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Concurrent assessment of time-to-isolation and temperature at 30 s as an innovative metric for predicting the persistence of pulmonary vein isolation using second-generation cryoballoons

Mei-Qiong Wu[1,2], Lin Chen[1,2], Liang-Hua Lian[1,2], Jian-Quan Chen[1,2], Yi-Ming Peng[1,2], Xue-Wen Liao[1,2], Ya-Zhou Lin[1,2*] and Jian-Cheng Zhang[1,2*]

Abstract

Background We attempted to establish correlations between intraoperative variables such as time-to-isolation (TTI) and temperature (T) at the 30-second mark, and the sustained efficacy of pulmonary vein isolation.

Methods One hundred patients underwent repeat procedures subsequent to their index ablation. Five time intervals were delineated based on TTI metrics of 30, 35, 40, 45, and 60 s during the initial procedure. Subsequently, temperatures of -25 °C, -29 °C, -30 °C, and − 31 °C were determined at 30 nodes during repeat procedures, guided by the findings from the initial intervention. The prevalence of re-established pulmonary vein (PV) potentials was assessed both prior to and post each TTI and temperature assessment at the 30-second node.

Results The incidence of reconnected PV potentials demonstrated a noteworthy reduction in the group with TTI < 30 s group than in the TTI ≥ 30. Similarly, there was a notable decrease in the incidence of reconnected PV potentials in the group with T at 30 s of < -31 ℃ than ≥ -31 ℃. The sensitivity, specificity, and positive predictive values (PPVs) for predicting durable pulmonary vein isolation were 13.19%, 94.44%, and 83.72%, respectively, in cases where the TTI was < 30 s and T at 30 s was < -31 ℃.

Conclusion Integrating both TTI30s and T30s could potentially serve as an effective method for predicting the persistence of pulmonary vein isolation using second-generation cryoballoons.

Keywords Atrial fibrillation, Catheter ablation, Durability, Physiological feedback, Pulmonary vein, Temperature

*Correspondence:
Ya-Zhou Lin
yazhoulina@126.com
Jian-Cheng Zhang
zhangjiancheng_zjc@163.com
[1]The Shengli Clinical Medical College, Fujian Medical University, Fuzhou 350001, Fujian Province, P.R. China
[2]Department of Cardiology, Fujian Provincial Hospital, Fuzhou University Affiliated Provincial Hospital, No.134 East Street, Fuzhou 350001, Fujian Province, P.R. China

Background

Pulmonary vein isolation (PVI) is the fundamental procedure for catheter ablation of atrial fibrillation (AF) [1]. Cryoballoon (CB) ablation, particularly using the second-generation cryoballoon CB2 (Arctic Front Advance, Medtronic Inc., Minneapolis, MN, USA), is commonly employed to isolate pulmonary veins in patients with AF. Clinical studies have shown that the use of CB2 offers favorable safety and efficacy outcomes [2–4]. However, the optimal cryoablation dosage for this technique remains unknown [1].

The time elapsed from the initiation of ablation to the development of acute PVI during CB ablation has been quantified with a physiological feedback parameter known as time-to-isolation (TTI). This metric can be assessed in real-time with a specialized CB inner-lumen circular diagnostic mapping catheter (Achieve; Medtronic Inc.) [5]. A TTI-guided approach has been advocated to facilitate the assessment and determination of circumferential and transmural lesion formation during CB ablation [6].

However, few clinical studies have thoroughly assessed the associations between TTI and the sustainability of PVI. The precise duration necessary to establish a comprehensive, enduring circumferential and transmural lesion with a recorded TTI remains unclear. Cryoballoon dosing strategies commonly emphasize TTI < 60 s, a threshold deemed insufficient for reliably predicting durable PVI. Alternatively, a temperature of -40 °C at 60 s can serve as a predictive indicator of sustained PVI without necessitating recorded TTI [1–7]. However, a rapid decline in temperature to below −40 °C within 30 s post-freezing may cause complications. Particularly, lower temperatures, notably within the left inferior (LIPV) and right superior (RSPV) pulmonary veins, may escalate the susceptibility to esophageal and phrenic nerve injuries [8]. However, the optimal temperature for achieving durable PVI warrants investigation. Therefore, in the current study, we endeavor to scrutinize the associations between combined TTI30s and T30s during the initial procedure and the subsequent durability of PVI.

Materials and methods

Basic information

A repeat procedure was conducted on 100 patients (female, $n = 38$ [38%]; mean age of 58 ± 10 years) using a 28-mm second-generation CB at a post-ablation-index of 23 ± 17.8 (range, 3.5–84) months. Supplementary table shows the clinical characteristics of the patients in this study. A 3-dimensional electroanatomical mapping system was used for all repeated ablations.

