Received: 6 January 2024 | Revised: 16 May 2024 | Accepted: 29 May 2024

DOI: 10.1002/joa3.13094

Journal of Arrhythmia Open Access WILEY

ORIGINAL ARTICLE

Blood pressure variability as a risk factor of recurrent paroxysmal atrial fibrillation after catheter ablation

Minoru Yambe MD, PhD | Yuki Kurose MD | Kaoru Hasegawa MD, PhD | Hisashi Kikuta MD | Takenori Sumiyoshi MD, PhD | Yuko Sekiguchi MD, PhD | Takeyoshi Kameyama MD, PhD | Tatsuya Komaru MD, PhD | Koji Kumagai MD, PhD

Tohoku Medical and Pharmaceutical University, Sendai, Japan

Correspondence
Koji Kumagai, Division of Cardiology, Faculty of Medicine, Tohoku Medical and Pharmaceutical University, 1-15-1 Fukumuro, Miyagino-ku, Sendai, Miyagi 983-8536, Japan.
Email: kumagai4917@tohoku-mpu.ac.jp

Abstract

Background: Blood pressure variability has been found to be a predictor of a stroke, heart failure, and ischemic heart disease that is independent of blood pressure control. This study used the variability independent of the mean (VIM) to evaluate the visit-to-visit blood pressure variability in patients previously undergoing catheter ablation (CA) of paroxysmal atrial fibrillation (PAF), and its relationship with AF recurrence was examined.

Method and Results: The subjects were 274 consecutive PAF patients who underwent CA at our hospital. Finally, 237 subjects were included in the analysis. The mean follow-up period was 29.6 months, during which 37 subjects had recurrences, and 200 did not. During the outpatient blood pressure examinations, the VIM of the systolic blood pressure (VIM SBP) was significantly higher in the recurrence group, suggesting that blood pressure variability is associated with recurrence. The Cox proportional hazards ratio of the VIM SBP was significantly higher in the recurrence (4.839) than no-recurrence group, even after an adjustment, suggesting that the extent of the variability was a risk factor of recurrence post-CA. In addition, the Cox proportional hazard ratio for recurrence was significantly lower in the patients taking dihydropyridine calcium channel blockers, suggesting that the risk of recurrence may differ depending on the type of antihypertensive drug.

Conclusions: Blood pressure variability may be a risk for AF recurrence after CA.

KEYWORDS
antihypertensive drugs, atrial fibrillation, blood pressure, catheter ablation, recurrence

1 | INTRODUCTION

Blood pressure variability has been found to be a predictor of a stroke, heart failure, and ischemic heart disease that is independent of blood pressure control.[1] Because it is also related to atherosclerotic factors and all-cause mortality, it is considered to be associated with a poor prognosis.[2] However, the specifics regarding the role of blood pressure variability, including the mechanism by which it contributes to cardiovascular events, remain unknown. Atrial fibrillation (AF) is associated with a poor prognosis of conditions such as cerebral

infarctions, and catheter ablation (CA) therapy is considered a more effective treatment than antiarrhythmic agents for AF, particularly paroxysmal atrial fibrillation (PAF).[3] Currently, electrical isolation of the pulmonary veins by CA is commonly used as a radical procedure. Although there have been reports of new-onset AF associated with blood pressure variability, literature on AF recurrence after CA and blood pressure variability is sparse.[4] Blood pressure variability is often evaluated using visit-to-visit blood pressure measurements, which are performed during outpatient examinations. The variability independent of the mean (VIM) is an index of the variability that is not dependent on the mean. Consequently, it is a more independent indicator of variability than previously used measures, such as the standard deviation. Although the VIM of the blood pressure has been found to be an index of the cardiovascular risk,[5] there have been no reports on the relationship between the blood pressure variability as determined using the VIM and AF recurrence after CA. This study used the VIM to examine the visit-to-visit blood pressure variability during outpatient visits after CA in patients with PAF and examined its relationship to the recurrence of AF and atrial tachycardia (AT).

2 | METHODS

2.1 | Subjects

The subjects consisted of 274 consecutive patients (repeat patients excluded) who underwent CA of PAF at our hospital between June 2018 and December 2022 and in whom the pulmonary vein isolation (PVI) was successful. The study subjects were patients in whom PAF was diagnosed by recording the AF rhythm preoperatively on a 12-lead electrocardiogram during an episode of AF. Patients with AF that persisted for 7 days or longer and patients for whom sinus rhythm was not recorded by 12-lead electrocardiography before CA were excluded because of the possibility of persistent AF.[6] Patients with a history of a PVI were also excluded ($n=3$). Also excluded were patients who were lost to follow-up because of death or interruption of their hospital visits during the follow-up period ($n=13$). Patients in the recurrence group who had a recurrence within 3 months after the CA were excluded from the analysis because those recurrences occurred during the blanking period and were, therefore, judged not to be recurrences. The patients were ultimately classified into a group with AF recurrence ($n=37$) and a group without AF recurrence ($n=200$, Figure 1). Valvular disease was evaluated by preoperative echocardiography, and patients with severe valvular disease were excluded from the study. Regarding coronary artery disease, myocardial ischemia was evaluated preoperatively by computed tomography (CT) coronary angiography or stress myocardial perfusion scintigraphy. In patients with significant myocardial ischemia, percutaneous coronary intervention (PCI) was performed after the CA ($n=1$).

