

Risk of Stroke in Patients With Short-Run Atrial Tachyarrhythmia

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Background and Purpose—The risk of stroke in patients with short-run atrial tachyarrhythmia (AT) remains unclear. This study aimed to investigate the relationship between short-run AT and the stroke and the use of the CHA₂DS₂-VASc score for the risk stratification.

Methods—From the registry of 24-hour Holter monitoring, 5342 subjects without known atrial fibrillation or stroke were enrolled. Short-run AT was defined as episodes of supraventricular ectopic beats <5 seconds.

Results—There were 1595 subjects (29.8%) with short-run AT. During the median follow-up period of 9.0 years, 494 subjects developed new-onset stroke. Patients with short-run AT had significantly higher stroke rates compared with patients without short-run AT (11.4% versus 8.3%; $P<0.001$). In patients with short-run AT, the number of strokes per 100 person-years for patients with CHA₂DS₂-VASc score of 0 and 1 were 0.23 and 0.67, respectively. However, the number of them for patients with CHA₂DS₂-VASc score of 2, 3, 4, and ≥ 5 were 1.62, 1.89, 1.30, and 2.91, respectively. In patients with CHA₂DS₂-VASc score of 0 or 1, age (>61 years old) and burden of premature atrial contractions (>25 beats/d) independently predicted the risk of stroke. In subgroup analyses, short-run AT patients were divided into 3 groups based on their CHA₂DS₂-VASc scores: low score (score of 0 [men] or 1 [women]; $n=324$), intermediate score (score of 1 [men] or 2 [women]; $n=275$), and high score (score of ≥ 2 [men] or ≥ 3 [women]; $n=996$). When compared with low score, intermediate and high scores were independent predictors for stroke (hazard ratio, 6.165; $P<0.001$ and hazard ratio, 8.577; $P<0.001$, respectively).

Conclusions—Short-run AT increases the risk of stroke. Therefore, the CHA₂DS₂-VASc score could be used for the risk stratification. Age and burden of premature atrial contractions were independent predictors for stroke in patients with CHA₂DS₂-VASc score of 0 or 1. (*Stroke*. 2017;48:3232-3238. DOI: 10.1161/STROKEAHA.117.018475.)

Key Words: CHA₂DS₂-VASc score ■ risk stratification ■ short-run atrial tachyarrhythmia ■ stroke

Atrial fibrillation (AF) is a leading cause of cardioembolic stroke and is associated with the development of cardiovascular events.^{1,2} Therefore, it is generally considered that identifying its presence is important to improve clinical prognosis. The CHA₂DS₂-VASc score is a risk assessment tool to predict stroke in patients with AF.³ Recent studies showed that the CHA₂DS₂-VASc score is useful for predicting ischemic stroke in patients with coronary artery disease without AF⁴ and cardiovascular events in patients with or without AF.^{5,6} Therefore, predictivity of the CHA₂DS₂-VASc score has been extended beyond the originally proposed AF field.

Short episodes of atrial tachyarrhythmia (AT) are a common finding on the Holter monitoring in general population which may be associated with the development of atrial remodeling

and AF inducibility.⁷ However, the relationship between short episodes of AT and the incidence of stroke is still controversial.^{2,8} In addition, it remains unclear whether short episodes of AT are related with the progression of AF. Therefore, the aim of the present study was to elucidate the association between short episodes of AT during a 24-hour Holter monitoring and clinical events, including stroke and AF. Another goal was to verify the value of the CHA₂DS₂-VASc score as a risk assessment tool for new-onset stroke in patients with short episodes of AT.

Methods

Study Population

We will not make our data, analytic methods, and study materials available to other researchers because the privacy of the study

