Characteristics of Phrenic Nerve Injury During Pulmonary Vein Isolation Using a 28-mm Second-Generation Cryoballoon and Short Freeze Strategy

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Background**—**The reported incidence of phrenic nerve injury (PNI) varies owing to different definitions, balloon generations, balloon size, freezing regimen, and protective maneuvers. We evaluated the incidence, predictors, and outcome of PNI during cryoballoon pulmonary vein isolation in a large population.

Methods and Results**—**Five hundred fifty atrial fibrillation patients underwent pulmonary vein isolation using one 28-mm second-generation cryoballoon and single 3-minute freeze strategy under diaphragmatic compound motor action potential (CMAP) monitoring. A total of 34 (6.2%) patients experienced PNI during the right superior and inferior pulmonary vein ablation in 30 and 4 patients, respectively. Applications were interrupted using double-stop techniques after 136 [104–158] second applications, and a pulmonary vein isolation was already achieved in all but one case. The baseline CMAP amplitude and timing of deflation ($CMAP_{def}$) were 0.75±0.30 and 0.17±0.17 mV, respectively. Persistent atrial fibrillation, larger right superior pulmonary vein ostia, and deeper balloon positions were associated with higher incidences of PNI. The $CMAP_{def}$ predicted a PNI recovery delay, and the best cutoff value for predicting PNI recovery by the next day was 0.20 mV (sensitivity 57.1%, specificity 100%). Among 6 patients undergoing second procedures 8.5 (6.7–15.0) months later, the right superior pulmonary vein was durable in 3 with >120 second applications. Despite active balloon deflation, no significant pulmonary vein stenosis was observed in 15 right superior pulmonary veins evaluated 6 (5–9) months later. No patients had symptoms, and the PNI recovered 1 day and 1 month postprocedure in 21 and 4 patients, respectively.

Conclusions**—**PNI resulting from cryoballoon ablation was reversible. The double-stop technique is safe, and immediate active deflation following a CMAP decrease appears to be essential for faster PNI recovery. **(*J Am Heart Assoc*. 2018;7:e008249. DOI: 10.1161/JAHA.117.008249.)**

Key Words: catheter ablation • complication • cryoballoon • phrenic nerve injury • pulmonary vein isolation

Pulmonary vein isolation (PVI) is an established strategy for drug-resistant atrial fibrillation (AF).[1] Recently, cryoballoon (CB) ablation has emerged as a valid alternative to radiofrequency ablation,[2–4] and a comparable efficacy and safety were demonstrated in a prospective randomized study.[4] Nevertheless, CB ablation is associated with a significant risk of phrenic nerve injury (PNI) due to the close proximity between the phrenic nerves and balloon position.[2–4] The reported incidence of PNI vary because of the different definitions, balloon generations, balloon size, freezing regimen, and protective maneuvers.[2–7] Currently, a single 28-mm-balloon use, proximal-seal technique, and active deflation when the compound motor action potential (CMAP) decreases have become the mainstay of PNI prevention. Continuous monitoring of the diaphragmatic CMAPs has also become an accepted technique in clinical practice.[8–11] Although a few preprocedural and intraprocedural predictors of PNI have been reported,[12,13] the prognostic factors for PNI recovery have not been evaluated. In addition, in clinical practice, it is still under debate whether any additional ablation should be applied following an interrupted freeze attributable to PNI. The present study aimed to clarify the detailed characteristics of PNI during the PVI using a single 28-mm second-generation

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Clinical Perspective

What Is New?

- The incidence of phrenic nerve injury (PNI) using 28-mm cryoballoons and a short freeze strategy during the procedure, on the next day, and 1 month after, was 6.2%, 2.4%, and 1.6%, respectively.
- The incidence of PNI was 5.5% and 0.7% during the right superior and inferior pulmonary vein ablation.
- Persistent atrial fibrillation, a larger right superior pulmonary vein ostium, and deeper balloon position were associated with a higher incidence of PNI.
- The compound motor action potentials amplitude during the emergent deflation predicted the timing of PNI recovery.

What Are the Clinical Implications?

- Patients at high risk for PNI can be recognized before and during the procedure.
- The timing of PNI recovery can be predicted during the procedure.

CB and short freeze strategy in a large consecutive patient series.

Methods

Study Population

This study consisted of 550 consecutive patients with AF who underwent their first PVI using a CB at Tsuchiura Kyodo Hospital. In all patients, a PVI was performed exclusively with a 28-mm second-generation CB (Arctic Front Advance, Medtronic) and single 3-minute freeze strategy (without any bonus applications after the isolation) under bilateral diaphragmatic electromyography monitoring.[14] AF was classified according to the latest guidelines.[1] All patients gave their written informed consent. The study protocol was approved by the hospital's institutional review board. The study complied with the Declaration of Helsinki. The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure because the original data included the patients' personal information.

