Renal Dysfunction, Stroke Risk Scores ($CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2), and the Risk of Thromboembolic Events After Catheter Ablation of Atrial Fibrillation

The Leipzig Heart Center AF Ablation Registry

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Background—There are limited data on the predictive value of stroke risk scores for thromboembolic events (TEs) after catheter ablation of atrial fibrillation (AF). Our objectives were to report the incidence of TEs after AF ablation in a large contemporary AF ablation cohort and to investigate the impact of renal dysfunction and the value of stroke risk stratification scores ($CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2) for predicting TE after AF ablation.

Methods and Results—Using the Leipzig Heart Center AF Ablation Registry, we documented TEs in patients undergoing radiofrequency AF catheter ablation. TE was defined as stroke, transient ischemic attack, or systemic embolism. Study population (N=2069; 66% men; 60±10 years; 62% paroxysmal AF; mean $CHADS_2$, 1.2±0.9; CHA_2DS_2-VASc, 2.1±1.4; and R_2CHADS_2, 1.3±1.1) were followed up for a median 18 (Q1–Q3, 12–29) months (ie, 3078 patient-years). Overall, 31 TEs occurred, with 16 events within 30 days of ablation and 15 TEs (0.72%) during the follow-up period. On multivariate analysis, $CHADS_2$ (P<0.001), R_2CHADS_2 (P<0.001), and CHA_2DS_2-VASc (P=0.003) scores were independent predictors of TEs during follow-up, and AF recurrence conferred a nonsignificant trend for increased TE risk (P=0.071–0.094). The CHA_2DS_2-VASc score further differentiated TE risk in patients with $CHADS_2$ and R_2CHADS_2 0 to 1 (0.13% if CHA_2DS_2-VASc was 0–1 and 0.71% if CHA_2DS_2-VASc was >2) and had the best predictive value in patients with AF recurrences (c-index 0.894, P=0.022 versus $CHADS_2$, P=0.031 versus R_2CHADS_2).

Conclusions—$CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores were associated with TE risk. The CHA_2DS_2-VASc score differentiated TE risk in the low-risk strata based on $CHADS_2$ and R_2CHADS_2 scores and may be superior in the subgroup with AF recurrences. **(*Circ Arrhythm Electrophysiol*. 2013;6:868-874.)**

Key Words: AF recurrences ■ atrial fibrillation ■ catheter ablation ■ CHA_2DS_2-Vasc score ■ thromboembolic complications

Catheter ablation of atrial fibrillation (AF) is an effective therapy for the reduction of AF burden, improvement of symptoms, and quality of life.[1,2] Major complications occur between 3.9% and 5.1% and can include thromboembolic complications in 1%.[3–6] Although the thromboembolic risk seems to be increased after ablation, there is the suggestion of a reduction in thromboembolic event (TE) rates during long-term follow-up.[7] Observational and registry studies have demonstrated low annual rates of TE (strokes and systemic embolism) during midterm follow-up after AF catheter ablation ranging between 0.5[8] and 1.7%,[9] thus reaching event rates that are broadly comparable with patients without AF.[7,9]

Clinical Perspective on p 874

There are only limited data on risk prediction scores for TE after AF ablation. Although previous studies suggest that both the $CHADS_2$ and CHA_2DS_2-VASc scores, as well as renal dysfunction, are useful predictors for thromboembolic complications after ablation, they are hampered by small sample sizes, inclusion of few high-risk patients, incomplete follow-up, and an unknown number of patients on anticoagulation with possible underuse.[4,10,11]

Renal dysfunction was incorporated in the R_2CHADS_2 risk score by adding 2 additional points for estimated glomerular

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filtration rate (eGFR) <60 mL/min per 1.73 m^2 as an additional risk factor to the $CHADS_2$ score and demonstrated marginal additive predictive power over the $CHADS_2$ score in predicting TE in a selected anticoagulated trial patient cohort with nonvalvular AF,[12] whereas in real-world cohorts, renal impairment did not independently add to stroke risk scores to improve their predictive value.[13,14] Despite this controversy, this score has not been evaluated in patients with AF after catheter ablation.

Our objectives were to report the incidence of TE (and its predisposing factors) after AF ablation in a large contemporary AF ablation registry and second, to investigate the impact of renal dysfunction and the value of stroke risk stratification scores ($CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2) for predicting TE after AF ablation.

