antiplatelet agents was considered. This was decided by the physicians responsible for treatment according to the individual characteristics of each patient.

Table 2 Univariate Cox Regression Analysis for Predictors of Adverse Events After Catheter Ablation

Variable	Hazard Ratio	95% CI	p Value
AF type (nonparoxysmal)	4.682	2.186–10.030	<0.001
Recurrence after multiple ablations	3.552	1.648–7.655	0.001
Left atrial diameter, mm	1.077	1.047–1.108	<0.001
LVEF, %	0.920	0.885–0.956	<0.001
$CHADS_2$ score	2.154	1.768–2.624	<0.001
CHA_2DS_2-VASc score	1.856	1.585–2.174	<0.001

CI = confidence interval; other abbreviations as in Table 1.

Abbreviations and Acronyms

AF = atrial fibrillation
INR = international normalized ratio
ROC = receiver-operator characteristic
TIA = transient ischemic attack

Definitions of the clinical endpoints and follow-up. The clinical endpoint was the combined occurrence of clinical events, including thromboembolic events (ischemic stroke, TIA, peripheral embolism, or pulmonary embolism) and death. Patients were followed-up every 1 to 3 months at our cardiology clinic or by referring physicians after catheter ablation. During each follow-up, patients were carefully examined, and 24-h Holter monitoring and/or cardiac event recording for 1 week were performed. AF recurrence was defined as an episode lasting longer than 1 min and confirmed by electrocardiograms 2 months after ablation. The status of patients who did not receive regular follow-up was assessed by chart reviews and telephone consultations to determine whether adverse events occurred. Our database was linked with the National Death Registry, and mortalities were further validated through a unique, lifelong personal identification number given to every Taiwan citizen.

Statistical analysis. Differences between continuous values were assessed using an unpaired 2-tailed *t* test for normally distributed continuous variables, the Mann-Whitney *U* test for skewed variables, and the chi-square test for nominal variables. Cox regression analysis was used to identify factors associated with adverse events. Details of the statistical analysis are provided in the Online Appendix.

Results

Clinical characteristics, adverse events, and predictors. Baseline characteristics of patients with and without events are shown in Table 1. During the follow-up period of 39.2 ± 22.6 months, 27 patients (4.8%) experienced adverse events, including death in 9 patients, ischemic stroke in 9, TIA in 6, pulmonary embolisms in 2, and peripheral embolism in 1. Three of the 27 patients experienced events within the blanking period after catheter ablation. Significant predictors of adverse events based on the univariate

Table 3 Multivariate Cox Regression Analysis for Predictors of Adverse Events After Catheter Ablation Using the $CHADS_2$ Score

Variable	Hazard Ratio	95% CI	p Value
AF type (nonparoxysmal)	1.804	0.752–4.328	0.186
Recurrence after multiple ablations	2.452	1.060–5.673	0.036
Left atrial diameter, mm	1.015	0.982–1.050	0.379
LVEF, %	0.977	0.936–1.021	0.308
$CHADS_2$ score	1.892	1.482–2.414	<0.001

Variables with p < 0.05 in Table 2 were adjusted with the $CHADS_2$ score in the multivariate Cox regression analysis.
Abbreviations as in Tables 1 and 2.

Table 4 Multivariate Cox Regression Analysis for Predictors of Adverse Events After Catheter Ablation Using the CHA_2DS_2-VASc Score

Variable	Hazard ratio	95% CI	p Value
AF type (nonparoxysmal)	1.927	0.800–4.644	0.144
Recurrence after multiple ablations	2.292	1.015–5.276	0.047
Left atrial diameter, mm	1.018	0.985–1.053	0.281
LVEF, %	0.973	0.931–1.017	0.219
CHA_2DS_2-VASc score	1.678	1.393–2.021	<0.001

Variables with $p < 0.05$ in Table 2 were adjusted with the CHA_2DS_2-VASc score in the multivariate Cox regression analysis.
Abbreviations as in Tables 1 and 2.

