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CLINICAL RESEARCH

Impact of cryoballoon application abortion due to phrenic nerve injury on reconnection rates: a YETI subgroup analysis

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Aims Cryoballoon (CB)-based pulmonary vein isolation (PVI) is an effective treatment for atrial fibrillation (AF). The most frequent complication during CB-based PVI is right-sided phrenic nerve injury (PNI) which is leading to premature abortion of the freeze cycle. Here, we analysed reconnection rates after CB-based PVI and PNI in a large-scale population during repeat procedures.

Methods and results In the YETI registry, a total of 17 356 patients underwent CB-based PVI in 33 centres, and 731 (4.2%) patients experienced PNI. A total of 111/731 (15.2%) patients received a repeat procedure for treatment of recurrent AF. In 94/111 (84.7%)

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patients data on repeat procedures were available. A total of 89/94 (94.7%) index pulmonary veins (PVs) have been isolated during the initial PVI. During repeat procedures, 22 (24.7%) of initially isolated index PVs showed reconnection. The use of a double stop technique did non influence the PV reconnection rate ($P = 0.464$). The time to PNI was 140.5 ± 45.1 s in patients with persistent PVI and 133.5 ± 53.8 s in patients with reconnection ($P = 0.559$). No differences were noted between the two populations in terms of CB temperature at the time of PNI ($P = 0.362$). The only parameter associated with isolation durability was CB temperature after 30 s of freezing. The PV reconnection did not influence the time to AF recurrence.

Conclusion In patients with cryoballon application abortion due to PNI, a high rate of persistent PVI rate was found at repeat procedures. Our data may help to identify the optimal dosing protocol in CB-based PVI procedures.

Clinical Trial Registration https://clinicaltrials.gov/ct2/show/NCT03645577?term=YETI&cntry=DE&draw=2&rank=1 ClinicalTrials.gov Identifier: NCT03645577.

Keywords Atrial fibrillation • Cryoballoon • Catheter ablation • Phrenic nerve injury

What´s new?

- Here, we analysed repeat procedures and reconnection rates after CB-based PVI and phrenic nerve injury in a large-scale population of the YETI registry
- A total of 89/94 (94.7%) index PVs have been isolated during the initial PVI. During the repeat procedures, 22 (24.7%) of initially isolated index PVs showed reconnection.
- The time to PNI was 140.5 ± 45.1 s in patients with persistent PVI and 133.5 ± 53.8 s in patients with reconnection ($P = 0.559$).
- The only parameter associated with isolation durability was CB temperature after 30 s of freezing. The PV reconnection did not influence the time to AF recurrence.

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in adults.[1] Pulmonary vein isolation (PVI) is the gold standard for the interventional treatment of AF. Since the non-inferiority of cryoballoon (CB)-based PVI when compared with radiofrequency (RF)-based PVI has been demonstrated, CB-based procedures became widely accepted for rhythm control strategy in AF patients.[2,3]

Differences still exist between centres regarding the CB ablation protocol. While the most recent data suggest that a time to isolation (TTI)-based approach is highly effective and safe, simultaneously reducing the energy transfer to myocardium, the fixed ablation protocols applying 180–240 s freezing cycles, sometimes followed by a bonus freeze are still in use.[4–8]

Phrenic nerve injury (PNI) is the most frequent procedural complication in CB-based PVI, with an incidence ranging from 1.1 to 6.2% of patients, and it is more common during isolation of the septal PVs.[2,3,9–12] Considering that most ablation protocols aims for an immediate stop of energy delivery, as well as no further ablation attempt for the right PVs, PNI occurrence might increase the risk of PV electrical reconnection and consequently the arrhythmia recurrence.[4,13] The data are sparse regarding the reconnection in patients who suffer PNI during CB-based PVI. To the best of our knowledge, only one single centre study with a limited number of patients addressed this subject so far.[14]

The present study represents a subanalysis of the YETI registry (worldwide survey on outcome after iatrogenic PNI during CB-based PVI), a retrospective, multicentre and multinational registry evaluating prognostic factors of PNI recovery after CB-based PVI.[15] Here, we sought to investigate the procedural characteristics that might influence PV reconnection in patients with premature energy delivery stop due to PNI.

Methods

Study design

The detailed protocol of the YETI registry has been published.[15] Briefly, this was a retrospective, multicentre and multinational registry which evaluated the incidence, characteristics, and prognostic factors for PNI recovery, as well as follow-up data of patients with PNI during CB-based PVI. All patients who underwent CB-based PVI between May 2012 and June 2019 and developed intraprocedural PNI were enrolled. Only patients treated with the second- (CB2), third- (CB3), or fourth- (CB4) generation CB (Arctic Front Advance, Medtronic Inc.) were eligible. Each participating centre provided baseline and periprocedural characteristics, as well as follow-up data based on a standardized and uniform protocol.[15]

The registry was approved by the local ethics committee of the University of Luebeck, Germany (AZ: 18–151A) and was registered on https://clinicaltrials.gov (NCT03645577). The study has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. All patients gave written informed consent, and all patient information was anonymized.

