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Clinical Outcomes of Intracardiac Echocardiography-Guided Contrast Agent-Free Cryoballoon Ablation in Atrial Fibrillation Patients With Renal Insufficiency

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AUTHOR'S SUMMARY

We investigated the efficacy and safety of cryoballoon ablation (CBA) in atrial fibrillation (AF) patients with chronic kidney disease (CKD) versus those without CKD and to evaluate the changes in renal function over 12 months after CBA in AF patients. In this prospective cohort study, all enrolled patients undergoing contrast agent-free CBA under intracardiac echocardiography guidance. There was no significant difference in clinical recurrence rate during a mean follow-up of 25.4±11.9 months between the two groups. The CKD patients showed a significant improvement in renal function over 12 months after CBA.

ABSTRACT

Background and Objectives: Previous studies have reported an association between impaired renal function and poor outcomes after radiofrequency catheter ablation in patients with atrial fibrillation (AF). However, outcomes of cryoballoon ablation (CBA) in patients with renal insufficiency are not fully elucidated. This study aimed to compare outcomes of CBA in AF patients with chronic kidney disease (CKD) versus those without CKD and to assess changes in renal function over 12 months following CBA.
Methods: A total of 839 patients (65.1% with non-paroxysmal AF [PAF]) who underwent de novo CBA were prospectively enrolled. We divided patients into two groups based on creatinine clearance rate (CCr) and performed intracardiac echocardiography (ICE)-guided contrast agent-free CBA.
Results: In comparison with patients without CKD (CCr >50, n=722), those with CKD (CCr ≤50, n=117) were older and predominantly female, had a lower body mass index, and showed a higher prevalence of heart failure and hypertension. Mean CHA_2DS_2-VAS score was significantly higher in CKD group than in non-CKD group. Procedure-related complications were not significantly different between two groups. During a mean follow-up period of

25.4±11.9 months, clinical recurrence occurred in 182 patients (21.7%) and not significantly different between two groups. In multivariate analysis, non-PAF and left atrial size were independent predictors of AF recurrence. CCr levels significantly improved over 12 months after CBA in CKD group.
Conclusions: ICE-guided contrast-agent-free CBA showed comparable long-term clinical outcomes without increasing procedure-related complications and improvement of renal function over 12 months following CBA in AF patients with CKD.

Keywords: Ablation; Atrial fibrillation; Echocardiography; Renal insufficiency

Conflict of Interest
The authors have no financial conflict of interest.

Data Sharing Statement
The data generated in this study is available from the corresponding author upon reasonable request.

Author Contributions
Conceptualization: Lim HE; Data curation: Lim HE; Formal analysis: Shin DG, Park SH; Investigation: Lim HE; Resources: Lim HE; Supervision: Han SJ, Lim HE; Writing - original draft: Shin DG; Writing - review & editing: Ahn J, Han SJ, Lim HE.

INTRODUCTION

Patients with chronic kidney disease (CKD) show a significantly higher incidence of atrial fibrillation (AF), and patients with AF also have a higher incidence of CKD in comparison with the general population.[1)2)] The management of AF patients with CKD can be quite challenging because renal impairment is associated with an increased risk of cardiovascular morbidity and mortality, and renal function may worsen over time.[3)] Antiarrhythmic drugs for rhythm control should be used cautiously in AF patients with CKD because of the risk of undesirable adverse reactions due to decreased drug clearance. Catheter ablation (CA) is an effective therapeutic modality for rhythm control in AF patients,[4)5)] and previous studies have reported its efficacy and safety in AF patients with CKD.[6)7)] Furthermore, several studies have suggested that renal function can be improved following radiofrequency CA (RFCA) in patients with AF.[8)9)] However, other studies have suggested that impaired renal function is associated with an increased AF recurrence rate and that RFCA is less effective in AF patients with CKD than in AF patients without CKD.[10-12)]

Cryoballoon ablation (CBA) is most widely used in AF patients and has shown similar efficacy and safety profile compared to RFCA. Traditionally, CBA is conducted on the basis of fluoroscopic imaging with contrast agent injection to confirm proper pulmonary vein (PV) occlusion with the cryoballoon.[13)] Contrast agent may worsen renal function in patients with chronic renal insufficiency. A few reports have described the influence of impaired renal function on clinical outcomes in AF patients who underwent CBA.[14-16)] However, the changes in renal function following CBA have not been fully elucidated. Thus, the purpose of this study was to compare the efficacy and safety of CBA in AF patients with CKD versus those without CKD and to evaluate the changes in renal function over 12 months after CBA in AF patients.

METHODS

Ethical statement

The study protocol was approved by the Hallym University Sacred Heart Hospital Institutional Review Board (IRB No.: 2020-01-010) and complied with the Declaration of Helsinki (2013). All the patients in this study provided written informed consent for their inclusion.