Cox regression analysis are shown in Table 2. The $CHADS_2$ and CHA_2DS_2-VASc scores remained independent predictors of adverse events in separate multivariate models (Tables 3 and 4). Besides the $CHADS_2$ and CHA_2DS_2-VASc scores, AF recurrence after multiple procedures was a significant predictor of adverse events. The event rate was higher in patients with recurrences than in patients without recurrences (9.6% vs. 2.8%, p = 0.001). When events were further divided into ischemic stroke/TIA, other embolic events, and death, the $CHADS_2$ and CHA_2DS_2-VASc scores remained significant predictors. Hazard ratios of each increment of the $CHADS_2$ scores to predict ischemic stroke/TIA, other embolic events, and death were 1.893 (95% confidence interval [CI]: 1.364 to 2.627, p < 0.001), 2.306 (95% CI: 1.116 to 4.764, p = 0.024), and 1.786 (95% CI: 1.159 to 2.754, p = 0.009), respectively. Similarly, hazard ratios of each increment of the CHA_2DS_2-VASc scores to predict ischemic stroke/TIA, other embolic events, and death were 1.694 (95% CI: 1.321 to 2.173, p < 0.001), 2.088 (95% CI: 1.1865 to 3.6789, p = 0.011), and 1.551 (95% CI: 1.108 to 2.171, p = 0.010), respectively. The usefulness of these 2 scoring systems in predicting strokes/TIAs was consistent in patients with and without recurrences.

$CHADS_2$ and CHA_2DS_2-VASc scores for prediction of adverse events. The event rates of patients continuously increased with increases in the $CHADS_2$ and CHA_2DS_2-VASc scores (Fig. 1). Figure 2 shows the receiver-operator characteristic (ROC) curves for predicting events after catheter ablation based on the $CHADS_2$ and CHA_2DS_2-VASc scores. At a cutoff point of 2 identified by the ROC curve, Kaplan-Meier survival analysis showed that patients with $CHADS_2$ scores of ≥2 (sensitivity, 59.3%; specificity, 83.5%) were associated with a higher event rate than the patients with $CHADS_2$ scores of <2 (15.2% vs. 2.4%, p < 0.001) during the follow-up period (Fig. 3A). Furthermore, a CHA_2DS_2-VASc score of ≥2 identified by the ROC curve (sensitivity, 85.2%; specificity, 66.5%) also significantly predicted occurrences of events (11.3% vs. 1.1%, p < 0.001) (Fig. 3B).

CHA_2DS_2-VASc scores and adverse events in low-risk patients with $CHADS_2$ scores of 0 or 1. In the subgroup analysis of 460 patients with $CHADS_2$ scores of 0 or 1, 11 (2.4%) patients experienced adverse events. The event rate progressively increased from 0.6% in patients with CHA_2DS_2-VASc scores of 0 to 11.8% in patients with CHA_2DS_2-VASc scores of 3 (Fig. 4). Using a CHA_2DS_2-VASc score of 2 as the cutoff point, patients with CHA_2DS_2-VASc scores of ≥2 were associated with a higher event rate as compared with patients whose CHA_2DS_2-VASc scores were <2 (7.1% vs. 1.1%, p = 0.003) (Fig. 5).

Discussion

Main findings. The main findings were as follows: $CHADS_2$ and CHA_2DS_2-VASc scores were useful parameters for predicting adverse events after catheter ablation of AF; and the CHA_2DS_2-VASc score was helpful in further risk stratifications among patients with $CHADS_2$ scores of 0 or 1.

