Original Article

Coronary Artery Dominance and Atrial Fibrillation Recurrence after Cryoballoon Pulmonary Vein Isolation

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Abstract

Background and Aim: Catheter-based atrial fibrillation (AF) ablation primarily for pulmonary vein isolation (PVI) has become a significant therapeutic alternative for symptomatic and drug-refractory AF patients. It is evident that AF time and left atrium diameter (LAD) have the most critical impact on AF recurrence. In this study, we aimed to evaluate the role of coronary artery dominance for predicting AF recurrence after cryoballoon PVI. **Methods:** We retrospectively analyzed clinical, laboratory, and angiographic data from consecutive patients who underwent coronary angiography and successful cryoballoon PVI. Images of the coronary angiography were retrospectively reviewed for the coronary artery dominance by two experienced observers. The coronary artery system was classified as right dominant (RD) and left dominant. **Results:** A total of 140 patients without coronary artery disease and structural heart disease who underwent successful cryoballoon PVI were included in the study. There were 101 RD (72%) and 39 left-dominant (28%) patterns. A total of 26 patients (22%) had developed AF recurrence during follow-up. AF recurrence rates were 41% in the left coronary-dominant group and 15% in the right coronary-dominant group ($P = 0.001$). According to AF recurrence after cryoballoon PVI, only follow-up time (15.7 ± 2.4 vs. 14 ± 1.8 months, $P = 0.001$), LAD (41.8 ± 2 vs. 40.6 ± 1.8 mm, $P = 0.003$) and coronary artery disease (CAD) (left CAD, 51.6% vs. 21.1%, $P = 0.001$) were significantly associated with AF recurrence. AF recurrence rates in multivariable logistic regression analysis according to AF recurrence after cryoballoon PVI, follow-up time, LAD, and CAD were independent predictors of AF recurrence. **Conclusions:** Our findings suggested that left CAD may be related to AF recurrence after cryoballoon PVI. Coronary artery dominance may be an additional predictor of AF recurrence if supported by larger prospective studies.

Keywords: Atrial fibrillation, coronary artery, cryoballoon, dominance, pulmonary vein

Introduction

Atrial fibrillation (AF) is the most common type of sustained cardiac arrhythmia in clinical practice.[1] Catheter-based AF ablation, primarily by pulmonary vein isolation (PVI), has

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emerged as a promising therapeutic alternative with improved efficacy and safety in symptomatic and drug-refractory AF patients.[2] Although there has been a significant improvement in procedural success through the use of recently developed ablation techniques, postprocedural AF recurrences continue to be a major clinical problem following catheter ablation, occurring in approximately 25%–50% of patients.[3]

Anatomical coronary dominance is defined based on the origin of the posterior descending artery (PDA) that supplies the posterior portion of the interventricular septum.[4,5] In a right-dominant (RD) circulation, the right coronary artery (RCA) gives off the PDA, while in a left-dominant (LD) circulation, the left circumflex (LCX) artery supplies this territory.[4,5] In the present study, we evaluate the relationship between coronary arterial dominance and AF recurrence after cryoballoon ablation (CA).

Methods

We analyzed retrospectively clinical, laboratory, and angiographic data of consecutive patients who underwent a coronary angiography and a successful CA for 12-lead confirmed, symptomatic, and drug-refractory paroxysmal AF. Patients whose episodes of AF terminated spontaneously within 7 days of onset were defined as having paroxysmal AF.

Patients with valvular disease, a thrombus in the left atrium (LA), thyroid dysfunction, preprocedural significant coronary artery stenosis, myocardial infarction, previous cardiac surgery, contraindication to anticoagulation, pregnancy, and an LA diameter (LAD) >50 mm were excluded from the study, along with subjects with recent infections, malignancies, blood dyscrasias, autoimmune or inflammatory diseases, renal failure, or hepatic failure.

The recorded patient data, accessed from the records from the time of CA, included both clinical and demographic characteristics, including age, gender, history of arterial hypertension (HT), diabetes mellitus (DM) and tobacco use, and echocardiographic parameters.