Mapping and Ablation Protocol

Preprocedural cardiac enhanced computed tomography was performed to evaluate the cardiac anatomy (Figure 1). No patients were excluded based on the computed tomographic characteristics. The surface ECG and bipolar intracardiac electrograms were continuously monitored and stored on a computer-based digital recording system (LabSystem PRO, Bard Electrophysiology, Lowell, Massachusetts). The bipolar electrograms were filtered from 30 to 500 Hz. The procedure was performed under moderate sedation obtained with dexmedetomidine. A 100 IU/kg body weight of heparin was administered immediately following the venous access, and heparinized saline was additionally infused to maintain the activated clotting time at 300 to 350 seconds. A single transseptal puncture was performed using a radiofrequency needle (Baylis Medical, Inc., Montreal, Quebec) and 8-Fr long sheath (SL0, AF Division, SJM, Minneapolis, Minnesota) under fluoroscopic guidance. The transseptal sheath was exchanged over a guidewire for a 15-Fr steerable sheath (Flexcath Advance, Medtronic, Minneapolis, Minnesota). A spiral mapping catheter (Achieve, Medtronic) was used to advance the 28-mm second-generation CB into the PV for support and to map the PV potentials. A 23-mm CB was not used in any cases. Following the verification of complete sealing with a contrast medium injection, a freeze cycle of 180 seconds was applied. The CB position in relation to the cardiac shadow under fluoroscopic guidance in the anteroposterior projection during the right superior pulmonary vein (RSPV) ablation was divided into 3 groups: completely inside the cardiac shadow (position A), one third outside the cardiac shadow (position B1), and one third or more outside the cardiac shadow (position B2) according to a prior report.[12] If the balloon temperature reached −60°C, the freezing was terminated. The procedural end point was defined as an electrical PVI, and no bonus applications were performed after the isolation. If electrical isolation was not achieved by a total of 3 CB applications per vein, touch-up ablation was performed with an 8-mm-tip cryocatheter for 2 minutes for each application or an irrigated-tip radiofrequency catheter.

Monitoring the Phrenic Nerve Function

The detailed technique has been previously described.[9,10,14] For monitoring the diaphragmatic CMAPs, two additional standard surface ECG electrodes were positioned 5 cm above the xiphoid process and 16 cm along the costal margin. During the CB applications, continuous pacing (10V, 2 ms) of the ipsilateral phrenic nerves was performed from the right and left subclavian veins. Ablation was terminated when the operator recognized any significant CMAP amplitude reduction from baseline, considering the amplitude variation, using a double-stop technique[11] (Figure 2). The diaphragmatic movement was evaluated throughout the procedure in the supine position.

A chest radiograph (standard posteroanterior view) was undertaken in a standing position 1 day before and the day after the ablation procedure in all patients. If the level of the right diaphragm was significantly elevated on the day after the

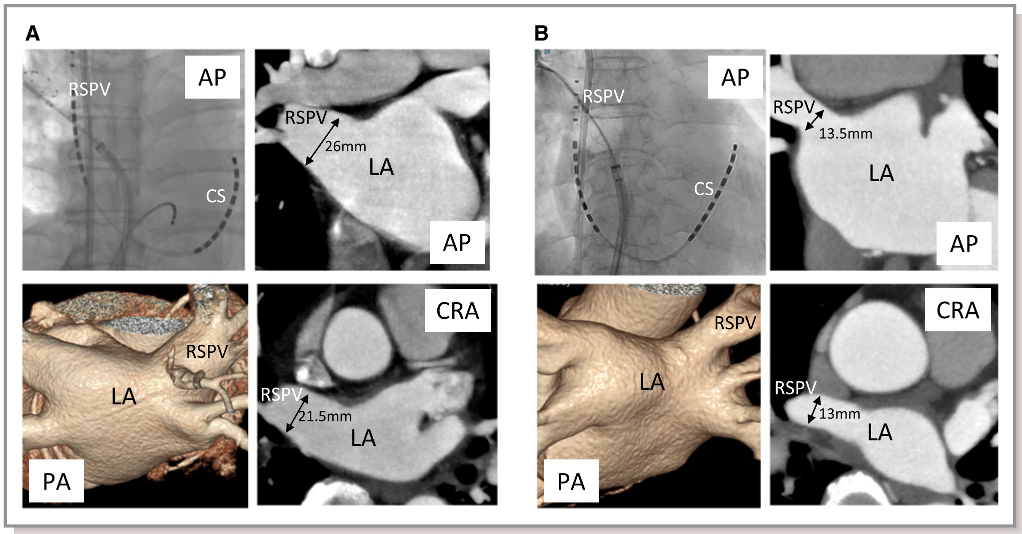

Figure 1. Representative balloon position on the chest radiograph and PV anatomy on cardiac CT in patients with PNI during RSPV applications. A, Deep balloon position due to the large RSPV ostium (26×21.5 mm) resulted in PNI. B, Despite a proximal balloon position attributable to a small RSPV ostium (13.5×13 mm), PNI occurred. AP indicates anteroposterior view; CRA, cranial view; CS, coronary sinus; LA, left atrium; PA, postero-anterior view; and RSPV, right superior pulmonary vein.

procedure relative to that before the procedure, we diagnosed it as a *persistent* PNI (Figure 3).