Methods

Patients and Risk Scores

The study population comprised 2069 consecutive patients with symptomatic AF who underwent radiofrequency catheter ablation at the Heart Center Leipzig between January 2007 and December 2011. Stroke risk was assessed using the $CHADS_2$ (Congestive heart failure, Hypertension, Age >75 years, Diabetes mellitus, and history of Stroke/transient ischemic attack [2 points])[15] and CHA_2DS_2-VASc (Congestive heart failure, Hypertension, Age >75 years [2 points], Diabetes mellitus, and history of Stroke/transient ischemic attack [2 points]–Vascular disease [history of myocardial infarction, peripheral artery disease, or vascular plaques], Age 65–74 years, and Sex category [female]) scores.[16,17] The R_2CHADS_2 score incorporated the components of the $CHADS_2$ score and also gave 2 points for renal dysfunction defined as eGFR <60 mL/min.[12] eGFR was calculated using the Cockroft–Gault equation: (140–age)×weight (kg)×(0.85 if female)/72×serum creatinine (mg/dL).

Catheter Ablation and Follow-Up

Left atrial catheter ablation was performed using a previously described approach.[18] Patients presenting with AF at the beginning of the procedure were electrically cardioverted, and ablation was performed during sinus rhythm (ie, AF termination with ablation was not attempted). In all patients circumferential left atrial ablation lines were placed around the antrum of the ipsilateral pulmonary veins (irrigated tip catheter, preselected tip temperature of 48°C, and maximum power of 30–50 W). In patients with persistent AF, additional linear lesions were added at the left atrial roof, the basal posterior wall, and the left atrial isthmus and according to low voltage areas. Ablation of complex fractionated electrograms was not performed. After circumferential line placement, voltage and pace mapping along the ablation line were used to identify and close gaps. The isolation of all pulmonary veins with bidirectional block was verified with a multipolar circular mapping catheter and was defined as the procedural end point. After ablation, class I and III antiarrhythmic drugs were not reinitiated, and proton pump inhibitors were added for 4 weeks.

According to the current guidelines,[16] oral anticoagulation was prescribed for 3 to 6 months after ablation and depending on the $CHADS_2$ or CHA_2DS_2-VASc score thereafter. Because of patient preferences, lack of symptoms, and ECG recordings of sinus rhythm, it was replaced by aspirin in some patients.[19]

All patients were followed up in the outpatient clinic for ≥12 months after the catheter ablation. During follow-up, serial 7-day Holter ECG recordings were performed immediately and at 3, 6, and 12 months after the procedure. Additional ECGs and Holter ECG recordings were obtained when patients' symptoms were suggestive of AF. AF recurrence was defined as a documented atrial arrhythmia episode lasting longer than 30 seconds after a 3-month blanking period.

Outcomes

The primary end point of this study was the composite of ischemic stroke, transient ischemic attack, and systemic embolism during follow-up excluding events within the first 30 days after ablation. Ischemic stroke was a clinical diagnosis that was made on the basis of typical symptoms lasting ≥24 hours. Brain imaging, which was available in the vast majority of patients, was not required but was recommended for the general diagnosis of stroke. A transient ischemic attack was defined as sudden-onset focal neurological deficit with duration of <24 hours. Systemic embolism was defined as TEs that occurred in peripheral organs (eg, spleen) or extremities.

Statistical Analysis

Data are presented as mean and SD for normally distributed continuous variables and as proportions for categorical variables. Continuous variables were tested for normal distribution using the Kolmogorov–Smirnov test. The differences between continuous values were assessed using an unpaired 2-tailed *t* test for normally distributed continuous variables, a Mann–Whitney test for skewed variables, and a χ^2 test for nominal variables.

Cox regression analyses were used to identify factors associated with TEs (stroke, transient ischemic attack, and systemic embolism). Multivariable analysis, which included variables with a *P* value <0.1 found on univariate analysis, was performed to identify independent predictors of TE. In addition, we performed multivariate analysis separately for every stroke risk stratification score with adjustment for renal dysfunction (for the $CHADS_2$ and CHA_2DS_2-VASc scores) or peripheral artery disease (for the $CHADS_2$ and R_2CHADS_2 scores).