In the present study, we analyse the subgroup of patients who exhibited PNI during the index PVI and received a repeat ablation procedure using a three-dimensional mapping system due to AF recurrence. This population was divided into two groups, based on the presence or absence of PV electrical reconnection as assessed during the repeated procedure. The two groups were compared in terms of baseline characteristics, procedural aspects, and follow-up data.

Patient management

Index procedure

Intraprocedural management of CB-based PVI has been described before. Each procedure was performed according to the individual centres' preferences, with four different ablation protocols used.[4,8,15–17] A bonus freeze protocol (protocol No. 1) comprised a fixed freezing-cycle duration of 240 s, followed by an additional bonus freeze of 240 s after successful PVI.[16] A no bonus freeze (240 s) protocol (protocol No. 2) applied a fixed freezing-cycle of 240 s without a bonus freeze after documentation of PVI.[8] A no bonus freeze (180 s) protocol (protocol No. 3) applied a fixed freezing-cycle of 180 s without a bonus freeze after documentation of PVI.[6] A TTI protocol (protocol No. 4) used a TTI-guided strategy based on continuous real-time recordings from the spiral mapping catheter.[4,5,18] The acute procedural success was defined as persistent PVI verified by the spiral mapping catheter recordings. A spiral mapping catheter (Achieve™, or Achieve Advance™, Medtronic) was used in all patients for real-time PV potentials recording, and the TTI was determined in all possible cases, even if it was not used for ablation time individualization. More details on the intraprocedural management can be found in the original paper.[15]

Phrenic nerve function monitoring

The comprehensive description of PN monitoring and PNI prevention techniques has been published before.[11,13,15,17,19] In this study, the safety algorithms for PNI avoidance were used according to the latest standards and recommendations and individual centres' protocol. Briefly, continuous PN pacing through a diagnostic catheter placed in the superior vena cava was carried out during freezing of the right PVs using the maximum output and pulse width at a cycle length of 1000–1200 ms. The PN capture was assessed using intermittent fluoroscopy and tactile feedback of diaphragmatic contractions. Moreover, the compound motor action potential (CMAP) was monitored as previously described.[19] In case of weakening or loss of diaphragmatic contraction as estimated by palpation or fluoroscopy, and/or at least 30% reduction of CMAP amplitude, the stability of the pacing catheter was reconfirmed and, in case of persistence, the PNI was diagnosed. Consequently, the energy delivery was stopped by either single or double stop technique.[13] Moreover, no additional freezing-cycle was applied at the level of the septal PVs. The PV where the freezing-cycle resulted in PNI was defined as 'index PV'.

Follow-up

The persistence of PNI was assessed prior discharge (1–3 days), as well as during each follow-up visit, by either fluoroscopy or chest X-ray scan. All patients were scheduled for follow-up visits at 3 and 6 months, and at 6-month interval thereafter. Symptomatic PNI was defined as proven PNI with otherwise not explained dyspnea.

Arrhythmia recurrence was evaluated by continuous electrocardiographic (ECG) monitoring during hospitalization, together with baseline 12-lead ECG and 24 h Holter ECG during follow-up visits. When available, implanted cardiac devices were also interrogated. Moreover, the rhythm was assessed using a 24 h Holter ECG each time a patient complained of arrhythmia-related symptoms.

Repeat ablation procedure

Patients with AF recurrence during the follow-up and suitable for a redo-PVI were scheduled for a second ablation procedure using a three-dimensional-mapping system. The techniques for left atrium (LA) mapping and RF-based PVI have been previously described.[8] The procedures were performed as per institutional standards.

