Predictors of a Persistent Status of Pulmonary Vein Electrical Isolation by a Cryoballoon Application for Drug-Refractory Atrial Fibrillation

Naohiko Kawaguchi, MD; Kaoru Okishige, MD; Yasuteru Yamauchi, MD; Manabu Kurabayashi, MD; Kenzo Hirao, MD

Background: Pulmonary vein isolation (PVI) using a cryoballoon (CB) is utilized for treating atrial fibrillation. This study aimed to assess the effect of the procedural characteristics of CB-based PVI (CB-PVI) on late PV reconnections.

Methods and Results: A total of 389 consecutive patients underwent the CB-PVI as their index procedure; 45 consecutive patients underwent re-do procedures (184±87 days after the index CB-PVI). A total of 146 of 178 PVs (82%) remained isolated. The occlusion grade was evaluated in 171 PVs. Complete PV occlusion by the CB (grade 4) was obtained in 122 of 171 PVs (71%) during the index CB-PVI and the PVI status was maintained in 111 PVs (91%). Among the remaining 49 CB-PVIs without complete PV occlusion (grades 1–3), 20 PVs (41%) had late PV reconnections despite successful PVI during the index CB-PVI. A “pull-down maneuver” was performed in 20 PVs because of leakage of blood at the inferior aspect of the PVs, and all those PVs with a successful pull-down maneuver maintained their PVI status. A multivariate analysis demonstrated that the presence of complete PV occlusion was the only independent predictor for persistence of PVI.

Conclusions: The occlusion grade was a reliable predictor of the long-term durability of PVI.

Key Words: Atrial fibrillation; Cryoballoon; Pulmonary vein isolation

Pulmonary vein isolation (PVI) is a widely accepted procedure for catheter ablation in patients with atrial fibrillation (AF). 1 The major cause of atrial tachyarrhythmias (ATs) after PVI is considered to be associated with PV reconnections. 2 PVI using the second-generation cryoballoon (CB) is regarded as highly effective for treating AF. 3 The durability of PVI after second-generation CB-based PVI (CB-PVI) may significantly contribute to the clinical outcome, but details of the results after CB-PVI have not been fully investigated. The aim of this study was to assess the clinical effect of CB-PVI during the index procedure on late PV reconnections examined during re-do procedures, and to find a predictor of the maintenance of PVI status after CB-PVI.

Methods

Inclusion and Exclusion Criteria

From July 2014 to March 2016, CB-PVI was performed in patients with drug-refractory AF. After the index CB-PVI procedure, re-do ablation procedures were performed in patients with drug-refractory recurrence of ATs. Consecutive patients undergoing a re-do procedure for a recurrence of an AT after the index CB-PVI procedure were enrolled in this study. AT recurrence was defined as documented AT lasting longer than 30 s on 12-lead ECG or 24-h Holter ECG examination after a 3-month blanking period. Exclusion criteria included severe valvular disease, severe coronary artery disease, a left atrial diameter >55 mm, and the existence of a thrombus in the left atrium (LA).

Written informed consent was given by all patients prior to the ablation procedure. This study protocol was approved by the institutional review board and conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Procedural Management

Cardiac computed tomography (CT) and transesophageal echocardiography (TEE) were performed the day before the ablation procedure to analyze the anatomy of the LA and PV and to rule out any intracardiac thrombi. Patients underwent conscious sedation with propofol combined with dexmedetomidine hydrochloride during the index and re-do ablation procedures. CB ablation was performed as previously described. 4 Briefly, a 14Fr deflectable sheath (FlexCath, Medtronic, Minneapolis, MN, USA) was introduced into the LA after a single transseptal puncture.
using a radiofrequency (RF) needle (Baylis Medical Inc., Montreal, Quebec, Canada) under fluoroscopic and intracardiac echocardiography guidance (AcuNav, Siemens AG Medical Solution, Munich, Germany). Immediately after the transseptal puncture 5,000 units of heparin were administered and additionally given to maintain an activated clotting time between 300 and 350s during the ablation procedure.

