Risk Management and Healthcare Policy Dovepress

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Impact of Paroxysmal Atrial Tachycardia on Thromboembolic Events and Major Adverse Cardiovascular Events: A Single-Center Retrospective Study

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Objective: Atrial fibrillation (AF) is known to increase the risk of thromboembolic events and major adverse cardiovascular events (MACE). The impact of paroxysmal atrial tachycardia (PAT) on these risks remains unclear.

Methods: This retrospective cohort study was conducted involving 889 patients diagnosed with PAT and 1106 control patients without PAT, all of whom underwent their initial 24-hour ECG monitoring between 2015 to 2020. Kaplan–Meier survival analysis and Cox regression analysis were used to evaluate the association between PAT and the study endpoints, including thromboembolic events and MACE.

Results: Over a mean follow-up period of 50.3 months, the incidence of thromboembolic events and MACE was significantly higher in the PAT group compared to the control group (6.5% vs 1.7% and 19.1% vs 9.9%, respectively). After adjusting for common risk factors and baseline imbalances, the PAT group exhibited a significantly elevated risk of thromboembolic events (hazard ratio [HR] 3.782, 95% confidence interval [CI] 2.212–6.467; P <0.001) and MACE (HR 1.795, 95% CI 1.398–2.305; P <0.001). However, the frequency of PAT episodes, heart rate, and maximum heart rate were not significantly associated with these outcomes. Within the PAT group, a history of stroke, transient ischemic attack, and chronic renal failure were identified as independent risk factors for thromboembolic events, while hypertension, coronary heart disease, heart failure, and chronic renal failure were independently associated with MACE.

Conclusion: PAT, as detected by 24-hour dynamic ECG, is associated with an increased risk of thromboembolic events and MACE.

Keywords: paroxysmal atrial tachycardia, thromboembolic events, ischemic stroke, transient ischemic attack, systemic thromboembolism, major adverse cardiovascular events

Introduction

Atrial tachycardia (AT) is a frequently encountered cardiac arrhythmia in clinical practice. Atrial fibrillation (AF) is a well-established independent risk factor for thromboembolic events, significantly increasing the risk of stroke. It is widely recognized that oral anticoagulants play a crucial role in reducing stroke risk in patients with AF, with direct oral anticoagulants now favored over vitamin K antagonists due to their superior safety profiles.[1–3] Beyond thromboembolic events, AF also predisposes patients to major adverse cardiovascular events (MACE), including nonfatal or fatal myocardial infarction (MI), coronary revascularization, cardiovascular death, and other cardiovascular incidents.[4,5] However, whether AT, often seen as a prelude to AF, similarly contributes to these adverse events remains unclear.

Received: 15 June 2024
Accepted: 18 October 2024
Published: 29 October 2024

Previous studies have reported that atrial high-rate episodes (AHRE) detected by implantable devices rather than clinically diagnosed AF, are linked to a markedly increased risk of ischemic stroke, systemic embolism, and the onset of AF.[6,7] Despite this, 24-hour dynamic ECG monitoring is more commonly employed in clinical practice due to its noninvasive, accessible, and cost-effective nature compared to implantable devices. Several studies have suggested that an increase in supraventricular ectopic activity, as recorded by 24-hour ECG, correlates with an elevated risk of AF and ischemic stroke.[8–12] In addition, a systematic review has found an association between paroxysmal supraventricular tachycardia (PSVT) and a higher risk of ischemic stroke.[13] Interestingly, while one study reported that AF is independently associated with thromboembolic stroke rather than PVST,[14] another study showed that PSVT was linked to a higher prevalence of embolic stroke but not with overall ischemic stroke.[15] Thus, the evidence regarding the use of anticoagulation therapy in patients with PSVTs remains inconclusive. Rapid runs of premature atrial contractions originating from arrhythmogenic foci in the pulmonary veins often precede episodes of AF in patients diagnosed with AF.[16] This leads us to hypothesize that nonsustained, clustered, and paroxysmal atrial tachycardia (PAT) might have a higher likelihood of progressing to AF and subsequently leading to AF-related complications.

PAT, previously defined as three or more consecutive premature atrial contractions lasting 30 seconds or less,[17] is frequently diagnosed and can be effectively detected and quantified using 24-hour ECG monitoring. However, it remains uncertain whether PAT identified by 24-hour ECG monitoring can predict the occurrence of thromboembolic events as well as other adverse cardiovascular outcomes. Given that PAT is closely associated with AHRE and rapid bursts of premature atrial contractions, our objective is to investigate the relationship between PAT detected by 24-hour ECG monitoring and the incidence of thromboembolic events and MACE. Furthermore, we aim to identify the specific characteristics of high-risk PAT patients.

Methods

Patients

This retrospective cohort study included consecutive patients aged over 18 years who underwent 24-hour ECG monitoring at Beijing Tsinghua Changgung Hospital between January 2015 and January 2020. The indication for 24-hour ECG monitoring in all patients was the presence of symptoms such as palpitations or chest tightness, regardless of their medical history. To ensure uniformity in the monitoring process, all tests were conducted using the SEER Light system (General Electric Company), with data analyzed using the MUSE analysis tool (General Electric Company). Each 24-hour ECG recordings exceeded 20 hours and met high quality, as reviewed by two independent cardiologists.