Study population

This prospective cohort study included 839 patients aged >18 years with drug-refractory AF who were referred for first-time CBA between January 2019 and April 2022. The patients were divided into two groups based on their creatinine clearance rate (CCr) value: the CKD group included patients with a CCr of ≤50 mL/min, and those with CCr >50 mL/min were included in the non-CKD group. CCr, which is an indicator of renal function required to administer non-vitamin K oral anticoagulants (NOACs) in patients with AF, was estimated using the Cockcroft-Gault equation: [(140−Age)×Mass (kg)×[0.85 if female]/72×[Serum Creatinine (mg/dL)]. Age, body weight, serum creatinine level, and sex were used to calculate the CCr at the time of the procedure and at 12 months after CBA.

Ablation procedure

Details regarding the contrast agent-free CBA technique and strategy have been described in previous studies.[17)18)] In brief, under deep sedation with continuous infusion of propofol and an intermittent bolus of fentanyl, the right femoral vein was percutaneously accessed using the Seldinger technique. A single transseptal puncture was performed under intracardiac echocardiographic guidance (ICE, ViewFlex™; Abbott, Inc., Abbott Park, IL, USA). The step-by-step process of CBA guided by ICE was as follows (**Supplementary Video 1**). A 28-mm cryoballoon catheter (Arctic Front Advance™; Medtronic, Inc., Minneapolis, MN, USA) assembled with an intraluminal mapping catheter (Achieve™; Medtronic, Inc.) was gently advanced into the left atrial (LA) cavity through a 15-Fr steerable sheath (FlexCath™; Medtronic, Inc.). The cryoballoon catheter was then advanced over the intraluminal mapping catheter, inserted into each PV, and inflated. The best-fit occlusion of the inflated cryoballoon in each PV antrum was confirmed using color Doppler ICE imaging, and a mapping catheter was used to obtain PV potential recordings for real-time monitoring of PV isolation (PVI). Subsequently, cryoenergy was delivered for 180 seconds if the time-to-isolation (TTI) of the PV was shorter than 30 seconds and for 240 seconds if the TTI of the PV was ≥30 seconds. Diaphragmatic stimulation with continuous pacing of the ipsilateral phrenic nerve was performed during right-sided CBA to avoid phrenic nerve paralysis. Four indicators were used to define proper PV occlusion: 1) TTI within 60 s after freezing if PV potentials were observed, 2) temperature drop of ≤30°C within 30 seconds and ≤40°C within 60 seconds after freezing, 3) absence of high-velocity color Doppler flow around the cryoballoon after freezing, and 4) presence of blood bubbles following deflation of the cryoballoon after thawing. If TTI was not achieved within 60 seconds or the temperature did not reach −40°C within 60 seconds, freezing was stopped, and the cryoballoon catheter was repositioned. If any remaining PV potential and atrial capture by high-output pacing inside the PVs were observed, an additional attempt with the same strategy was performed to achieve complete PVI. After PVI, the segmental non-occlusive technique was used to apply additional freezing for 150 seconds at a more proximal antrum than the previous CBA site to create a wide antral circumferential ablation. In cases involving documented or induced typical atrial flutter, linear ablation of the cavotricuspid isthmus was performed and additional procedures were performed according to the operator's judgment. After the procedure, hemostasis of the femoral vein was achieved using a Fisherman's knot suture without protamine injection. Oral anticoagulation (OAC) was performed at the scheduled time on the day of the procedure after confirming complete hemostasis or the absence of bleeding complications.

Follow-up

All patients received OACs for at least three months after CBA. Antiarrhythmic drugs were allowed for the first three months to avoid early recurrence but then discontinued if sinus rhythm (SR) was maintained. All patients were followed up at the outpatient clinic at 1, 3, 6, 9, and 12 months and every 6 months thereafter or whenever symptoms occurred after CBA. Twelve-lead electrocardiography (ECG) was performed at each visit or whenever a patient presented with palpitations, and 24-hour Holter monitoring was performed at 3, 6, and 12 months and every 12 months thereafter. Any ECG-documented atrial tachyarrhythmia (AF, atrial flutter, or atypical atrial flutter) lasting >30 seconds after the initial three-month blanking period was defined as clinical recurrence. Laboratory examinations, including hemoglobin levels, platelet counts, and renal and liver function tests, were performed at least annually.

Statistical analysis

All normally distributed continuous variables were expressed as mean and standard deviation. Continuous variables were analyzed using independent t-tests. Categorical variables are reported as counts and proportions and analyzed using Pearson's χ^2 test or Fisher's exact test, as appropriate. Variables found to be statistically significant in the univariate analysis were further analyzed using multivariate Cox regression to identify independent predictors of clinical recurrence of AF. Kaplan–Meier analysis with the log-rank test was performed to compare AF recurrence-free survival between the 2 groups. The R package (version 4.1.1, The R Foundation for Statistical Computing, Vienna, Austria) and SPSS (version 26.0, IBM, Armonk, NY, USA) were used to conduct all statistical analyses. $p \leq 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics

The patient population consisted of 722 patients (86.1%) in the non-CKD group and 117 patients (13.9%) in the CKD group. The clinical characteristics of the enrolled patients are summarized in **Table 1**. Mean age was 63.6±10.3 years, and 293 patients (34.9%) had paroxysmal AF (PAF). Patients with CKD were older (75.2±8.6 vs. 61.7±9.3 years, p<0.001), predominantly female (47.9% vs. 20.2%, p<0.001), had a lower BMI (23.7±3.6 vs. 25.5±3.4 kg/m^2, p<0.001), and showed a higher prevalence of HF (60.7% vs. 28.9%, p<0.001) and hypertension (82.1% vs. 72.7%, p=0.022) than those without CKD. The mean CHA_2DS_2-VAS score was significantly higher in the CKD group than in the non-CKD group (4.3±1.5 vs. 2.4±1.5, p<0.001).

