



Reconduction After Second-Generation Cryoballoon-Based Pulmonary Vein Isolation

— Impact of Different Ablation Strategies —

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Background: The second-generation cryoballoon (CB2) has demonstrated high procedural efficacy and convincing clinical success rates for pulmonary vein isolation (PVI). Nevertheless, data on the impact of different ablations protocols on durability are limited. The aim was to comparing the durability of PVI following 3 different ablation strategies in patients with recurrence of atrial fibrillation or atrial tachycardia undergoing repeat procedures.

Methods and Results: In 192 patients, a total of 751 PVs were identified. All PVs were successfully isolated during index PVI. Thirty-one out of 192 (16%) patients were treated with a bonus-freeze protocol (group 1), 67/192 (35%) patients with a no bonus-freeze protocol (group 2), and 94/192 (49%) patients with a time-to-effect-guided protocol (group 3). Persistent PVI was documented in 419/751 (55.8%) PVs, and in 41/192 (21%) patients, all PVs were persistently isolated. The total rate of PV reconnection was not significantly different between the groups ($P=0.134$) and the comparison of individual PVs revealed no differences (P -values for RSPV: 0.424, RIPV: 0.541, LSPV: 0.788, LIPV: 0.346, LCPV: 0.865). The procedure times were significantly reduced by omitting the bonus-freeze and applying individualized application times (group 1: 123.4 ± 31.5 min, group 2: 112.9 ± 39.8 min, group 3: 86.67 ± 28.4 min, $P<0.001$).

Conclusions: Comparing 3 common ablation protocols, no differences for durable PVI were detected. Procedure times were significantly reduced by omitting the bonus-freeze cycle and by applying individualized application times.

Key Words: Atrial fibrillation; Clinical follow up; Cryoballoon; Electrical reconduction; Pulmonary vein isolation

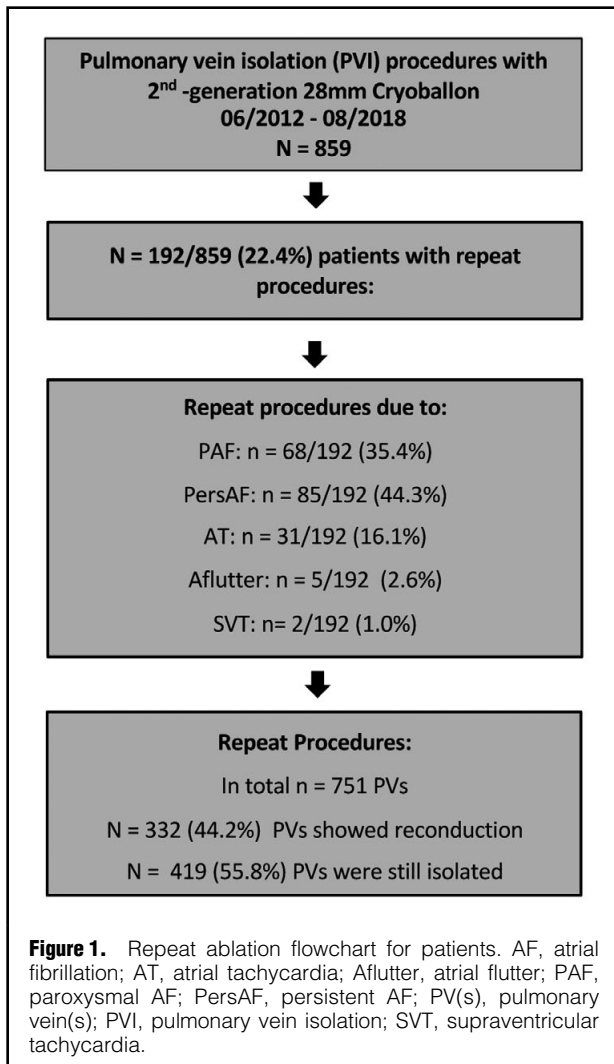
Pulmonary vein isolation (PVI) forms the cornerstone of invasive treatment of atrial fibrillation (AF). Latest AF guidelines state that PVI should be performed using either radiofrequency (RF) or cryoballoon (CB) catheters.¹ The second-generation CB (CB2; Arctic Front Advance, Medtronic Inc., Minneapolis, MN, USA) has demonstrated high procedural success rates, relatively short procedure times, high durability of PVI and convincing long-term clinical success rates.² Ablation strategies predominantly imply fixed freeze-cycle durations of 180–240s, oftentimes followed by a bonus-freeze cycle.³ To potentially reduce complications as well as procedure duration, the protocols were modified, aiming for shorter

and fewer CB applications and demonstrated comparable clinical outcomes.^{3,4} After identifying the time to PVI (time-to-effect, TTE) as an essential indicator for durability of PVI, latest ablation strategies implemented the individual TTE.⁵ Reducing the ablation time, omitting the bonus-freeze cycle and implementing the TTE to recent protocols resulted in shorter procedure duration and reduced periprocedural complications without affecting clinical outcomes.³ Nevertheless, data on the impact of different ablations protocols on durability after CB2-based PVI are limited.⁶ The present study aimed to evaluate the rate of electrical reconduction in patients presenting for repeat ablation due to recurrence of atrial tachyarrhythmia

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mias (ATA) following initial CB2-based PVI and the impact of different ablation protocols.