Statistical Analysis

Continuous data are expressed as the mean±standard deviation for normally distributed variables or as the median [25th, 75th percentiles] for non–normally distributed variables, and were compared using a Student *t* test or Mann-Whitney *U*-test, respectively. Categorical variables were compared using the chi-square test. Among 550 total patients, the RSPV diameters in patients with and without any PNI were compared. A multiple logistic regression analysis was used to determine the predictors of the occurrence of PNI among the clinical parameters. Among 34 patients with PNI, the CMAP amplitude at the timing of the active deflation in patients with and without *persistent* PNI were compared. The optimal cutoff point was chosen as the combination with the highest sensitivity and specificity using receiver operating characteristic curves. A probability value of $P<0.05$ indicated statistical significance.

Results

Clinical Characteristics and Procedure Results

A total of 34 (6.2%) patients experienced PNI with a significant CMAP amplitude reduction during the procedure. All were right PNI, and occurred during an RSPV and right inferior pulmonary vein (RIPV) ablation in 30 (5.5%) and 4 (0.7%) patients, respectively. The patient characteristics are summarized in Table 1. In the 34 patients, a total of 136 PVs were identified. Overall, 131 of 136 (96.3%) PVs were isolated successfully using exclusively 28-mm second-generation CBs. Touch-up lesions were applied in a total of 5 (3.7%) PVs, including 1, 1, 1, and 2 in the left superior PV, left inferior PV, RSPV and RIPV, respectively. Among the 5 PVs, PVI by the CB was abandoned due to PNI in 2 PVs (one RSPV and RIPV each). The mean number of CB applications was 1.3±0.4, 1.3±0.7, 1.2±0.5, and 1.1±0.4 for the RSPV, RIPV, left superior, and left inferior PVs, respectively. No other complications except for right PNI were observed in any of the patients.

Procedural Detail

In the 34 patients, the applications were terminated using a double-stop technique at a median of 136 (104–158) seconds from starting the applications. The applications related to PNI were the first application for the targeted vein in 28 (82.3%) patients, and the second application following a failed first application in 4 (11.8%). In the remaining 2 (5.9%) patients, PNI occurred during both the first and second applications. A retrospective analysis clarified that the CMAP amplitude started to decrease a median of 104 (76–122) seconds from starting the cryoapplications, and the delay until the emergent deflation was a median of 16 (7–30) seconds. The mean CMAP amplitude at baseline and during the active deflation was 0.75±0.30 and 0.17±0.17 mV, respectively (Figure 2). The amplitude was 0 mV during the active deflation in 10 (29.4%) patients.