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patients is protected by the institutional review board regulation. This retrospective, observational study was based on the database of Registry of 24-hour ECG monitoring at Taipei Veterans General Hospital.⁹ Taipei Veterans General Hospital is a large tertiary referring medical center providing comprehensive medical services to >6 million populations in north Taiwan. A total of 5903 consecutive patients, who were >18 years of age, were referred for 24-hour Holter monitoring between January 1, 2002, and December 31, 2004, for the following indications: palpitations, syncope, and suspected arrhythmia; hospitalized patients were excluded from the study. The extent of clinical follow-up for each patient was determined by physician decision. Clinical features for these patients, including past medical history, comorbidities, and medications, were obtained from hospital discharge diagnoses, outpatient visits, emergency visits, and the Collaboration Center of Health Information Application, Ministry of Health and Welfare in Taiwan.⁹⁻¹¹ The exclusion criteria in our study were as follows: participants with past history of stroke, permanent pacemaker, catheter ablation, pulmonary hypertension or hypertrophic cardiomyopathy, and valvular heart disease. In addition, patients with AF/atrial flutter and any supraventricular ectopic beats >5 seconds in this Holter study were excluded. The final sample included 5342 patients for analysis. This methodology has been validated in our previous studies.⁹⁻¹² Furthermore, the institutional review board at Taipei Veterans General Hospital, Taipei, Taiwan, approved this study (Veterans General Hospital institutional review board number: 2013-08-002AC#1).

Follow-Up and Event Ascertainment

Patients with regular medications received scheduled follow-up every 1 to 3 months depending on their clinical course. Alternatively, those patients without regular medications were followed-up based on physician decision or after a new event as defined in this study. Follow-up data of all participants was retrieved from Taipei Veterans General Hospital, Taiwan National Health Insurance Research Database, and Collaboration Center of Health Information Application.⁹⁻¹¹ The clinical end points of this study were cardiovascular-related hospitalization, new-onset stroke, or new-onset AF. These clinical end points were investigated in detail based on initial identification through *International Classification of Diseases, Ninth Edition*, with reference to diagnostic codes or mention of an end point on discharge summary, and the database of the Collaboration Center of Health Information Application and National Health Insurance Research Database which had been previously validated.^{9,11-14} For detailed information, see the [online-only Data Supplement](#). The overall end of follow-up was February 28, 2013.

Assessment of Short-Run Atrial Tachyarrhythmia

All subjects underwent 24-hour Holter monitoring (see the [online-only Data Supplement](#)); the details of Holter monitoring used in this study were mentioned in a previous work.⁹ The definition of supraventricular ectopic beat has been previously described.¹⁵ The basic classification of supraventricular ectopic beat were (1) the coupling interval to the preceding QRS complex was $\leq 70\%$ of the mean RR interval of basic rhythm before the event, (2) QRS complexes had to be a length of <0.11 seconds when aberration was not suspected, and (3) the post-contraction pause had to be noncompensatory. In the APAF study (A Controlled Randomized Trial of CPVA Versus Antiarrhythmic Drug Therapy in for Paroxysmal AF),¹⁶ sustained AT (including both AF and atrial tachycardia) was defined as lasting >5 seconds although there are some definitions of long episodes of AT.^{2,8} Therefore, short-run AT was defined as ≥ 3 consecutive supraventricular ectopic beats with mean P–P interval ≤ 600 ms and lasting <5 seconds.

Determination of Risk Factors

Data were collected based on demographic characteristics (age and sex). Target comorbidities, such as diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, heart failure, chronic kidney disease, and thyroid disease, were determined by using the *International Classification of Diseases, Ninth Edition*, codes derived

from patient medical charts and Collaboration Center of Health Information Application at the time of examination. Left ventricular ejection fraction data were collected from the transthoracic echocardiography reports. Medical history with antiarrhythmic agent (classes I and III antiarrhythmic drug), antihypertension medication (including β -blocker, calcium channel blocker, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker), and statin was confirmed by medical chart review.

Statistical Analysis

Baseline patient characteristics were reported as means \pm SDs for continuous variables and as percentages for categorical variables. Continuous and categorical variables were compared using the Student *t* test and χ^2 test with Yates' correction, respectively. Kaplan–Meier survival curves were used to analyze survival data in patients with or without short-run AT. The log-rank test was used to compare survival curves. Then, the use of CHA₂DS₂-VASc score for the risk stratification of new-onset stroke was investigated in the patients with short-run AT (patients were given: 1 point for an age 65 to 74 years, female sex, heart failure, hypertension, diabetes mellitus, and vascular disease; and 2 points for an age 75 years or older). Incidence rates of new-onset stroke were calculated by dividing the number of events by person-time at risk. The variables selected for testing in the multivariate analysis were those with a $P < 0.05$ in the univariate models (see the [online-only Data Supplement](#)). Kaplan–Meier survival curves were used to analyze survival data (ie, time to adverse event) among the CHA₂DS₂-VASc score class. The CHA₂DS₂-VASc score to predict clinical outcome (new-onset stroke) in the Cox proportional hazards regression model was analyzed. $P < 0.05$ was considered as significant. The analysis was performed by a biostatistician using SPSS statistical software (version 22.0, SPSS Institute, Chicago, IL).