Receiver operating characteristic curves were generated for graphical illustration of $CHADS_2$, R_2CHADS_2, and CHA_2DS_2-VASc scores' performance in predicting TE, with the area under the curve being equivalent to the c-index for determining the predictive value for a score. The c-indexes (ie, areas under the receiver operating characteristic curves) for the 3 scores were compared using DeLong method.[20] A *P* value of <0.05 was considered statistically significant. All analyses were performed with SPSS statistical software version 17.

Results

Patient Characteristics and TEs

The clinical characteristics are summarized in Table 1. Complete rhythm follow-up was available in 1557 patients (75.3%) revealing AF recurrences in 25.8%.

Overall, TE occurred in 31 patients (1.5%). Sixteen patients (0.8%) had TE within first 30 days after catheter ablation.

During the follow-up period of median of 18 (Q1–Q3, 12–29) months (ie, 3078 patient-years), 15 (0.72%) experienced TE, including 5 ischemic strokes, 9 transient ischemic attacks, and 1 systemic embolism. The characteristics of those patients with TEs during follow-up are shown in Table I in the online-only Data Supplement. The median (Q1–Q3) time to event was 11 (6–19) months. All patients with TE were anticoagulated at the time of event. The mean international normalized ratio at discharge for the patients on vitamin K antagonists in TE cohort was 1.5±0.5 and 2.37±0.75 at the time of TE.

Common Risk Scores as Predictors of TEs

Patients with TE had more frequently a history of previous TE, renal dysfunction, and recurring AF, as well as higher $CHADS_2$, R_2CHADS_2, and CHA_2DS_2-VASc scores (Table 1). Using 3 separate multivariate Cox regression (Table 2) analyses of the entire cohort, the $CHADS_2$, R_2CHADS_2, and CHA_2DS_2-VASc scores were significant predictors of TEs.

Table 1. Baseline Characteristics of the Study Population Stratified According to TEs During Follow-Up

	Total	TE in Follow-Up		
%	N=2069	No (n=2054)	Yes (n=15)	*P* Value
Age, y	60±10	60±10	64±11	0.214
Men	66	66	60	0.601
AF type (paroxysmal)	63	63	53	0.443
FU months, median (Q1–Q3)	18 (12–29)	18 (12–28)	26 (20–35)	0.184
BMI, kg/m^2	28±5	29±5	27±5	0.363
eGFR, mL/min per 1.73 m^2	100±34	100±34	88±25	0.147
Hypertension	71	71	93	0.055
Diabetes mellitus	15	15	27	0.211
Coronary artery disease	14	14	27	0.172
Chronic heart failure	7	7	13	0.351
Peripheral artery disease	8	8	20	0.078
Renal dysfunction	7	7	20	0.047†
Previous thromboembolic events	9	9	33	0.001†
Peri-interventional stroke/TIA	0.8	0.8	0	0.731
$CHADS_2$	1.2±0.9	1.2±0.9	2.1±1.3	<0.001†
R_2CHADS_2	1.3±1.1	1.3±1.1	2.5±1.6	<0.001†
CHA_2DS_2-VASc	2.1±1.4	2.1±1.4	3.5±1.7	<0.001†
LVEF, %	59±10	59±10	53±16	0.233
LVEDd, mm	49±8	49±7	51±12	0.479
LAD, mm	43±6	43±6	45±9	0.392
No. of ablations (mean±SD) Median (Q1–Q3)	1.42±0.73 1 (1–2)	1.42±0.73 1 (1–2)	1.47±0.74 1 (1–2)	0.801
AF recurrence*	25.8	25.6	53.3	0.014†

AF indicates atrial fibrillation; BMI, body mass index; eGFR, estimated glomerular filtration rate; LAD, left atrial diameter; LVEDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; TE, thromboembolic event; and TIA, transient ischemic attack.

*Complete rhythm follow-up was available for 1557 patients.

†indicates significant *P* value.

Based on receiver operating characteristic curve analysis, all 3 risk stratification scores had good predictive value (c-indexes: 0.720 [0.700–0.739] for $CHADS_2$ and 0.736 [0.716–0.755] for both R_2CHADS_2 and CHA_2DS_2-VASc scores) for predicting TE ($P<0.05$ for all scores) without any significant difference among the scores (Figure 1). As shown in Figure 2, the CHA_2DS_2-VASc score was able to further differentiate TE risk in patients with $CHADS_2$ and R_2CHADS_2 0 to 1. In those patients, TE occurred in 0.13% if CHA_2DS_2-VASc was 0 to 1 and 0.62% to 0.71% if the CHA_2DS_2-VASc score was ≥2.