Patients were excluded if they had documented AF/atrial flutter (AFL) or AF/AFL diagnosed during 24-hour ECG monitoring, high-grade atrioventricular block (AVB), sustained supraventricular tachycardia (SVT) lasting >30 seconds, frequent premature ventricular contraction (PVC, burden ≥15%), ventricular tachycardia (VT), ventricular fibrillation (VF), chronic rheumatic heart disease, severe mitral stenosis, acute heart failure (AHF), cardiomyopathy, inherited arrhythmia syndrome, use of oral anticoagulants (OAC), a history of malignancy, acute myocardial infarction (AMI), or stroke at the acute stage before enrollment.

After exclusion, the final study population included 1995 patients. Of these, 889 patients diagnosed with PAT by the first 24-hour ECG monitoring at Beijing Tsinghua Changgung Hospital were assigned to the PAT group, while 1106 patients without PAT were assigned to the control group. Personal medical histories and comorbidities were retrospectively collected at baseline. Informed consent was waived due to the retrospective nature of the study, and the data were anonymized. This study complies with the ethical principles of the Declaration of Helsinki, and was approved by the Beijing Tsinghua Changgung Hospital Institutional Review Board (#23605-6-01).

Endpoints

The primary endpoint was the occurrence of thromboembolic events, including ischemic stroke, transient ischemic attack (TIA), and systemic thromboembolism. Ischemic stroke was defined as a new ischemic lesion detected by computed tomography or magnetic resonance imaging, or a persistent cerebrovascular neurological deficit lasting over 24 hours.[18] TIA was defined as a sudden focal neurological deficit of presumed vascular origin lasting < 24 hours. Systemic

thromboembolism was defined based on documented loss of end-organ perfusion through imaging, surgery, or autopsy. Secondary endpoints were MACE, including MI, cardiac revascularization, acute heart failure, life-threatening arrhythmias, and cardiovascular death or hospitalization.

Follow-Up

The date of each patient`s first 24-hour ECG monitoring at Beijing Tsinghua Changgung Hospital was defined as the enrollment date. Patients were observed for the outcome of thromboembolic events as well as MACE and followed from the enrollment date until the date of the event, death, or March 31, 2021 (whichever came first). Follow-up data were collected from hospital records and verified through telephone interviews, and only outcome events confirmed at Beijing Tsinghua Changgung Hospital or other hospitals were included.

Statistical Analysis

Continuous variables were expressed as mean (standard deviation, SD) or median with interquartile range (IQR), depending on their distribution. The Mann–Whitney *U*-test was used for non-normally distributed and ordinal data, while the independent samples *t*-test was used for normally distributed data. Categorical variables were expressed as numbers and percentages and compared using Pearson's chi-square test. Kaplan–Meier survival curves and Log rank tests were used to compare event-free survival between the PAT and control groups. Cox regression models with time-dependent covariates were used to assess the association between PAT and thromboembolic events or MACE, adjusting for age, sex, prior stroke or TIA, history of diabetes mellitus, high blood pressure, coronary heart disease and other baseline factors. A *P*-value <0.05 was considered statistically significant, and all analyses were performed using the SPSS Statistics software (version 25.0; IBM SPSS Inc).

Results

Demographic Data

The flowchart in Figure 1 illustrates patient enrollment, including a total of 1995 patients, with 889 in the PAT group and 1106 in the control group. The median age of all participants was 61 years (IQR, 53–67), and 63.1% of the cohort were women. The baseline demographic characteristics and comorbid disorders in the PAT and control groups are shown in Table 1. The mean follow-up duration was 50.3 months. During this period, 24 patients died, including 16 in the PAT group and 8 in the control group. Among these, it is possible that three deaths in the PAT group were due to ischemic stroke, and four may have been attributed to MACE, while in the control group, one patient may have died from ischemic stroke and another from MACE.

PAT and Thromboembolic Events

During the mean follow-up of 50.3 months, 58 (6.5%) thromboembolic events occurred in the PAT group, including 37 ischemic strokes, 16 TIAs, and five systemic thromboembolisms. The mean time to event was 32.6 ± 17.1 months. There were 19 (1.7%) thromboembolic events in the control group, including 10 ischemic strokes and 9 TIAs, with a mean time to event was 31.3 ± 17.2 months. Kaplan-Meier survival curves showed significantly reduced event-free survival in the PAT group compared to the control group (log-rank *P* <0.001, Figure 2). Cox regression identified PAT as an independent predictor of thromboembolic events (hazard ratio [HR] 3.782; 95% confidence interval [CI] 2.212–6.467; *P* <0.001), even after adjusting for covariates including age, sex, prior stroke or TIA, history of diabetes mellitus, high blood pressure, coronary heart disease, heart failure, chronic renal failure, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea syndrome (OSAS) and smoking history. After further adjustment for platelet count, triacylglycerol, and low-density lipoprotein cholesterol, PAT remained an independent predictor of thromboembolic events (HR 3.348; 95% CI 1.939–5.780; *P* <0.001), as shown in Table 2.