Results

Baseline Characteristics

The 5342 patients were followed-up through clinical evaluation and investigation of medical records, nursing records, and Bureau of National Health Insurance of Taiwan data. The median follow-up period of the patients with and without short-run AT were 9.0 and 9.1 years, respectively. Table 1 shows the baseline clinical characteristics of the study subjects. Patients with short-run AT were generally older, with a higher prevalence in man, in those with hypertension and coronary artery disease. There were no significant differences in the prevalence of diabetes mellitus, dyslipidemia, heart failure, chronic kidney disease, thyroid dysfunction and baseline antiarrhythmic, hypertensive drugs, and statin between these 2 groups. In the 24-hour Holter monitoring, the total number of premature atrial contraction (PAC) was significantly higher in patients with short-run AT than in those without short-run AT.

Clinical End Points

During the follow-up period, there were 494 (9.2%) patients with new-onset stroke and 413 (7.7%) cases of new-onset AF. Patient with short-run AT had a significantly higher prevalence of new-onset stroke and new-onset AF compared with patients without short-run AT (new-onset stroke, 11.4 versus 8.3%; new-onset AF, 9.8 versus 6.8%; $P < 0.001$, respectively). The results of applying Kaplan–Meier survival curve for different significant events are presented in Figure 1. In Kaplan–Meier analysis, patients with short-run AT had lower event-free rates for new-onset stroke and new-onset AF compared with patients without short-run AT (log-rank $P < 0.001$, respectively).

Table 1. Comparison of Clinical Characteristics in Patients With or Without Short-Run Atrial Tachyarrhythmia

	Atrial Tachyarrhythmia (-; n=3747)	Atrial Tachyarrhythmia (+; n=1595)	P Value
Age	58.8±18.5	68.3±16.9	<0.001
Gender (male)	2123 (56.6%)	1076 (67.4%)	<0.001
Underlying disease			
Hypertension	1256 (33.5%)	642 (40.2%)	<0.001
Diabetes mellitus	369 (9.8%)	155 (9.7%)	0.884
Dyslipidemia	140 (3.7%)	59 (3.6%)	0.948
Heart failure	164 (4.3%)	82 (5.1%)	0.223
Coronary artery disease	1059 (28.2%)	514 (32.2%)	0.004
Chronic kidney disease	36 (0.9%)	20 (1.2%)	0.336
Thyroid dysfunction	49 (1.3%)	25 (1.5%)	0.457
Holter monitoring			
PAC	274.7±1448.6	736.2±1944.6	<0.001
PVC	423.2±1364.0	415.0±1399.3	0.841
LVEF	64.0±5.0	63.9±5.2	0.419
Medical therapy			
Antiarrhythmic drugs	27 (0.7%)	10 (0.6%)	0.706
Antihypertensive drugs			
β-Blocker	105 (2.8%)	37 (2.3%)	0.316
Calcium channel blocker	276 (7.3%)	137 (8.5%)	0.125
ACE-I/ARB	184 (4.9%)	78 (4.8%)	0.975
Statin	133 (3.5%)	58 (3.6%)	0.876

ACE-I indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; LVEF, left ventricular ejection fraction; PAC, premature atrial complex; and PVC, premature ventricular complex.

New-Onset Stroke in Patients With Short-Run AT

During the follow-up period, there were 182 (11.4%) new-onset stroke in patients with short-run AT. In those patients, 33 patients (18.1%) had lacunar infarction and 149 patients had major territory stroke (81.9%). The main stroke localization was in the partial territory of middle cerebral artery (n=81), full territory of middle cerebral artery (n=25), territory of anterior cerebral artery (n=31), and territory of posterior cerebral artery or basilar artery (n=12). Multiple territory infarctions were found in 45 patients. Both of the median follow-up period in short-run AT patients with and without stroke were 9.0 years. Table 2 shows the clinical characteristics in short-run AT patients with or without stroke. The patients with stroke in short-run AT were generally older, with a higher prevalence of man, hypertension, diabetes mellitus, dyslipidemia, and medication of angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker and statin. There were no significant differences in the prevalence of heart failure, coronary artery disease, chronic kidney disease, thyroid dysfunction, Holter monitoring findings, and baseline antiarrhythmic drugs