2.2 | Electrophysiological study and the CA procedure

The CARTO®3 system (Biosense Webster®) or EnSite NavX™ system (Abbott) was used as the three-dimensional mapping system for the CA.

Radio frequency ablation: The PVI was performed with radio frequency (RF) ablation. New findings for the techniques performed in addition to the PVI have been reported for CA performed for AF.[7,8] The CA procedure was as follows. All CA procedures were performed under sedation and anesthesia induced by an intravenous injection of dexmedetomidine and thiopental. A septal puncture was performed under intracardiac echocardiography guidance. A single 5000-unit bolus of heparin was administered after the septal puncture. Physiological saline containing heparin was administered

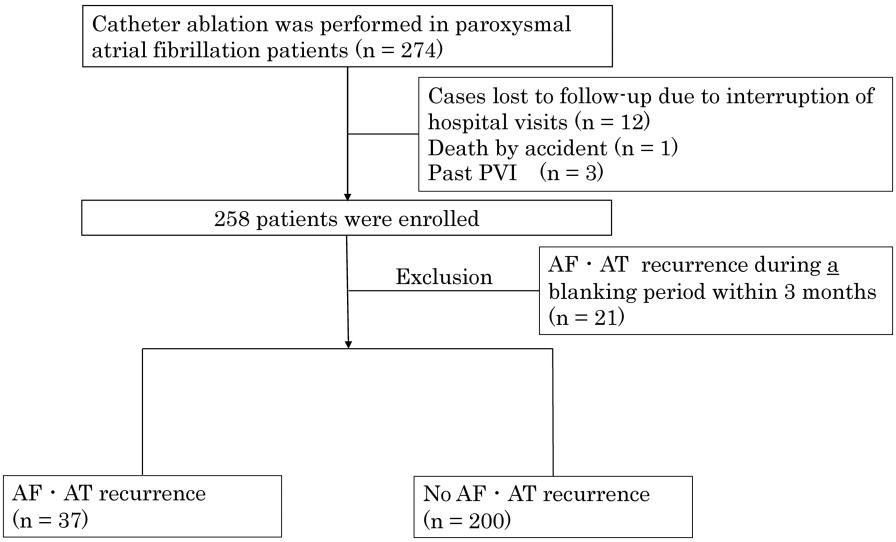

FIGURE 1 Patient flowchart of this study. AF, atrial fibrillation; AT, atrial tachycardia.

continuously to maintain an active coagulation time (ACT) of 300–350 s. For the RF ablation, a 5-French deflectable catheter was inserted into the coronary sinus (CS) from the right femoral vein. After the septal puncture, an 8.5-French SL0 sheath and an Agilis™ NxT sheath (Abbott) were advanced into the left atrium. The three-dimensional left atrium geometry was constructed using a 7-French decapolar circular catheter (EPstar Libero, Japan Lifeline). The PVI was performed using a 7-French decapolar circular catheter placed in the pulmonary vein. The RF catheters used were the FlexAbility™ (Abbott), TactiCath™ SE (Abbott), or TactiFlex™ SE (Abbott) when using the EnSite NavX™ system and the Thermocool Smarttouch® SF (Biosense Webster®) when using the CARTO®3 system. The RF applications when using the FlexAbility™ were delivered for 20 s (5–8 s for sites near the esophagus) at a temperature of 42°C and output of 30 W using a 4.0-mm irrigated-tip RF catheter with an irrigation flow rate of 13 mL/min. The RF applications when using the TactiCath™ SE were delivered for 20 s (5–8 s for sites near the esophagus) at a temperature of 42°C and output of 30 W using a 3.5-mm irrigated-tip RF catheter with an irrigation flow rate of 17–31 mL/min. The RF applications when using the TactiFlex™ SE were delivered for 15 s (5–8 s for sites near the esophagus) at a temperature of 42°C and output of 45 W using a 4.0-mm irrigated-tip RF catheter with an irrigation flow rate of 13 mL/min. The RF applications when using the Thermocool Smarttouch® SF were delivered for 15 s (5–8 s for sites near the esophagus) at a temperature of 42°C and output of 45 W using a 3.5-mm irrigated-tip RF catheter with an irrigation flow rate of 8 mL/min. After the PVI, induction was performed with pacing at an output of 10 mA and pulse width of 2 ms (10 ms steps from 250 to 200 ms, 10 s). Isoproterenol was not administered. Electrical cardioversion was performed if the AF or AT persisted. A cavo-tricuspid isthmus (CTI) ablation was also performed when an atrial flutter that included the CTI in the circuit was induced. In the present study, an electrical isolation of the superior vena cava, box isolation, and CTI ablation were added as necessary.