Table 1. Baseline characteristics and post-procedure medication

	Overall (n=839)	non-CKD (n=722)	CKD (n=117)	p value
Age (years)	63.6±10.3	61.7±9.3	75.2±8.6	<0.001
Sex, male (%)	637 (75.9)	576 (79.8)	61 (52.1)	<0.001
BMI (kg/m^2)	25.3±3.5	25.5±3.4	23.7±3.6	<0.001
Paroxysmal AF	293 (34.9)	252 (34.9)	41 (35.0)	0.977
Medical history				
Heart failure	280 (33.4)	209 (28.9)	71 (60.7)	<0.001
Hypertension	621 (74.0)	525 (72.7)	96 (82.1)	0.033
Diabetes mellitus	236 (28.1)	202 (28.0)	34 (29.1)	0.809
Stroke/TIA	128 (15.3)	107 (14.8)	21 (17.9)	0.383
Vascular disease	94 (11.2)	75 (10.4)	19 (16.2)	0.063
CHA_2DS_2-VASc score	2.6±1.6	2.4±1.5	4.3±1.5	<0.001
Creatinine	1.1±0.8	1.0±0.2	1.9±1.8	<0.001
Echocardiographic value				
LA diameter (AP) (mm)	44.7±7.4	44.5±7.4	46.1±7.2	0.089
LV ejection fraction (%)	58.5±9.8	58.7±9.3	57.0±12.3	0.075
Post-procedure medication				
Antiarrhythmic drugs	289 (34.4)	254 (35.2)	35 (29.9)	0.266
Beta-blocker	179 (21.3)	153 (21.2)	26 (22.2)	0.801
Calcium channel blocker	253 (30.2)	214 (29.6)	39 (33.3)	0.419

Values are presented as mean ± standard deviation or number (%).
AF = atrial fibrillation; AP = anteroposterior; BMI = body mass index; LA = left atrium; LV = left ventricle; TIA = transient ischemic attack.

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Procedural outcomes

Successful PVI was achieved using a contrast agent-free CBA technique under ICE guidance in all enrolled patients. Procedural data are presented in **Table 2**. The average total procedure and LA indwelling times were 74.9±13.3 minutes and 58.1±11.1 minutes, respectively, and they did not differ between the 2 groups. The average ablation time was 1,735.1±453.9 seconds, and it was longer in the non-CKD group than in the CKD group (p=0.038). Procedure-related complications did not differ between the 2 groups.

Clinical outcomes

Table 3 shows the clinical outcomes of CBA. Over a mean follow-up period of 25.4±11.9 months, clinical recurrence occurred in 182 patients (21.7%). There were no significant differences in post-procedure medication (**Table 1**) and follow-up period between the CKD group and the non-CKD group. (25.27±9.36 months, 25.42±8.82 months, respectively). **Figure 1** shows the Kaplan–Meier analysis of the clinical recurrence-free survival rate, which revealed a comparable outcome between the two groups overall (**Figure 1A**, log-rank p=0.370) and in patients with PAF (**Figure 1B**, log-rank p=0.144) and those with non-PAF (**Figure 1C**, log-rank p=0.749).

Table 4 shows the results of univariate and multivariate Cox regression analyses aimed at identifying the potential predictors of clinical recurrence. Multivariate analysis revealed that non-PAF (hazard ratio [HR], 2.422; 95% confidence interval [CI], 1.427–4.110; p=0.001) and larger LA size (LA diameter of ≥50 mm) (HR, 2.024; 95% CI, 1.344–3.050; p=0.001) were independent predictors of clinical recurrence.

Renal outcomes

Figure 2 shows the changes in the CCr before and after CBA. The baseline CCr did not significantly change over 12 months after CBA in the overall (**Figure 2A**) and non-CKD groups (**Figure 2B**). However, in the CKD group (**Figure 2C**), the CCr over 12 months following CBA improved significantly in comparison with the baseline CCr. **Figure 3** shows the changes in CCr before and after CBA according to the AF type with or without recurrence. The baseline CCr and the CCr over 12 months after CBA did not differ significantly in PAF (**Figure 3A**) and non-PAF patients (**Figure 3B**). In addition, the CCr over 12 months following CBA did not change significantly in comparison with the baseline CCr, regardless of whether clinical recurrence developed (**Figure 3C and D**).