There was no association between antiarrhythmic drug usage after catheter ablation and TE at follow-up ($P=0.810$). Anticoagulation regimes at discharge and at 6-month

Table 2. Clinical Predictors for TE in the Entire Cohort (N=2069)

Cox Regression	UV			MV*		Model 1	MV		Model 2	MV		Model 3
Variables	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Hypertension	5.3	0.69–40.4	0.107									
PAD	3.2	0.89–11.3	0.093	2.2	0.61–8.0	0.229	2.2	0.6–7.8	0.241			
Previous TE	5.3	1.8–15.4	0.002†									
RD	3.5	0.99–12.5	0.052	2.3	0.6–8.5	0.195				1.9	0.52–7.1	0.327
$CHADS_2$	2.0	1.4–2.9	<0.001†	1.9	1.3–2.8	0.001†						
R_2CHADS_2	1.8	1.4–2.5	<0.001†				1.8	1.3–2.4	<0.001†			
CHA_2DS_2-VASc	1.7	1.3–2.3	<0.001†							1.6	1.2–2.2	0.001†

CI indicates confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; MV, multivariate analysis; PAD, peripheral artery disease; RD, renal dysfunction (eGFR <60 mL/min per 1.73 m^2); TE, thromboembolic events; and UV, univariate analysis.

*Although hypertension and previous TE had a *P* value <0.1 in univariate analysis, we did not include them into multivariate analysis because of their inclusion in to all risk scores.

†indicates significant *P* value.

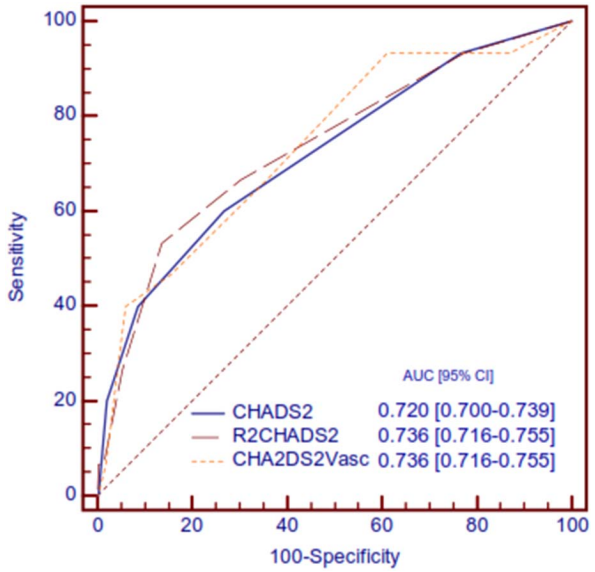

Figure 1. Receiver operating characteristic curves for the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores in predicting thromboembolic events in the entire cohort (N=2069). Significance levels: $CHADS_2$ vs R_2CHADS_2, *P*=0.617; $CHADS_2$ vs CHA_2DS_2-VASc, *P*=0.674; and R_2CHADS_2 vs CHA_2DS_2-VASc, *P*=0.996. AUC indicates area under the curve (equivalent to c-index); and CI, confidence interval.

follow-up were also not associated with TE (*P*=0.901 and *P*=0.138).

Impact of AF Recurrences

The importance of AF recurrences on TE occurrence after catheter ablation was examined in a subgroup of 1557 patients (75.3%) with complete rhythm follow-up data

Predictors for TE in patients with available rhythm outcomes are presented in Table II in the online-only Data Supplement. All 3 stroke risk stratification scores were associated with TE, whereas AF recurrence conferred a nonsignificant trend for increased TE risk (depending on the multivariable model *P*=0.056–0.077).

In patients with AF recurrence (n=402; 26%), all 3 risk scores were also associated with TE (Table III in the online-only Data Supplement), with the CHA_2DS_2-VASc score having the best c-index (0.894; 95% confidence interval, 0.860–0.923; Figure I in the online-only Data Supplement), superior to $CHADS_2$ (*P*=0.022) and R_2CHADS_2 (*P*=0.031).