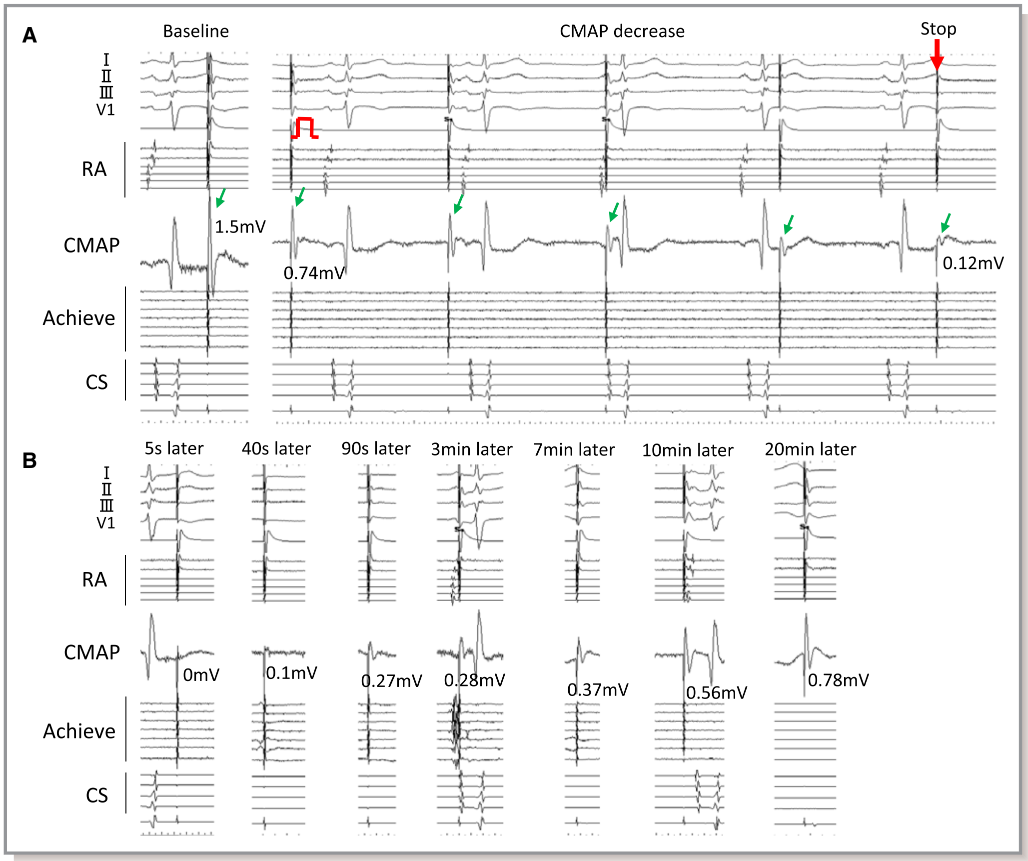

Figure 2. Representative time course of diaphragmatic CMAPs in a patient with PNI. A, The baseline CMAP amplitude was 1.5 mV. The cryoapplication was terminated (red arrow) following the CMAP amplitude reduction (green arrows, 0.12 mV). B, The CMAP amplitude further reduced to 0 mV following the emergent termination; however, it gradually recovered to 0.78 mV over 20 minutes after termination. CMAP indicates compound motor action potential; and RA, right atrium.

In 17 (47.2%) of 36 applications related to PNI, real-time monitoring of the PV potentials was possible, and the time-to-isolation was a median of 28 (19.5–35) seconds. All 17 applications were interrupted after achieving the PVI. In the remaining 19 (52.8%) applications, during which real-time PV potentials were not visible, subsequent mapping by a ring catheter confirmed the PVI in 17 applications but not in the remaining 2 in 1 patient (detailed description below).

After the occurrence of PNI, no additional ablation was performed in all except for 2 patients. In the first patient with long-standing persistent AF, the time-to-isolation of the RSPV was 27 seconds, and the application was interrupted 33 seconds after starting the application due to a CMAP amplitude decrease, which resulted in a reconnection. Following the CMAP amplitude recovery, a second application was applied, but was again interrupted 134 seconds after starting the application because of a CMAP amplitude decrease. The time-to-isolation during the second application was 45 seconds, and no further ablation was added. In the second patient with persistent AF, the first and second applications for the RSPV were interrupted 123 and 105 seconds after starting the application because of a CMAP amplitude decrease. No real-time PV potentials were visible, and RSPV potentials still remained after the 2 applications. Thus, additional touch-up ablation was required for the isolation. In 34 total patients, the total freezing duration was a median of 143 (116–177) seconds.

Predictors of PNI

In the 30 patients with the occurrence of PNI during the RSPV ablation, the diameter of the RSPV ostium in the coronal and horizontal views on cardiac computed tomography was 19.5±4.2 and 15.7±3.8 mm, respectively. A proximal-seal technique was used in 11 (36.7%) patients, but not in the remaining 19 (63.3%). The CB positions in relation to the cardiac shadow under fluoroscopic guidance were positions A, B1, and B2, in 12, 13, and 3 patients, respectively. The nadir balloon temperature was −53.5±4.5°C, and the time to