Methods

Patients Characteristics

All patients referred to 2 EP centres in Hamburg, Germany, were analysed retrospectively. Consecutive patients with initial paroxysmal AF (PAF) or persistent AF (PersAF) and recurrent symptomatic and documented ATA after previous CB2-based PVI were admitted for reablation and included in the study. The study was approved by the local ethical review board. All patients gave written informed consent and all patient information was anonymized. All data were evaluated retrospectively.

Intraprocedural Management

Transesophageal echocardiography was performed prior to ablation in all patients to rule out intracardiac thrombi. No additional pre-procedural imaging was performed. All procedures were performed in deep sedation using midazolam, fentanyl, and propofol. Double (index procedure) or triple (repeat procedure) puncture of the right femoral vein was performed and one diagnostic catheter was posi-

tioned inside the coronary sinus. A single (index procedure) or double (repeat procedure) transseptal puncture was performed under fluoroscopic guidance using a modified Brockenbrough technique and 1 or 2x 8.5F transseptal sheaths (TS; SL1, St. Jude Medical, Inc., St. Paul, MN, USA). Heparin was administered to maintain an activated clotting time of ≥ 300 s.

Index-PVI

Intraprocedural management of CB2-based PVI has been described earlier.^{7,8} In brief, selective PV angiographies were performed after transseptal access. The regular TS was exchanged over a guidewire for a 12F steerable sheath (Flexcath Advance, Medtronic, Inc.). The CB2 was advanced into the LA and directed towards the target PV via a spiral mapping catheter (20 mm diameter; Achieve™, Medtronic). The CB was inflated proximal to the PV ostium and gently pushed against the PV ostium aiming for complete antral PV occlusion, as verified by contrast medium injections distal to the balloon. If complete antral occlusion was achieved, the freeze was started. The acute procedural endpoint was defined as persistent PVI verified by spiral mapping catheter recordings. In all patients, an esophageal temperature probe (Sensitherm; St. Jude Medical, Inc.) was inserted to monitor intraluminal esophageal temperatures during energy delivery. The intraluminal esophageal temperature cut-off was set to 12–15°C according to previous evaluations.^{9,10} During ablation of the septal PVs, continuous phrenic nerve (PN) pacing at maximum output and pulse width (12 mA, 2.9 ms) at a cycle length of 1,200 ms was performed using a diagnostic catheter positioned in the superior vena cava. PN capture was monitored by tactile feedback of diaphragmatic contraction and registration of the compound motoric activation potential (CMAP) of the right diaphragm. Energy delivery was stopped immediately in case of weakening or loss of diaphragmatic movement or if the CMAP amplitude decreased by 30%.⁶

Ablation Protocols

Three different ablation protocols were consecutively applied during the course of the study. The first protocol (bonus-freeze protocol, protocol #1, group 1) comprised a fixed freeze-cycle duration of 240 s, followed by an additional bonus-freeze of 240 s after successful PVI.⁷ The second protocol (no-bonus-freeze protocol, protocol #2, group 2), applied a fixed freeze-cycle of 240 s without a bonus-freeze cycle after documentation of PVI.³ The third ablation protocol (time-to-effect protocol, protocol #3, group 3) used a “time-to-effect” guided strategy based on continuous real-time recordings from the circular mapping catheter. After documentation of PVI, the freeze cycle was prolonged for additional 120 s. If no real-time PV signal recording could be obtained, an empiric freeze cycle duration of 180 s was applied. No bonus-freeze cycle was applied in protocol #3.⁵

Repeat Procedures

Techniques of repeat procedures have been reported before.⁶ Briefly, in patients admitted for a repeat procedure due to ATA recurrence, an electroanatomical LA-map (Carto 3™; Biosense Webster, Inc., Diamond Bar, CA, USA) was conducted and the PV ostia tagged on the LA map according to selective PV angiographies and electrical information. Persistent PVI or electrical reconnection of