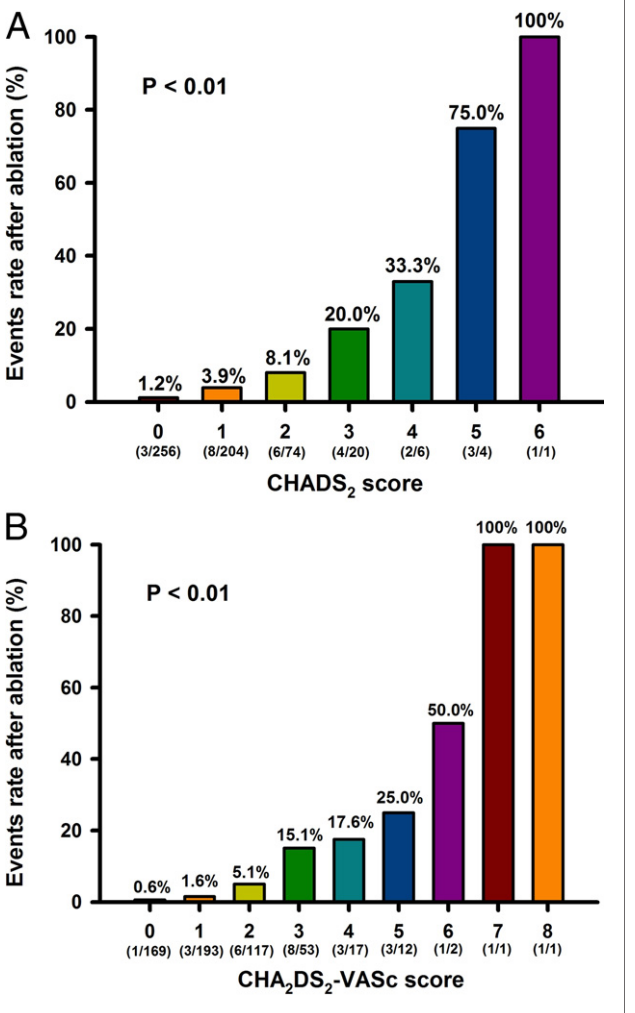

Figure 1 Event Rates and Scores

The adverse event rates continuously increased when the $CHADS_2$ **(A)** and CHA_2DS_2-VASc **(B)** scores became higher.

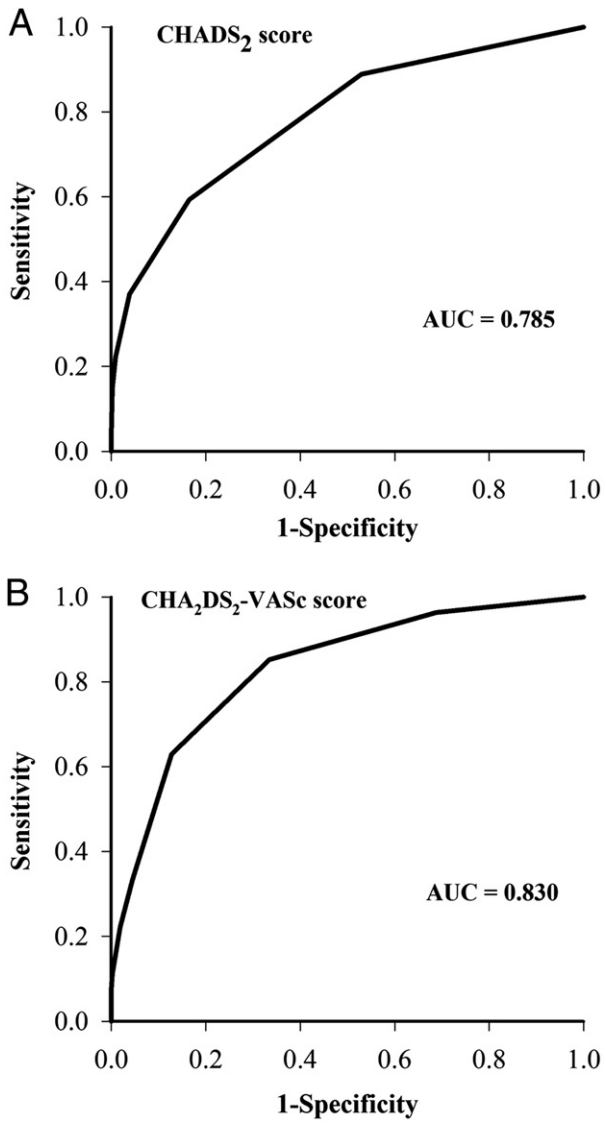

Figure 2 **ROC Curves for the $CHADS_2$ and CHA_2DS_2-VASc Scores for Predicting Events**

The areas under the curves (AUCs) for the $CHADS_2$ **(A)** and CHA_2DS_2-VASc **(B)** scores for predicting adverse events were 0.785 and 0.830, respectively ($p = 0.116$). ROC = receiver-operator characteristic.