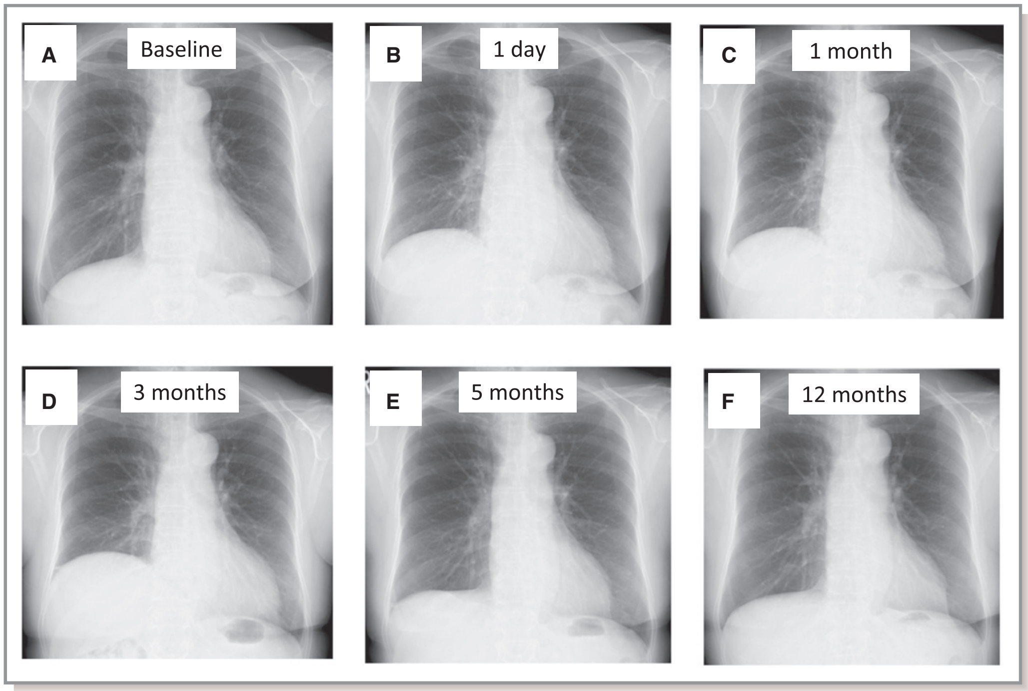

Figure 3. The representative time course of right PNI on the chest radiograph (A, baseline; B, 1 day; C, 1 month; D, 3 months; E, 5 months; and F, 12 months after the procedure). In this case, the timing of the emergent deflation was delayed by 50 seconds after a significant CMAP reduction (same patient as Figure 1B) and complete PNI recovery required 12 months.

−30°C and time to −40°C were 27.0±3.1 and 39.5±7.9 seconds, respectively (Table 2).

Among the preprocedural parameters, the AF type (paroxysmal versus persistent AF 4.9% versus 5.8%: odds ratio [OR] =1.204, 95% CI=0.443–3.271; *P*=0.716; paroxysmal versus longstanding persistent AF 4.9% versus 23.1%: OR=5.850, 95% CI=1.502–22.781; *P*=0.011) (Figure 4A), RSPV coronal diameter (OR=1.200, 95% CI=1.074–1.341; *P*=0.001), and RSPV horizontal diameter (OR=1.194, 95% CI=1.066–1.338; *P*=0.002) were significantly associated with the occurrence of PNI (Table 2). The best cutoff value of the coronal and horizontal RSPV diameters to predict the occurrence of PNI was 18.2 mm (sensitivity 73.3%, specificity 60.0%) and 16.3 mm (sensitivity 46.7%, specificity 78.1%), respectively. Among the intraprocedural parameters, the use of a proximal-seal technique reduced the incidence of PNI, but the difference did not reach statistical significance. The balloon position relative to the cardiac shadow was associated with the occurrence of PNI (A versus B1: OR=5.241, 95% CI=2.307–11.907; *P*<0.0001, A versus B2: OR=13.821, 95% CI=3.180–60.080; *P*<0.0001), but the temperature drop parameters were not (Table 2, Figure 4B). Figure 1A is a representative PNI case with a large RSPV ostium and deep balloon position; however, PNI could occur even in cases with small RSPV ostia and a proximal balloon position as in Figure 1B.

Table 1. Characteristics of the PNI Patients

N	34
Age, y	62.1±10.5
Paroxysmal AF, n (%)	22 (6.5%)
Initial procedure, n (%)	34 (100%)
Female, n (%)	14 (41.2%)
Structural heart disease, n (%)	5 (14.7%)
Hypertension, n (%)	16 (47.0%)
Body mass index, kg/m^2	23.8±3.5
LA diameter, mm	36.3±5.9
LV ejection fraction, %	63.5±10.5
Pro-brain natriuretic peptide, pg/mL	250±545
Estimated GFR, mL/min per 1.73 m^2	71.5±18.8

AF indicates atrial fibrillation; GFR, glomerular filtration ratio; LA, left atrial; and LV, left ventricular.