**Index CB-PVI Procedure**

Only a 28-mm CB (Arctic Front Advance, Medtronic) was used, and inserted into the LA through a long guiding sheath (FlexCath, Medtronic). The CB was further advanced through a decapolar circular mapping catheter (Achieve, Medtronic), which was inserted into the distal portion of each PV, in an “over-the-wire” fashion. The CB was inflated and advanced against the ostium of each PV, and ablation of the PV antrum was attempted. In patients with a left common trunk, the CB was applied individually to each distal branch of the left common PV (LCPV). PV angiography and measurement of the PV potentials were carried out both before and after the PVI procedure with the use of an Achieve catheter. The occlusion status of each PV was assessed by venous angiography. The occlusion grade was verified by an injection of contrast medium into the PVs via the central lumen of the CB followed by a freezing energy application. The occlusion grade was categorized into 4 groups according to described criteria.5 Grade 4= no leakage of contrast media from the PV to the LA; Grade 1= massive outflow leakage from the PV to the LA. The occlusion grade was evaluated by 2 observers blinded to the present study. The CB was positioned as proximal as possible at each PV without sacrificing a better occlusion status. The freezing time was set for 180 s per PV. In cases of massive leakage of contrast medium through the space between the CB and PV, especially around the inferior aspect of the targeted PV, a “pull-down maneuver” was performed. The pull-down maneuver was undertaken as one of the methods to make the occlusion grade higher.6,7 At first, cryothermal energy was applied to the superior aspect of the targeted PV to make the CB adhere to the superior aspect of the PV. After the CB temperature reached $-10^\circ$C, and never at a lower temperature, both the Flexcath sheath and CB were pulled downward to make the CB attach to the inferior aspect of the surface of the PV for complete PV occlusion status. The occlusion grade was evaluated before and after the pull-down maneuver, and final classification of the occlusion grade was performed according to the results of the pull-down maneuver. The initial 100 patients underwent bonus freezing after successful PVI, whereas the following patients received no bonus freezing when the first freezing was able to achieve successful PVI. In the first 21 patients, we performed PVI using the CB in following order: left superior (LS) PV, left inferior (LI) PV, right superior (RS) PV, and right inferior (RI) PV, and in all remaining patients we changed the order of the CB applications as follows: LSPV, LIPV, RIPV, and then RSPV.

When PVI could not be achieved with a maximum of a double-freezing cycle for CB ablation, supplementary touch-up RF ablation was performed using a 3.5-mm tip-irrigated catheter (Smart touch, Biosense Webster, Diamond Bar, CA, USA or FlexAbility, St. Jude Medical, Minneapolis, MN, USA). During the touch-up ablation, a circular mapping catheter (Lasso, Biosense Webster or Libero, Japan Lifeline, Tokyo, Japan) was inserted into the PV ostium, and RF energy was delivered at the site of the earliest inscription of the PV potential indicative of conduction gap (CG) sites. During CB ablation, the luminal esophageal temperature was continuously monitored by an esophageal temperature probe (Sensitherm, St. Jude Medical, or Esophaster, Japan Lifeline). The CB ablation was prematurely terminated when the esophageal temperature reached 15°C. An electrode catheter was advanced and positioned at the superior vena cava (SVC) for right-sided phrenic nerve stimulation and into the left subclavian vein for left-sided stimulation. The phrenic nerve was paced continuously during the CB ablation at a rate of 40 beats/min. The CB ablation was also prematurely terminated when the maximum amplitude of the compound motor activation potential decreased by more than 30% or there was a sudden decrease in diaphragmatic contraction.8,9 Emergency deflation of the CB, so-called “double-stop technique”, which can make the temperature of the CB rise immediately, was performed for the prevention of cryothermal esophageal injury and phrenic nerve paralysis, if necessary.