Table 1. Baseline Data of N=192 Patients			
Variable	Bonus-Freeze	No-Bonus-Freeze	Time-to-Effect
Number of patients	31	67	94
Age (years)	64 (56, 69)	65 (55, 72)	66 (58, 73)
Duration of AF (months)	31 (21, 60)	17 (7, 44)	28 (14, 68)
Initial paroxysmal AF	24 (77.4)	41 (61.2)	43 (45.7)
LA diameter (mm)	44 (40, 46)	45 (40, 49)	45 (40, 50)
Coronary artery disease	2 (6.5)	8 (11.9)	6 (6.4)
Diabetes mellitus type 2	4 (12.9)	9 (13.4)	7 (7.4)
Art. hypertension	17 (5.5)	45 (67.2)	63 (67.0)
Heart failure	1 (3.2)	8 (11.9)	14 (14.9)
Female	16 (51.6)	30 (44.8)	57 (60.6)
Stroke/TIA	2 (6.5)	7 (10.4)	4 (4.3)
CHA ₂ DS ₂ VASc-Score=1	4 (12.9)	9 (13.4)	19 (20.2)
CHA ₂ DS ₂ VASc-Score=2	9 (29.0)	15 (22.4)	25 (26.6)
CHA ₂ DS ₂ VASc-Score=3	4 (12.9)	15 (22.4)	15 (16.0)
CHA ₂ DS ₂ VASc-Score=4	4 (12.9)	11 (16.4)	16 (17.0)
CHA ₂ DS ₂ VASc-Score=5	1 (3.2)	2 (3.0)	2 (2.1)
CHA ₂ DS ₂ VASc-Score=6	0 (0)	2 (3.0)	1 (1.1)

Test of no regression: P=0.0615. Continuous data are summarized as medians (25th and 75th percentiles). Categorical data are presented as N (%). AF, atrial fibrillation; TIA, transitory ischemic attack.

previously isolated PVs was assessed by the presence or absence of electrical conduction into the PV according to spiral mapping catheter signals (Lasso™, Biosense-Webster). Identified reconduction gaps were assigned to 4 segments (antero-superior, antero-inferior, postero-superior, postero-inferior) and targeted and isolated by RF ablation using a 3.5mm irrigated-tip catheter (Biosense Webster, Navi-Star™, Thermo-Cool™). To identify the site of LA-PV reconduction in patients presented in sinus rhythm, a spiral mapping catheter was positioned at the proximal PV ostium. If LA-PV reconduction was present, the PV spike sequence was analyzed to identify the earliest site of PV activation, and RF ablation was guided by local map potentials along the tagged PV ostium and PV activation sequence. Gap location was defined as the site of successful reisolation of the individual PV (one gap) or the site of clear change in the PV electric activation pattern (2 or more gaps). In patients presenting in AF, re-PVI was performed after electrical cardioversion. In patients presenting with atrial tachycardia (AT), PV gap assessment was performed after AT termination, as described above, and re-PVI was performed in sinus rhythm.

In patients with persistent isolation of all PVs and admitted in SR, fractionated ostial potentials along previously performed ablation lines were identified and ablated and/or linear lesion sets were applied according to individual bipolar information. In patients admitted in AF or AT and persistent isolation of all PVs, ostial potentials were identified and ablated followed by ablation of complex fractionated atrial electrograms (CFAE) and/or deployment of linear lesion sets.⁶

Endpoints

The primary endpoints were PV reconduction and localization of PV reconduction gaps after index CB2-based PVI comparing the 3 groups. The secondary endpoints were index and repeat ablation procedural parameters and complications.

Postprocedural Care

Following ablation, all patients underwent transthoracic echocardiography to rule out pericardial effusion. All patients were treated with proton-pump inhibitors twice daily for 6 weeks. Low molecular-weight heparin was administered in patients on vitamin K antagonists and an INR <2.0 until a therapeutic INR of 2–3 was achieved. Novel oral anticoagulants were re-initiated 6h post ablation at a half regular daily dose and at full dose the following day. Anticoagulation was continued for at least 3 months and thereafter based on the individual CHA₂DS₂-VASc score. Previously ineffective antiarrhythmic drugs were continued for 3 months.

Statistical Analysis

Differences of continuous variables between 2 groups were analyzed with t-tests if the data were normally distributed, or otherwise with Wilcoxon-Mann Whitney U-tests. Differences between categorical variables were evaluated with the Chi-squared test. The primary aim of these analyses was to compare reconnection rates between 3 different ablation protocols and between PVs of 192 patients. Effects of ablation protocols and PVs on the occurrence of reconductions were analyzed using a generalized linear mixed model. Post-hoc tests were applied to compare the equality of reconnection rates between each of 2 PVs. The Tukey method was applied to adjust for multiple comparisons. All P-values were 2-sided and a P-value <0.05 was considered significant. All calculations were performed with the statistical analysis software R (R Core Team, 2018).