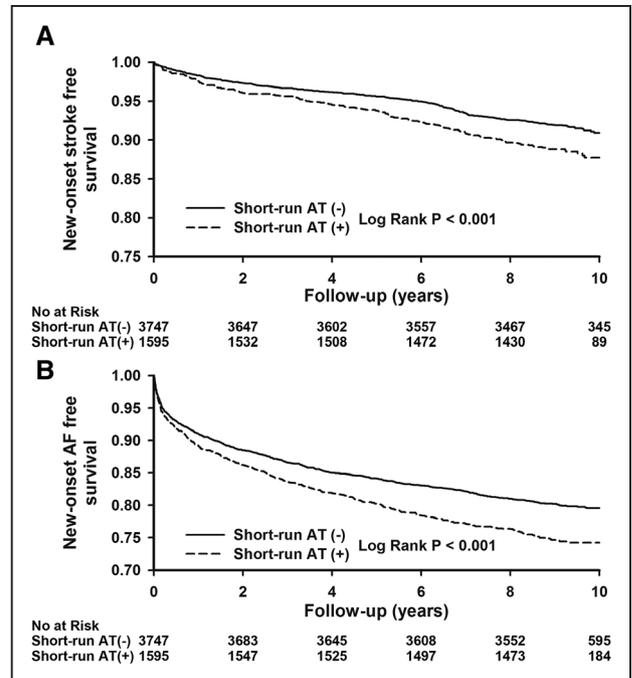


Figure 1. Kaplan–Meier analysis for clinical events in patients with or without short-run atrial tachyarrhythmia (AT). **A**, Kaplan–Meier curve of new-onset stroke-free survival in patients with or without short-run AT. **B**, Kaplan–Meier curve of new-onset atrial fibrillation (AF)-free survival in patients with or without short-run AT.

between these 2 groups. The short-run AT with stroke had a significantly lower prevalence of CHA₂DS₂-VASc score 0 and 1 and higher prevalence of score 2 and 3 when compared with short-run AT without stroke.

Table 3 shows the number of new-onset strokes per 100 person-years for short-run AT patients among the CHA₂DS₂-VASc score class. The number of strokes per 100 person-years for patients with CHA₂DS₂-VASc score of 0 and 1 were 0.23 and 0.67, respectively. However, the number of strokes per 100 person-years for patients with CHA₂DS₂-VASc score of 2, 3, 4, and ≥5 were 1.62, 1.89, 1.30, and 2.91, respectively. In short-run AT patients with CHA₂DS₂-VASc score of 0 or 1, the univariate analysis showed that age, sex, and the burden of PACs were significantly associated with new-onset stroke ($P<0.001$, $P=0.022$, and $P=0.001$, respectively) while the multivariate analysis showed that age and the burden of PACs were independent predictors for new-onset stroke ($P=0.002$ and $P=0.014$, respectively). On the receiver operator characteristics analysis for the prediction of new-onset stroke, the best cut-off value for age and the burden of PACs were 61 years old (area under the curve: 0.797; sensitivity: 87.5%; specificity: 66.5%) and 25 beats/d (area under the curve: 0.622; sensitivity: 83.3%; specificity: 39.6%), respectively. Next, the short-run AT with CHA₂DS₂-VASc score of 0 or 1 (n=496) were divided into 3 groups based on age and the burden of PACs: group 1 (age ≤61 years old and the burden of PACs ≤25 beats/d; n=161), group 2 (age >61 years old or the burden of PACs >25 beats/d; n=186), and group 3 (age >61 years old and the burden of PACs >25 beats/d; n=149). As shown in Figure 2A, new-onset stroke was significantly higher

Table 2. Comparison of Clinical Characteristics in Short-Run Atrial Tachyarrhythmia With or Without Stroke