**Re-Do Procedure**

A re-do ablation procedure was performed in patients with a recurrence of AT after a 3-month blanking period. During the re-do procedure, PV-LA reconnections were evaluated by a circular mapping catheter located at ostium of each PV. If PV-LA reconnections were observed, irrigated RF energy was delivered at the site of the earliest PV potential recording sites through the irrigated RF catheter. In the case of a recurrence of any AT, activation mapping was performed utilizing a 3D mapping system (CARTO 3, Biosense Webster or NavX, St. Jude Medical) and focal or linear ablation was performed to terminate the ATs. Further ablation, including isolation of the SVC, and additional LA linear ablation were performed at the operator’s discretion. We investigated the prevalence of PV reconnection, localization of CGs, and results of RF touch-up ablation for CGs. The localization of the CGs was divided into 7 segments for both the left- and right-sided PVs (roof, anterosuperior, anteroinferior, posteroseptal, posteroinferior, bottom and carina segments). We also investigated the characteristics of the PV anatomy, such as the PV diameter and the existence of an LCPV and right middle PV (RMPV). The maximal and minimal diameters of each PV ostium were measured by reference to the cardiac CT.9 An LCPV was defined when the distance of a common trunk of a left-sided PV was >10 mm, and an RMPV was defined as an accessory right-sided PV between the RSPV and RIPV.9,10

The definition of the thawing time was the period from the termination of freezing to the passive deflation of the CB (balloon temperature reaching at 20°C). The procedural characteristics of the CB ablation and anatomic characteristics of the PVs were compared to assess the predictors of persistence of PVI status after the CB-PVI procedure between the groups successfully and unsuccessfully maintaining PVI status.

**Statistical Analysis**

Continuous data are expressed as the mean±SD. Statistical comparisons were performed using Student’s t-test, Mann-Whitney U test, and Fisher’s exact test, as appropriate. Univariate analyses were conducted with the logistic
Occlusion Grade-Guided Cryoballoon Ablation

Finally, all 178 PVs were successfully isolated by CB ablation in combination with a touch-up RF ablation (this procedure was defined as CB-PVI). The average nadir balloon temperature during freezing was $-51.9\pm7.4^\circ C$, mean freezing cycle $1.4\pm0.5$ times, and average total freezing time $242\pm86$ s. The occlusion grade could be evaluated in 171 of 178 (96.1%) PVs. Complete PV occlusion by the CB (grade 4) was observed in 122 PVs (71.3%).

Bonus freezing after successful PVI by CB ablation was performed in 15 (33.3%) patients and not in the other 30 (66.7%). Although transient right phrenic nerve paralysis was observed in 2 patients during CB ablation of the RSPV, the motion of the diaphragm had fully recovered by the end of the ablation session. There were no other complications during the index CB ablation procedure.

Re-Do Procedure
A re-do procedure was performed 184±87 days after the index CB-PVI procedure in 45 patients. Of them, 18 (40.0%) underwent a re-do procedure and were enrolled in the present study.

Study Population
Among 389 consecutive patients who underwent a CB-PVI for drug-refractory AF, the proportions of paroxysmal and persistent AF patients were 309 (79.4%) and 80 (20.6%), respectively. Of the 389 patients, 63 (16.2%) (39 [10.0%] with paroxysmal, and 24 [6.2%] with persistent AF) had a recurrence of AT after a 3-month blanking period. Of those 63 patients, 45 (11.6%) underwent a re-do procedure and were enrolled in the present study.

Baseline Patient Characteristics
The mean age was 66.7±11.0 years and 35 (77.8%) patients were male. The patients’ characteristics are shown in Table 1. The proportions of paroxysmal and persistent AF patients were 25 (56.0%) and 20 (44.0%), respectively. The targeted number of PVs during the index ablation procedure was 180. Of those 180 PVs, 2 RIPVs were isolated by RF irrigated catheter in an encircling PVI fashion because of transient right phrenic nerve paralysis during CB ablation of the RSPV. Therefore, a total of 178 PVs undergoing CB-PVI were evaluated.