Cryoballoon ablation: The Arctic Front Advance® system (Medtronic) was used for cryoballoon ablation. For the cryoballoon ablation, a 12-French deflectable catheter was placed in the left atrium using a guidewire after the septal puncture, and a 28-mm cryoballoon was advanced into the left atrium. The deflectable sheath was aligned with the angle of the targeted PV and provided primary support during PV occlusion by the inflated cryoballoon. A spiral mapping catheter (Achieve, Medtronic) was placed in the target pulmonary vein, and the cryoballoon was positioned at the pulmonary vein ostium. After cryoballoon positioning at the PV antrum, an injection of contrast provided venographic evidence of a cryoballoon occlusion or leak detection. The cryoballoon was inflated and pulmonary venography was performed to confirm the pulmonary vein occlusion. The ablation time was 180–240 s. With the best-fit occlusion, the mapping catheter was repositioned to obtain PV potential recordings; otherwise, it is withdrawn proximally after the end of the freezing application to assess for the disappearance of the potentials.[9] Because of the presence of the phrenic nerve, phrenic nerve pacing was performed from the superior vena cava. The esophageal temperature was monitored during ablation, which was stopped when the esophageal temperature decreased to 15°C or lower.

Laser balloon ablation: The Heart Light® system (CardioFocus) was used for the laser balloon ablation. For the laser balloon ablation, a visually guided laser balloon (VGLB; HeartLight®, CardioFocus) was used. After the septal puncture, a VGLB catheter was advanced into the left atrium through a 12-French deflectable sheath, and the balloon was inflated at the ostium of the target pulmonary vein. The ablation site was established endoscopically as a contiguous, overlapping, and circumferential area in the pulmonary vein. The electrical PVI was evaluated using a circular mapping catheter. If the electrical PVI was inadequate, the VGLB catheter was placed again, and additional ablation was performed.

2.3 | Follow-up and the blood pressure measurement method

The blood data used were data from blood collected before the CA. For the visit-to-visit blood pressure, it was known that the variability was smaller after three or more visit opportunities, and to confirm the variability, three or more measurement occasions were considered sufficient for consideration.[10] Furthermore, even the variability of three blood pressure measurements has been shown to be a useful predictor of the prognosis.[11] The patients returned for outpatient hospital visits at 1, 2, 3, 6, and 12 months after the CA. They were subsequently examined when symptoms recurred or during periodic examinations from 6 months to 1 year after the CA. During each examination, the rhythm was determined by 12-lead electrocardiography, and Holter electrocardiography was also performed 12 months after the CA. AF·AT that persisted for at least 30 s was considered a recurrence. If AF·AT was confirmed, the patient was assigned to a recurrent case and the blood pressure at that time was excluded. Outpatient blood pressure measurements were performed during the examinations after the rhythm was determined by 12-lead electrocardiography. The blood pressure was measured according to the 2017 ACC/AHA guidelines.[12] The patients remained at rest for at least 5 min before the measurements, which were performed with the patient seated. The blood pressure measurements were performed using a cuff that covered 80% of the upper arm. Two measurements were performed 1–2 min apart, and the mean was used. If only 1 measurement was performed, that result was used. The blood pressure was measured using an oscillometric automatic sphygmomanometer (OMRON HBP-9020; Omron Healthcare; Kyoto, Japan) and measured at least three times during the outpatient visits during the follow-up period.

2.4 | Visit-to-visit blood pressure variability

The blood pressure variability was quantified using the VIM as the index. The VIM was determined by dividing the standard deviation (SD) by the mean raised to an exponent, as shown in the

equation below. The power x was calculated from a nonlinear regression model for the entire sample. The data were modeled using an SD = a × (Mean[SBP])^x with the calculation performed using the PROC NLIN procedure of the SAS package.[5,13] In this study, the VIM was calculated individually for the SBP and the diastolic blood pressure (DBP) and was used as an index of the blood pressure variability, and its relationship with AF recurrence was examined.

$$\mathrm{VIM} = \frac{\text{Standard Deviation(SBP)}}{\text{Mean(SBP)}^x}$$

$$\mathrm{SD} = a \times \left(\text{Mean}\left[\mathrm{SBP}\right]\right)^x.$$

2.5 | Statistical analysis

The *t*-test, chi-squared test, and Fisher exact test were used to test for significant differences. Factors with nonnormal distributions were compared using logarithms. Hazard ratios were calculated using the Cox proportional hazards ratio.