	Stroke (–; n=1413)	Stroke (+; n=182)	P Value
Age	67.4±17.6	75.1±6.9	<0.001
Gender (male)	938 (66.3%)	138 (75.8%)	0.011
Underlying disease			
Hypertension	547 (38.7%)	95 (52.1%)	<0.001
Diabetes mellitus	128 (9.0%)	27 (14.8%)	0.013
Hyperlipidemia	45 (3.1%)	14 (7.6%)	0.002
Heart failure	77 (5.4%)	5 (2.7%)	0.120
Coronary artery disease	451 (31.9%)	63 (34.6%)	0.464
Chronic kidney disease	18 (1.2%)	2 (1.0%)	0.842
Thyroid dysfunction	23 (1.6%)	2 (1.0%)	0.589
Holter monitoring			
PAC	738.3±1963.9	720.0±1792.5	0.905
PVC	420.1±1428.5	375.0±1150.3	0.682
LVEF	63.9±5.3	64.3±4.1	0.277
Medical therapy			
Antiarrhythmic drugs	9 (0.6%)	1 (0.5%)	0.888
Antihypertensive drugs			
β-Blocker	35 (2.4%)	2 (1.0%)	0.245
Calcium channel blocker	116 (8.2%)	21 (11.5%)	0.131
ACE-I/ARB	63 (4.4%)	15 (8.2%)	0.026
Statin	44 (3.1%)	14 (7.6%)	0.002
CHA ₂ DS ₂ -VASc score			
Score 0 (n=143)	140 (9.9%)	3 (1.7%)	<0.001
Score 1 (n=353)	332 (23.5%)	21 (11.5%)	<0.001
Score 2 (n=499)	430 (30.4%)	69 (37.9%)	0.041
Score 3 (n=437)	369 (26.1%)	68 (37.4%)	0.001
Score 4 (n=136)	121 (8.6%)	15 (8.2%)	0.884
Score ≥5 (n=24)	21 (1.5%)	6 (3.3%)	0.115
Follow-up			
New-onset AF	128 (9.0%)	29 (15.9%)	0.003
Cardiovascular-related hospitalization	334 (30.9%)	69 (37.9%)	<0.001
Antithrombotic therapy	226 (15.9%)	42 (23.0%)	0.016

ACE-I indicates angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; LVEF, left ventricular ejection fraction; PAC, premature atrial complex; and PVC, premature ventricular complex.

in group 3 than in group 1 and group 2 ($P=0.003$ and $P=0.002$, respectively).

Furthermore, in subgroup analyses, the patients with short-run AT were divided into 3 groups based on their CHA₂DS₂-VASc scores: low score (score of 0 [men] or 1 [women]; n=324), intermediate score (score of 1 [men] or 2 [women]; n=275), and high score (score of ≥2 [men] or ≥3

Table 3. Risk of New-Onset Stroke per 100 Person-Years Among the CHA₂DS₂-VASc Score Class

	No. of New-Onset Stroke (%)	Person-Years	Incidence*
CHA ₂ DS ₂ -VASc score class			
Score 0 (n=143)	3 (2.0)	1299.8	0.23
Score 1 (n=353)	21 (5.9)	3125.2	0.67
Score 2 (n=499)	69 (13.8)	4236.7	1.62
Score 3 (n=437)	68 (15.5)	3592.5	1.89
Score 4 (n=136)	15 (11.0)	1150.1	1.30
Score ≥5 (n=24)	6 (25)	205.9	2.91
CHA ₂ DS ₂ -VASc score among 3 groups			
Low score (n=324)	6 (1.8)	2936.5	0.20
Intermediate score (n=275)	30 (10.9)	2375.8	1.26
High score (n=996)	146 (14.6)	8297.9	1.75

*Number of ischemic stroke per 100 person-years of follow-up.

[women]; n=996). As shown in Table 3, the number of strokes per 100 person-years for patients with low score, intermediate score, and high score were 0.20, 1.26, and 1.75, respectively. Figure 2B shows Kaplan–Meier analysis for the event-free rates of new-onset stroke among the 3 groups (log-rank $P<0.001$). The multivariable Cox proportional hazard analysis showed that the intermediate and high scores were independent predictors of stroke (C-statistics: 0.616; 95% confidence interval: 0.578–0.654; $P=0.001$ and $P<0.001$, respectively) when compared with low score (Table 4).