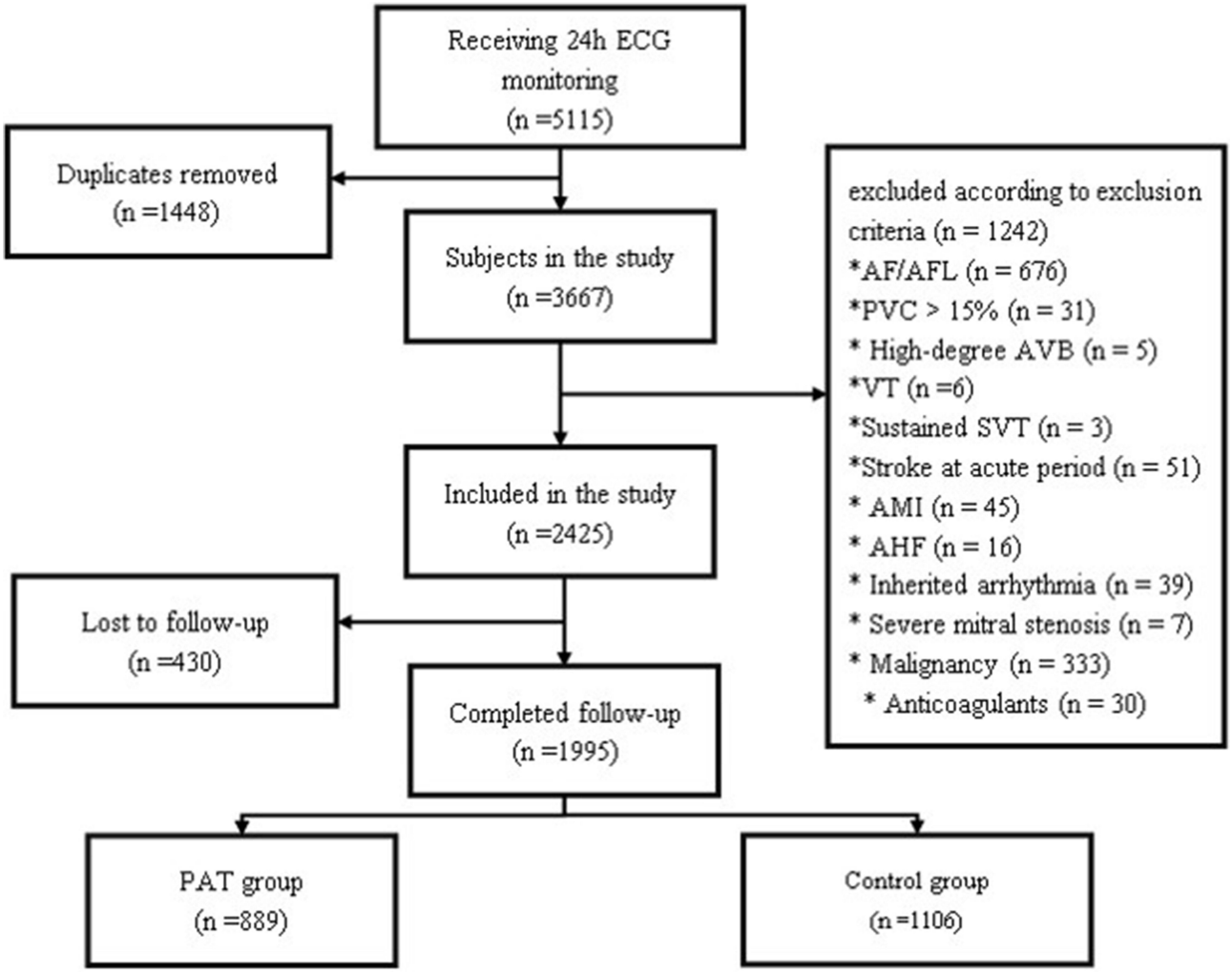

Figure 1 Study flowchart.

Risk Factors for Thromboembolic Events in PAT Patients

In PAT group, Multivariate Cox regression analysis revealed that prior stroke or TIA (HR 3.093; 95% CI 1.464–6.533; P = 0.003) and chronic renal failure (HR 3.182; 95% CI 1.543–6.561; P = 0.002) independently correlated with thromboembolic events (Table 3). Unadjusted Kaplan-Meier survival curves represented a significantly higher risk of thromboembolic events in PAT group compared to the control group (Log-rank P< 0.001, Figure 2A). However, further stratification analysis by tertiles or quartiles of 24-hour ECG parameters, showed no significant trends across tertiles of PAT episodes (Tertile 1[T1], 1 episode. Tertile 2 [T2], 2–3 episodes. Tertile 3 [T3] ≥4 episodes), quartiles of the number of beats at PAT per 24 hours (Quartile 1[Q1], 3–5 beats; Quartile 2 [Q2], 6–10 beats; Quartile 3 [Q3], 11–22 beats; Quartile 4 [Q4], 23–18773 beats), and quartiles of maximum heart rate during PAT (Q1, < 115 bpm; Q2, 115–131 bpm; Q3, 132–149 bpm; Q4, ≥150 bpm), with all log-rank P values > 0.05 (Figure 2B–D). Cox regression models for 24-hour ECG parameters did not reveal a significant association between the number of PAT episodes, number of beats, or maximum heart rate. Cox regression analysis showed that episodes of PAT (HR 0.961; 95% CI 0.864–1.070; P = 0.471), number of beats of PAT per 24 hours (HR 1.001; 95% CI 0.998–1.004; P = 0.621), and maximum heart rate during PAT (HR 0.939; 95% CI 0.854–1.033; P = 0.196) were not statistically significant predictors of thromboembolic events after adjusting for covariates, including prior stroke, TIA, and chronic renal failure.