Periprocedural interventions related to the catheter CA were performed as outlined in the current guidelines and studies.[3,6,7] The study participants continued to receive the anticoagulation and antiarrhythmic drug regimen prescribed prior to the ablation procedure for the following 3 months. When the patients developed symptoms compatible with recurrent AF, follow-up visits were made in the 3rd, 6th, and 12th months and then at most every 6 months afterward. In the postprocedural 3rd month, a 24–48-h Holter electrocardiograph (ECG) was made, and antiarrhythmic treatment was ceased if no arrhythmia was detected. At the 3rd month and every 6 months thereafter, another 24–48-h Holter ECG was performed and recorded. The requirement for oral anticoagulation was also assessed after the 3rd month, based on the CHA2DS2-VASc score.[8] The time from the date of ablation to the date of recurrence or the last follow-up was used to calculate the AF-free period. The blanking period was defined as the first 3 months following AF ablation. No atrial arrhythmias that arose during the blanking period were defined as a recurrence. The detection of AF (at least 30 s when evaluated with ECG or Holter ECG monitoring) occurring more than 3 months after the AF ablation procedure was used to define AF recurrence.

Images of the coronary angiography were obtained using standardized angiographic projections, based on the guidelines of the American College of Cardiology/American Heart Association, and stored digitally.[9] All images were reviewed retrospectively for coronary dominance by two experienced observers. The coronary artery system was classified as RD if the RCA gave off the PDA and as LD if the LCX supplied this territory. Significant coronary artery disease (CAD) was defined as a ≥50% narrowing of luminal diameter in at least one projection of at least one major epicardial artery, and these subjects were excluded.

The study was in compliance with the principles outlined in the Declaration of Helsinki and approved by the institutional ethics committee.

Statistical analysis

The normality of distribution of all study parameters was evaluated. For the comparison of continuous data with normal distribution, a Student's *t*-test was used. A Mann–Whitney U-test was used to compare data with skewed distribution. A Chi-square test was used to compare categorical variables. Continuous variables are presented as mean ± SD, whereas categorical data are presented as percentages. To clarify the clinical predictors of outcomes, a univariate Cox proportional analysis was performed initially. Sequentially, all variables with $P < 0.10$ in the univariate analyses were included in a multivariate analysis, and hazard ratios and 95% confidence intervals were calculated. For all tests, a two-tailed $P < 0.05$ was considered statistically significant. The statistical analysis made using SPSS version 20.0 software (IBM Corp., Armonk, NY, USA).

Results

A total of 140 patients without significant CAD who underwent CA for AF were included. The mean age of the cohort was 41.8 ± 7.8 years; 59% were men; 13% had diabetes; 38% had HT; and 27% were smokers. Of the 140 patients enrolled in the study, 31 (22%) had AF recurrence, 101 (72%) had RD circulation, and 39 (28%) had LD circulation. The baseline characteristic features of the study population are presented in Table 1.

The patients were divided into two groups, based on the recurrence of AF. There were no significant differences between the two groups in the mean age; gender ratio; mean body mass index (BMI); smoking rate; or frequency of DM, HT, or hyperlipidemia. No significant difference was detected in any other baseline laboratory parameters. LAD was larger in the AF recurrence group than that in the AF nonrecurrence group (41.8 ± 2.0 mm vs. 40.6 ± 1.8 mm, $P = 0.003$). Similarly, when compared to the AF nonrecurrence

Table 1: Baseline characteristics and demographical features of the study population