Results

Patient Characteristics

Between August 2012 and August 2018 a total of 859 patients underwent CB2/CB3-based PVI in 2 centers (St. George Hospital and Harburg Hospital, Hamburg, Germany) and 192 patients presented for a repeat ablation

Table 2. Procedural Data of Index Procedure From N=192 Patients

Variable	Group 1 (Bonus-Freeze)	Group 2 (No-Bonus-Freeze)	Group 3 (Time-to-Effect)	P value
Number of patients	31	67	94	
Number of PVs	120	262	369	
Total CB freezes per PV	2 (2, 2)	1 (1, 1)	1 (1, 1)	<0.001
Total CB freezes per PV until PVI	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.630
Mean minimal CB temperature (°C)	-49.0 (-44.8, -53.0)	-47.0 (-43.0, -52.0)	-46.0 (-42.0, -51.0)	<0.001
Mean time to PVI (s)	50 (22, 76)	49 (27, 82)	40 (24, 54)	0.436
Mean minimal eso temperature (°C)	33.2 (34.9, 35.5)	33.4 (35.0, 35.6)	32.5 (34.7, 35.4)	0.505
All PVs isolated (%)	120/120 (100)	262/262 (100)	369/369 (100)	0.999
Fluoroscopy time (min)	20.2±9.1	20.2±8.7	19.9±10.0	0.473
Contrast medium (mL)	119.5±64.4	119.1±42.1	117.2±32.2	0.358
Procedure time (min)	123.4±31.5	112.9±39.8	86.67±28.4	<0.001
Radiofrequency touch up (%)	0 (0)	0 (0)	0 (0)	0.999
Major complications (%)	3 (9.7)	2 (3.0)	6 (6.4)	0.386
Phrenic nerve injury (%)	1 (3.2)	2 (3.0)	2 (2.1)	0.919
Puncture site bleeding (%)	2 (6.5)	0 (0)	3 (3.2)	0.743
Tamponade (%)	0 (0)	0 (0)	0 (0)	0.999
Stroke/TIA (%)	0 (0)	0 (0)	1 (1.1)	0.864
Death (%)	0 (0)	0 (0)	0 (0)	0.999
Pulmonary bleeding (%)	0 (0)	0 (0)	0 (0)	0.999

Continuous data are summarized as medians (25th and 75th percentiles) or means and standard deviations. PV, pulmonary vein; CB, cryoballoon; PVI, pulmonary vein isolation; TIA, transitory ischemic attack.

due to recurrence of ATA (PAF: 69/192 [35.9%], PersAF: 84/192 [43.8%], AT: 32/192 [16.7%], common type flutter: 5/192 [2.6%], supraventricular tachycardia: 2/192 [1%]) (Figure 1). The patients' baseline characteristics are shown in Table 1. No differences were observed between the 3 groups.

Index PVI

A total of 751 PVs were identified in 192 patients (192 right superior PVs [RSPV], 192 right inferior PVs [RIPV], 175 left superior PVs [LSPV], 175 left inferior PVs [LIPV] and 17 left common PVs [LCPV]). All PVs (751/751, 100%) have been successfully isolated during the index PVI procedure (Table 2). Thirty-one out of 192 (16%) patients were treated with a bonus-freeze protocol (group 1), 67/192 (35%) patients with a no bonus-freeze protocol (group 2), and 94/192 (49%) patients with a "time-to-effect"-guided ablation protocol without bonus-freezes (group 3). The number of total CB cycles per PV and the mean procedure time were significantly different between the groups. The mean minimal CB temperature showed significantly higher temperatures for groups 2 and 3 compared to group 1. No differences were observed with regard to periprocedural complications.

Primary Endpoints: PV Reconnection and Localization of PV Reconnection Gaps

In a total of 332/751 (44.2%) PVs, LA-to-PV reconnection was demonstrated while persistent PVI was documented in 419/751 (55.8%) PVs. In 41/192 (21.4%) patients, all PVs were persistently isolated. Details regarding incidence of PV reconnection and localization of reconnection gaps are shown in Table 3, Figure 2 and Figure 3. Significant differences were found when comparing reconnection rates for different PVs (P=0.001). Post-hoc tests between all PVs showed significant differences between RIPV and LIPV

(P=0.004), RIPV and LSPV (P>0.001), as well as RIPV and RSPV (P=0.017). Differences between LSPV and LIPV (P=0.866), LSPV and RSPV (P=0.535), and RSPV and LIPV (P=0.946), were not significant. In total, 204 reconnection gaps were identified in 192 patients and distributed, as shown in Figure 3.

Comparison of PV Reconnection for Different Ablation Protocols

For the total incidence of PV reconnection, there were no significant differences demonstrated for the 3 groups (P=0.134). According to this finding, the comparison of individual PVs also showed no differences for different ablation protocols (P-values for RSPV: 0.424, RIPV: 0.541, LSPV: 0.788, LIPV: 0.346, LCPV: 0.865). The number of patients with 4, 3, 2, 1 or 0 persistent isolated PVs was also not significant between the groups (P=0.594, P=0.092, P=0.625, P=0.802, and P=0.600, respectively). The comparison of the number of reconnection gaps for the predefined segments between the groups revealed no significant differences.