The proportional hazards assumption was examined by constructing a model that generated time-dependent covariates by creating an interaction between the predictors and the survival time function. If any time-dependent covariates were significant, then their predictors were not proportional. A *p*-value of <0.05 was considered significant. SAS system version 9.4 software (SAS Institute, Cary, NC) was used for the statistical analysis.

3 | RESULTS

3.1 | Clinical characteristics

The mean follow-up period was 29.6 months. Patients with a history of a PVI were excluded (*n* = 3). Follow-up observations could not be performed in 13 of the 274 patients (12 lost to follow-up and, 1 accidental death). Of the 258 subjects enrolled in the study, recurrence, including early recurrence, was seen in 58. Twenty-one subjects with early recurrence during the 3-month blanking period were excluded from the analysis. Thus, 237 subjects were ultimately included in the analysis (37 in the recurrence group, and 200 in the no-recurrence group). Of those 237 subjects, 34 were asymptomatic. The mean age of the subjects was 64.7 years; 156 were men, and 81 were women. The methods of CA used were an RF PVI (*n* = 220), cryoballoon ablation (*n* = 36), and laser balloon ablation (*n* = 12). When the PVI was performed, a CTI and superior vena cava ablation were also performed as needed. There were no patients for whom an electrical PVI could not be achieved by CA.

3.2 | Blood pressure variability and the risk of AF recurrence

The brain natriuretic peptide (BNP) level, VIM of the systolic blood pressure (VIM SBP) and VIM of the diastolic blood pressure (VIM DBP) were nonnormally distributed, and their logarithmic values were, therefore, used in the analysis. A figure of the distribution and the quantile–quantile plot (QQ plot) showed a normal distribution (Data S1). In comparing the patients with recurrence and no-recurrence, significant differences were seen for the following: gender (proportion of females), smoking, logarithmic BNP (Log BNP), standard deviation of the SBP (SD SBP), logarithmic VIM SBP (Log VIM SBP), dyslipidemia, and the use of dihydropyridine calcium channel blockers and antiarrhythmic drugs at discharge. The Log VIM SBP was significantly higher in the patients with recurrence (Table 1). A multivariate analysis was performed using the gender, duration of the PAF, dihydropyridine calcium channel blockers, use of antiarrhythmic drugs after CA, and the Log VIM SBP, which were significant in the univariate analysis. The Cox proportional hazards ratio test showed a significantly high hazard ratio of 4.554 for the Log VIM SBP. When adjusted for the gender, when the duration of the PAF and the use or nonuse of dihydropyridine calcium channel blockers or antiarrhythmic drugs were used the hazard ratio for the Log VIM SBP remained significant (4.839). The Cox proportional hazard ratio for the duration of the PAF was significant, but low (1.006). The gender was not a significant risk factor for AF·AT recurrence after the CA in this study. The results suggested that the blood pressure variability may be a risk factor for AF·AT recurrence after CA. In addition, the duration of the PAF was also suggested to be a possible risk factor for recurrence (Table 2).

This study was conducted excluding missing values. In cases of recurrence, the observation period may have been shortened, so we assumed that the follow-up was performed for 1 year and performed a multiple imputation method. To impute the missing values, we constructed multiple regression models including variables potentially related to the fact that the values were missing also variables correlated with that outcome. Thirty multiple imputations by a fully conditional specification were performed with the PROC MI in SAS. The Cox proportional hazard ratios for each factor were similarly significant (Data S2).

4 | DISCUSSION

4.1 | Blood pressure variability and AF recurrence

Blood pressure variability is considered a risk factor and is associated with a poor prognosis for conditions such as a stroke, myocardial infarction, and heart failure.[1] Moreover, a large blood pressure variability has been reported to be a risk factor for new-onset AF.[14] However, regarding the relationships between the blood pressure variability and cardiovascular and cerebrovascular events, aspects such as the underlying mechanism have not been elucidated, and many points are unclear. There have been previous reports regarding the relationship between blood pressure variability as determined using the standard deviation and AF recurrence after CA, as well as new-onset AF.[4] However, the relationship between the VIM, which is considered an independent index of blood pressure variability, and AF recurrence

TABLE 1 Baseline characteristics and clinical characteristics.