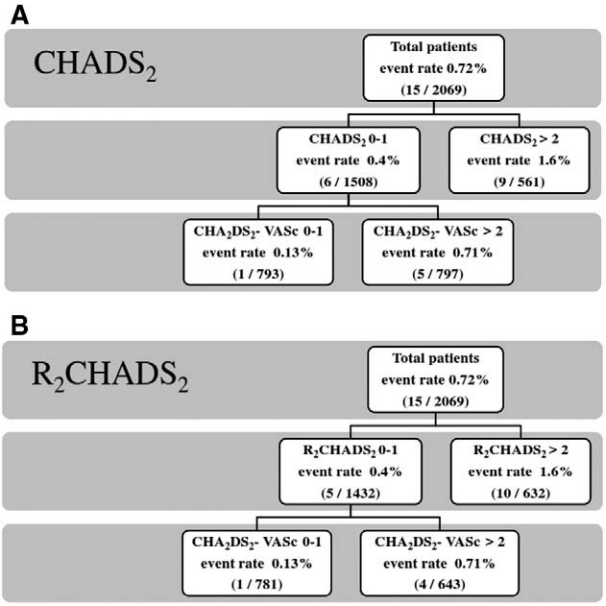

Figure 2. Thromboembolic events according to different scoring systems**. A**, $CHADS_2$ score. **B**, R_2CHADS_2 score.

Discussion

To the best of our knowledge, this is the largest study assessing the incidence and risk factors for thromboembolic complications after AF catheter ablation during midterm follow-up with a special focus on renal dysfunction and stroke risk stratification scores. The main findings are that TE after AF catheter ablation are rare, but all 3 stroke risk stratification scores (ie, $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2) are associated with TE risk. The CHA_2DS_2-VASc was useful to differentiate stroke risk in low-thromboembolic risk strata according to the $CHADS_2$ and R_2CHADS_2 scores. Also, the CHA_2DS_2-VASc had the best predictive value for TE in the subgroup with AF recurrences.

Several studies have suggested lowered stroke rates after catheter ablation.[21,22] With 4212 patients included and followed up for ≥3 years, Bunch et al[9] reported that AF ablation may not only reduce stroke, but also reduce mortality risk compared with patients with AF without ablation, with event rates even reaching levels seen among patients without AF. More recently, Lin et al[11] reported a small cohort showing a significant risk reduction of TE in patients after catheter ablation compared with those who received antiarrhythmic medication (2.3% versus 8.6%). In our study with >2000 patients with drug-refractory AF undergoing catheter ablation, we have observed a low rate of TE, which is in accordance with several studies[7,8] The strength of our study is the use of a large contemporary cohort of consecutive patients undergoing ablation therapy for AF with guideline-adherent peri- and postprocedural anticoagulation.

The importance of $CHADS_2$ and CHA_2DS_2-VASc scores in prediction of long-term cardiovascular outcomes and mortality has been of interest for several years.[11,23,24] There are only limited data on stroke predictors in patients after AF catheter ablation. Chao et al[4] demonstrated that both $CHADS_2$ and CHA_2DS_2-VASc scores could provide an estimation of the risk of adverse events in patients undergoing catheter ablation. More recently, the same group demonstrated the predictive value of added renal dysfunction to the CHA_2DS_2-VASc score, as an additional risk factor for TE, with a small but significant improvement in prediction value for thromboembolism.[10] However, there were limited patient numbers with relatively high occurrence of TE (2.9%) perhaps because of a high percentage of nonanticoagulated patients.

We did not find a significant independent effect of renal dysfunction on TE risk, and this may reflect that many of the risk factor components of $CHADS_2$ and CHA_2DS_2-VASc scores (ie, age, heart failure, diabetes mellitus, vascular disease, etc) are themselves related to renal dysfunction. The association between renal dysfunction and

thromboembolism in the general population and its role in AF-related strokes is well known and has been studied for several years.[25–27] In the AnTicoagulation and Risk factors In Atrial fibrillation (ATRIA) study, proteinuria and reduced eGFR were associated with a significant TE risk increase.[28] In the Danish National Patient Registry, renal failure increased stroke risk ≤83%.[25] In another study, eGFR <60 mL/min per 1.73 m^2 was a significant predictor of stroke and cardiovascular events among patients with AF, independent of the $CHADS_2$ score,[29] in accordance with recently published studies.[25,30]