$CHADS_2$ and CHA_2DS_2-VASc scores and adverse events after catheter ablation. In the current study, both scores proved to be useful predictors of events after catheter ablation of AF in separate multivariate models. These results provide evidence for extending the usefulness of $CHADS_2$ and CHA_2DS_2-VASc scores to predict adverse events in AF patients who have received catheter ablation. In view of the ROC curves based on the $CHADS_2$ and CHA_2DS_2-VASc scores in predicting events, the differences between the areas under the curves did not reach statistical significance ($p = 0.116$). This may be because of the low event rate of the current study. Therefore, further trials with a larger sample size may be able to demonstrate a significant statistical difference with sufficient power.

Although the predictive accuracies of the $CHADS_2$ and CHA_2DS_2-VASc scores assessed by the ROC curves did not differ significantly, the CHA_2DS_2-VASc scores could further stratify the patients with $CHADS_2$ scores of 0 or 1 into 2 groups with different risks of events at the cutoff value of 2. According to the flowchart of the current guidelines of the European Society of Cardiology on the use of oral anticoagulants after catheter ablations, the $CHADS_2$ scheme should be used as a simple initial means of assessing stroke risk, and chronic oral anticoagulant therapy is recommended for patients with $CHADS_2$ scores of ≥ 2. For patients with a $CHADS_2$ score of 0 or 1, it is recommended that the CHA_2DS_2-VASc scoring system be used for a more comprehensive assessment of the risks (3). However, this recommendation was mainly based on consensus among experts, and the data in patients who received catheter ablation of AF were insufficient. The results

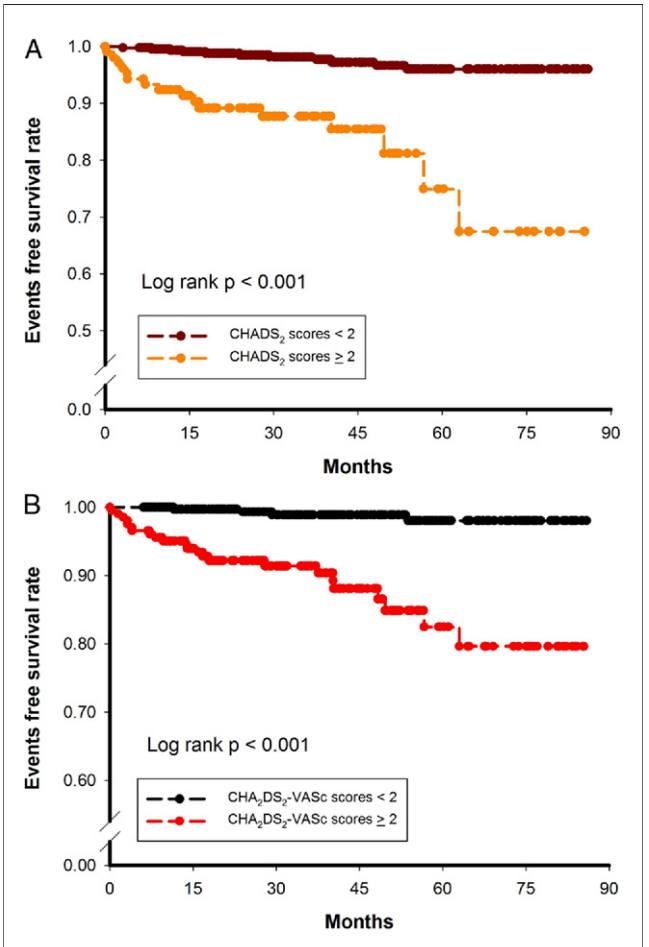

Figure 3 **Event-Free Survival Curves for Patients With Different $CHADS_2$ and CHA_2DS_2-VASc Scores**