Variables	All ($n=237$) *n* (%)	Recurrence ($n=37$) *n* (%)	No-recurrence ($n=200$) *n* (%)	*p*-value (recurrence vs. no-recurrence)
Age (year)	64.7 ± 10.9	65.1 ± 13.5	64.6 ± 10.3	.8248
Female	81 (34.1)	18 (48.7)	53 (26.5)	.0107*
Body mass index (kg/m^2)	24.5 ± 3.6	24.2 ± 4.5	24.6 ± 3.4	.6007
Duration of PAF (month)	29.7 ± 53.1	44.35 ± 59.4	27.1 ± 51.7	.0692
Past CA (CTI)	5 (2.1)	1 (2.7)	4 (2.0)	.5754
Alcohol	136 (57.3)	17 (46.0)	119 (59.5)	.1487
Smoking (current and past)	128 (53.2)	14 (35.1)	114 (56.5)	.0472*
Symptomatic paroxysmal atrial fibrillation	206 (86.9)	34 (91.9)	172 (86.0)	.4324
CHA_2DS_2-VAS_C score	2.1 ± 1.5	2.2 ± 1.7	2.1 ± 1.4	.6935
History of strokes	24 (10.1)	4 (10.8)	20 (10.0)	.7744
History of ischemic heart disease				
Prior angina pectoris	19 (8.0)	5 (13.5)	14 (7.0)	.1895
Prior myocardial infarction	6 (1.6)	1 (2.7)	5 (2.5)	1.0
Echography				
LVEF (%)	61.5 ± 7.6	62.3 ± 6.0	61.4 ± 7.8	.4972
Left atrial dimension (mm)	39.5 ± 6.6	38.1 ± 6.5	39.7 ± 6.6	.1932
E/e'	7.34 ± 2.94	6.99 ± 2.1	7.39 ± 3.1	.3545
eGFR (mL/min/1.73m^2)	68.9 ± 15.0	68.8 ± 16.6	70.2 ± 16.1	.5446
HbA1c (%)	6.02 ± 0.65	6.04 ± 0.11	5.95 ± 0.65	.4924
BNP (pg/mL), median (IQR)	31.5 (15.4, 60.6)			
Log BNP (Unit)	1.50 ± 0.45	1.65 ± 0.44	1.47 ± 0.44	.0245*
PVI methods				
RF EnSite NavX™	194 (81.9)	35 (94.6)	159 (79.5)	.0344
RF CARTO®3	16 (6.8)	1 (2.7)	15 (7.5)	.4783
Cryoballoon	36 (15.2)	2 (5.4)	34 (17.0)	.0824
Laser balloon	12 (5.1)	2 (5.4)	10 (5.0)	1.0
Additional ablation				
CTI isolation	38 (16.0)	4 (10.81)	34 (17)	.4667
BOX isolation	2 (0.8)	0 (0)	2 (1.0)	1.0
SVC isolation	12 (5.1)	3 (8.1)	9 (4.5)	.4068
Mean SBP (mmHg)	128.9 ± 12.9	129.5 ± 11.1	128.8 ± 13.1	.7934
Mean DBP (mmHg)	74.3 ± 8.9	74.7 ± 7.5	74.2 ± 9.2	.7479
SD SBP	9.1 ± 5.5	11.2 ± 7.2	8.7 ± 5.0	.0115*
SD DBP	5.8 ± 3.7	6.1 ± 3.4	5.7 ± 3.7	.5549
VIM SBP, median (IQR)	0.1180 (0.081, 0.171)			
VIM DBP, median (IQR)	1.768 (1.157, 2.425)			
Log VIM SBP (Unit)	−0.928 ± 0.240	−0.851 ± 0.251	−0.9423 ± 0.237	.0359*
Log VIM DBP (Unit)	0.241 ± 0.254	0.275 ± 0.265	0.235 ± 0.235	.3932
Hypertension	146 (61.6)	19 (51.4)	127 (63.5)	.1980
Antihypertensive agent after CA				
Dihydropyridine Calcium channel blocker	101 (32.6)	10 (27.3)	91 (45.5)	.0461*
Angiotensin receptor blocker	89 (37.6)	10 (27.3)	79 (39.5)	.1958
Angiotensin-converting enzyme inhibitor	6 (1.6)	0 (0)	6 (3.0)	.5937

TABLE 1 (Continued)

Variables	All ($n=237$) *n* (%)	Recurrence ($n=37$) *n* (%)	No-recurrence ($n=200$) *n* (%)	*p*-value (recurrence vs. no-recurrence)
Angiotensin receptor neprilysin inhibitor	3 (1.2)	0 (0)	3 (1.5)	1.0
Beta blocker	77 (32.4)	6 (16.2)	69 (34.5)	.0336*
Alpha blocker	6 (2.5)	1 (2.7)	5 (2.5)	1.0
Thiazide	18 (7.5)	1 (2.7)	17 (8.5)	.3214
Diabetes mellitus	45 (19.0)	4 (10.8)	41 (20.5)	.2523
Dyslipidemia (total)	107 (45.1)	10 (27.0)	97 (48.5)	.0191*
Statin	76 (32.1)	9 (24.3)	67 (33.5)	.3389
Chronic heart failure	9 (3.8)	1 (2.7)	8 (4.0)	1.0
Digoxin	5 (2.1)	1 (2.7)	4 (2.0)	.5754
AAD after CA (total)	53 (22.3)	15 (40.5)	38 (19.0)	.0086*
Cibenzoline	2 (0.8)	1 (2.7)	1 (0.5)	1.0
Flecainide	18 (7.6)	7 (18.9)	11 (5.5)	.0112*
Verapamil	18 (7.6)	6 (16.2)	18 (9.0)	.2301
Pilsicainide	5 (2.1)	1 (2.7)	4 (2.0)	.5754
Bepridil	13 (5.5)	1 (2.7)	12 (6.0)	.6979