Despite the known association between renal dysfunction and TE in AF, renal dysfunction has not been included in any of the current stroke stratification schemes although it was previously proposed that the small c in CHA_2DS_2-VASc score could represent informally chronic renal impairment.[31] In 2012, Piccini et al[12] proposed the R_2CHADS_2 score, in which renal dysfunction (eGFR<60mL/min per 1.73 m^2 using Cockroft–Gault formula) was assigned 2 points, but this was derived from anticoagulated clinical trial cohort, where the whole range of renal function was not studied (patients with eGFR<30 mL/min were excluded) and the broad range of stroke risk was not evident (the trial population excluded those with a $CHADS_2$ scores 0–1 and even $CHADS_2$=2 was capped at 10%). In the real-life cohorts studying a broad range of stroke risk, renal function, and nonanticoagulated subjects, an independent additive value of renal dysfunction to risk scores for TE was not found.[30,32] In accordance with some previous studies, we found that $CHADS_2$ and CHA_2DS_2-VASc scores had strong predictive value for TE during midterm follow-up in nonvalvular AF.[4,11] A new observation in our study was the use of R_2CHADS_2 in the prediction of TE, but there was no added advantage of this score compared with the classic $CHADS_2$ and CHA_2DS_2-VASc scores.

In the nationwide Danish cohort study, Olesen et al[24] found that those defined as low risk using a $CHADS_2$ score=0 had a stroke risk ranging from 0.8% to 3.2%/y, suggesting improvement of classification of patients with AF without oral anticoagulation at low and moderate risk for TE, when compared with $CHADS_2$ score. Similar results had been shown in a trial cohort of patients with $CHADS_2$ score=1 and treated with antiplatelet therapy, where a very low risk group (1% per year stroke risk) was separated from other patients.[23] Potpara et al[33] found that CHA_2DS_2-VASc offered best predictive performance for the absence of ischemic stroke when compared with the $CHADS_2$ and van Walraven scores.

In our study, we show the usefulness of CHA_2DS_2-VASc score to further discrimination those patients classed as being at low to moderate risk by the $CHADS_2$ and R_2CHADS_2 scores of 0 or 1. Although patients with low $CHADS_2$ and R_2CHADS_2 seemed to have a lower risk for TE compared with those with a score ≥2, further subanalysis of these groups using the CHA_2DS_2-VASc score reclassified patients into a truly low or moderate risk (CHA_2DS_2-VASc=0–1) and high risk (CHA_2DS_2-VASc≥2). Our data show almost the same TE risk (0.71% and 0.62%) with a previous study although their event rate was much higher.[4] In the subgroup followed up for AF recurrence, the CHA_2DS_2-VASc score has the best c-index compared with $CHADS_2$ or R_2CHADS_2.

Hunter et al[8] demonstrated that an AF ablation strategy was associated with lower rates of stroke and death during the long term compared with patients on medical treatment. It remains possible that AF is a risk marker of more serious cardiac disease rather than a causative factor, and freedom from AF was the strongest predictor of stroke-free survival.[8] Although the association between TE and AF recurrences in our subpopulation did not reach significance, our results demonstrated a 4.2-fold risk for TE in patients with AF relapses in univariate analyses. Similar to previous data,[8] we did not find any association between antiarrhythmic drug use after catheter ablation and TEs at follow-up. Of note, anticoagulation regimes at discharge and at 6-month follow-up were also not associated with TEs, but the majority of our patients were anticoagulated.

Limitations

This study is limited by its registry design although we had careful follow-up data in a large consecutive series. Prospective randomized trials are required to confirm whether the incidence of TE is reduced in the catheter ablation–treated patients. We had relatively low event rates, but on receiver operating characteristic curve analysis, all scores exhibited broadly similar prediction levels. The ability of the CHA_2DS_2-VASc score to discriminate between high- and low-risk patients using net reclassification improvement was also restricted by the low number of events.

Taken together, although the low event rate may affect statistical power, our findings are consistent and reveal plausible associations.

Rhythm follow-up was complete in 75%, but underdetection of silent AF remains an issue that may contribute to the nonsignificance of AF recurrences as TE predictor. Finally, TE was assumed to be thromboembolic based on clinical history and brain imaging but other pathogenesis may be possible.