Typically, LA electroanatomic reconstruction was performed using either a multipolar mapping catheter or an ablation catheter. Each individual

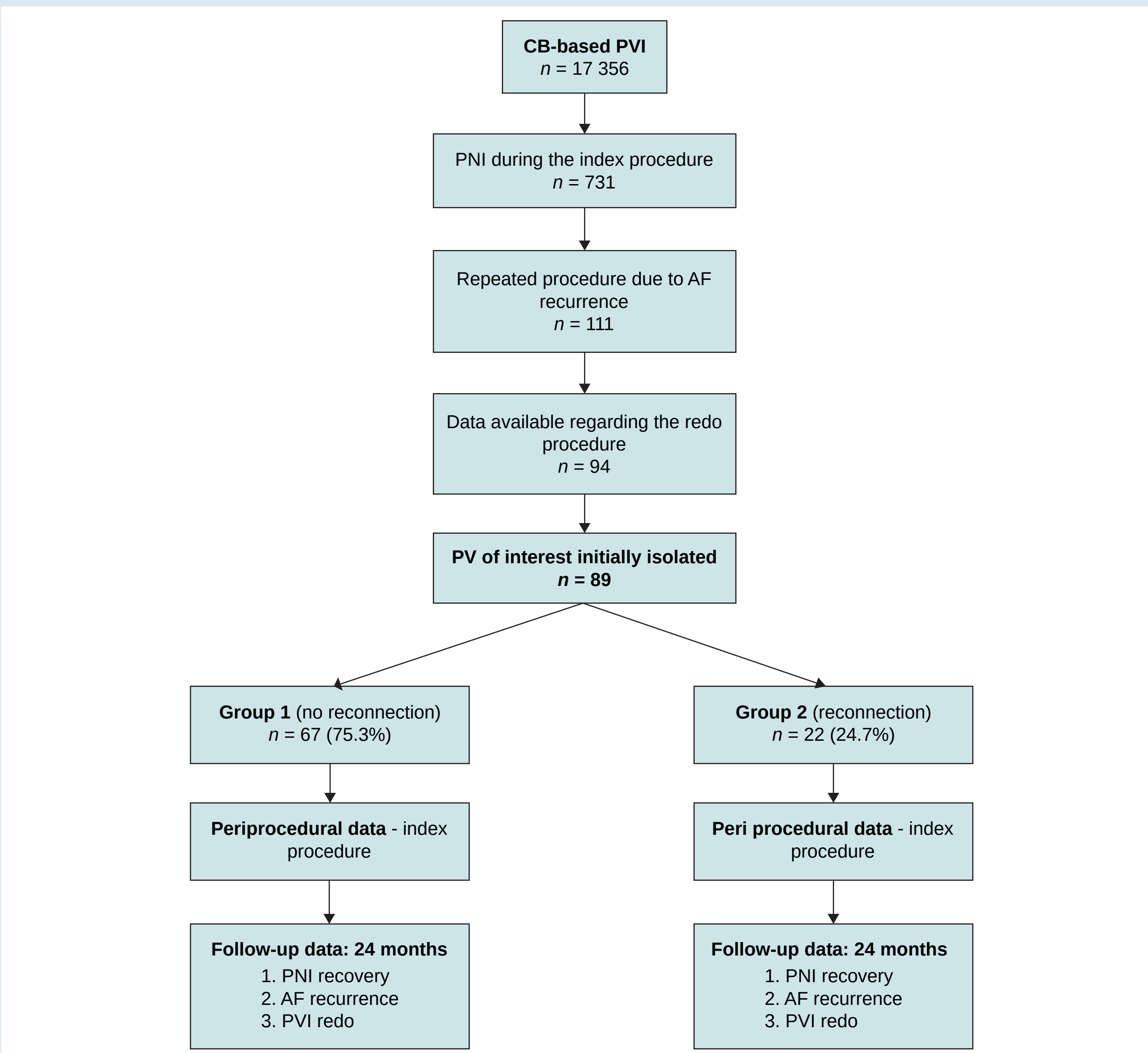

Figure 1 Flow chart. CB, cryoballoon; PVI, pulmonary vein isolation; PNI, phrenic nerve injury; AF, atrial fibrillation; PV, pulmonary vein; PV of interest, PV where PNI occurred during PVI.

PV was evaluated for electrical reconnection using the spiral catheter recordings. When non-isolated PVs were identified, an RF-based, point by point PVI was carried out as per institutional standard.

Statistical analysis

All categorical variables are reported as counts and relative frequencies and were compared using the χ^2 test or Fischer's exact test, as appropriate. Continuous variables were tested for normal distribution using the Shapiro-Wilk test. They were reported as mean ± standard deviation (SD) if normally distributed, or as median and interquartile range (first quartile and third quartile) otherwise. The comparison of continuous variables was performed using the Student's *t*-test if the data had normal distribution. The corresponding nonparametric test (Mann–Whitney *U* test) was used for not normally distributed data.

The cumulative rate of PNI recovery was estimated using the Kaplan-Meier method, and the two groups were compared using the log-rank test. All *P*-values are two-sided, and a *P*-value <0.05 was considered significant. All analyses were performed using SPSS software version 28 (IBM SPSS Statistics).