Abbreviations: AAD, antiarrhythmic drug; BNP, brain natriuretic peptide; CA, catheter ablation; CTI, cavo-tricuspid isthmus; DPB, diastolic blood pressure; eGFR, estimate glomerular filtration rate; HbA1c, hemoglobin A1c; IQR, interquartile range; Log, logarithmic; LVEF, left ventricle ejection fraction; PAF, paroxysmal atrial fibrillation; PVI, pulmonary vein isolation; RF, radio frequency; SBP, systolic blood pressure; SD, standard deviation; SVC, superior vena cava; VIM, variability independent of means.

*$p<0.05$.

after CA has not been determined. The present study evaluated the PAF recurrence after CA and visit-to-visit blood pressure variability for PAF using the VIM. The results suggested that blood pressure variability was related to the recurrence of PAF after CA as an independent predictor. Blood pressure control has previously been emphasized in the management of the blood pressure, with target blood pressures being recommended. However, the results of the present study suggested that, although it is important to achieve antihypertensive targets in controlling the blood pressure after CA, it may also be important to control the blood pressure variability.

Atrial fibrillation is not triggered only by the pulmonary veins. There are other triggers, such as nonpulmonary vein foci. The pattern of recurrence may differ depending on the trigger. In the present study, there was no significant difference in recurrence rate among the patients who underwent additional ablation other than the PVI. Further studies are considered necessary because of the small number of cases, for further follow-up of the cases and a reexamination of the second CA.

4.2 | Blood pressure variability and antihypertensive agents

The Cox proportional hazard ratio for AF recurrence was low in patients who were taking a dihydropyridine calcium channel blocker as an antihypertensive therapy in this study, suggesting that dihydropyridine calcium channel blockers may reduce the risk of recurrence. From the perspective of blood pressure variability, a study comparing dihydropyridine calcium channel blockers and beta blockers found that dihydropyridine calcium channel blockers provided a greater reduction in the blood pressure variability.[15] Dihydropyridine calcium channel blockers were also found to reduce the blood pressure variability more than angiotensin receptor blockers (ARBs) and angiotensin-converting enzyme inhibitors (ACE-I). The reduction in the blood pressure variability provided by dihydropyridine calcium channel blockers may serve as a mechanism for reducing the rate of AF recurrence. However, although a comparison of the groups taking dihydropyridine calcium channel blockers in the recurrence and no-recurrence groups in the present study showed a trend toward a lower Log VIM SBP in the no-recurrence group, the difference was not significant. An investigation with a larger number of patients is needed. When an episode of PAF occurs, many patients complain of palpitations because of tachycardias, and a beta blocker may, therefore, be selected as an antihypertensive drug. The results of the present study indicated that dihydropyridine calcium channel blockers may be superior for inhibiting recurrence after CA and that an antihypertensive drug that is likely to reduce the blood pressure variability needs to be selected before the CA.

On the other hand, patients who were taking an antiarrhythmic drug at discharge had a significantly high hazard ratio for recurrence. These were patients who after CA experienced frequent supraventricular premature beats or AT·AF that persisted for less than 30 s and started taking an antiarrhythmic drug, suggesting that

TABLE 2 Cox proportional hazard model for the recurrence of paroxysmal atrial fibrillation.

	Unadjusted			Multivariate adjusted		
	HR	95% CI	*p*-value	HR	95% CI	*p*-value
Age	1.003	0.972–1.035	.8552			
Female	1.945	1.000–3.782	.0499*	1.842	0.932–3.641	.0789
Body mass index	0.969	0.880–1.067	.5233			
Duration of PAF	1.005	1.000–1.009	.0419*	1.006	1.001–1.010	.0159*
Left atrium dimension	0.959	0.909–1.011	.1220			
eGFR	1.003	0.981–1.025	.7996			
Log BNP	1.851	0.918–3.735	.0855			
SD SBP	1.066	1.015–1.119	.0104*			
SD DBP	1.019	0.936–1.108	.6683			
Log VIM SBP	4.554	1.032–20.091	.0453*	4.839	1.038–22.555	.0447*
Log VIM DBP	1.694	0.421–6.462	.4731			
Hypertension	0.613	0.319–1.180	.1429			
Dihydropyridine calcium channel blocker	0.431	0.203–0.917	.0289*	0.387	0.179–0.836	.0158*
Angiotensin receptor blocker	0.675	0.324–1.405	.2935			
Angiotensin-converting enzyme inhibiter	0.00	0-	.9897			
Angiotensin receptor neprilysin inhibitor	0.00	0-	.9908			
Beta blocker	0.421	0.175–1.013	.0535			
Alpha blocker	1.113	0.152–8.131	.9161			
Thiazide	0.381	0.052–2.784	.3419			
Diabetes mellitus	0.537	0.190–1.522	.2425			
Dyslipidemia (total)	0.367	0.172–0.781	.0093*			
Statin	0.576	0.262–1.266	.1700			
Chronic heart disease	0.778	0.107–5.686	.8050			
Digoxin	1.236	0.169–9.029	.8346			
AAD after CA (total)	2.237	1.140–4.388	.0192*	2.327	1.167–4.642	.0165*
Cibenzoline	4.308	0.589–31.517	.1504			
Verapamil	1.986	0.824–4.783	.1262			
Pilsicainide	1.236	0.169–9.029	.8346			
Flecainide	2.237	0.907–5.518	.0804			
Bepridil	0.464	0.063–3.390	.4492			