In conclusion, TE after AF catheter ablation is rare, but all 3 stroke risk stratification scores (ie, $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2) were associated with TE risk. The CHA_2DS_2-VASc score was useful to differentiate TE risk in the low-thromboembolic risk strata based on $CHADS_2$ and R_2CHADS_2 scores and may be superior in the subgroup with AF recurrences. It is important to stress that the risk scores were useful in light of AF reduction by catheter ablation and use of anticoagulation. This suggests that high-risk patients identified by the risk scores would need optimized anticoagulation through intensified warfarin therapy or novel oral anticoagulants and intensified rhythm control. However, further studies are needed to address and support this concept.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Several different scores (eg, $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2) are used for stroke risk stratification in patients with atrial fibrillation (AF), which informs clinical decisions for oral anticoagulation. This risk assessment is particular relevant after AF catheter ablation. In the current study, we report the incidence of thromboembolic events (TE) in a large, contemporary AF ablation cohort while under guideline-recommended oral anticoagulation treatment and investigate the value of renal dysfunction and stroke risk stratification scores in predicting TE. Also, we examined the association between TE and AF recurrences. All stroke scores were predictors for TE after catheter ablation. The CHA_2DS_2-VASc score was better for refining TE risk assessment in patients designated the low risk based on the $CHADS_2$ and R_2CHADS_2 scores. CHA_2DS_2-VASc was also a better predictor in the subgroup with AF recurrences. In summary, all risk scores were useful for TE risk stratification, despite AF burden reduction by catheter ablation and the use of oral anticoagulation. CHA_2DS_2-VASc seemed to offer additional advantages in defining those at low risk.

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Supplemental Material

eTable 1. Clinical characteristics of patients with TE events

	Gender	Age	Stroke risk stratification scores			eGFR	Event	Time to event	OAC	AF recurrence
			$CHADS_2$	R_2CHADS_2	CHA_2DS_2-VASc	ml/min/1.73m^2		(months)	Event time	
#1	Female	32	1	1	2	80	Stroke	2	Aspirin, clopidogrel, LMWH*	no
#2	Male	54	1	1	2	>100	Stroke	37	Warfarin	no
#3	Female	54	3	3	5	69	Stroke	11	LMWH	yes
#4	Female	57	4	5	5	>100	Stroke	24	Warfarin	no
#5	Male	58	2	2	2	100	Stroke	16	Warfarin	no
#6	Male	64	3	3	4	>100	Stroke	5	Aspirin, clopidogrel	no
#7	Male	64	0	0	0	75	TIA	9	Dabigatran	no
#8	Male	66	4	6	6	59	A. poplitea embolism	40	Warfarin	yes
#9	Female	68	3	3	5	88	TIA	6	Warfarin	yes
#10	Female	69	1	1	3	77	TIA	15	Warfarin	yes
#11	Male	71	4	4	5	93	TIA	5	Warfarin	yes
#12	Male	72	1	1	3	97	TIA	11	Warfarin	yes
#13	Male	72	1	3	2	58	TIA	3	Warfarin	no
#14	Male	76	2	4	4	55	Stroke	10	Warfarin	yes
#15	Female	76	2	2	5	82	TIA	17	Warfarin	yes

* status post pulmonary venous stent due to pulmonary vein stenosis
Abbreviation: LMWH – low molecular weight heparin

eTable 2. Clinical predictors for TE events in cohort with complete follow up for rhythm outcomes (n=1,557)

Cox regression	**UV**				**MV**	Model 1		**MV**	Model 2		**MV**	Model 3
Variables	HR	95% CI	*P*-value	HR	95% CI	*P*-value	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Hypertension	5.6	0.73 – 42.5	0.097									
PAD	3.7	1.02 – 13.0	**0.046**	2.2	0.59 – 8.0	0.329	2.2	0.6 – 8.2	0.230			
Previous TE	5.8	2.0 – 17.1	**0.001**									
RD	3.9	1.1 – 14.0	**0.034**	2.2	0.62 – 8.2	0.220				1.8	0.48 – 6.7	0.386
AF recurrences	3.4	1.2 – 9.3	**0.019**	2.6	0.92 – 7.4	0.071	2.6	0.9 – 7.2	0.077	2.7	0.98 – 7.7	0.056
$CHADS_2$	2.1	1.5 – 3.0	**<0.001**	1.9	1.3 – 2.8	**0.001**						
R_2CHADS_2	1.9	1.4 – 2.6	**<0.001**				1.8	1.3 – 2.4	**<0.001**			
CHA_2DS_2-VASc	1.8	1.3 – 2.4	**<0.001**							1.7	1.2 – 2.3	**0.001**