	Minimum-Maximum	Median	Mean±SD/*n* (%)
Age	19.0-63.0	43.0	41.8±7.8
Sex			
Female			57 (41)
Male			83 (59)
BMI	21.3-34.6	28.9	29.4±4.3
Coronary dominance			
Right			101 (72)
Left			39 (28)
Smoking			38 (27)
DM			18 (13)
HT			53 (38)
Recurrence			
Yes			31 (22)
No			109 (78)
LAD, mm	37.0-47.0	40.0	40.8±1.9
Follow-up time	12.0-20.0	14.0	14.4±2.1
WBC, $\times 10^9$/L	4.1-14.2	7.1	7.4±2.0
Neutrophil, $\times 10^9$/L	1.9-11.2	4.4	4.5±1.5
Lymphocytes, $\times 10^9$/L	1.0-6.6	2.2	2.4±0.9
Hgb, g/dL	9.6-18	13.9	14.1±1.5
PLT, $\times 10^9$/L	122-472	262	267±65
Glucose, mg/dL	81-373	96	98±28
Creatinine, mg/dL	0.5-1.2	0.8	0.8±0.1
Total protein, g/dL	5.8-8.5	7.4	7.4±0.5
Albumin, g/dL	3.7-5.1	4.5	4.5±0.3
TG, mg/dL	70-760	144	180±144
Total cholesterol, mg/dL	101-360	200	202±48
HDL, mg/dL	28-77	47	47±11
LDL, mg/dL	58-255	118.0	120±38
NLR	0.8-6.2	20	2.0±0.8
PLR	43-286	20	120±41

BMI: Body mass index; DM: Diabetes mellitus, HT: Hypertension, Hgb: Hemoglobin, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, LAD: Left atrium diameter, NLR: Neutrophil-to-lymphocyte ratio, PLT: Platelet, PLR: Platelet-to-lymphocyte ratio, TG: Triglyceride, WBC: White blood count, SD: Standard deviation

group, the follow-up period was longer in the AF recurrence group (14.0 ± 1.8 months vs. 15.7 ± 2.4 months, $P = 0.001$). A comparison of the baseline characteristics and laboratory parameters of the AF recurrence and AF nonrecurrence groups is presented in Table 2.

In the AF recurrence group, LD circulation was observed in 16 cases (51.6%) and RD circulation was observed in 15 cases (48.4%). RD circulation was significantly more common than LD circulation in the AF nonrecurrence group (86 cases [78.9%] vs. 23 cases [21.1%], respectively, $P = 0.001$). The rate of LD circulation correlated significantly with AF recurrence [Table 3 and Figure 1]. In the multivariate logistic regression analysis, LD circulation, LAD, and duration of follow-up were independent predictors of AF recurrence ($P < 0.05$) [Table 4].

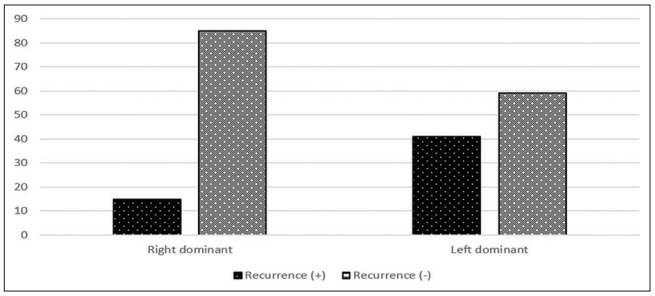

Figure 1: The relationship between coronary artery dominance and recurrence of paroxysmal atrial fibrillation after cryoballoon pulmonary vein isolation

Discussion

The findings of the present study suggest an association between LD circulation and AF recurrence after PVI CA. Moreover, a larger LAD and a longer follow-up time were identified as other independent predictors of AF recurrence. In the present study, the rate of recurrence after CA was 22%, which is similar to the results of other studies.[10-12]

Previous studies indicate that several factors, including age, HT, duration of AF, early recurrence of AF, obesity, LAD,

Table 2: Baseline characteristics and laboratory parameters of the study population according to atrial fibrillation recurrence after cryoballoon pulmonary vein isolation