Follow-Up: Clinical Events in Patients With Short-Run AT

During the follow-up period, there were subsequent 157 (9.8%) new-onset AF, 403 (25.2%) cardiovascular-related hospitalization, and 268 additional antithrombotic therapy (16.8%) in patients with short-run AT (n=1595). The prevalence of those clinical events and antithrombotic therapy was significantly higher in short-run AT with stroke than in that without stroke (Table 2). Those patients were excluded, and the multivariable Cox proportional hazard analysis for new-onset stroke was performed again. When compared with low CHA₂DS₂-VASc score, intermediate and high CHA₂DS₂-VASc scores were still independent predictors for new-onset stroke (Table I in the [online-only Data Supplement](#)).

Discussion

Main Findings

For the first time, we demonstrated that short-run AT was associated with the development of new-onset stroke and AF. The CHA₂DS₂-VASc score provides useful information for predicting new-onset stroke in patients with short-run AT. Although the annual risk for new-onset stroke were low in short-run AT patients with CHA₂DS₂-VASc score of 0 or 1, age (>61 years old) and the burden of PACs (>25 beats/d) were independent predictors for new-onset stroke in those patients. In subgroup analyses, intermediate (score of 1 [men]

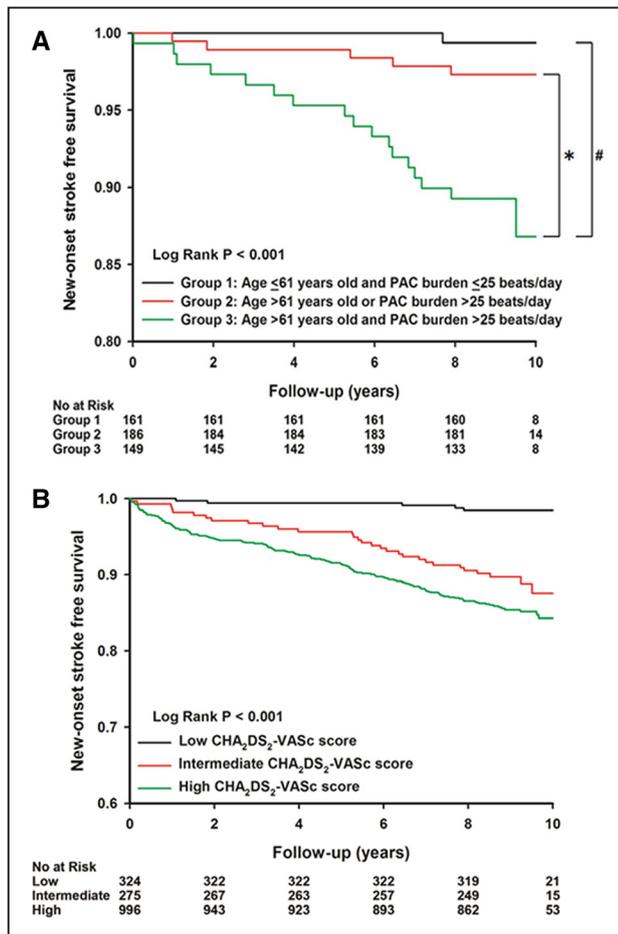


Figure 2. Kaplan–Meier analysis for new-onset stroke in short-run atrial tachyarrhythmia. **A**, Kaplan–Meier analysis for new-onset stroke in short-run atrial tachyarrhythmia with CHA_2DS_2-VASc score of 0 or 1 ($n=496$) among group 1 ($n=161$), group 2 ($n=186$), and group 3 ($n=149$). $*P=0.002$ and $\#P=0.003$. **B**, Kaplan–Meier analysis for new-onset stroke in short-run atrial tachyarrhythmia ($n=1595$) among low ($n=324$), intermediate ($n=275$), and high ($n=996$) CHA_2DS_2-VASc scores. PAC indicates premature atrial contraction.

or 2 [women]) and high (score of ≥ 2 [men] or ≥ 3 [women]) scores were independent predictors of new-onset stroke in the patients with short-run AT.