Results

Study Population
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Index CB-PVI Procedure
All 45 patients underwent CB-PVI as the index procedure. As mentioned before, in 2 patients, the RIPVs were isolated by RF catheter ablation in a point-by-point fashion. As a result, the RSPV in both patients was successfully isolated as ascertained by complete disappearance of the PV potentials. Of the total 178 PVs enrolled, 161 (90.4%) were isolated solely by CB application. Supplementary touch-up RF applications (mean 4.6±4.1 times) after the CB ablation were required for the remaining 17 (9.6%) PVs (3 RSPVs, 4 LIPVs and 10 RIPVs). All LSPVs were isolated solely by CB ablation. Finally, all 178 PVs were successfully isolated by CB ablation in combination with a touch-up RF ablation (this procedure was defined as CB-PVI). The average nadir balloon temperature during freezing was $-51.9\pm7.4^\circ C$, mean freezing cycle $1.4\pm0.5$ times, and average total freezing time $242\pm86$ s. The occlusion grade could be evaluated in 171 of 178 (96.1%) PVs. Complete PV occlusion by the CB (grade 4) was observed in 122 PVs (71.3%).

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Re-Do Procedure
A re-do procedure was performed 184±87 days after the index CB-PVI procedure in 45 patients. Of them, 18 (40.0%) underwent a re-do procedure and were enrolled in the present study.

Table 1. Clinical Characteristics of the Study Population With Drug-Refractory AF

| n     | 45              |
|-------|-----------------|
| Age (years) | 66.7±11.0         |
| Male sex (%) | 35 (78)          |
| Paroxysmal AF (%) | 25 (56)          |
| AF duration (months) | 61.7±75.8       |
| CHADS2 score | 1.1±1.1          |
| Heart failure (%) | 4 (9)            |
| Hypertension (%) | 17 (38)          |
| Diabetes mellitus (%) | 9 (20)         |
| Stroke/TIA (%) | 5 (11)           |
| LA diameter (mm) | 42.5±7.1         |
| LVEF (%) | 62.4±8.9          |

AF, atrial fibrillation; LA, left atrium; LVEF, left ventricular ejection fraction; TIA, transient ischemic attack.

Figure. Localization of conduction gaps during re-do ablation procedures. A total of 38 conduction gaps (*) in 32 reconnected PVs were observed. The site of the conduction gaps was predominantly observed at the posteroinferior and bottom aspects of the right inferior pulmonary veins (RIPVs) (19/38=50.0%). LI, left inferior; LS, left superior; RS, right superior.
(8 patients with paroxysmal and 10 with persistent AF) had no PV reconnections. There were no significant differences in the number of patients without PV reconnections between those with paroxysmal and persistent AF (8/25 [32.0%] vs. 10/20 [50.0%], P=0.24). Of the 178 PVs evaluated, persistent PVI status was observed in 146 PVs (82.0%); 23 patients (15 paroxysmal, 8 persistent AF) had 1 reconnected PV, 3 (2 paroxysmal, 1 persistent AF) had 2 reconnected PVs, and 1 with persistent AF had 3 reconnected PVs. There were no patients with all 4 PV reconnected. Therefore, a total of 32 reconnected PVs was observed during the re-do ablation procedures.

The distribution of the 32 reconnected PVs was 5 (15.6%) LSPVs, 6 (18.8%) LIPVs, 4 (12.5%) RSPVs, and 17 (53.1%) RIPVs. The exact locations of the CGs during the re-do procedure are shown in Figure. The total number of CGs was 38 in the 32 reconnected PVs. The site of the CG was predominantly observed at the RIPV, especially the posteroinferior and bottom segments of the RIPV (19/38 [50.0%]). All reconnected PVs were successfully isolated by a mean of 4.1±3.4 touch-up RF applications.

With respect to PV anatomy, an LCPV and RMPV were observed in 6 and 12 patients, respectively. The maximal and minimal PV diameters were 21.6±2.5 mm and 17.8±2.7 mm for the LSPVs, 18.7±2.1 mm and 14.1±2.4 mm for the LIPVs, 21.3±3.0 mm and 18.4±3.2 mm for the RSPVs, 18.1±2.4 mm and 14.7±1.9 mm for the RIPVs.