Abbreviations: AAD, antiarrhythmic drug; BNP, brain natriuretic peptide; CA, catheter ablation; DPB, diastolic blood pressure; eGFR, estimate glomerular filtration rate; Log, logarithmic; PAF, paroxysmal atrial fibrillation; SBP, systolic blood pressure; SD, standard deviation; VIM, variability independent of means.

*$p < .05$.

patients with postoperative supraventricular arrhythmias have high recurrence rates even with antiarrhythmic drug administration. In a previous report, no significant difference was found between dihydropyridine calcium channel blockers and ARBs with respect to the prevention of PAF recurrences.[16] However, the results of the present study suggested that dihydropyridine calcium channel blockers may be more effective than other antihypertensive drugs in preventing such recurrences.

Moreover, the present study showed that the recurrence group had significantly more patients who were receiving drug therapy for hyperlipidemia. However, when the drugs were classified as statins and other lipid-lowering drugs and their hazard ratios were determined, no significant differences were seen. Blood pressure variability has been found to be reduced in a group receiving statins.[15] Consequently, further investigation is needed in this regard, including investigations that determine the actual status of lipid management.

4.3 | Duration of PAF

In addition, the results of the present study suggested that the time from the PAF diagnosis to CA may play a role in recurrence, although the Cox proportional hazard ratio for this factor was not

high. That suggested that it is also important to perform CA sooner after PAF is diagnosed. CA is becoming the common treatment for PAF. Although it is important to carefully consider the indication, CA ought to be performed as soon as PAF is diagnosed. Subsequently, adequate consideration must be given not only to blood pressure control but also to blood pressure variability.

4.4 | Clinical implications

Evidence suggests that large blood pressure variability is associated with a poor prognosis for conditions such as cardiovascular and cerebrovascular disorders.[15] However, it has also been found not to be a significant index compared with a blood pressure reduction,[13,17] and further investigation of its role as a prognostic factor is needed. Much also remains unknown about its role as a prognostic factor after heart disease treatment. Patients with large blood pressure variability have a high incidence of a stroke. AF may also play a causal role in cerebral infarctions, but the mechanism has not been elucidated in the investigations that have so far been conducted.[18] Although the present study examined patients who underwent CA of PAF, the relationship between blood pressure variability and recurrence after CA of PAF and other arrhythmias also needs to be examined in a large population.

5 | CONCLUSION

The present results suggested blood pressure variability may be a risk for AF recurrence after CA. In addition, the risk of recurrence varied depending on the type of antihypertensive drug used, with the risk being low in the group that took dihydropyridine calcium channel blockers. Thus, the results also suggested that differences in the change in blood pressure variability depending on the antihypertensive drug used may play a role in recurrence.

5.1 | Limitations

Although the subjects included patients with asymptomatic PAF, symptomatic PAF was significantly more common in patients with recurrence. There may be patients with recurrences who are not identified because they are asymptomatic. Methods such as periodic at-home ECG checks by means such as a smart watch technology offer promise in this regard.

In the present study, postcatheter ablation cases were considered. Ideally, a preoperative blood pressure variability evaluation is necessary because the effect of antiarrhythmic drugs on the blood pressure variability and the ablation itself on the blood pressure variability cannot be ruled out. Further, we could not conduct a survey on the adherence to medication. We would like to consider additional surveys in the future.

ACKNOWLEDGMENTS

The authors are indebted to Professor Hirohito Metoki and Dr. Michihiro Satoh of the Tohoku Medical and Pharmaceutical University, Division of Public Health, Hygiene and Epidemiology for their advice on the statistical analysis.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest associated with this manuscript.

DATA AVAILABILITY STATEMENT

The deidentified participant data will not be shared.

ETHICS STATEMENT

The protocol of this study was reviewed and approved by the Ethics Committee of Tohoku Medical and Pharmaceutical University (No. 2023-2-031).

PATIENT CONSENT STATEMENT

Informed consent was obtained in the form of opt-out on the website. Those who rejected were excluded.