Table 1 Baseline Characteristics of PAT Group and Control Group

Baseline Variables	PAT group (n = 889)	Control group (n = 1106)	P-value
Age (years)	64 (59–70)	58 (47–64)	< 0.001
Female	595 (66.9)	663 (59.9)	0.001
Prior stroke or TIA	38 (4.3)	52 (4.7)	0.648
High blood pressure	517 (58.2)	545 (49.3)	< 0.001
Coronary heart disease	116 (13.0)	112 (10.1)	0.041
Heart failure	10 (1.1)	15 (1.4)	0.644
Diabetes mellitus	215 (24.2)	217 (19.6)	0.014
Chronic renal failure	47 (5.3)	44 (4.0)	0.164
COPD	39 (4.4)	56 (5.1)	0.481
OSAS	94 (10.6)	116 (10.5)	0.951
Smoking	135 (15.2)	203 (18.4)	0.061
eGFR (ml/min/1.73 m^2)	93.7 (85.6–99.9)	98.3 (90.3–106.4)	< 0.001
Platelet count (*10^9/L)	216 (179–252)	224 (188–265)	< 0.001
TC (mmol/L)	4.67 (3.99–5.47)	4.73 (4.08–5.40)	0.690
TG (mmol/L)	1.34 (0.98–1.94)	1.45 (1.03–2.05)	0.008
LDL-c (mmol/L)	2.76 (2.16–3.45)	2.88 (2.24–3.53)	0.023

Notes: Values are presented as number (percentage, %) or median (Quartile 1 to Quartile 3, Q1 to Q3).

Abbreviations: PAT, paroxysmal atrial tachycardia; COPD, chronic obstructive pulmonary disease; OSAS, obstructive sleep apnea syndrome; eGFR, estimated glomerular filtration rate; TC, Total cholesterol; TG, triacylglycerol; LDL-c, low density lipoprotein cholesterol.

CHA2 DS2 -VASc Score Analysis for Thromboembolic Events in PAT Patients

The median CHA2 DS2-VASc score was 2 in the PAT group and 1 in the control group. In the PAT group, the CHA2 DS2 VASc score of 52 patients was 0, and these patients had a stroke frequency of 0.5/100 person-years. The CHA2DS2-VASc score of 247 patients was 1, and these patients had a stroke frequency of 0.83 per 100 person-years. A total of 255 patients had a CHA2 DS2-VASc score of 2 and the number of strokes per 100 person-years was 1.13. A total of 199 patients had a CHA2 DS2-VASc score of 3 and the number of strokes per 100 person-years was 2.77. A total of 105 patients had a CHA2 DS2-VASc score of 4 and the number of strokes per 100 person-years was 2.3. 31 patients had a CHA2 DS2-VASc score > 5, and the number of strokes per 100 person-years in these patients was 3.0 (Table 4). These data suggested that stroke rates increased with higher CHA2 DS2-VASc scores, with patients scoring >5 having the highest stroke incidence.

PAT and MACE

In the PAT group, 170 MACE (19.1%) occurred, including 55 MIs /cardiac revascularizations, 12 acute heart failures, 3 life-threatening arrhythmias, 5 cardiac arrests, and 103 cardiovascular hospitalizations. The mean time to MACE was 29.4 ± 17.3 months. In the control group, 110 MACE (9.9%) occurred, including 40 MIs /cardiac revascularizations, 6 acute heart failures, one life-threatening arrhythmias, and 70 cardiovascular hospitalizations, with a median time to MACE was 20.5 months. Kaplan-Meier survival analysis showed significantly reduced event-free survival in the PAT group (log-rank, P <0.001, Figure 3). Cox analysis demonstrated that the presence of PAT was an independent predictor of MACE (HR 1.795; 95% CI 1.398–2.305; P <0.001) after adjusting for age, sex and comorbidities. Further adjustment for covariates such as platelet count, triacylglycerol, and low-density lipoprotein cholesterol, PAT remained an independent predictor of MACE (HR 1.713; 95% CI 1.324–2.216; P <0.001), as shown in Table 5.

Risk Factors for MACE in PAT Patients

In the PAT group, multivariate Cox regression analysis (Table 6) demonstrated that a history of high blood pressure (HR 1.448; 95% CI 1.021–2.052; P = 0.038), coronary heart disease (HR 1.575; 95% CI 1.081–2.295; P = 0.018), heart