**Investigation of the Procedural and Anatomical Characteristics During the Re-Do Procedure**

A higher prevalence of complete PV occlusion (grade 4; 111/140 [79.3%] vs. grade 1–3; 11/31 [35.4%], P<0.001), lower nadir balloon temperature (−52.7±7.3°C vs. −48.2±6.4°C, P=0.002), and longer thawing time (48.5±19.7 vs. 40.0±22.1 s, P=0.008) were observed in the persistently isolated PVs than in the reconnected PVs (Table 2). The number of PVs isolated solely by CB ablation during the index procedure was significantly higher in the persistently isolated PVs than in the reconnected PVs (137/146 [93.8%] vs. 24/32 [75.0%], P=0.004). The number of freezing cycles and total freezing time between the persistently isolated PVs and reconnected PVs did not reach statistical significance.

The existence of an LCPV or RMPV, which did not reach statistical significance with regard to the occlusion grade of the CB, was not associated with PV reconnection, and there was also no significant difference in the maximal

| Table 2. Comparison of the Procedural Characteristics of the Index Cryoballoon Ablation Procedure Between Those With and Without Persistent PVI |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Persistent PVI (n=146) | Reconnected PVs (n=32) | P value |
| Freezing cycle (times) | 1.3±0.5 | 1.4±0.5 | 0.400 |
| Bonus freezing (%) | 49 (34) | 9 (28) | 0.552 |
| Total freezing time (s) | 239±87 | 255±83 | 0.357 |
| PVI solely by cryoballoon ablation (%) | 137 (94) | 24 (75) | 0.004 |
| Nadir balloon temperature (°C) | −52.7±7.3 | −48.2±6.4 | 0.002 |
| Complete PV occlusion (occlusion grade 4) (%) | 111 (79) | 11 (35) | <0.001 |
| Thawing time (s) | 48.5±19.7 | 40.0±22.1 | 0.008 |

PV, pulmonary vein; PVI, pulmonary vein isolation.

| Table 3. Comparison of the Anatomical Characteristics Between Patients With and Without Persistent PVI |
|-------------------------------------------------|-----------------|-----------------|-----------------|
|-------------------------------------------------|-----------------|-----------------|-----------------|
| LSPV (n=45) | Persistent PVI (n=146) | Reconnected PVs (n=32) | P value |
| Maximal diameter, mm | 21.5±2.3 | 22.3±3.4 | 0.68 |
| Minimal diameter, mm | 17.7±2.6 | 18.5±3.2 | 0.63 |
| Existence of LCPV (%) | 6 (15) | 0 (0) | 1.0 |
| LIPV (n=45) | 39 | 6 | |
| Maximal diameter, mm | 18.8±2.2 | 18.2±0.5 | 0.17 |
| Minimal diameter, mm | 14.2±2.5 | 13.8±1.2 | 0.55 |
| Existence of LCPV (%) | 5 (13) | 1 (17) | 1.0 |
| RSPV (n=45) | 41 | 4 | |
| Maximal diameter, mm | 21.1±3.0 | 23.1±2.5 | 0.26 |
| Minimal diameter, mm | 18.3±3.2 | 19.9±3.3 | 0.47 |
| Existence of RMPV (%) | 11 (27) | 1 (25) | 1.0 |
| RIPV (n=43) | 26 | 17 | |
| Maximal diameter, mm | 18.1±2.3 | 18.0±2.6 | 0.81 |
| Minimal diameter, mm | 14.7±2.1 | 14.5±1.6 | 0.69 |
| Existence of RMPV (%) | 8 (31) | 3 (18) | 0.48 |

LCPV, left common PV; LIPV, left inferior PV; LSPV, left superior PV; RMPV, right middle PV; RIPV, right inferior PV; RSPV, right superior PV. Other abbreviations as in Table 2.
and minimal PV diameters of each of the 4 PVs between those with persistently isolated PVs or reconnected PVs (Table 3). Univariate analysis for predicting the persistence of the PVI status demonstrated the presence of complete PV occlusion, longer thawing time, accomplishment of PVI solely by CB ablation, and lower nadir balloon temperature. Multivariate analysis demonstrated that the presence of complete PV occlusion (odds ratio 4.93, P<0.001) during the index procedure was the only independent predictor of persistent PVI status (Table 4).