Table 2. Procedural data

	Overall (n=839)	non-CKD (n=722)	CKD (n=117)	p value
Procedure time (min)	74.9±13.3	75.0±13.4	74.4±12.6	0.679
Ablation time (sec)	1735.1±453.9	1748.7±462.5	1649.1±386.6	0.038
LA indwelling time (min)	58.1±11.1	58.3±11.4	56.7±9.0	0.196
CTI ablation	276 (32.9)	227 (31.4)	49 (41.9)	0.026
Procedure-related complications	52 (6.2)	42 (5.8)	10 (8.5)	0.256

Values are presented as mean ± standard deviation or number (%).
CKD = chronic kidney disease; CTI = cavotricuspid isthmus; LA = left atrium

Table 3. Clinical outcome

	Overall (n=839)	non-CKD (n=722)	CKD (n=117)	p value
Early recurrence	209 (24.9)	182 (25.2)	27 (23.1)	0.616
Clinical recurrence	182 (21.7)	153 (21.2)	29 (24.8)	0.386
AF	141 (16.8)	121 (16.8)	20 (17.1)	
Atypical AFL/AT	41 (4.9)	32 (4.4)	9 (7.7)	

Values are presented as number (%).
AF = atrial fibrillation; AFL = atrial flutter; AT = atrial tachycardia; CKD = chronic kidney disease.

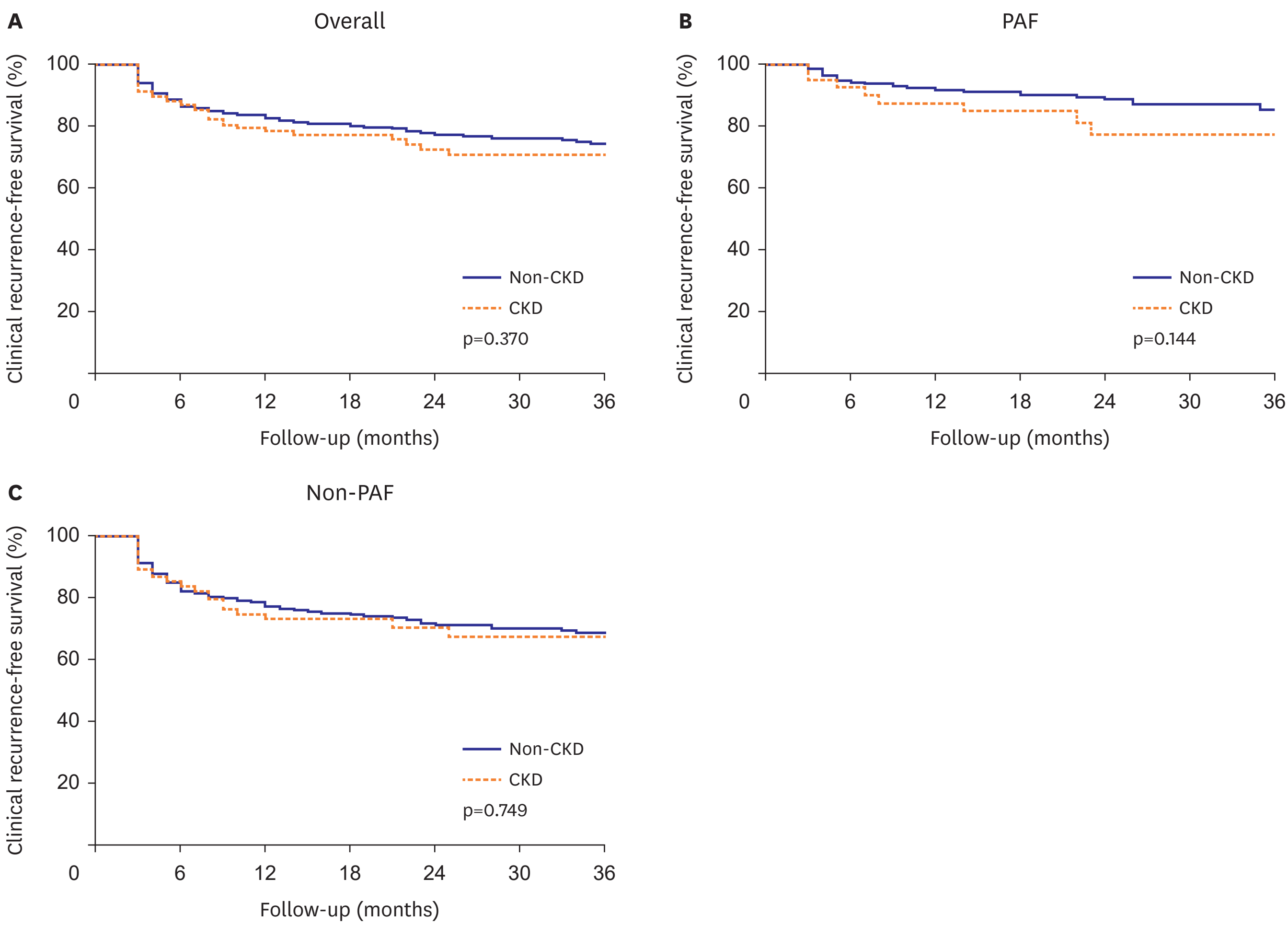

Figure 1. Kaplan-Meier survival curves for clinical recurrence-free survival rate in overall, PAF, and non-PAF patients.
CKD = chronic kidney disease; PAF = paroxysmal atrial fibrillation.