Kaplan-Meier survival analysis showed that the patients with $CHADS_2$ scores of ≥ 2 were associated with a higher event rate compared with the patients with $CHADS_2$ scores of <2 (15.2% vs. 2.4%, $p < 0.001$) **(A)**. Furthermore, a CHA_2DS_2-VASc score of ≥ 2 identified by the receiver-operator characteristic curve also significantly predicted occurrences of events (11.3% vs. 1.1%, $p < 0.001$) **(B)**.

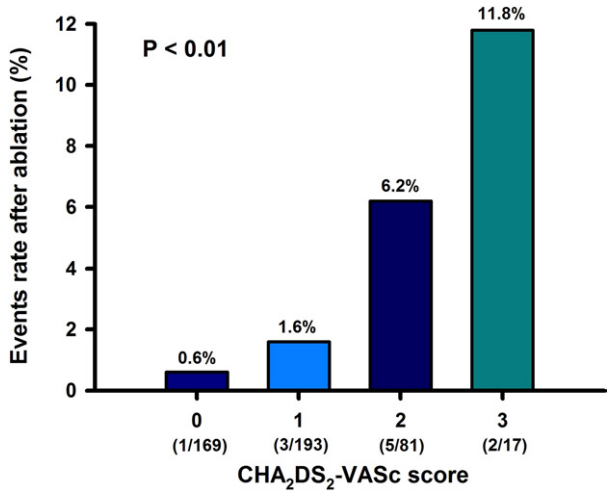

Figure 4 Event Rates in the Patients With $CHADS_2$ Scores of 0 or 1

The event rates progressively increased from 0.6% to 11.8% in patients with different CHA_2DS_2-VASc scores.

of the present study may provide the evidence for the basis of the previously mentioned flowchart.

Clinical applications of $CHADS_2$ and CHA_2DS_2-VASc scores. Oral et al. (5) reported that discontinuation of anticoagulant therapy appears to be safe after successful ablation of AF. Recently, Bunch et al. (6) reported that among patients with AF, the stroke risk was lower in patients who underwent catheter ablation than in those who did not. The 3-year stroke rate (2% to 3%) was similar to that of our study. However, these previous studies did not provide a useful method to identify patients with high risk of events. According to the results of the present study, the $CHADS_2$ scoring scheme can be used to screen patients with $CHADS_2$ scores of ≥2 who are predisposed to adverse events after catheter ablation. Furthermore, a more detailed CHA_2DS_2-VASc scoring scheme can further identify patients with risk of events among patients with $CHADS_2$ scores of <2. The clinical use of CHA_2DS_2-VASc scores should be emphasized because among patients with $CHADS_2$ scores of 0 or 1 who were traditionally assumed to be at low risk, those with CHA_2DS_2-VASc scores of 3 can have an event rate as high as 11.8%. Among the 9 patients who experienced stroke, 2 patients were receiving long-term medication with warfarin and had an INR within the therapeutic range at the time the events occurred. Five and 8 patients had $CHADS_2$ and CHA_2DS_2-VASc scores of ≥2, respectively. Of the 4 patients with $CHADS_2$ scores of 0 or 1, 3 had CHA_2DS_2-VASc scores of ≥2. This may further demonstrate the important role of the CHA_2DS_2-VASc score in identifying low-risk patients who are at risk of stroke; an anticoagulant should be prescribed to lower this risk. Furthermore, for patients with scores indicating a high risk of stroke and who are receiving warfarin treatment, it may be helpful to monitor the INR level more closely to avoid suboptimal treatment. However, a further prospective and large-scale trial is necessary to prove this supposition.