Results

Patients population

Thirty-three experienced electrophysiological centres from 10 countries participated in the YETI registry. A total of 17 356 patients underwent CB2-, CB3-, or CB4-based PVI and 731 (4.2%) patients experienced periprocedural PNI. During the follow-up, 111/731 (15.2%) patients received redo procedures using a three-dimensional mapping system, due to AF recurrence. Data on the repeat procedures were available for 94 (84.7%) patients. Despite the premature stop of energy delivery, the index PV was reported to be isolated at the end of the index procedure in 89/94 (94.7%) patients. These 89 patients were divided into two groups, based on the presence or absence of PV electrical reconnection as documented during the second ablation procedure (*Figure 1*). Group 1 comprises patients with persistent isolation of the studied PV ($n = 67$; 75.3%), while Group 2 includes those patients where PV reconnection was reported ($n = 22$; 24.7%). The baseline characteristics of the patients are depicted in *Table 1*. No significant differences were noted between the groups.

Index procedure data

Procedural data were available for all 89 patients and are presented in *Table 2*. The total procedure time was 101 (80, 130) minutes for Group 1 and 97 (75.5, 118.5) minutes for Group 2 ($P = 0.710$). The 28 mm CB was used predominantly, with no difference between the groups ($P = 0.568$). PN pacing during septal PVs ablation was used in all patients, while the tactile feedback of the diaphragmatic movements was used in 91% of the patients in Group 1 and in 100% of them in Group 2 ($P = 0.330$). The CMAP monitoring served for PN function monitoring in 26/67 (38.8%) patients in the first group and in 10/22 (45.5%) patients in the second group ($P = 0.623$), while a CMAP amplitude loss of >30% was noted in 17 patients in Group 1 and eight patients in Group 2 ($P = 0.413$). No differences were noted between the groups in terms of immediate stop of freezing and the use of double stop technique in the case of PNI recognition ($P = 1$ and $P = 0.464$, respectively).

The most common ablation site which led to PNI was the right superior PV (RSPV; 83.6% in Group 1 vs. 86.4% in Group 2; $P = 1$), followed by the right inferior PV (RIPV; 14.9 vs. 13.6%; $P = 1$) and left superior PV (LSPV; 1.5 vs. 0%; $P = 1$). No case of PNI was noted during isolation of the left inferior PV (LIPV). The reconnection rate was similar in the right PVs (25.3% for RSPV vs. 23.1% for RIPV; $P = 1$).

A bonus freeze protocol was used in 22/67 (32.8%) patients in Group 1 and in 10/22 (45.5%) patients in Group 2 (0.314). PNI during the first freezing cycle was more common in the reconnection group (86.4 vs. 76.1%), while PNI during the second freezing cycle was more common in the no reconnection group (22.4 vs. 13.6%).

Table 1 Baseline characteristics

$n = 89$		Group 1 (no reconnection) $n = 67$ (75.3%)	Group 2 (reconnection) $n = 22$ (24.7%)	*P*-value
Age, years		61.7 ± 11.5	58.8 ± 11.5	0.316
Paroxysmal AF, *n* (%)		39/67 (58.2%)	12/22 (54.5%)	0.807
Male sex, *n* (%)		35/67 (52.2%)	12/22 (54.5%)	1
Arterial hypertension, *n* (%)		43/67 (64.2%)	14/22 (63.6%)	1
Diabetes, *n* (%)		5/67 (7.5%)	2/22 (9.1%)	1
Coronary artery disease, *n* (%)		16/67 (23.9%)	2/22 (9.1%)	0.220
BMI, Kg/m^2		26.2 ± 4.4	25.6 ± 3.9	0.570
Congestive heart failure, *n* (%)		12/67 (17.9%)	4/22 (18.2%)	1
Implantable cardiac device, *n* (%)		5/62 (8.1%)	0/20 (0%)	0.328
LA-diameter (millimetres)		42.9 ± 7.2	41.4 ± 8.4	0.439
LVEF (%)		55 (50, 62.3)	56.5 (55, 63)	0.609
Previous TIA/stroke, *n* (%)		4/67 (6%)	1/22 (4,5%)	1
CHA2DS2-VASc Score, *n* (%)	0	4/67 (6%)	3/22 (13.6%)	0.358
	1	19/67 (28.4%)	6/22 (27.3%)	1
	2	17/67 (25.4%)	6/22 (27.3%)	1
	3	12/67 (17.9%)	4/22 (18.2%)	1
	≥4	15/67 (22.4%)	3/22 (13.6%)	0.543

Values are counts, *n* (%) or mean ± SD or median (first quartile and third quartile). AF, atrial fibrillation; BMI, body mass index; LA, left atrium; LVEF, left ventricular ejection fraction; TIA, transient ischaemic attack.