Table 4. Univariate and multivariate Cox regression analysis for predictors of clinical recurrence

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p value	HR (95% CI)	p value
Age	1.007 (0.991–1.023)	0.425	0.983 (0.962–1.005)	0.129
Sex, male	1.096 (0.741–1.621)	0.646	1.128 (0.692–1.837)	0.630
BMI	1.016 (0.969–1.065)	0.508	0.977 (0.922–1.036)	0.440
Non-paroxysmal AF	2.665 (1.785–3.980)	<0.001	2.422 (1.427–4.110)	0.001
Medical history				
Heart failure	1.361 (0.967–1.915)	0.077	1.102 (0.722–1.682)	0.652
Hypertension	1.165 (0.806–1.684)	0.418	1.188 (0.761–1.854)	0.448
Diabetes mellitus	0.805 (0.563–1.151)	0.234	0.788 (0.535–1.161)	0.228
Stroke/TIA	1.026 (0.647–1.626)	0.914	0.917 (0.562–1.496)	0.728
Renal impairment (CCr <50)	0.848 (0.535–1.344)	0.482	0.974 (0.522–1.815)	0.933
Echocardiography				
LA diameter (≥50 mm)	2.218 (1.522–3.231)	<0.001	2.024 (1.344–3.050)	0.001
LV ejection fraction	0.994 (0.978–1.011)	0.501	1.005 (0.985–1.025)	0.619

AF = atrial fibrillation; BMI = body mass index; CCr = creatinine clearance rate; LA = left atrium; LV = left ventricle; TIA = transient ischemic attack.

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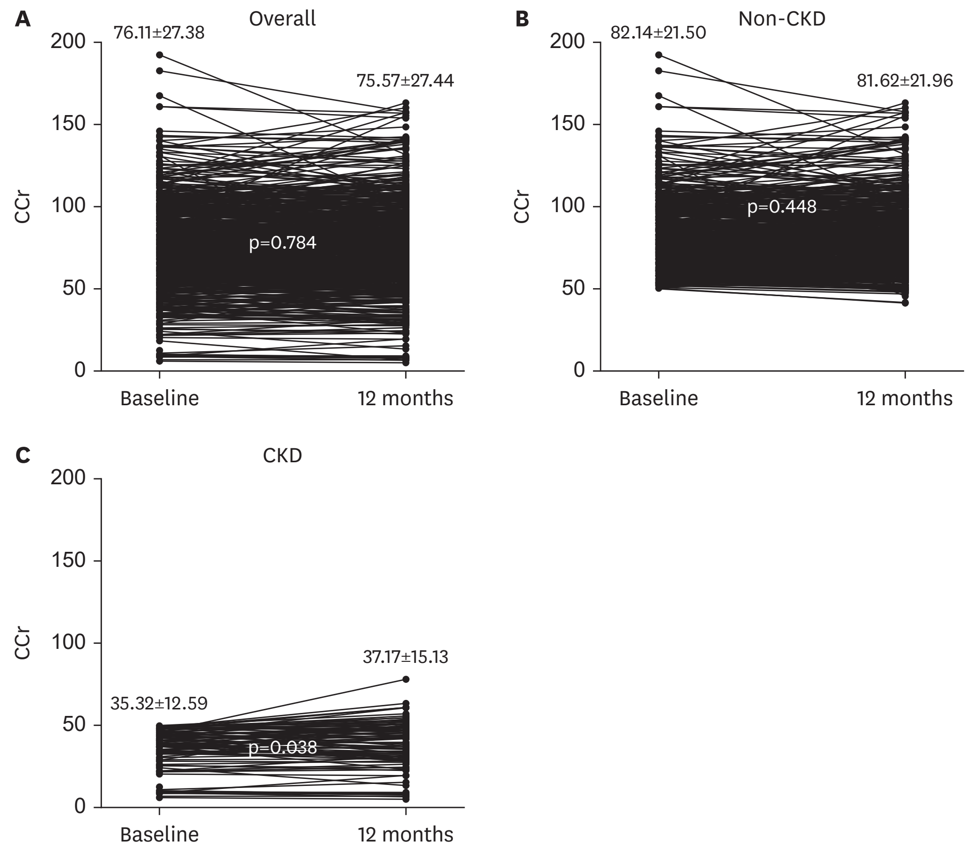

Figure 2. The changes in CCr between baseline and 12 months after cryoballoon ablation in overall, non-CKD, and CKD patient.
CCr = creatinine clearance rate; CKD = chronic kidney disease.

DISCUSSION

The efficacy and safety of RFCA in AF patients with CKD remain controversial, and limited data regarding the clinical outcomes of CBA in these patients have been presented to date. To the best of our knowledge, this is the first prospective cohort study to evaluate the long-term clinical outcomes, including the changes in renal function, in AF patients with chronic renal insufficiency who underwent de novo CBA. The present study yielded several noteworthy findings: 1) successful PVI was achieved by an ICE-guided contrast agent-free CBA method in all enrolled patients; 2) procedural data and procedure-related complications did not differ significantly between the non-CKD and the CKD groups; 3) the clinical recurrence-free survival rate was comparable between the two groups over a mean follow-up period of 25.4±11.9 months after CBA; 4) renal function was significantly improved over 12 months after CBA in CKD patients.