The association of the presence of complete PV occlusion with the procedural parameters and anatomical characteristics is shown in Table 5. The occlusion grade could be evaluated in 171 PVs. Complete PV occlusion (grade 4) was observed in 122 (71.3%) PVs. Leakage of contrast medium from the PV to the LA (grades 1–3) was observed in the remaining 49 (28.7%) PVs. CB ablation with complete PV occlusion during the index procedure was significantly associated with a lower nadir balloon temperature, longer thawing time, and higher prevalence of PVI solely by CB ablation.

CB-PVI with occlusion grade 4 (122 PVs) accomplished persistent PVI status in 111 PVs (91.0%), whereas CB-PVI with occlusion grade 1–3 (49 PVs) had a late PV reconnection in 20 PVs (40.8%) despite 100% accomplishment of an acute successful PVI during the index CB-PVI. The maximal and minimal PV diameters were smaller in all 4 PVs with complete PV occlusion than in those without; however, this did not reach statistical significance.

### Table 4. Univariate and Multivariate Analyses for Predicting Persistent PVI

|                          | OR       | 95% CI    | P value |
|--------------------------|----------|-----------|---------|
| Complete PV occlusion    | 7.27     | 3.13–16.9 | <0.001  |
| Thawing time             | 1.03     | 1.01–1.06 | <0.001  |
| PVI solely by cryoballoon ablation | 5.07 | 1.78–14.4 | <0.001  |
| Nadir balloon temperature| 1.10     | 1.03–1.16 | <0.001  |

### Table 5. Association of Complete PV Occlusion With Procedural Parameters and Anatomical Characteristics

|                | Presence of complete PV occlusion | Absence of complete PV occlusion | P value |
|----------------|-----------------------------------|----------------------------------|---------|
| No. of PVs (n) | 122                               | 49                               |         |
| Nadir balloon temperature (°C) | −53.5±6.9 | −48.3±6.9 | <0.001  |
| Thawing time (s) | 51.0±19.8 | 39.2±17.8 | <0.0002 |
| PVI solely by cryoballoon ablation (%) | 118 (97) | 38 (78) | <0.003  |
| Acute PVI at the index CB-PVI (%) | 122 (100) | 49 (100) | 1.0     |

### Abbreviations as in Tables 2, 3.
significant differences in these parameters between the successfully occluded PVs with and without a pull-down maneuver (P=0.76 for the nadir balloon temperature, P=0.27 for the thawing time, and P=0.35 for the total freezing time). Persistent PVI status was maintained during the re-do procedure in all 10 PVs with a successful pull-down maneuver. The other 10 PVs without complete PV occlusion even with a pull-down maneuver had 5 reconnected PVs during the re-do procedure (50.0% of the PV reconnection rate). There were no complications in the patients undergoing a pull-down maneuver during the index procedure.

Discussion

The major findings of the present study were (1) 40% of the patients had no PV reconnections and 82% of the PVs were persistently isolated during the re-do ablation procedure by the CB-PVI procedure, (2) the presence of complete PV occlusion was the only independent predictor of a persistent PVI status, (3) CB-PVI without complete PV occlusion had late PV reconnections with a probability of 41% despite 100% accomplishment of an acute successful PVI during the index procedure, and (4) all CB-PVIs with a successful pull-down maneuver maintained a persistent PVI status.

Our study demonstrated the importance of the presence of complete PV occlusion for a durable PVI status. CB-PVI with complete PV occlusion was able to maintain persistent PVI status in more than 90% of the patients during the re-do ablation procedure. Univariate analysis demonstrated the importance of the presence of complete PV occlusion, thawing duration, successful PVI solely by CB application, and nadir balloon temperature. However, the multivariate analysis demonstrated the presence of complete PV occlusion as the only independent predictor of persistent PVI status. Although several previous studies have reported the predictors of persistent PVI status after CB ablation, the most crucial predictor of persistent PVI status was the durability of the PVI before the delivery of cryothermal energy. An evaluation of the occlusion grade by injecting contrast medium is routinely performed in almost all cases immediately prior to the CB ablation procedure. 

Achieving a complete PV occlusion was an absolute requirement for the successful PVI achievement using either the first- or second-generation CB. Therefore, in the case of an occlusion grade less than 4, re-positioning of the CB in order to obtain a higher occlusion grade has to be performed.