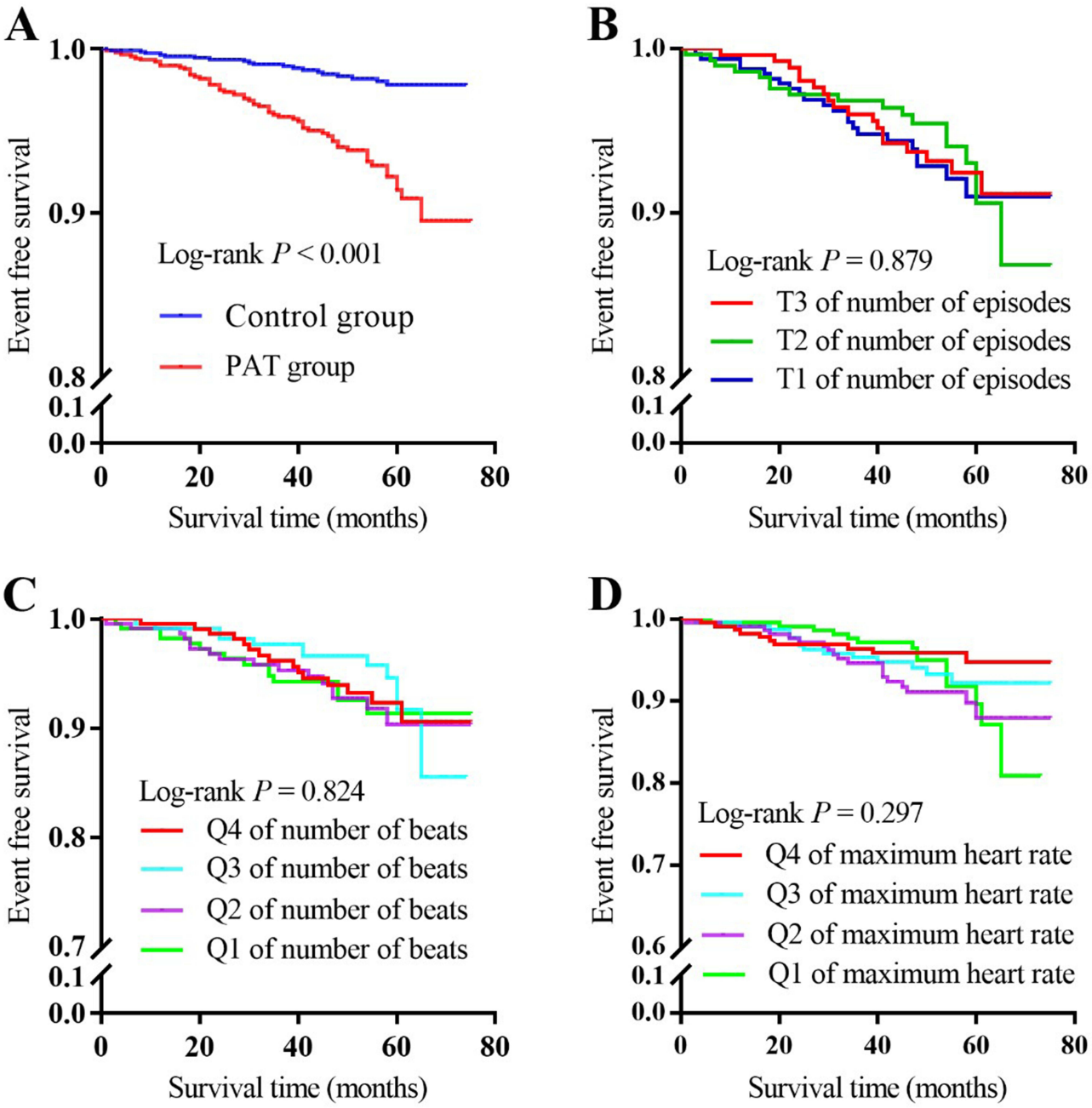

Figure 2 Kaplan-Meier survival curves comparing free from thromboembolic events among patients with and without PAT (**A**). Kaplan-Meier curves representing the incidence of thromboembolic events by three tertile groups (T1, T2 and T3) with episodes of PAT (**B**). Kaplan-Meier curves representing the incidence of thromboembolic events by number of beats at PAT (**C**). Kaplan-Meier curves representing the incidence of thromboembolic events by maximum heart rate at PAT (**D**).
Abbreviation: PAT, Paroxysmal atrial tachycardia; T, tertile.

failure (HR 5.025; 95% CI 2.307–10.948; P <0.001), and chronic renal failure (HR 2.942; 95% CI 1.834–4.718; P <0.001) was independently associated with MACE. Unadjusted Kaplan-Meier survival curves represented a significantly higher risk of MACE in PAT group compared to the control group (Log-rank P< 0.001, Figure 3A). However, further stratification analysis by tertiles or quartiles of 24-hour ECG parameters, showed no significant trends across tertiles of PAT episodes (T1, 1 episode; T2, 2–3 episodes; T3, ≥4 episodes), quartiles of the number of beats at PAT per 24 hours (Q1, 3–5 beats; Q2, 6–10 beats; Q3, 11–22 beats; Q4, 23–18773 beats), and quartiles of maximum heart rate during PAT (Q1, < 115 bpm; Q2, 115–131 bpm; Q3, 132–149 bpm; Q4, ≥150 bpm), with all log-rank P values > 0.05 (Figure 3B–D). Cox regression models for 24-hour ECG parameters did not reveal an association between the

Table 2 The Association Between PAT and Incidence of Thromboembolic Events Analyzed by Using Cox Regression

Adverse events	No-PAT (n=1106)	PAT (n=889)	Model 1		Model 2	
			HR* (95% CI)	*P*-value	HR* (95% CI)	*P*-value
Thromboembolic events	19 (1.7%)	58 (6.5%)	3.782 (2.212–6.467)	< 0.001	3.348 (1.939–5.780)	< 0.001
Ischemic stroke	10 (0.9%)	37 (4.2%)	4.308 (2.102–8.827)	< 0.001	3.920 (1.899–8.090)	< 0.001
TIA	9 (0.8%)	16 (1.8%)	2.661 (1.094–6.473)	0.031	2.377 (0.915–6.174)	0.076
Systemic thromboembolism	0 (0%)	5 (0.6%)	-	–	–	–

Notes: Model 1: adjusted with age, sex, prior stroke or TIA, history of diabetes mellitus, high blood pressure, coronary heart disease, heart failure, chronic renal failure, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea syndrome (OSAS), smoking history. Model 2: adjusted for model 1 plus platelet count, triacylglycerol, and low-density lipoprotein cholesterol. *Hazard ratio of PAT for adverse events.
Abbreviation: PAT, paroxysmal atrial tachycardia; HR, hazard ratio; CI, confidence interval; TIA, transient ischemic attack.