Reablation Results

Re-isolation of all PVs was successfully performed using RF energy. In 27/192 (14.1%) patients, complete wide-area circumferential ablation lines around the ipsilateral PVs were applied. In addition, ablation of ostial potentials was performed in 56/192 (29.2%) patients, CFAE ablation in 15/192 (7.8%) patients, and ablation of linear lesions in 62/192 (32.3%) patients (n=15 mitral isthmus lines, n=35 anterior lines, n=12 roof lines). In 4 patients (2.1%) with isolated PVs, the left atrial appendage (LAA) was isolated due to ablation of a combination of an anterior line, mitral isthmus line and roof line.¹¹ A bidirectional CTI block was performed in 33/192 (17.2%) patients due to documented typical CTI-dependent atrial flutter. In 3 patients (1.6%), a

Table 3. Data of Repeat Procedures for N=192 Patients					
Variable	Total	Bonus-Freeze	No-Bonus-Freeze	Time-to-Effect	P value
Number of patients	192	31	67	94	
Total number of PVs	751	120	262	369	
Total PV reconnection	332/751 (44.2)	46/120 (38.3)	110/262 (42.0)	176/369 (47.7)	0.134
RSPV reconnection	81/192 (42.2)	11/31 (35.5)	26/67 (38.1)	44/94 (46.8)	0.424
RIPV reconnection	110/192 (57.3)	15/31 (48.4)	39/67 (58.2)	56/94 (59.6)	0.541
LSPV reconnection	62/175 (35.4)	9/27 (33.3)	20/61 (33.8)	33/87 (37.9)	0.788
LIPV reconnection	69/175 (39.4)	9/27 (33.3)	21/61 (34.4)	39/87 (44.8)	0.346
LCPV reconnection	10/17 (58.8)	2/4 (50.0)	4/6 (66.7)	4/7 (57.1)	0.865
All PVs isolated	41 (21.4)	9 (29)	13 (19.4)	19 (20.2)	0.594
3 PVs isolated	38 (19.3)	5 (16.1)	19 (28.4)	14 (14.9)	0.092
2 PVs isolated	69 (35.9)	10 (32.3)	22 (32.8)	37 (39.4)	0.625
1 PVs isolated	11 (5.7)	1 (3.2)	4 (6)	6 (6.4)	0.802
0 PVs isolated	33 (17.2)	6 (19.4)	9 (13.4)	18 (19.1)	0.600
Rate of reisolation	192 (100)	120 (100)	262 (100)	369 (100)	0.999
Procedure time, repeat procedure (min)	121.2±42.0	120.5±39.6	118.4±44.3	116.9±40.0	0.852
Fluoroscopy time, repeat procedure (min)	16.4±7.8	16.3±8.3	16.2±8.3	16.0±7.3	0.912
Individual pulmonary vein segments					
RSPV (antero-superior)	23 (12.0)	3 (9.7)	9 (13.4)	11 (11.7)	0.862
RSPV (postero-superior)	14 (7.3)	2 (6.5)	4 (6.0)	8 (8.5)	0.814
RSPV (antero-inferior)	11 (5.8)	1 (3.2)	5 (7.5)	5 (5.3)	0.683
RSPV (postero-inferior)	2 (1.0)	1 (3.2)	1 (1.5)	0 (0)	0.696
RIPV (antero-superior)	6 (3.1)	1 (3.2)	1 (1.5)	4 (4.3)	0.670
RIPV (postero-superior)	5 (2.6)	0 (0)	1 (1.5)	4 (4.3)	0.610
RIPV (antero-inferior)	34 (17.7)	3 (9.7)	15 (22.4)	16 (17.0)	0.300
RIPV (postero-inferior)	34 (17.7)	8 (25.8)	15 (22.4)	11 (11.7)	0.094
LSPV (antero-superior)	21 (11.4)	3 (11.1)	3 (4.9)	15 (17.2)	0.069
LSPV (postero-superior)	14 (7.6)	2 (7.4)	6 (9.8)	6 (6.9)	0.810
LSPV (antero-inferior)	3 (1.6)	0 (0)	1 (1.6)	2 (2.3)	0.855
LSPV (postero-inferior)	0 (0)	0 (0)	0 (0)	0 (0)	0.999
LIPV (antero-superior)	0 (0)	0 (0)	0 (0)	0 (0)	0.999
LIPV (postero-superior)	1 (0.5)	0 (0)	1 (1.6)	0 (0)	0.912
LIPV (antero-inferior)	19 (10.3)	2 (7.4)	8 (13.1)	9 (10.3)	0.692
LIPV (postero-inferior)	14 (7.6)	2 (7.4)	6 (9.8)	6 (7.6)	0.810

Values are presented as n or n (%). LCPV, left common pulmonary vein; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; PV, pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.