Several predictors of recurrence after AF ablation have been identified in previous studies.[19)20)] Of these, comorbidities such as renal, cardiac, and lung diseases can influence the clinical outcomes after AF ablation. However, the effects of chronic renal insufficiency on ablation outcomes remain controversial. Several studies have reported that CKD is significantly associated with recurrence after RFCA for AF,[10-12)] whereas a large cohort study demonstrated that the presence of CKD did not affect clinical outcomes, including repeat AF ablation.[6)] Therefore, CKD is still not included in various risk scores for predicting recurrence after AF ablation.[21-26)]

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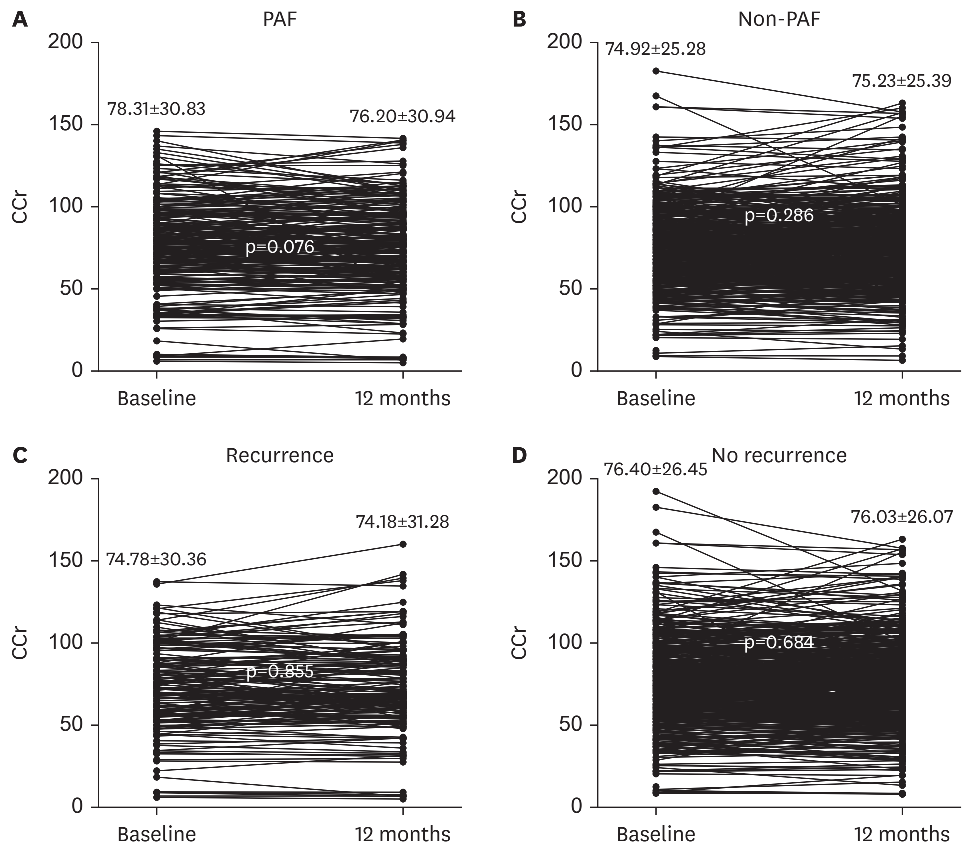

Figure 3. The changes in CCr between baseline and 12 months after cryoballoon ablation according to the type of AF (A, B) and clinical recurrence (C, D).
AF = atrial fibrillation; CCr = creatinine clearance rate; PAF = paroxysmal atrial fibrillation.

Most results regarding clinical outcomes following AF ablation in patients with CKD are based on data from RFCA studies, and data from CBA studies are limited. Yanagisawa et al.[14] reported that a low estimated glomerular filtration rate at baseline was an independent predictor of recurrence after CBA in patients with PAF. Boriani et al.[15] revealed that mild-to-moderate reductions in renal function was associated with a higher risk of AF recurrence after CBA. These results contradict the findings of the present study. This difference may be due to differences in the characteristics of the enrolled population, follow-up periods, and ablation techniques. In comparison with two previous studies that only included patients with PAF, our cohort study prospectively enrolled not only patients with PAF but also patients with non-PAF. Therefore, the majority of enrolled participants in our study were patients with non-PAF (n=546, 65.1%). Moreover, the mean follow-up period in the present study was much longer than that in previous studies (25.4±11.9 months vs. 9 months, respectively). The most striking difference was observed in the CBA strategy. Previous studies used a conventional CBA technique on the basis of fluoroscopic imaging with contrast agent injection. This method has been considered routine during CBA to confirm proper PV occlusion with cryoballoon.[27] However, all enrolled patients in our study underwent a contrast agent-free CBA technique under ICE guidance. This protocol will benefit patients with renal impairment because contrast media can cause deterioration of renal function. In addition, this protocol greatly reduces radiation exposure by omitting the contrast-confirmation step in fluoroscopic cine imaging. Consequently, in the present study, renal function did not significantly change

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before and 12 months after CBA in all patients and significantly improved over 12 months following CBA in AF patients with CKD.