Table 3 Cox Regression Analysis of Risk Factors for Thromboembolic Events in PAT Patients

Variables	Univariable Analysis		Multivariable Analysis	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age (years)	1.000 (1.000–1.001)	0.247	–	–
Female	0.552 (0.329–0.924)	0.024	0.668 (0.392–1.137)	0.137
Prior stroke or TIA	4.256 (2.090–8.666)	< 0.001	3.093 (1.464–6.533)	0.003
High blood pressure	1.768 (0.994–3.145)	0.052	–	–
Coronary heart disease	1.495 (0.775–2.883)	0.230	–	–
Heart failure	5.459 (1.705–17.478)	0.004	2.870 (0.847–9.723)	0.090
Diabetes mellitus	1.706 (0.992–2.934)	0.053	–	–
Chronic renal failure	3.935 (1.931–8.018)	< 0.001	3.182 (1.543–6.561)	0.002
COPD	1.012 (0.316–3.238)	0.984	–	–
OSAS	1.217 (0.552–2.683)	0.626	–	–
Smoking	0.675 (0.290–1.571)	0.361	–	–

Abbreviations: PAT, Paroxysmal atrial tachycardia; HR, hazard ratio; CI, confidence interval; TIA, transient ischemic attack; COPD, chronic obstructive pulmonary disease; OSAS, obstructive sleep apnea syndrome.

Table 4 Risk of Thromboembolic Events per 100 Person-Years Among the CHA2 DS2 -VASc Score Class

CHA_2DS_2-VASc score	Thromboembolic Events	Person-Years	Incidence*
Score 0 (n = 52)	1	199.3	0.50
Score 1 (n = 247)	8	966	0.83
Score 2 (n = 255)	12	1061	1.13
Score 3 (n = 199)	23	830.75	2.77
Score 4 (n = 105)	10	435.5	2.30
Score ≥ 5 (n = 31)	4	133.25	3.00

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

number of PAT episodes, number of beats, or maximum heart rate and MACE risk even after adjusting for covariates, such as high blood pressure, coronary heart disease, heart failure, and chronic renal failure (all $P > 0.05$).

Discussion

To date, this is a novel study evaluating the risk of thromboembolic events as well as MACE in relation to PAT using convenient 24-hour Holter monitoring. Our finding revealed that PAT was significantly linked to an increased incidence

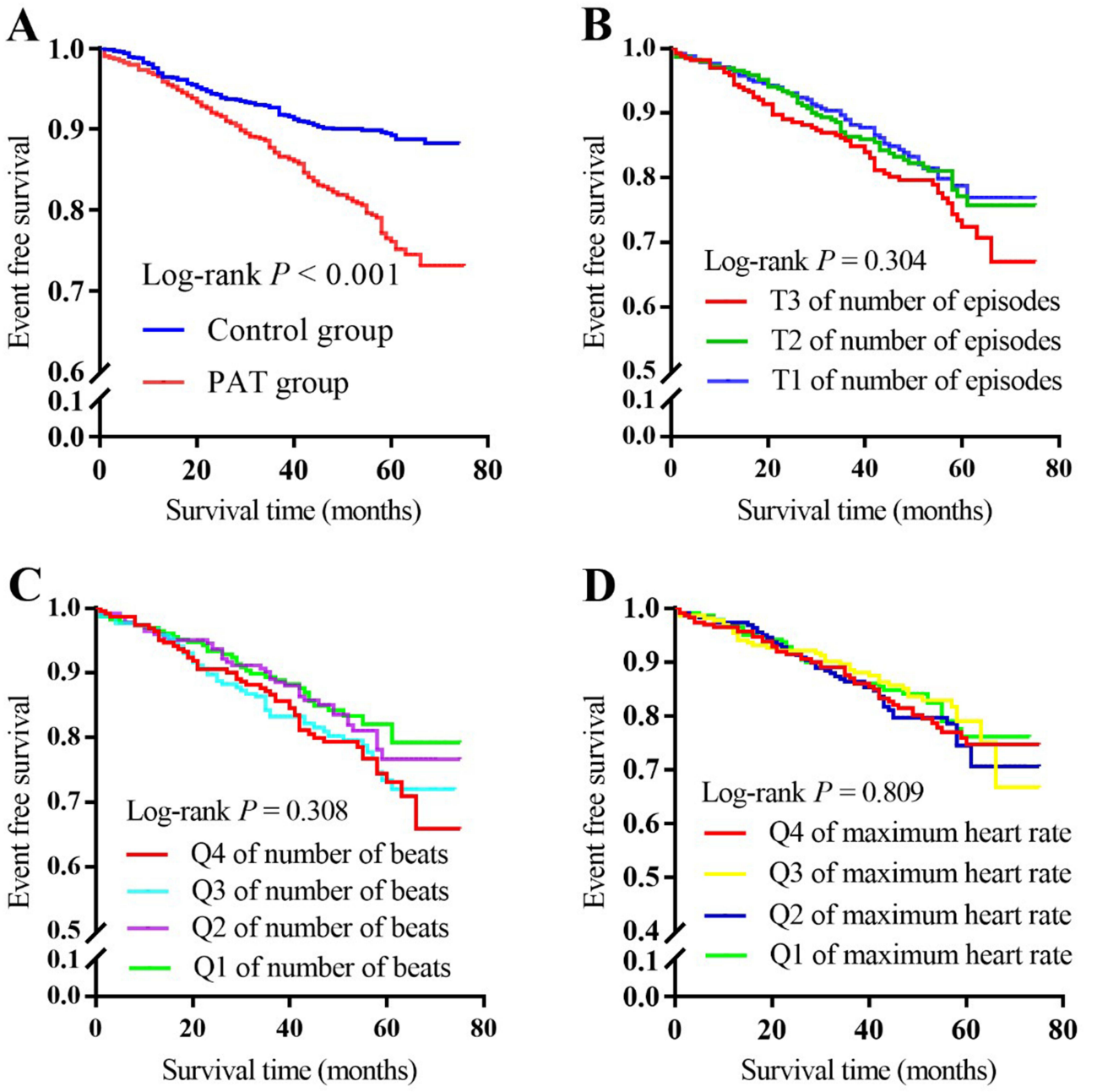

Figure 3 Kaplan-Meier curves comparing free from MACE among patients with and without PAT (**A**). Kaplan-Meier curves representing the incidence of MACE by three tertile groups with episodes of PAT (**B**). Kaplan-Meier curves representing the incidence of MACE by number of beats at PAT (**C**). Kaplan-Meier curves representing the incidence of MACE by maximum heart rate at PAT (**D**).