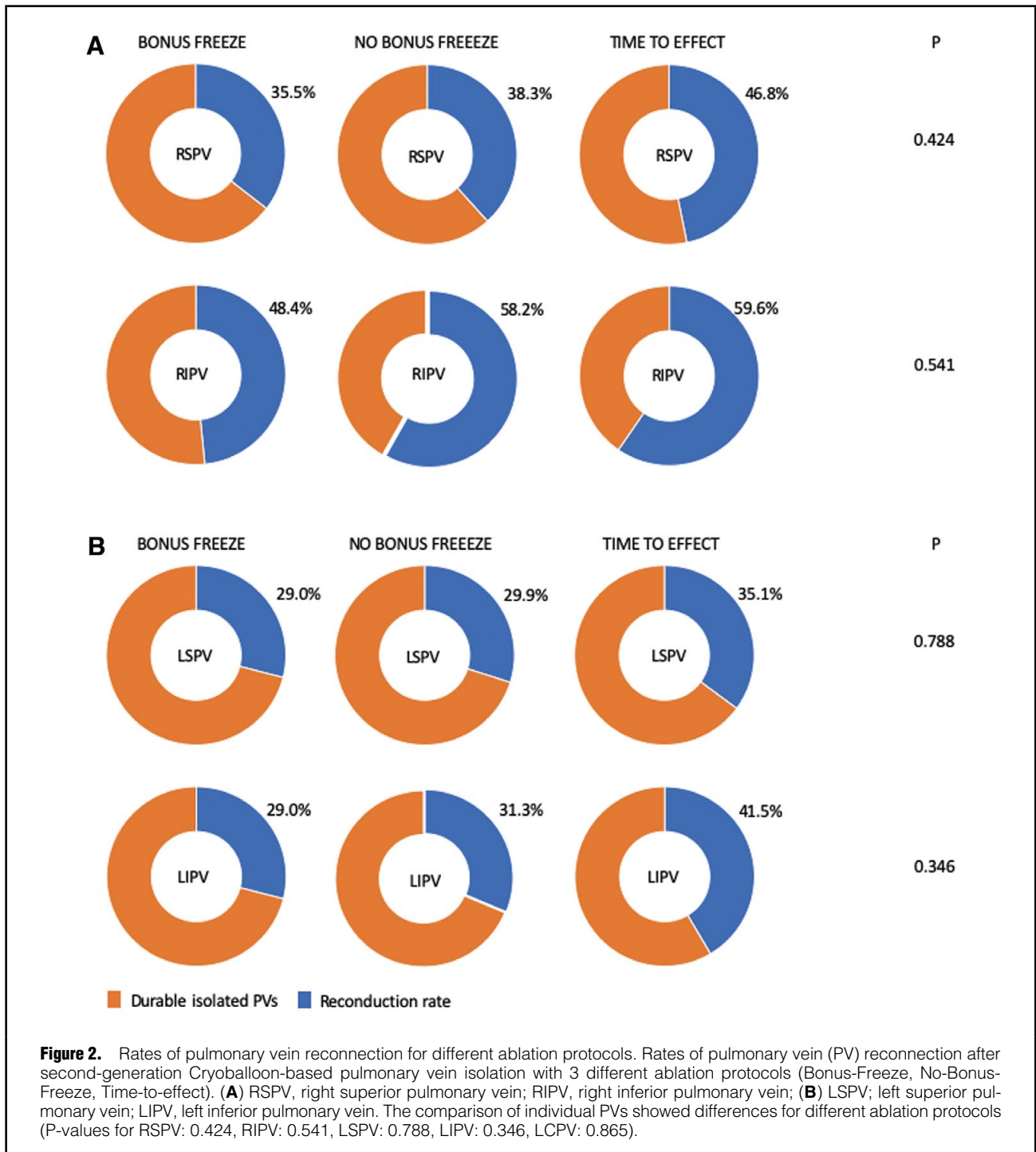
pericardial tamponade requiring epicardial puncture occurred. All patients were successfully treated without the need of open-heart surgery. Periprocedural stroke occurred in 1/192 (0.5%) patient. One patient (0.5%) developed a procedure-related hematoma of the right groin without surgical treatment or blood transfusion. Two patients (1.1%) suffered from severe groin hematoma, making a blood transfusion without surgical treatment necessary. No additional complications were documented. Periprocedural data are reported in **Table 3**.

Discussion

To the best of our knowledge, the current study is the first to compare durability of PVI between 3 common ablation protocols utilizing the CB2 and CB3. The study demonstrated that omitting the bonus-freeze cycle and reducing freezing durations by using individualized protocols results in comparable PVI durability and significantly shorter procedure duration without comprising the safety profile.