Pull-Down Maneuver

The various locations of late PV reconnection sites after CB ablation have been reported. In our study, the majority of the CGs were observed in the posteroinferior and bottom segments of the RIPVs. Poor CB adhesion to the atrial tissue in this area may cause this eccentric distribution of the CGs. The pull-down maneuver was an effective method of improving the CB occlusion status, which abolished leakage, predominantly around the inferior aspect of the targeted PVs. Although the results of the pull-down maneuver utilizing first-generation CB have been reported, this maneuver utilizing second-generation CB has not been clearly investigated. In this study, complete PV occlusion achieved with the pull-down maneuver resulted in no late PVs reconnections during the re-do ablation procedure, and this procedure did not cause any serious complications.

On the other hand, further improvement in the pull-down maneuver should be considered because complete PV occlusion was obtained in only 50% of the targeted PVs undergoing the maneuver. In the present study, the pull-down maneuver was undertaken when the CB temperature reached −10°C. If adherence between the CB and the superior aspect of the targeted PV is insufficient, the pull-down maneuver could provide new leakage around the superior aspect of the targeted PVs. Although relatively late timing of the pull-down maneuver might be advocated for better adherence of the CB to the PV tissue, it could lead to occlusion of the central lumen of the CB by crystal formation, which would make it impossible to evaluate the occlusion grade. Further investigation is required to evaluate the best method of performing the pull-down maneuver.

Complications

Complications associated with second-generation CB ablation are rare, but serious problems such as esophageal cryothermal injury, phrenic nerve paralysis, and PV stenosis have been reported. In our study, no major complications were observed during the index procedure. Phrenic nerve paralysis was provoked in 2 patients, but had resolved by the end of the ablation procedure. No patients reported any dyspnea or other symptoms suggestive of PV stenosis during the follow-up.

CB ablation with the second-generation CB has improved its effectiveness in terms of the clinical outcome. The improvement in the durability of the PVI status might have contributed this clinical outcome. In the present study, the prevalence of an acute successful PVI solely by CB application was 90% during the index procedure. This was relatively low in comparison with previously published reports. Our method of CB ablation, in which the number of CB applications was limited to ≤2 and the cryothermal energy was applied as proximal as possible at each PV ostium, may be associated with the results achieved during the index procedure. However, the prevalence of persistent PVI status during the re-do procedure was almost similar in the present study to that reported in previously published studies. Although our protocol may have overestimated the results of the CB ablation itself, because approximately 10% of the PVs were isolated with first-generation CB, but CB ablation without complete PV occlusion was still unsatisfactory even with the second-generation CB.
by CB ablation combined with touch-up RF ablation, the results of our study could show that PVI by a combination of CB ablation and focal RF touch-up applications for the CGs may be useful and effective with a low risk of CB-associated complications.

**Study Limitations**

This study was a nonrandomized analysis of consecutive patients including our initial patients treated with a novel CB device. However, all operators were well trained in CB ablation and were beyond the learning curve, minimizing any time-dependent confounders.

It was a retrospective, single-center trial. The study population was relatively small and not all patients with recurrence of AT underwent a re-do procedure. This might have influenced the results. This study did not enroll patients without AT recurrence. Therefore, the prevalence of PV reconnection might be estimated as higher than the actual prevalence. The retrospective evaluation of the occlusion grade of the PVs was sometimes difficult to categorize or arbitrarily categorize. The occlusion grade was evaluated not by intracardiac echocardiography, but by the fluoroscopic images of the leakage of contrast medium. A combined use of fluoroscopy and intracardiac echocardiography might improve the ability to detect a tiny leakage, and therefore, PVs with a tiny leakage might be categorized as a grade 4 complete PV occlusion. The study results were derived from the combination of the CB and RF treatments, so the results might have overestimated the results of the CB ablation in poorly occluded PVs. Larger, prospective, multicenter studies are needed to identify the other important predictors during long-term follow-up.

**Conclusions**

The occlusion grade might predict the persistence of PVI status. Appropriate manipulation of the CB for a better occlusion status may be crucial for a successful CB-PVI procedure.

**Disclosures**

The authors have no conflicts of interest to declare.

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