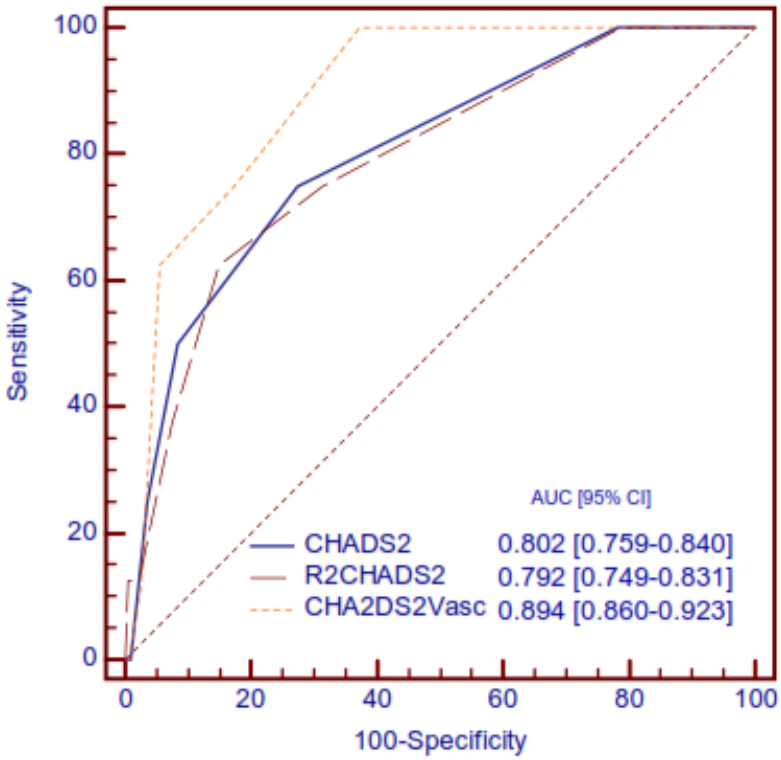
Abbreviations: UV – univariable analysis, MV – multivariable analysis, PAD – peripheral artery disease, TE – thromboembolic events, RD – renal dysfunction (eGFR <60 ml/min/1.72m^2)

eTable 3. Clinical predictors for thromboembolic events in patients with AF recurrence (n=402)

Cox regression	**UV**				**MV**	Model 1		**MV**	Model 2		**MV**	Model 3
Variables	HR	95% CI	*P*-value	HR	95% CI	*P*-value	HR	95% CI	*P*-value	HR	95% CI	*P*-value
PAD	7.4	1.7 – 32	**0.007**	3.5	0.74 – 16.1	0.114	4.4	0.98 – 20.2	0.053			
Previous TE	5.3	1.3 – 22.1	**0.023**									
RD	3.5	0.7 – 17.1	0.128	2.2	0.5 – 9.4	0.304				1.1	1.4 – 3.4	0.869
$CHADS_2$	2.3	1.4 – 3.7	**0.001**	2.0	1.2 – 3.3	**0.011**						
R_2CHADS_2	1.9	1.3 – 2.8	**0.001**				1.8	1.2 – 2.7	**0.004**			
CHA_2DS_2-VASc	2.3	1.5 – 3.4	**<0.001**							2.2	1.4 – 3.4	**<0.001**

Abbreviations: as in eTable 2.

Figure e1. ROC curves for the $CHADS_2$, CHA_2DS_2-VASc and R_2CHADS_2 scores in predicting TE events in patients with AF recurrences (n=402).



Abbreviations as in Figure 1

Significance levels:

$CHADS_2$ vs R_2CHADS_2	p=0.661
$CHADS_2$ vs CHA_2DS_2-VASc	p=0.022
R_2CHADS_2 vs CHA_2DS_2-VASc	p=0.031