Clinical Outcome and Prognostic Factors of PNI Recovery

No patients complained of symptoms related to PNI. Complete recovery of PNI was confirmed the next day and 1 month after the procedure in 21 (61.8%) and 4 (11.8%) patients, respectively. PNI persisted more than 1 month in the remaining 9 (26.5%) patients. PNI completely recovered within

Table 2. Parameters Associated With the Occurrence of PNI During RSPV Applications

	PNI During RSPV	No PNI	
N	30	520	*P* Value
Age, y	62.1±10.6	63.6±11.2	0.479
AF type			0.017
Paroxysmal AF, n	22 (73.3%)	429 (82.5%)	
Persistent AF, n	5 (16.7%)	81 (15.6%)	
Long-standing persistent AF, n	3 (10.0%)	10 (1.9%)	
Female, n	12 (40%)	155 (29.8%)	0.238
Body mass index, kg/m^2	24.4±3.2	24.3±3.7	0.867
LA diameter, mm	37.4±5.3	38.0±5.6	0.540
LV ejection fraction, %	64.0±11.1	65.8±7.5	0.215
RSPV diameter (coronal), mm	19.5±4.2	17.7±2.8	0.001
RSPV diameter (horizontal), mm	16.0±4.7	14.4±2.6	0.001
Proximal-seal technique	11 (36.7%)	269 (51.7%)	0.09
Balloon position on chest radiograph	N=28	N=474	<0.0001
A	12 (42.9%)	387 (81.6%)	
B1	13 (46.4%)	80 (16.9%)	
B2	3 (10.7%)	7 (1.5%)	
Nadir balloon temperature, °C	−53.5±4.5	−54.7±5.0	0.213
Time to −30°C, s	27.0±3.1	28.2±4.5	0.150
Time to −40°C, s	39.5±7.9	44.0±17.2	0.166

AF indicates atrial fibrillation; LV, left ventricular; LA, left atrial; PNI, phrenic nerve injury; and RSPV, right superior pulmonary vein.

6 and 12 months after the procedure in 4 and 3 patients, respectively (Figure 3A through 3F), while the remaining 2 patients still had PNI during 1 month of follow-up.

In patients who required a longer time for PNI recovery, the timing of the CMAP amplitude decrease after starting the application was earlier and the emergent deflation delay from the start of the CMAP amplitude reduction was longer than in the patients requiring a shorter time for recovery. The CMAP amplitude during the emergent deflation significantly correlated with the PNI recovery delay (P=0.002, Table 3). For the association between the CMAP amplitude during the emergent deflation and *persistent* PNI, an area under the curve of 0.846 (95% CI=0.717–0.975) was observed. The best cutoff value of the CMAP amplitude when the freezing was interrupted to predict the PNI recovery on the day after the procedure was 0.20 mV (sensitivity 57.1%, specificity 100%) (Figure 4C and 4D).

Durability and Safety of Active Deflation

A second procedure was performed at a median of 8.5 (6.7–15.0) months after the initial procedure in 6 (17.6%) patients. PNI occurred during the RSPV ablation in all. During the second procedure, 3 RSPVs were reconnected and the remaining 3 were still isolated. The detailed procedural data during the initial procedure is presented in Table 4.

Fifteen (44.1%) patients underwent follow-up CT at a median of 6 (5–9) months after the procedure. Despite the use of active balloon deflation, no PV stenosis was observed in any cases except for 1 (6.7%) with mild RSPV stenosis (25%).

Discussion

We found the following: (1) The incidence of PNI using single 28-mm balloons and a short freeze strategy during the procedure, on the next day, and 1 month after, was 6.2%, 2.4%, and 1.6%, respectively. (2) The incidence of PNI was 5.5% and 0.7% during the RSPV and RIPV ablation, but 0% during the left PV ablation. (3) Persistent AF, a larger RSPV ostium, and deeper balloon position were associated with a higher incidence of PNI. (4) PNI generally occurred after achieving an electrical PVI. (5) The CMAP amplitude during the emergent deflation predicted the timing of PNI recovery. (6) The RSPV was durable in all patients who underwent application of >120 seconds despite emergent interruptions. (7) No significant PV stenosis was observed in any PVs despite active balloon deflations.

Incidence of PNI

The reported incidence of PNI varies because of the different definitions, balloon generations, balloon size, freezing regimen, and protective maneuvers.[2–7] Currently, a single 28-mm-balloon use, continuous CMAP monitoring, short freeze duration, and active deflation when the CMAP decreases >30% from baseline are recommended to anticipate PNI.[8–11] However, the major limitation of CMAP monitoring in clinical practice was the amplitude variations with respiratory movements and body habitus, especially during conscious sedation.[8,10] Micro-dislodgement of pacing catheters is also an important limitation. Early termination likely leads to a false positive, and prolongs the procedure time and makes it difficult to decide the optimal freeze dosing of subsequent applications. These factors could be misleading for the optimal emergent deflation timing. Our study clarified the incidence of PNI at different timings after the procedure when single 28-mm balloons and a short freeze strategy were applied. All patients with PNI, except the patients with short follow-up periods, recovered during the follow-up period, which was in accordance with the published literature.[7]