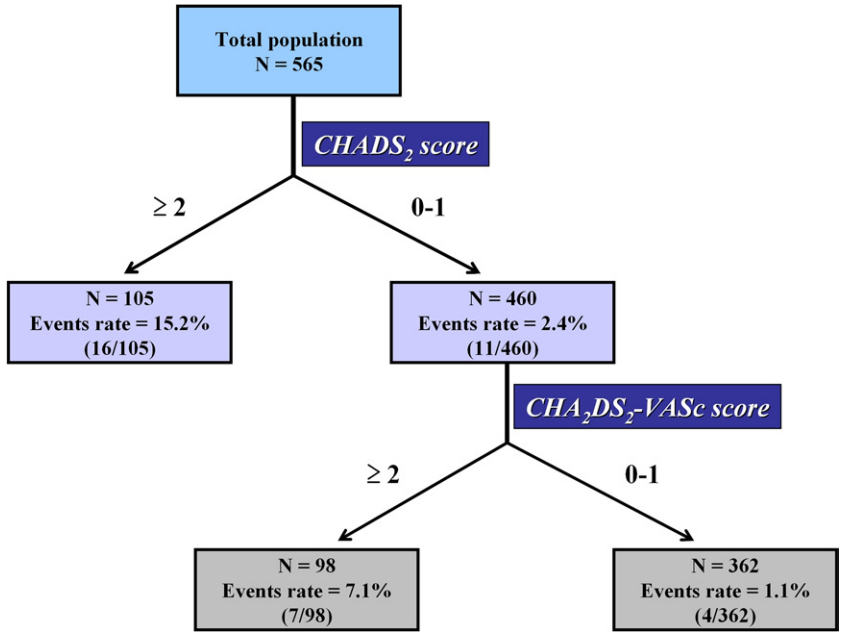

Figure 5 Flowchart of Event Rates and Scores

A flowchart demonstrating the event rates in the patients stratified according to the $CHADS_2$ and CHA_2DS_2-VASc scores.

Study limitations. First, although the follow-up was not uniform for every patient, more than 70% of the study population underwent follow-up regularly at the cardiology clinics, and the remaining patients were completely assessed through telephone consultations. The accuracy of mortality events was further confirmed through the National Death Registry of Taiwan. Second, the strategy about the use of warfarin was determined by the physicians responsible for treatment according to the individual characteristics of each patient. However, the management was based on the same principle for individuals with similar risk. Moreover, long-term use of warfarin after catheter ablation was not a significant predictor of adverse events based on the analysis and therefore may not confound the results of the present study. Last, although only 18.6% of the patients in the study had $CHADS_2$ scores ≥ 2, the mean person-years of follow-up was $>1{,}500$, which was sufficient to show statistical significance in a population with low event rates.

Conclusions

$CHADS_2$ and CHA_2DS_2-VASc scores can provide an estimate of the risk of adverse events in patients who undergo catheter ablation of AF. Among patients with $CHADS_2$ scores of 0 or 1, CHA_2DS_2-VASc scores were useful to further identify which patients were predisposed to adverse events.

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REFERENCES

1. Wolf PA, Mitchell JB, Baker CS, et al. Impact of atrial fibrillation on mortality, stroke, and medical costs. Arch Intern Med 1998;158:229–34.
2. Lip GY, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro heart survey on atrial fibrillation. Chest 2010;137:263–72.
3. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J 2010;31:2369–429.
4. Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA 2001;285:2864–70.
5. Oral H, Chugh A, Ozaydin M, et al. Risk of thromboembolic events after percutaneous left atrial radiofrequency ablation of atrial fibrillation. Circulation 2006;114:759–65.
6. Bunch TJ, Crandall BG, Weiss JP, et al. Patients treated with catheter ablation for atrial fibrillation have long-term rates of death, stroke, and dementia similar to patients without atrial fibrillation. J Cardiovasc Electrophysiol 2011;22:839–45.

Key Words: atrial fibrillation ■ catheter ablation ■ $CHADS_2$ score ■ CHA_2DS_2-VASc score.

APPENDIX

For an expanded Methods section, please see the online version of this article.