AF is a well-known adverse prognostic factor for CKD because it has thrombogenic potential, which can lead to recurrent renal micro-infarction.[28] Furthermore, AF increases systemic inflammation and activates the renin-angiotensin-aldosterone system, which can contribute to left ventricular dysfunction and CKD progression.[29,30] Therefore, maintenance of SR and/or substantial reduction of the AF burden can prevent renal function decline in AF patients with renal impairment. In support of this theory, several studies demonstrated that renal function was improved after RFCA for AF.[8,9] The main mechanism underlying these positive effects on renal function is widely believed to be an improvement in hemodynamics through the restoration of SR.

However, the effect of CBA on renal function has not been fully elucidated because the traditional CBA strategy requires a substantial amount of contrast agent, which can result in deterioration of renal function, especially in patients with chronic renal insufficiency. In our study, renal function was improved over 12 months after CBA in patients with CKD, irrespective of AF type and/or clinical recurrence. Although the exact mechanism is still unclear, improvement of renal perfusion through the restoration of SR or a greatly reduced AF burden after contrast agent-free CBA may influence renal function recovery in patients with AF and impaired renal function. Diaz et al.[16] reported that CBA for AF may be associated with improved renal function despite recurrence, particularly among patients with a reduced baseline estimated glomerular filtration rate. This finding is consistent with the results of our study. Consistent with previous findings, non-PAF and an enlarged LA were independent predictors of AF recurrence.

Our results cannot be generalized because all procedures were performed by highly experienced operators using ICE-guided contrast agent-free CBA. The results may differ if AF ablation is conducted with conventional CBA using a fluoroscopic cine imaging with contrast agent injection. Furthermore, the efficacy may be overestimated, since continuous long-term ECG monitoring was not performed during the follow-up period. However, the long-term recurrence-free rate over a mean follow-up period of 25.4±11.9 months was not significantly different between the non-CKD and CKD groups. Moreover, the overall success rate (78.3%) was similar to that of the largest cohort including >1,000 procedures by Bordignon et al.[27] A prospective, large-scale, multicenter study is required to assess the generalizability of the findings from our study.

In conclusion, contrast agent-free CBA was performed safely and effectively under ICE guidance. PVI was achieved in all enrolled patients by using our CBA method, which showed comparable long-term clinical outcomes between patients with impaired and preserved renal function. Renal function was improved at 12 months after CBA in AF patients with impaired renal function. Therefore, contrast agent-free CBA may be an effective ablation strategy in AF patients with CKD.

SUPPLEMENTARY MATERIAL

Supplementary Video 1

Step-by-step process of CBA guided by ICE.