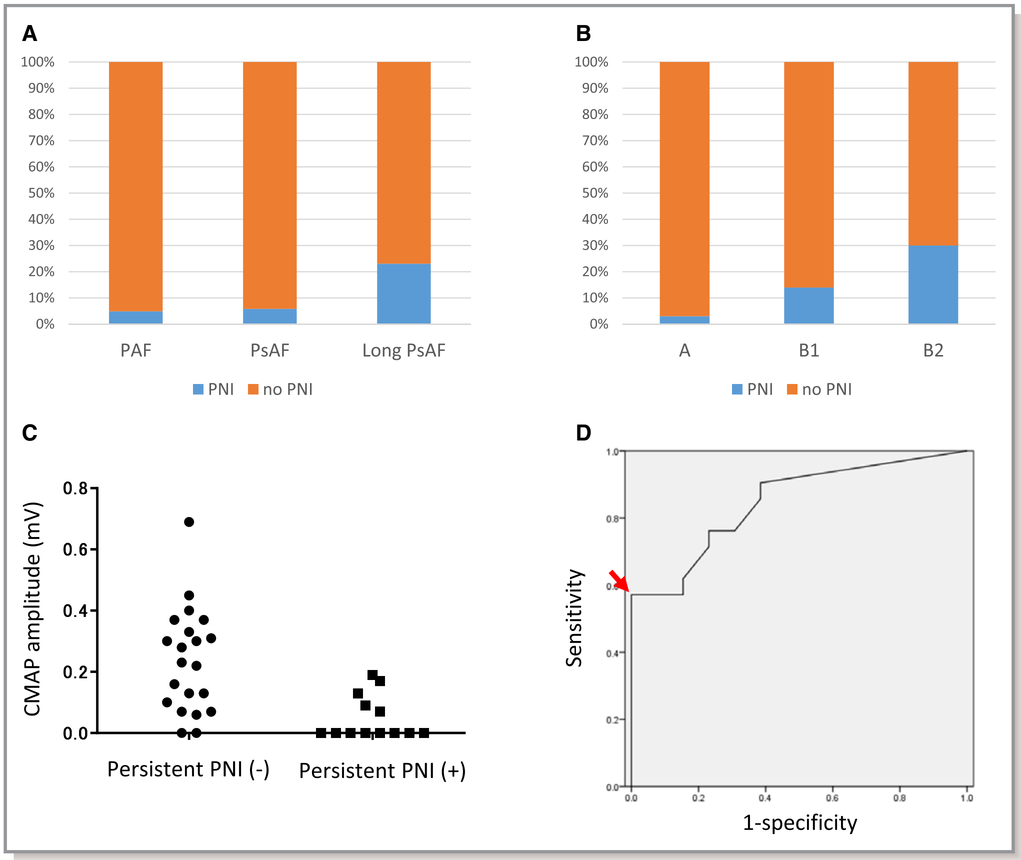

Figure 4. A, The incidence of PNI in patients with different AF (atrial fibrillation) types. B, The incidence of PNI at different balloon positions on chest radiograph during the procedure. C, The CMAP (compound motor action potential) amplitude during the balloon deflation in patients with and without *persistent* PNI (phrenic nerve injury). D, Receiver operating characteristic curve to evaluate the best cutoff value (red arrow) of the CMAP amplitude when freezing was interrupted to predict PNI recovery by the next day of the procedure. PAF indicates paroxysmal atrial fibrillation; PsAF, persistent atrial fibrillation.

Preprocedural and Intraprocedural Predictors of PNI

A few studies have shown that larger PV diameters, deeper balloon positions on fluoroscopy, and rapid temperature drops during freezing phases are associated with a higher incidence of PNI.[12,13] A single-center study in 19 PNI patients among 165 patients showed that PNI occurrences were 0.9%, 10.6%, and 90.1% in positions A, B1, and B2, respectively.[12] The same group reported, by comparing 41 PNI patients to 123 control patients, that low temperatures during the early freezing cycle phases predicted PNI, and an RSPV diameter of 23.5×17.9 mm significantly predicted PNI occurrences.[13] Our study results are in line with these data except for the temperature drop parameters, presumably because we tried to isolate RSPVs as proximal as possible in the majority of patients. In addition, we clarified that the AF type was also a predictor for PNI occurrence. The concept of “AF begets AF”

Table 3. Intraprocedural Parameters Associated With PNI Recovery

Timing of PNI Recovery	<24 h	<1 mo	>1 mo	
N	21	4	9	*P* Value
Baseline CMAP amplitude, mV	0.79±0.33	0.75±0.27	0.64±0.20	0.454
Timing of CMAP amplitude reduction, s	105 (85–129)	121 (109–131)	80 (62–97)	0.054
Delay of emergent balloon deflation, s	10 (6–25)	28 (16–34)	21 (15–35)	0.094
CMAP amplitude at the timing of emergent deflation, mV	0.24±0.17	0.11±0.09	0.02±0.05	0.002

CMAP indicates compound motor action potential; and PNI, phrenic nerve injury.