	Recurrence (+) (*n*=31)		Recurrence (−) (*n*=109)		*P*
	Mean±SD/*n* (%)	Median	Mean±SD/*n* (%)	Median	
Age	42.6±5.9	42	41.6±8.3	43	0.850 (M)
Sex					
Female	15 (48.4)		42 (38.5)		0.324χ^2
Male	16 (51.6)		67 (61.5)		
BMI	30.3±3.7	29.7	29.2±4.4	27.8	0.070 (M)
Coronary dominance					
Right	15 (48.4)		86 (78.9)		0.001 (χ^2)
Left	16 (51.6)		23 (21.1)		
Smoking	7 (22.6)		31 (28.4)		0.517 (χ^2)
DM	2 (6.5)		16 (14.7)		0.217 (χ^2)
HT	10 (32.3)		43 (39.4)		0.466 (χ^2)
LAD, mm	41.8±2.0	42.0	40.6±1.8	40.0	0.003 (M)
Follow-up time, months	15.7±2.4	15.0	14.0±1.8	14.0	0.001 (M)
WBC, $\times10^9$/L	7.6±1.9	7.1	7.4±2.1	7.2	0.547 (M)
Neutrophil, $\times10^9$/L	4.7±1.4	4.6	4.5±1.5	4.2	0.221 (M)
Lymphocytes, $\times10^9$/L	2.6±0.8	2.5	2.4±0.9	2.1	0.073 (M)
Hgb, g/dL	14.1±1.3	14.4	14.0±1.6	13.7	0.511 (M)
PLT, $\times10^9$/L	263±61	258	268±67	263	0.648 (M)
Glucose, mg/dL	93±19	96	99±29	95.0	0.530 (M)
Creatinine, mg/dL	0.8±0.1	0.9	0.8±0.1	0.8	0.239 (M)
Total protein, g/dL	7.3±0.4	7.4	7.4±0.5	7.4	0.337 (*t*)
Serum albumin, g/dL	4.4±0.3	4.3	4.5±0.3	4.5	0.076 (M)
TG, mg/dL	163±69	151	185±59	139	0.962 (M)
Total cholesterol, mg/dL	208±54	193	200±46	200	0.646 (M)
HDL, mg/dL	48.8±12.6	46	46.9±10.8	47	0.614 (M)
LDL, mg/dL	126.5±43.7	121	117.9±36.1	118	0.462 (M)
NLR	2.0±0.7	2.0	2.0±7	1.8	0.681 (M)
PLR	110.4±42	107	122.2±0.9	118	0.054 (M)

t=*T*-test, M=Mann-Whitney U-test, χ^2=Chi-squared test. BMI: Body mass index, DM: Diabetes mellitus, HT: Hypertension, Hgb: Hemoglobin, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol, LAD: Left atrium diameter, NLR: Neutrophil-to-lymphocyte ratio, PLT: Platelet, PLR: Platelet-to-lymphocyte ratio, TG: Triglyceride, WBC: White blood count

Table 3: The relationship between coronary artery dominance and recurrence of paroxysmal AF after cryoballoon PVI

	Recurrence(+) *n* = 31 (22%)	Recurrence(-) *n* = 109 (78%)	*P* value
Right coronary dominance *n* = 101, (72%)	15 (15%)	86 (85%)	0.001
Left coronary dominance *n* = 39, (28%)	16 (41%)	23 (59%)	

inflammation, and LA fibrosis (determined by magnetic resonance imaging), are predictors of AF recurrence.[10,12-14] In the present study, LD circulation was found to be associated with AF recurrence in patients who underwent PVI CA for paroxysmal AF. In addition, in line with the findings of previous studies, LAD and a longer follow-up time were identified as independent predictors of AF recurrence also in the present study. However, we found no association between AF recurrence and demographic data such as age, HT, DM or BMI, or inflammatory markers such as neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and albumin. In our study, similar to some previous studies,[7,10,11] gender and smoking were not associated with AF recurrence. However, there are studies in the literature that smoking and female gender are independent predictors of AF recurrence.[15-17] This inconsistency may be due to the age of the patients in our study being younger than other studies. In addition, this inconsistency could be explained by the fact that our study consisted of only paroxysmal AF patients and its small and retrospective design. Further studies are warranted to confirm and assess the possible mechanisms of these links.