Table 2 Periprocedural characteristics

n = 89	Group 1 (no reconnection) *n* = 67	Group 2 (reconnection) *n* = 22	*P*-value
Procedure time, min	101 (80, 130)	97 (75.5, 118.5)	0.710
Fluoroscopy time, min	18 (9.8, 22.5)	12 (5.2, 24.6)	0.513
Amount of contrast medium, mL	55 (30.5, 96.25)	71 (42.5, 95)	0.340
CB diameter: 28 mm, *n* (%)	63/67 (94%)	22/22 (100%)	0.568
Utilization of PN pacing, *n* (%)	67/67 (100%)	22/22 (100%)	1
Utilization of PN tactile feedback, *n* (%)	61/67 (91%)	22/22 (100%)	0.330
Utilization of CMAP, *n* (%)	26/67 (38.8%)	10/22 (45.5%)	0.623
CMAP amplitude loss of >30%, *n* (%)	17/67 (25.4%)	8/22 (36.4%)	0.413
Immediate stop of freezing if PNI recognized, *n* (%)	66/67 (98.5%)	22/22 (100%)	1
Double stop technique, *n* (%)	40/67 (59.7%)	11/22 (50%)	0.464
Pull-back manoeuver, *n* (%)	14/67 (20.9%)	5/22 (22.7%)	1
PNI during ablation of RSPV, *n* (%)	56/67 (83.6%)	19/22 (86.4%)	1
PNI during ablation of RIPV, *n* (%)	10/67 (14.9%)	3/22 (13.6%)	1
PNI during ablation of LSPV, *n* (%)	1/67 (1.5%)	0/22 (0%)	1
PNI during ablation of LIPV, *n* (%)	0/67 (0%)	0/22 (0%)	1
Bonus freeze protocol	22/67 (32.8%)	10/22 (45.5%)	0.314
PNI during the first freezing cycle, *n* (%)	51/67 (76.1%)	19/22 (86.4%)	0.382
PNI during the second freezing cycle, *n* (%)	15/67 (22.4%)	3/22 (13.6%)	0.543
PNI during the third freezing cycle, *n* (%)	1/67 (1.5%)	0/22 (0%)	1
PNI during bonus freeze cycle	4 (6)	1 (4.5)	0.801
CB temperature at the time of PNI, °C	−49 (−52.2, −43)	−49.5 (−54, −45)	0.362
Time of PNI during freezing cycle, s	140.5 ± 45.1	133.5 ± 53.8	0.559
CB temperature at the time of PNI (Bonus freeze), °C	−47.5 (−52.2, 40.7)	−50.5 (−53.2, −46.7)	0.160
Time of PNI during freezing cycle (Bonus freeze), s	154.5 (131, 204.5)	160.5 (123.5, 192.5)	0.854
CB temperature at the time of PNI (no bonus freeze), °C	−49.5 (−52.7, −43.5)	−47.5 (−54.7, −44.2)	0.896
Time of PNI during freezing cycle (no bonus freeze), s	134.5 (110, 165)	92.5 (69.5, 156)	0.120
Freezing time—TTI, s	88.6 ± 42.5	82.1 ± 36.1	0.340
Cumulative freezing time to PNI, s	151.5 (115.3, 194.3)	151.5 (82.8, 206)	0.454
Time to isolation, s	51 (30, 71)	36 (28, 74.7)	0.575
Time to isolation <60 s, *n*	23 (34.3)	10 (45.5)	0.349
Time to CB temperature of −30°C, s	23.2 ± 3.5	25 ± 3.4	0.344
CB temperature after 30 s, °C	−40.5 ± 2.8	−33.7 ± 5.1	0.011
PV diameter (PNI vein), mm	19.2 ± 4.7	20.4 ± 3.8	0.381

Values are counts, *n* (%) or mean ± SD or median (first quartile and third quartile). CB, cryoballoon; PN, phrenic nerve; CMAP, compound motor action potential; PNI, phrenic nerve injury; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; TTI, time to isolation; PV, pulmonary vein

However, statistical significance level was not reached. Only one patient from Group 1 exhibited PNI during the third freezing cycle.

The CB temperature at the time of PNI was −49 (−52.2, −43) °C in Group 1 and −49.5 (−54, −45) °C in Group 2 ($P = 0.362$). The comparison of time to PNI ($P = 0.559$) and freezing time—TTI (0.340) were not statistically significant. A large range of freezing times led to either durable PVI (min 15; max 240 s) or PV reconnection (min 58, max 240 s). The cumulative freezing time, defined as total freezing time including multiple freezing cycles, was calculated for the PV of interest, and no significant difference was seen between the groups ($P = 0.454$).