Abbreviation: PAT, paroxysmal atrial tachycardia; MACE, major adverse cardiovascular events; T, tertile.

of thromboembolic events, even after adjusting for conventional risk factors and baseline imbalances. Furthermore, PAT was also independently associated with the occurrence of MACE during the follow-up period. Notably, our analysis suggested that 24h-ECG parameters, including the number of episodes of PAT, number of heartbeats, and maximum heart rate during PAT, were not predictive of thromboembolic events or MACE, highlighting the need for further research in this area.

AF remains a leading cause of stroke, heart failure, sudden death, and cardiovascular morbidity worldwide. A previous study have showed that approximately 25% of patients with AF-related stroke are diagnosed with AF only at the time of the stroke, which precludes them from receiving primary preventive therapy.[19] As a result, there has been

Table 5 The Association Between PAT and Incidence of MACE Analyzed by Using Cox Regression

Adverse events	No-PAT n=1106	PAT n=889	Model 1		Model 2	
			HR* (95% CI)	*P*-value	HR* (95% CI)	*P*-value
MACE	110 (9.9%)	170 (19.1%)	1.795 (1.398–2.305)	< 0.001	1.713 (1.324–2.216)	< 0.001
MI/CR	40 (3.6%)	55 (6.2%)	1.417 (0.929–2.163)	0.106	1.454 (0.940–2.250)	0.093
Acute heart failure	6 (0.5%)	12 (1.3%)	1.864 (0.652–5.332)	0.246	1.963 (0.613–6.285)	0.256
Life-threatening arrhythmias	1 (0.1%)	3 (0.3%)	6.741 (0.486–93.543)	0.155	8.810 (0.395–196.580)	0.170
Cardiovascular death	0 (0%)	5 (0.6%)	–	–	–	–
Cardiovascular hospitalization	70 (6.3%)	103 (11.6%)	1.645 (1.198–2.258)	0.002	1.499 (1.083–2.074)	0.015

Notes: Model 1: adjusted with age, sex, prior stroke or TIA, history of diabetes mellitus, high blood pressure, coronary heart disease, heart failure, chronic renal failure, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea syndrome (OSAS), smoking history. Model 2: adjusted for model 1 plus platelet count, triacylglycerol, and low-density lipoprotein cholesterol. *Hazard ratio of PAT for adverse events.

Abbreviation: PAT, paroxysmal atrial tachycardia. HR, hazard ratio. CI, confidence interval. MI, myocardial infarction. CR, cardiac revascularization.

Table 6 Cox Regression Analysis of Risk Factors for MACE in PAT Patients

Variables	Univariable Analysis		Multivariable Analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (years)	1.001 (1.000–1.001)	0.014	1.000 (1.000–1.001)	0.364
Female	0.738 (0.542–1.004)	0.053	-	-
Prior stroke or TIA	1.003 (0.470–2.137)	0.995	-	-
High blood pressure	1.758 (1.261–2.450)	0.001	1.448 (1.021–2.052)	0.038
Coronary heart disease	2.029 (1.414–2.911)	< 0.001	1.575 (1.081–2.295)	0.018
Heart failure	6.304 (2.953–13.459)	< 0.001	5.025 (2.307–10.948)	< 0.001
Diabetes mellitus	1.831 (1.336–2.509)	< 0.001	1.357 (0.970–1.899)	0.075
Chronic renal failure	3.671 (2.343–5.752)	< 0.001	2.942 (1.834–4.718)	< 0.001
COPD	0.930 (0.457–1.893)	0.841	–	–
OSAS	1.506 (0.978–2.320)	0.063	–	–
Smoking	1.414 (0.962–2.077)	0.078	–	–

Abbreviations: PAT, Paroxysmal atrial tachycardia. HR, hazard ratio. CI, confidence interval. TIA, transient ischemic attack. COPD, chronic obstructive pulmonary disease. OSAS, obstructive sleep apnea syndrome.

growing interest in identifying supraventricular activity, beyond AF, to aid in the prevention of cardioembolic strokes. Early identification of patients with atrial tachycardia who are at risk of cardioembolic stroke may facilitate timely intervention to prevent these complications.

Several key studies have established the predictive role of atrial contractions in AF development. The Cardiovascular Health Study (CHS) identified premature atrial contraction as a predictor of incident AF and premature atrial contraction count was associated with a significant increase in AF risk,[9] while the Copenhagen Holter Study confirmed a high frequency of premature atrial contractions (≥30 per hour) or more than 20 consecutive premature atrial contractions was associated with a greater risk of ischemic stroke and death.[12] The Malmö Diet and Cancer Study (MDCS) further linked supraventricular tachycardia to incident AF.[20] However, these studies did not distinguish atrial tachycardia or premature atrial contractions based on the duration of tachycardia, and they did not separately investigate the role of PAT. Here, we hypothesize that nonsustained, clustered, and paroxysmal atrial tachycardia is more likely to progress into AF and trigger cardioembolic strokes. This study provides evidence that PAT is an independent predictor of thromboembolic events.