Short-Run AT and Clinical Events

It is considered that patients with paroxysmal or chronic AF have similar risks of ischemic stroke.^{17,18} However, the relationship between short episodes of AT and the incidence of

Table 4. Cox Proportional Hazard Model of New-Onset Stroke in Short-Run Atrial Tachyarrhythmia ($n=1595$): Impact of CHA_2DS_2-VASc Score

	HR (95% CI)	P Value
CHA_2DS_2-VASc score		
Low score ($n=324$)	Reference	
Intermediate score ($n=275$)	6.165 (2.566–14.811)	<0.001
High score ($n=996$)	8.577 (3.791–19.406)	<0.001

CI indicates confidence interval; and HR, hazard ratio.

stroke is still controversial and little is known about the clinically significant duration of the short AT episodes related with future stroke events. In the RATE Registry (Registry of Atrial Tachycardia and Atrial Fibrillation Episodes), short episodes of atrial tachycardia/AF were not associated with increased risk of stroke events compared with patients without documented atrial tachycardia/AF.² In that study, short episodes of atrial tachycardia/AF were defined as episodes in which both the onset and offset of atrial tachycardia/AF were present within a single electrogram recording in patients with device implantation. However, in the Copenhagen Holter Study, excessive supraventricular ectopic activity, defined as the presence of either ≥ 30 PACs/h daily or any runs of ≥ 20 PACs using 48-hour ambulatory electrocardiography, was associated with an increased risk of ischemic stroke.⁸ In the SMART Registry (The Stroke and Monitoring for PAF in Real Time), 10.3% patients with paroxysmal AF, defined as the standard electrocardiographic criteria for AF¹⁶ and a minimum event duration of 5 seconds, had ischemic stroke events.¹⁹ In our present study, short-run AT was defined as ≥ 3 consecutive supraventricular ectopic beats (rate ≥ 100 bpm) and lasting < 5 seconds, which was different from previous studies. As a result, Kaplan–Meier analysis showed that patients with short-run AT had lower event-free rates for new-onset stroke compared with patients without short-run AT (log-rank $P < 0.001$). Our study suggested that even patients with short-run AT < 5 seconds still had a risk for stroke events.

In addition to stroke, the relationship between short episodes of AT and new-onset AF is also controversial.^{2,15} In the present study, Kaplan–Meier analysis showed that patients with short-run AT had lower event-free rates for new-onset AF compared with patients without short-run AT (log-rank $P < 0.001$). Our results suggested that patients with short-run AT also had a risk for the development of new-onset AF.

Short-Run AT and the CHA_2DS_2-VASc Score

In the present study, we calculated the number of new-onset strokes per 100 person-years for short-run AT patients among the CHA_2DS_2-VASc score class. In patients with AF, the proposed anticoagulant treatment thresholds for balancing ischemic stroke reduction against serious bleeding were 1.7% per year for warfarin therapy and 0.9% per year for the use of nonvitamin K antagonist oral anticoagulants.²⁰ The annual risk for new-onset stroke in short-run AT patients with CHA_2DS_2-VASc score of 2, 3, 4, and ≥ 5 were 1.62, 1.89, 1.30, and 2.91, respectively. Therefore, CHA_2DS_2-VASc score ≥ 2 can predict new-onset stroke in the patients with short-run AT. Although the annual risk for new-onset stroke in short-run AT patients with CHA_2DS_2-VASc score of 0 and 1 was low (0.23 and 0.67, respectively), age (> 61 years old) and the burden of PACs (> 25 beats/d) are useful predictors for new-onset stroke. These findings provide useful information for the management of the patients with short-run AT. On the current clinical guidelines,^{3,21} the use of CHA_2DS_2-VASc score for stroke risk stratification is suggested, and oral anticoagulants should be prescribed for patients with a CHA_2DS_2-VASc score ≥ 2 (class I recommendation) and omitted for male patients with a CHA_2DS_2-VASc score of 0 and female patients with a CHA_2DS_2-VASc score of 1 in patients with AF. For patients

with 1 risk factor in addition to sex (ie, CHA₂DS₂-VASc score 1 [men] or 2 [women]), the European Society of Cardiology guidelines suggest that stroke prevention with oral anticoagulants should be considered. Therefore, the patients with short-run AT were divided into 3 groups: low score (score of 0 [men] or 1 [women]), intermediate score (score of 1 [men] or 2 [women]), and high score (score of ≥ 2 [men] or ≥ 3 [women]). As a result, the multivariable Cox proportional hazard analysis showed that intermediate and high scores were independent predictors of new-onset stroke. Therefore, female patients with sex alone (CHA₂DS₂-VASc score of 1) were truly low risk in short-run AT, which was almost identical to patients with AF. Although it is considered that AF is an important risk factor of cardioembolic stroke,¹ only 29 (1.8%) of the patients with short-run AT (n=1595) developed both new-onset AF and stroke during the follow-up period. Short-run AT patients with stroke had higher prevalence of AF compared with short-run AT patients without stroke. However, the incidence of AF after stroke (n=16) was high compared with it before stroke (n=13). Therefore, short-run AT is associated with the incidence of new-onset stroke but not with a clinical manifestation of AF.