Table 4. Procedural Data in Patients Who Underwent Second Procedures

Patient	TTI, s	PVI by CB Alone?	CB Application Time, s	Nadir Balloon Temperature, °C	Follow-Up, mo	Durability
#1	19	Yes	155	−50	8	Durable
#2	29	Yes	68	−49	9	Reconnection
#3	NA	Yes	120	−54	15	Durable
#4	NA	Yes	58	−45	15	Reconnection
#5	NA	No	228+Touch-up	−51 and −56	8	Reconnection
#6	30	Yes	166	−50	3	Durable

CB indicates cryoballoon; NA, not available; PVI, pulmonary vein isolation; and TTI, time-to-isolation.

remains a cornerstone in the understanding of the natural history of AF progression, and an increasing AF burden is associated with progressive atrial remodeling, which can contribute to the persistence of AF.[1] It is plausible that advanced atrial remodeling might be associated with a higher incidence of PNI. Although CB ablation could be an alternative strategy for catheter ablation of persistent AF, the reported single procedure outcome is limited as compared to paroxysmal AF.[15] All these data highlight the importance of a proximal CB position during the application. The proximal-seal technique was initially proposed by Su et al to avoid deep CB positioning.[8] If no leak is visible on venography, withdraw the CB slightly and allow a leak around the PV-balloon interface to better define the PV ostium and ensure a proximal ablation. Then, reapply only the minimal amount of pressure needed to regain occlusion before ablation. Since the CB size slightly becomes larger when the freezing starts, a small leakage is generally sealed by CB applications. However, it should be noted that PNI could occur even if the RSPV size is small, presumably because the phrenic nerve course varies among patients. Therefore, careful CMAP monitoring is mandatory during applications regardless of the RSPV size.

Predictors of PNI Recovery

Our study initially showed that the CMAP amplitude during the active deflation was significantly associated with a delay of the PNI recovery. When the amplitude was >0.2 mV, it recovered by the next day in all cases. This was in line with the results of an animal study showing that the functional and histologic severity of PNI parallels the degree of the CMAP amplitude reduction.[16] Data showing that an early timed CMAP decrease was associated with a PNI recovery delay could be explained by experimental study results showing that phrenic nerve cooling to subzero temperatures consistently leads to a loss of function and the functional recovery is delayed if it is cooled at faster rates and to lower temperatures.[17] Earlier recognition of CMAP amplitude reductions and immediate active deflations appear to be essential to anticipate *persistent* PNI.

Although active balloon deflation has safety concerns of tissue/vascular injury, our data clarified that no significant stenosis was observed in PVs following active deflation. The data were in accordance with the animal study data that active deflation is associated with faster balloon rewarming, but not with significant differences in the mean or maximum neointimal thickness.[18]

Durability After Interrupted Applications With Active Deflation

In all but 1 case, the timing of PNI occurrence was after achieving the PVI regardless of the capability of real-time PV potential monitoring. It is still unknown whether additional ablation is necessary after interrupting applications because of PNI. Additional CB ablation would increase the risk of exacerbating the PNI, and additional RF ablation might be challenging if there are no PV potentials if the PVI was already achieved by interrupting applications. Moreover, the expected lesion size differed between standard CB applications (single-stop) and actively interrupted applications (double-stop) despite the same freezing duration because cryolesions are created during the freezing phase and also the thawing phase. Although the number of evaluable cases was limited, according to our data, 1-minute freezes seem to be insufficient, however, 2-minute freezes might be sufficient to obtain good durability. Further study is necessary to explore this issue.

Study Limitations

The study was a single-center observational study, and the number that experienced PNI was relatively low. We could not analyze the association between the location of the transseptal puncture site and PNI, and between the sheath location during the application and PNI. Overlap of the CMAP amplitudes was observed during the recovery time; nevertheless, all PNIs recovered by the next day if a CMAP amplitude of >0.20 mV remained. Our study results should be further confirmed in a prospective study.

Conclusions

In second-generation CB ablation, the incidence of PNI during, 1 day after, and 1 month after the procedure was 6.2%, 2.4%, and 1.6%, respectively; however, all were reversible during the follow-up period. Persistent AF, a larger RSPV ostium, and deeper balloon position on fluoroscopy were associated with a higher incidence of PNI. The CMAP amplitude during the emergent deflation predicted the delay in the PNI recovery, and all PNI recovered by the next day in patients with a remaining CMAP amplitude >0.2 mV. The double-stop technique is safe, and early recognition of CMAP amplitude reductions and subsequent immediate active deflations appears to be essential for early recovery of PNI.

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Disclosures

None.

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