To date, CB2-based PVI has been established as a rou-

tine AF ablation procedure worldwide. Concerning dosing of cryothermal energy initially, a freeze duration of 240s followed by an empiric bonus-freeze cycle of 240s was accepted and generally applied. The Fire and Ice trial also followed this recommendation, and it was adopted by most centers worldwide.¹² However, to possibly reduce periprocedural complications and to decrease procedure time, freeze protocols with shorter energy transfer and omitting the bonus-freeze cycle have been evaluated in clinical practice.^{3,7,8} Concerning clinical outcome, no differences have been observed for the comparison of a bonus-freeze protocol (240s plus empirical application of another 240s after isolation) and a no-bonus-freeze protocol (240s and omitting the bonus-freeze). The procedure time was significantly reduced.³ A large comparison of periprocedural complications found favorably less complications in protocols with shorter freezing duration and without bonus-freezes.¹³ Therefore, TTE-guided protocols with less and shorter freezes might be favorable for patient's safety. Although comparisons of acute efficacy and clinical outcomes between different protocols showed no differences



for the data on the durability of CB2-based PVI, data comparing different ablation protocols are sparse. Recently, PVI durability of an “ICE-T”-guided CB2 ablation (target freeze duration: 180s vs. 240s) in patients undergoing a repeat procedure have been evaluated in a total of 106 patients.¹⁴ A remarkable high rate of durable PVI (83%) was detected. A freeze duration of 240s vs. 180s was associated with a significantly increased lesion durability, particularly at the left-sided PV. The rate of PVI durability assessed by other groups was described at 69–77%^{6,15} in

redo procedures due to ATA recurrence and 91% in patients with invasive check-ups, irrespective of ATA recurrence.¹⁶ In our analysis, 55.8% of PVs showed persistent PVI following index-PVI. The comparison of the 3 different ablation protocols (240s+240s bonus-freeze, 240s no-bonus-freeze and time-to-effect+120s) found no differences for PV reconnection rates.

As expected, utilizing the time-to-effect-guided protocol resulted in significantly reduced procedure times. Yet, no differences were detected for periprocedural complications.