Limitation

First, there is some degree of bias in the study with regard to follow-up, treatment, and considerable variability because this was depended on the clinical decision of the treating physician. Further prospective study with regular follow-up is necessary to validate our study results. Second, interactions between stroke and the different clinical events or additional antithrombotic therapy during the follow-up period could not be fully adjusted. Finally, intra-atrial clot and extracranial atherosclerosis were not evaluated during the follow-up period. However, short-run AT patients with stroke had a higher incidence of vascular risk factors. These results suggested that short-run AT might be a marker of the progression of stroke.

Conclusions

Short-run AT is associated with incidence of new-onset stroke and AF. The CHA₂DS₂-VASc score is a useful tool for the risk stratification of new-onset stroke in the patients with short-run AT. Short-run AT patients with CHA₂DS₂-VASc score ≥ 2 have higher risk of new-onset stroke. Age and the burden of PACs were independent predictors for new-onset stroke in patients with CHA₂DS₂-VASc score of 0 or 1.

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Disclosures

None.

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Supplemental Material

The identification of clinical events during the follow-up

The clinical events (i.e., cardiovascular-related hospitalization, new-onset stroke or new-onset AF) were investigated in detail based on initial identification through International Classification of Diseases diagnostic codes or mention of an endpoint on the hospital face sheet, previous discharge summary, outpatient clinic report and the database of the Collaboration Center of Health Information Application which had been described previously.¹⁻³ Cardiovascular-related hospitalization was defined as an overnight stay in a hospital ward for the treatment of cardiovascular disease, excluding the visits in the Emergency Department. Additional medical therapies for clinical event were considered at each attending physician's discretion.

Holter monitoring

In addition to the automatic analysis, the ECG strip were reviewed and manually edited by two experienced technicians. Then, two physicians reviewed the whole ECG recording of all arrhythmic episodes and all unknown strips. Finally, one licensed electrophysiologist confirmed the Holter report.

Univariate and multivariate analyses

In patients with low risk of stroke, the association between selected parameters (i.e., age, gender, hypertension, diabetes mellitus, hyperlipidemia, heart failure, coronary artery disease, chronic kidney disease, thyroid dysfunction and the burden of premature atrial complexes and premature ventricular complexes) and new-onset stroke was studied by the Cox proportional hazards regression model. The variables selected for testing in the multivariate analysis were those with a $p < 0.05$ in the univariate models.

Supplementary Table I. Cox Proportional Hazard Model of new-onset stroke in short-run AT: impact of CHA₂DS₂-VASc score

	HR (95% CI)	P value
Short-run AT without new-onset AF (n=1438)		
CHA ₂ DS ₂ -VASc score:		
Low score (n=307)	Reference	
Intermediate score (n=249)	5.341 (2.191-13.019)	<0.001
High score (n=882)	7.640 (3.366-17.341)	<0.001
Short-run AT without cardiovascular-related hospitalization (n=1192)		
CHA ₂ DS ₂ -VASc score:		
Low score (n=283)	Reference	
Intermediate score (n=204)	4.594 (1.683-12.542)	0.003
High score (n=705)	7.994 (3.250-19.665)	<0.001
Short-run AT without anti-thrombotic therapy (n=1327)		
CHA ₂ DS ₂ -VASc score:		
Low score (n=298)	Reference	
Intermediate score (n=236)	6.012 (2.286-15.815)	<0.001
High score (n=793)	9.058 (3.698-22.188)	<0.001
Short-run AT without new-onset AF, cardiovascular related hospitalization and/or anti-thrombotic therapy (n=957)		
CHA ₂ DS ₂ -VASc score:		
Low score (n=252)	Reference	
Intermediate score (n=168)	4.207 (1.339-13.213)	0.014
High score (n=537)	7.907 (2.878-21.724)	<0.001

AT: atrial tachycardia; HR: hazard ratio; CI: confidence interval; and AF: atrial fibrillation.

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