Previous studies indicate that RCA is dominant in 85% of patients, while about half of the remaining 15% appear to have left coronary artery (LCA)-dominant circulation.[18] Previous studies also suggest a prognostic association between coronary artery dominance and CAD, acute ST-elevation myocardial infarction (STEMI), and chronic total coronary artery occlusion.[19-21] Although the available data are inconclusive,

Table 4: Multivariate logistic regression analysis showing independent predictors of atrial fibrillation recurrence after cryoballoon pulmonary vein isolation

Variables	Odds ratio	95% CI	*P*
PLR	0.840	0.650-1.250	0.358
Albumin	0.753	0.135-4.215	0.747
LAD	1.670	1.266-2.203	<0.001
Follow-up time	1.518	1.182-1.950	0.001
Coronary dominance	5.701	1.994-16.301	0.001

LAD: Left atrium diameter, PLR: Platelet-to-lymphocyte ratio, CI: Confidence interval

previous studies involving patients who underwent PCI demonstrated that LD was associated with increased risk of death or re-infarction during long-term follow-up.[22-24] Similarly, patients with an LD or codominant coronary artery system had lower left ventricular ejection fraction early after STEMI.[25,26] An LD coronary artery tree may have a less well-balanced circulation than other systems, resulting in a larger area of myocardium at risk in the face of various cardiovascular diseases. In patients with LD, blood supply to the sinoatrial node may be disturbed and may predispose patients to arrhythmias such as AF.

A P-wave duration (PWD) in sinus rhythm preablation has been hypothesized to be a noninvasive ECG marker associated with increased AF recurrence after PVI.[27,28] There is a newer study showed that prolonged PWD with a cutoff of >120 ms to >150 ms in sinus rhythm before ablation may be associated with AF recurrence after PVI regardless of age, gender, left atrial size, and the presence of structural heart disease.[29] Nabi Aslan *et al*. investigated the relationship between coronary dominance and AF from PWD and P-wave dispersion in a previous study.[30] At the end of their study, they suggested that atrial blood flow may depend mainly on the RCA, as the RCA territory is relatively weak in LD patients, and left dominancy may increase the risk of AF.[30] Likewise, in the present study, AF recurrence was more common in patients with LD circulation than in patients with RD circulation, leading us to hypothesize that blood supply to the sinoatrial node is disturbed in patients with LD circulation.

Blood flow within a coronary branch located close to an radiofrequency (RF) electrode renders a protective effect via convective cooling, hindering RF energy from overheating the vascular endothelium,[31] and this "heat sink" protects the coronary arteries. On the other hand, it may also limit the success of ablation procedures as a result of the "shadow effect" phenomenon. It is thought that blood flow through the small intramyocardial vessels may disrupt the formation of transmural lesions, may preserve conduction through an RF lesion, and in this way, may prevent complete conduction block.[32,33] In the present study, AF ablation was achieved through CA rather than RF, although similar mechanisms may have taken place in both procedures. The arteries supplying the LA are among the earliest branches of the LCA, usually from the LCX.[34] We suggest that better circulation of the LA may be seen in patients with LD circulation, thus preventing the success of CA. This may be the reason why AF recurrence is more common in patients with LD circulation.

Study limitations

Our study had several limitations. First, the study was performed in a single center and included only paroxysmal AF patients. The second limitation is the fact that although follow-up visits and questioning of symptoms were performed and all participants underwent 24–48-h Holter monitoring, some patients with recurrent AF may have been overlooked. Finally, the sample size was relatively small and the retrospective design of the study does not make it possible to draw conclusions about cause-effect relationship.

Conclusions

The findings of the present study suggest an increased risk of AF recurrence after PVI CA in patients with left-dominant coronary artery circulation. Coronary artery dominance may be considered an additional predictor of AF recurrence, provided that the findings of the present study can be confirmed in future prospective controlled studies.

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Conflicts of interest

There are no conflicts of interest.

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