When analysing the prematurely stopped freezing cycle, the time needed for the CB to reach −30°C was 23.2 ± 3.5 s in Group 1 and 25 ± 3.4 s in Group 2 ($P = 0.344$). A more abrupt temperature drop in the first 30 s of the freezing cycle was noted in Group 1 when compared with Group 2 (−40.5 ± 2.8 vs. −33.7 ± 5.1°C; $P = 0.011$).

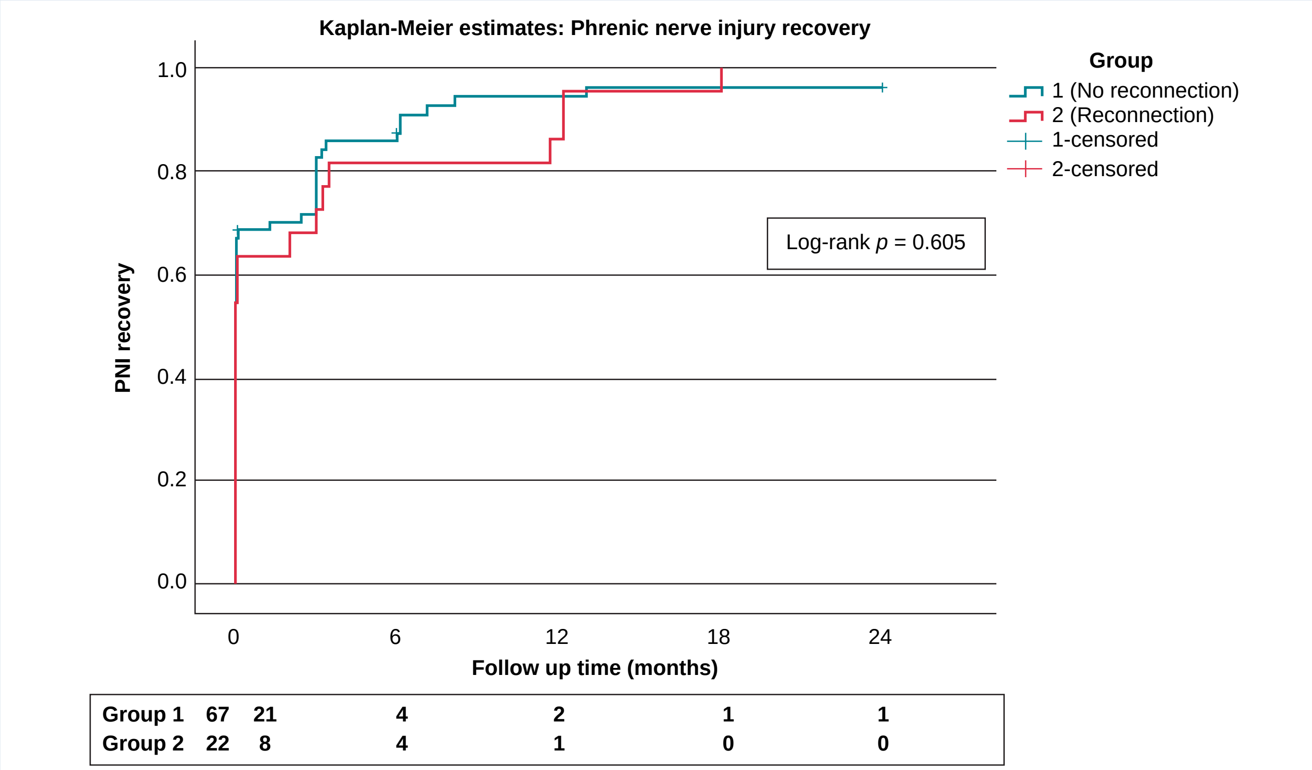

Figure 2 The phrenic nerve injury recovery during follow-up. PNI, phrenic nerve injury.

Follow-up

Excepting three patients from Group 1 who were lost during follow-up, all the others ($n = 86$) were followed for 24 months after the CB-based procedure.

Phrenic nerve injury recovery

Figures 2 and *3* illustrate PNI recovery during the follow-up. The log-rank test *P*-value was 0.605, showing no differences between groups. The results were confirmed when analysing the PNI recovery rate for each prespecified follow-up check-point. Only one patient from Group 1 had irreversible PNI. However, symptomatic PNI persisted only for 6 months post-procedural in this case.

Time to AF recurrence

The median time to AF recurrence was 5 (2, 12) months for Group 1 and 5 (3, 16.5) months for Group 2 ($P = 0.897$).

Time to redo

The median time to reintervention was 10 (6.25, 19.75) months for Group 1 and 9.5 (6.75, 15.5) months for Group 2 ($P = 0.770$).