ORCID

Minoru Yambe https://orcid.org/0009-0001-7983-3464

REFERENCES

1. Rothwell PM, Howard SC, Dolan E, O'Brien E, Dobson JE, Dahlöf B, et al. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. Lancet. 2010;375(9718):895–905.
2. Lau KK, Wong YK, Chan YH, Teo KC, Chan KH, Wai Li LS, et al. Visit-to-visit blood pressure variability as a prognostic marker in patients with cardiovascular and cerebrovascular diseases–relationships and comparisons with vascular markers of atherosclerosis. Atherosclerosis. 2014;235(1):230–5.
3. Hakalahti A, Biancari F, Nielsen JC, Raatikainen MJ. Radiofrequency ablation vs antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: systematic review and meta-analysis. Europace. 2015;17(3):370–8.
4. Kamioka M, Kaneshiro T, Hijioka N, Amami K, Nodera M, Yamada S, et al. Visit-to-visit blood pressure variability predicts atrial fibrillation recurrence after pulmonary vein isolation in patients with Hypertension and atrial fibrillation. Circ Rep. 2021;3(4):187–93.
5. Ebinger JE, Driver M, Ouyang D, Botting P, Ji H, Rashid MA, et al. Variability independent of mean blood pressure as a real-world measure of cardiovascular risk. EClinicalMedicine. 2022;13(48):101442.
6. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016;37(38):2893–962.
7. Kumagai K, Minami K, Sugai Y, Sumiyoshi T, Komaru T. Effect of ablation at high-dominant frequency sites overlapping with low-voltage areas after pulmonary vein isolation of nonparoxysmal atrial fibrillation. J Cardiovasc Electrophysiol. 2019;30(10):1850–9.
8. Kumagai K, Sato T, Kurose Y, Sumiyoshi T, Hasegawa K, Sekiguchi Y, et al. Predictors of recurrence of atrial tachyarrhythmias after pulmonary vein isolation by functional and structural mapping of nonparoxysmal atrial fibrillation. J Arrhythm. 2021;38(1):86–96.

9. Georgiopoulos G, Tsiachris D, Manolis AS. Cryoballoon ablation of atrial fibrillation: a practical and effective approach. Clin Cardiol. 2017;40(5):333–42.
10. Hartley RM, Velez R, Morris RW, Souza MF, Heller RF. Confirming the diagnosis of mild hypertension. Br Med J (Clin Res Ed). 1983;286(6361):287–9.
11. Alpérovitch A, Blachier M, Soumaré A, Ritchie K, Dartigues JF, Richard-Harston S, et al. Blood pressure variability and risk of dementia in an elderly cohort, the Three-City study. Alzheimers Dement. 2014;10(5 Suppl):S330–S337.
12. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the Prevention, Detection, Evaluation, and management of high blood Pressure in Adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018;71(6):e13–e115.
13. Asayama K, Kikuya M, Schutte R, Thijs L, Hosaka M, Satoh M, et al. Home blood pressure variability as cardiovascular Risk factor in the population of Ohasama. Hypertension. 2013;61(1):61–9.
14. Lee SR, Choi YJ, Choi EK, Han KD, Lee E, Cha MJ, et al. Blood pressure variability and incidence of new-onset atrial fibrillation: a nationwide population-based study. Hypertension. 2020;75(2):309–15.
15. Rothwell PM, Howard SC, Dolan E, O'Brien E, Dobson JE, Dahlöf B, et al. Effects of beta blockers and calcium-channel blockers on within-individual variability in blood pressure and risk of stroke. Lancet Neurol. 2010 May;9(5):469–80.
16. Yamashita T, Inoue H, Okumura K, Kodama I, Aizawa Y, Atarashi H. Randomized trial of angiotensin II-receptor blocker vs. dihydropiridine calcium channel blocker in the treatment of paroxysmal atrial fibrillation with hypertension (J-RHYTHM II study). Europace. 2011;13(4):473–9.
17. Hara A, Thijs L, Asayama K, Jacobs L, Wang JG, Staessen JA. Randomised double-blind comparison of placebo and active drugs for effects on risks associated with blood pressure variability in the systolic Hypertension in Europe trial. PLoS One. 2014;9(8):e103169.
18. Gosmanova EO, Mikkelsen MK, Molnar MZ, Lu JL, Yessayan LT, Kalantar-Zadeh K, et al. Association of systolic blood pressure variability with mortality, coronary heart disease, stroke, and renal disease. J Am Coll Cardiol. 2016;68(13):1375–86.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Yambe M, Kurose Y, Hasegawa K, Kikuta H, Sumiyoshi T, Sekiguchi Y, et al. Blood pressure variability as a risk factor of recurrent paroxysmal atrial fibrillation after catheter ablation. J Arrhythmia. 2024;40:858–866. https://doi.org/10.1002/joa3.13094