REFERENCES

1. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016;37:2893-962. PUBMED | CROSSREF
2. Soliman EZ, Prineas RJ, Go AS, et al. Chronic kidney disease and prevalent atrial fibrillation: the Chronic Renal Insufficiency Cohort (CRIC). *Am Heart J* 2010;159:1102-7. PUBMED | CROSSREF
3. Boriani G, Savelieva I, Dan GA, et al. Chronic kidney disease in patients with cardiac rhythm disturbances or implantable electrical devices: clinical significance and implications for decision making-a position paper of the European Heart Rhythm Association endorsed by the Heart Rhythm Society and the Asia Pacific Heart Rhythm Society. *Europace* 2015;17:1169-96. PUBMED | CROSSREF
4. Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339:659-66. PUBMED | CROSSREF
5. Khan AR, Khan S, Sheikh MA, Khuder S, Grubb B, Moukarbel GV. Catheter ablation and antiarrhythmic drug therapy as first- or second-line therapy in the management of atrial fibrillation: systematic review and meta-analysis. *Circ Arrhythm Electrophysiol* 2014;7:853-60. PUBMED | CROSSREF
6. Ullal AJ, Kaiser DW, Fan J, et al. Safety and clinical outcomes of catheter ablation of atrial fibrillation in patients with chronic kidney disease. *J Cardiovasc Electrophysiol* 2017;28:39-48. PUBMED | CROSSREF
7. Sairaku A, Yoshida Y, Kamiya H, et al. Outcomes of ablation of paroxysmal atrial fibrillation in patients on chronic hemodialysis. *J Cardiovasc Electrophysiol* 2012;23:1289-94. PUBMED | CROSSREF
8. Takahashi Y, Takahashi A, Kuwahara T, et al. Renal function after catheter ablation of atrial fibrillation. *Circulation* 2011;124:2380-7. PUBMED | CROSSREF
9. Navaravong L, Barakat M, Burgon N, et al. Improvement in estimated glomerular filtration rate in patients with chronic kidney disease undergoing catheter ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2015;26:21-7. PUBMED | CROSSREF
10. Li M, Liu T, Luo D, Li G. Systematic review and meta-analysis of chronic kidney disease as predictor of atrial fibrillation recurrence following catheter ablation. *Cardiol J* 2014;21:89-95. PUBMED | CROSSREF
11. Lee WC, Wu PJ, Fang CY, Chen HC, Chen MC. Impact of chronic kidney disease on atrial fibrillation recurrence following radiofrequency and cryoballoon ablation: a meta-analysis. *Int J Clin Pract* 2021;75:e14173. PUBMED | CROSSREF
12. Chung I, Khan Y, Warrens H, Seshasai RK, Sohal M, Banerjee D. Catheter ablation for atrial fibrillation in patients with chronic kidney disease and on dialysis: a meta-analysis and review. *Cardiorenal Med* 2022;12:155-72. PUBMED | CROSSREF
13. Kuck KH, Brugada J, Fürnkranz A, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. *N Engl J Med* 2016;374:2235-45. PUBMED | CROSSREF
14. Yanagisawa S, Inden Y, Kato H, et al. Impaired renal function is associated with recurrence after cryoballoon catheter ablation for paroxysmal atrial fibrillation: a potential effect of non-pulmonary vein foci. *J Cardiol* 2017;69:3-10. PUBMED | CROSSREF
15. Boriani G, Iacopino S, Arena G, et al. Chronic kidney disease with mild and mild to moderate reduction in renal function and long-term recurrences of atrial fibrillation after pulmonary vein cryoballoon ablation. *J Cardiovasc Dev Dis* 2022;9:126. PUBMED | CROSSREF
16. Diaz CL, Kaplan RM, Peigh G, et al. Improvement in renal function following cryoballoon ablation for atrial fibrillation. *J Interv Card Electrophysiol* 2021;60:513-20. PUBMED | CROSSREF
17. Ahn J, Shin DG, Han SJ, Lim HE. Does isolation of the left atrial posterior wall using cryoballoon ablation improve clinical outcomes in patients with persistent atrial fibrillation? A prospective randomized controlled trial. *Europace* 2022;24:1093-101. PUBMED | CROSSREF
18. Ahn J, Shin DG, Han SJ, Lim HE. Safety and efficacy of intracardiac echocardiography-guided zero-fluoroscopic cryoballoon ablation for atrial fibrillation: a prospective randomized controlled trial. *Europace* 2023;25:euad086. PUBMED | CROSSREF
19. Garvanski I, Simova I, Angelkov L, Matveev M. Predictors of recurrence of AF in patients after radiofrequency ablation. *Eur Cardiol* 2019;14:165-8. PUBMED | CROSSREF
20. Njoku A, Kannabhiran M, Arora R, et al. Left atrial volume predicts atrial fibrillation recurrence after radiofrequency ablation: a meta-analysis. *Europace* 2018;20:33-42. PUBMED | CROSSREF
21. Kornej J, Hindricks G, Shoemaker MB, et al. The APPLE score: a novel and simple score for the prediction of rhythm outcomes after catheter ablation of atrial fibrillation. *Clin Res Cardiol* 2015;104:871-6. PUBMED | CROSSREF

22. Mesquita J, Ferreira AM, Cavaco D, et al. Development and validation of a risk score for predicting atrial fibrillation recurrence after a first catheter ablation procedure - ATLAS score. *Europace* 2018;20:f428-35. PUBMED | CROSSREF

23. Canpolat U, Aytemir K, Yorgun H, Şahiner L, Kaya EB, Oto A. A proposal for a new scoring system in the prediction of catheter ablation outcomes: promising results from the Turkish Cryoablation Registry. *Int J Cardiol* 2013;169:201-6. PUBMED | CROSSREF

24. Winkle RA, Jarman JW, Mead RH, et al. Predicting atrial fibrillation ablation outcome: the CAAP-AF score. *Heart Rhythm* 2016;13:2119-25. PUBMED | CROSSREF

25. Bisbal F, Alarcón F, Ferrero-de-Loma-Osorio A, et al. Left atrial geometry and outcome of atrial fibrillation ablation: results from the multicentre LAGO-AF study. *Eur Heart J Cardiovasc Imaging* 2018;19:1002-9. PUBMED | CROSSREF

26. Mujović N, Marinković M, Marković N, Shantsila A, Lip GY, Potpara TS. Prediction of very late arrhythmia recurrence after radiofrequency catheter ablation of atrial fibrillation: the MB-LATER clinical score. *Sci Rep* 2017;7:40828. PUBMED | CROSSREF

27. Bordignon S, Chen S, Bologna F, et al. Optimizing cryoballoon pulmonary vein isolation: lessons from >1000 procedures- the Frankfurt approach. *Europace* 2021;23:868-77. PUBMED | CROSSREF

28. Suwanwongse K, Shabarek N. Does atrial fibrillation increase the risk of developing end-stage renal disease in patients with chronic kidney disease? *Cureus* 2020;12:e6908. PUBMED | CROSSREF

29. Iravanian S, Dudley SC Jr. The renin-angiotensin-aldosterone system (RAAS) and cardiac arrhythmias. *Heart Rhythm* 2008;5:S12-7. PUBMED | CROSSREF

30. Li J, Solus J, Chen Q, et al. Role of inflammation and oxidative stress in atrial fibrillation. *Heart Rhythm* 2010;7:438-44. PUBMED | CROSSREF