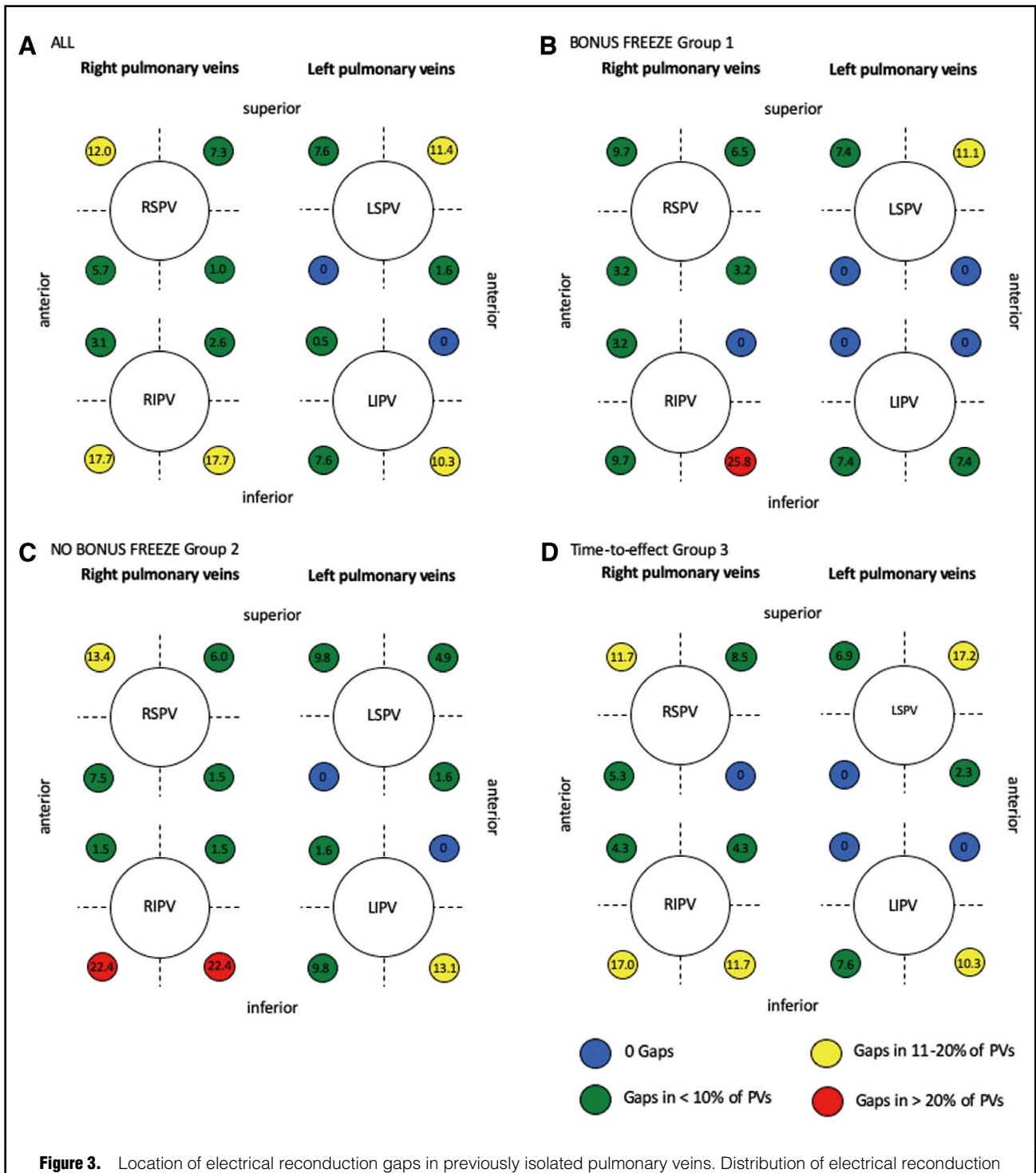


Figure 3. Location of electrical reconduction gaps in previously isolated pulmonary veins. Distribution of electrical reconduction gaps in previously isolated pulmonary veins for the total population (A) and for patients treated with a bonus-freeze protocol (B), a no-bonus-freeze protocol (C) and a time-to-effect-guided protocol (D). Septal and lateral pulmonary vein ostia are divided into 4 segments (antero-superior, antero-inferior, postero-superior, postero-inferior). Numbers express the number of reconduction gaps found in each segment. Data for a left common pulmonary vein (n=17) are not shown. RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein. Post-hoc tests between all PVs showed significant differences between RIPV and LIPV (P=0.004), RIPV and LSPV (P>0.001), as well as RIPV and RSPV (P=0.017). Differences between LSPV and LIPV (P=0.866), LSPV and RSPV (P=0.535), RSPV and LIPV (P=0.946) were not significant.

As it was recently shown for clinical outcomes,³ recent data brought evidence that the bonus-freeze cycle seems to be not necessary for durable PVI and potentially also not for PVI durability.¹⁷ Our data are presenting evidence that longer freezing times and bonus-freeze cycles may not improve durability. As no difference in PVI durability was detected for different ablation protocols and the time-to-effect-guided protocol resulted in significantly reduced procedure times, this latter protocol might be suitable for durable PVI.

As shown previously, the right inferior PVs were demonstrated to have the highest incidence of electrical reconnection. It is remarkable to state that utilizing the time-to-effect +120s protocol, the antero-superior aspect of the LSPV reveals the highest rate of PV reconnection. In our opinion, this reflects the relatively short freezing duration along the LSPV–LAA ridge and might indicate a border zone of minimal freezing duration to achieve durable PVI in this area, which is characterized by thick muscular tissue.

The high proportion of patients with recurrent ATA and persistent isolation of all PVs raises the question about the best treatment strategy during repeat procedures. As additional LAA isolation was recently found to possibly improve clinical outcome after catheter ablation, this strategy might offer a potential treatment for PVI non-responders when applying the CB2.^{11,18,19} Another study demonstrated that especially for PersAF, isolation of the posterior wall using the CB2 might also bring additional benefit.²⁰

Study Limitations

The presented findings are based on a retrospective 2-center experience. As only patients with ATA recurrence were evaluated, the population represents a subgroup of patients after CB2-based PVI. Furthermore, not all patients with ATA recurrences agreed to a repeat ablation procedure. Repeat ablation procedures were scheduled and performed at individual points of time after the index ablation procedure and not after a scheduled and predefined period. As invasive repeat procedures for all patients, irrespective of whether patients have ATA recurrences, might be unethical and unnecessary, the present study offers a reasonable approximation of PV durability after CB2-based PVI in a large patient population. Optimal ablation strategies going beyond closing reconnection gaps to achieve re-PVI are currently unknown. Therefore, it is difficult to decide what to do for patients with persistently isolated PVs at invasive check-up, despite ATA recurrences. Assessment of clinical outcomes following different ablation protocols was not part of the recent study, but will be performed in a future analysis.

Conclusions

In patients with recurrent ATAs presenting for a repeat procedure after the index CB2-based PVI, a relatively high rate of the persistent PVI was found. When comparing the 3 common ablation protocols, no differences in the PVI durability were detected, yet the procedure times were significantly reduced by omitting the bonus-freeze cycles and applying individualized application times. As shorter procedure times might reduce collateral damage and be beneficial for patients, these observations could lead to further evaluation of shorter and individualized ablation

protocols.

Disclosures

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