Our analysis also indicated that a history of stroke or transient ischemic attack (TIA) and chronic renal failure were independently associated with thromboembolic events in patients with PAT, indicating that PAT patients with such comorbidities were at a particularly high risk of experiencing thromboembolic events. The Cox regression model adjusted for these variables confirmed that PAT remains an independent risk factor for thromboembolic events.

Consistent with the MDCS findings, our study observed that the duration of supraventricular tachycardia or heart rate of supraventricular tachycardia was not associated with incident AF. Our results indicate that episodes of PAT, number of

beats at PAT, and maximum heart rate during PAT were not significantly associated with the occurrence of thromboembolic events or MACE. However, the prognosis for PAT patients with underlying conditions, such as high blood pressure, coronary heart disease, heart failure, or chronic renal failure, remains poor in terms of both thromboembolic events and MACE. These results underscore the importance of individual patient tolerance to PAT and support the value of risk factor control in managing these patients.

We also found that a history of high blood pressure, coronary heart disease, heart failure, and chronic renal failure was independently associated with MACE in PAT patients, indicating that PAT patients with one or more risk factors face a higher risk of MACE. A mismatch between the blood supply and the demand of coronary arteries is a critical risk factor in the pathogenesis of ischemic heart disease. In patients with a history of coronary heart disease or heart failure, PAT may lead to an increase in blood pressure and aggravate myocardial ischemia, heart failure, and other adverse cardiovascular events.

Although the NOAH-AFNET trial showed that anticoagulation with edoxaban did not significantly reduce the incidence of a composite of cardiovascular death, stroke, or systemic embolism in patients with AHREs detected by implantable devices compared to placebo, patients in the placebo group seemed to be more affected by these adverse events than those in edoxaban group.[21] We believe that for PAT, greater emphasis should be placed on controlling the risk factors rather than solely focusing on anticoagulant therapy. The results of this study suggest that reducing the risk of thromboembolic events and MACE in PAT patients could be achieved through preventive measures, such as targeted risk factor management. For patients with PAT, appropriate risk factor modification and closer follow-up may facilitate better management and prevention of these complications.

Strengths and Limitations

One of the strengths of this study is its specific focus on patients with PAT rather than on those generalized supraventricular tachycardia or sustained atrial tachycardia. To the best of our knowledge, this is the first study to evaluate the risks of thromboembolic events and MACE specifically associated with PAT. We adjusted for many conventional risk factors, including age, sex, prior stroke or TIA, history of diabetes mellitus, high blood pressure, coronary heart disease, and smoking status. Furthermore, we minimized potential confounding factors such as triacylglycerol levels, low-density lipoprotein cholesterol, and platelet count. Therefore, we do not believe that such confounders would have a substantial effect on the results. Additionally, we utilized consistent data from a single type of 24-hour monitoring device (SEER 12 holter recorder) at Beijing Tsinghua Changgung Hospital to avoid heterogeneity caused by various ECG monitoring devices. The 24-hour ECG is non-invasive, cost-effective, and easy to perform, making it a practical tool for screening high-risk PAT patients with PAT and for use in future prospective studies.

However, this study has several limitations. Being retrospective in nature, it did not include certain previously reported independent predictors for thromboembolic events or MACE, such as troponin, NT-proBNP, or body mass index, to avoid biases due to missing data. The follow-up process, which relies on hospital records and telephone calls, may not capture all individuals who have experienced a transient ischemic attack (TIA). Additionally, the detection of AF, particularly asymptomatic AF, may have been inaccurate, limiting the predictive values of PAT and other 24-hour ECG parameters for AF. Most patients in this study did not undergo intracardiac electrophysiological examination, making it challenging to determine the origin of atrial tachycardia or differentiate between focal and re-entrant tachycardia. Lastly, this study was conducted at a single center, which may limit the generalizability of our results to other medical institutions.

Conclusion

PAT measured by 24-hour ECG predicts thromboembolic events independently of other known risk factors. PAT was also associated with an increased incidence of MACE independent of conventional risk factors. Furthermore, thromboembolic events and MACE were linked to underlying comorbidities in PAT patients. Episodes of PAT, the number of beats during PAT, and maximum heart rate during PAT were not associated with thromboembolic events or MACE occurrence. Risk factor modification and close follow-up are essential for managing PAT patients to reduce the associated risks of thromboembolic events and MACE.

Abbreviations

AF, Atrial fibrillation; PAT, Paroxysmal atrial tachycardia; MACE, major adverse cardiovascular events; TIA, Transient ischemic attack; CIEDs, Cardiac implanted electronic devices; AHRE, Atrial high-rate episode; AFL, Atrial flutter; AT, Atrial tachycardia; ECG, Electrocardiographic; VT, Ventricular tachycardia; VF, Ventricular fibrillation; OAC, Oral anticoagulants; IQR, interquartile range; CHS, Cardiovascular Health Study; MDCS, Malmö Diet and Cancer Study; T, tertile.

Declaration of Helsinki

This study adheres to the ethical principles of the Declaration of Helsinki. The study was approved by institute review board of Beijing Tsinghua Changgung Hospital, which waived the need for patient consent for retrospectively acquired clinical data.

Funding

This work was supported by Beijing Municipal Administration of Hospitals' Ascent Plan (DFL20190902), Tsinghua University Spring Breeze Fund (Grant No. 100003001) and Natural Science Foundation of Inner Mongolia Autonomous Region (Grant No. 2023QN08004).

Disclosure

Peng Liu, Tingting Lv, and Yuanwei Liu are co-first authors for this study. The authors report no conflicts of interest in this work.

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