Discussion

To the best of our knowledge, this is the largest study to assess the impact of premature energy delivery stop due to PNI during CB-based PVI on PV electrical reconnection. The main findings are:

(1) In patients with premature freeze cycle termination due to PNI, a high rate of persistent PVI rate was found.
(2) A steep temperature drop during freezing (temperature at 30 s) was associated with durable PVI.
(3) In patients undergoing a repeat procedure the PV electrical reconnection did not influence the time to AF recurrence and the time to reintervention.
(4) Single stop and double stop technique resulted in similar PV reconnection rates.
(5) The use of the bonus freeze protocol and the number of freezing cycles applied during PVI did not affect reconnection rates.
(6) There was no predilection for the reconnection of a certain PV.

Today PVI represents the cornerstone of interventional AF treatment and CB-based procedures proved to be safe and efficient in this purpose.[1–3] The most common complication of this procedure is right PNI during ablation of the septal PVs.[9,11,12] In this case, the freezing cycle needs to be immediately interrupted to avoid further damage of the PN.[10,13] Moreover, many protocols aim for no additional cryoablation attempt at the level of the right PVs.[4,11,12,15,17] The YETI registry showed a 82.5% rate of acute PVI despite the premature cessation of energy delivery.[15] However, little is known about the durability of isolation in these veins and the procedural factors that might influence the electrical reconnection.

The predictors of PV chronic isolation in patients with completed freezing cycles have been studied before, and the PV occlusion grade, the nadir balloon temperature, the balloon warming time, and the PV diameter were found to predict the PVI durability. However, in our study, the only factor associated with PVI persistence was the CB temperature after 30 s of freezing, suggesting that a more abrupt balloon cooling leads to a more durable isolation. This observation is confirming the findings of previous studies were a temperature of at least −30°C after 30 s was shown to improve the durability of PVI.[5]

Several publications reported rates of PV reconnection after completed CB-based PVI procedures ranging between 20.4 and 52%. Compared with these data, our results (24.7%) did not show an increased risk of PV reconnection, suggesting that the premature

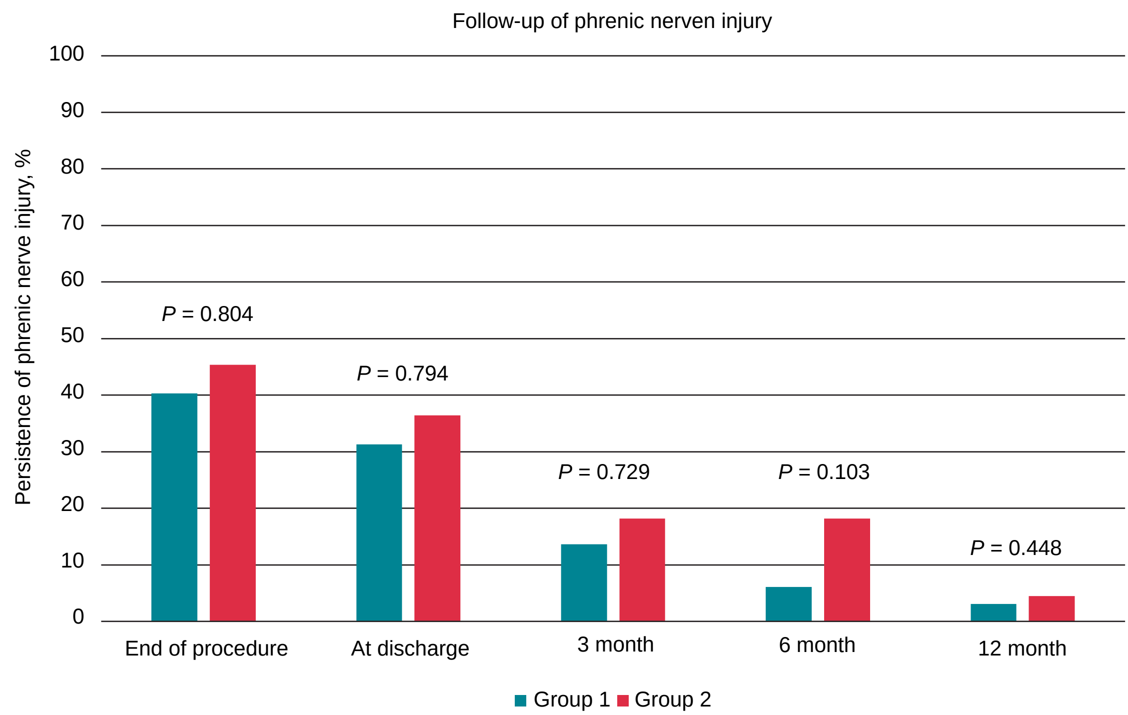

Figure 3 Phrenic nerve injury follow-up. Follow-up of phrenic nerve injury and comparison between the two groups (Group 1: no PV reconnection, Group 2: PV reconnection).

cessation of cryoablation due to PNI might not influence the reconnection rate, once the targeted vein was isolated. However, a head to head comparison is required to draw a clear conclusion.

Miyazaki *et al*. were the first to explore the RSPV isolation durability after the premature interruption of the freezing cycle in 14 patients exhibiting PNI during CB-based PVI. In this study, the reconnection rate was 38.5%. The authors reported a significantly longer freezing time in the durable PVI when compared with reconnected veins (160 vs. 68 s; $P = 0.032$).[14] In our study, the freezing time was slightly longer in the persistent PVI group, however, the difference did not reach statistical significance (140.5 vs. 133.5 s; $P = 0.559$). Moreover, it is important to note that we did not find a cut-off freezing time which led to reconnection in all studied PVs, as the authors reported in the previous study. Our results confirm that a shorter freezing time of less than the commonly used 180 s could be effective for durable PVI which has been recently shown in other studies.[4] Furthermore the data show that a large range of freezing durations can lead to either durable PVI (min 15; max 240 s) or PV reconnection (min 58; max 240 s).

It has been demonstrated that the temperature of the phrenic nerve, as well as the length of the cooling is strongly associated with the durability of PNI. The double stop technique for freezing interruption in case of PNI has been introduced aiming to limit the PN damage and consequently the PNI persistence.[17] The YETI registry showed that the immediate stop of the freezing cycle using a double stop technique is the strongest prognostic factor for PNI recovery.[15] These results are in line with other studies.[13] However, the counterpart of this approach is a potentially higher incidence of PV reconnection. In the present study, we found that the use of the double stop technique was not associated with a higher rate of PV reconnection. Thus, we strongly recommend the implementation of this approach in order to facilitate the PNI recovery, without compromising the PVI durability.

Multiple studies including patients with completed PVI reported a higher incidence of PV reconnection in the RSPV. Even so, the reconnection rate in our study was 25,3% for the RSPV and 23.1% for the RIPV, with no statistical differences between the two ($P = 1$). Thus, no predilection for the reconnection of any of the PVs was noted.

Chierchia *et al*. found that the AF recurrence rate is similar in patients with premature stop of cryoablation due to PNI and those with complete freezing of the septal PVs. As the authors noted, this might be explained by a more complex substrate modification during cryoablation in the LA or by the fact that the incriminated PV may not be the vein responsible for triggering the arrhythmia.[20] However, it has been demonstrated that the most common reason for AF recurrence after PVI is the electrical reconnection of the PVs. Thus, the understanding of PVI persistence in this particular population can offer essential information regarding the best therapeutical approach. It is important to note that in the above-mentioned study, the authors did not find any clinical or procedural predictors of AF recurrence. Our results show that the presence of PV reconnection due to premature stop of PVI did not influence the time to arrhythmia recurrence and reintervention. Based on these results, we advise for no additional therapeutical strategy in isolated PVs in which the freezing cycle was prematurely interrupted to avoid further damage of the PN.

Limitations

The present study is based on the YETI registry and represents a retrospective analysis. However, it is a multicentre, worldwide database aiming to present real-life information. Another limitation is the fact that only patients exhibiting AF recurrence were reassessed for PV reconnection, even if this phenomenon might also appear in arrhythmia-free individuals.

A third limitation is that the study was not designed to assess the procedural factors that might influence the acute isolation of the PVs. In consequence, this issue cannot be addressed here. Moreover, the comparison between the reconnection rate in patients with and without premature freezing interruption can only be performed using the data from the literature, as the present study did not evaluate the reconnection rate in patients with completed PVI.

A fourth limitation is the fact that the order of treated PVs was not assessed in the YETI registry; therefore, we are not able to provide this data. Finally, even if 111 patients from the YETI registry underwent reintervention, data on the repeat procedure were available only in 94 patients.

Conclusions

In patients with premature CB application abortion due to PNI, a high rate of persistent PVI was found at repeat procedures. The only procedural parameter statistically associated with PVI durability was the CB temperature after 30 s of freezing. The double stop technique and the use of a bonus freeze protocol did not influence the PVI durability. PV reconnection was not associated with shorter times to arrhythmia recurrence and reintervention.

Supplementary material

Supplementary material is available at *Europace* online.

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Data availability statement

Due to ethical reasons the data will not be available for researchers outside the YETI group.

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