Study participants

All patients underwent repeat procedures due to the recurrence of atrial tachyarrhythmia (ATa) lasting ≥ 30 s following a 3-month blanking period post-PVI using an Arctic Front Advance cryoballoon (CB-Adv) (Medtronic Inc.). Routine follow-up was conducted for all patients included in this study. However, patients with an intracavitary thrombus, segmental pulmonary vein isolation surgery, uncontrolled heart failure, moderate or severe valvular disease, left atrium (LA) diameter ≥ 55 mm, and/or contraindications to anesthesia were excluded. Approval for this study was obtained from the Institutional Ethics Committee on Human Research at our institution.

Preoperative preparation

The CHA2DS2-VASc scores of the patients were assessed upon admission to assess their risk for AF. Transthoracic echocardiography was used to measure the left atrial diameter and left ventricular ejection fraction. Left atrial thrombi were identified and excluded through transesophageal echocardiography and pulmonary venous computed tomography angiography. Assessment of the left atrium size and pulmonary vein anatomy was conducted using computed tomography angiography (CTA). Detailed preoperative explanations of the procedure were provided to all patients, who subsequently provided written informed consent to participate in this study.

CB ablation as index procedure

The CB ablation index procedure for AF was conducted by three operators on patients under local anesthesia, midazolam (Xuzhou Enhua Pharmaceutical Group Co. Ltd., Xuzhou, China), and fentanyl (Yichang Renfu Pharmaceutical Co. Ltd., Yichang, China). A decapolar catheter (Abbott Laboratories, Chicago, IL, USA) was inserted into the coronary sinus through the left femoral vein. Additionally, a quadripolar diagnostic catheter (Abbott Laboratories) was positioned at the superior vena cava to prevent phrenic nerve injury, while ipsilateral phrenic nerve was stimulated using a 1,000-ms cycle and a 10-mA output. Subsequently, a transseptal needle, sheath, and catheter (Medtronic) were placed at the target location based off a right femoral venous approach. Heparinization was administered based on body weight (80–100 U/kg) of the patients. Upon accessing the left atrium, the inner lumen Achieve mapping catheter (Medtronic) was advanced into each PV ostium using a steerable FlexCath Advance 15 Fr sheath (Medtronic). An Arctic Front Advance 28-mm CB-Adv (Medtronic) was then positioned in each PV ostium, ensuring optimal vessel occlusion, confirmed by selective contrast injection demonstrating complete contrast retention without backflow to the atrium. Cryothermal energy was subsequently delivered for a minimum of 180 s, followed by a bonus ablation lasting 120 s. Termination of the freezing procedure occurred upon reaching a balloon temperature of −55 °C or a significant decrease in diaphragmatic electromyography amplitude. This protocol adhered to the recommendations outlined in the 2020 Chinese Expert Consensus on Catheter Ablation via CB (Fig. 1). Electrical signals were captured throughout the CB ablation procedure using Achieve. Prior to ablation in each vein, PV activity was recorded proximally at the ostium using Achieve. TTI was documented when PVs were detectable at the onset of energy delivery, prior to their disappearance or dissociation from left atrial activity during energy delivery. Assessment of PVI durability was conducted at least 20 min post-cryothermal energy delivery. Additional heparin infusions of 1,000 IU were administered hourly as needed to maintain an activated clotting time>250 s throughout the procedure [9]. The total procedure duration was defined as the interval between achieving femoral venous access and catheter removal. The patients whose pulmonary vein potentials were not recorded at the time of the first freeze, or whose TTI was greater than 60 s at the time of the first freeze.

Repeat ablation procedure

Between June 2016 and October 2022, repeat ablation procedures were performed on 45 patients with paroxysmal AF and 55 patients with persistent AF using an RF irrigated-tip CF catheter (Abbott Laboratories) due to ATa recurrences.

All patients provided consent for repeat ablation procedures, which involved double-transseptal puncture and 3-dimensional LA reconstruction geometry using the EnSite NavX 3D-mapping system (Abbott Laboratories). A circular mapping catheter was used to identify potential PV reconnection sites and locate conduction gaps in each proximal PV ostium. Late PV reconnection was characterized by LA-PV electric reconduction that occurred during the repeat procedure, with the location of conduction gaps along previously deployed circumferential lesions in four distinct anatomical regions of the PV antrum indicating reconnection sites.

Statistical analysis

Categorical variables are presented as absolute and relative frequencies, while continuous variables are expressed as means±SD. Student t-tests and the chi-squared or Fisher's exact tests were used to compare continuous and binomial variables, respectively. Statistical significance was defined as two-tailed $P<0.05$. Predictors of PV reconnection were identified through multivariable analysis using Cox proportional hazards regression models. Statistical analyses were performed using GraphPad Prism v. 8.0.1.244 (GraphPad Software Inc., San Diego, CA, USA) and SPSS v. 23 (IBM Corp., Armonk, NY, USA).

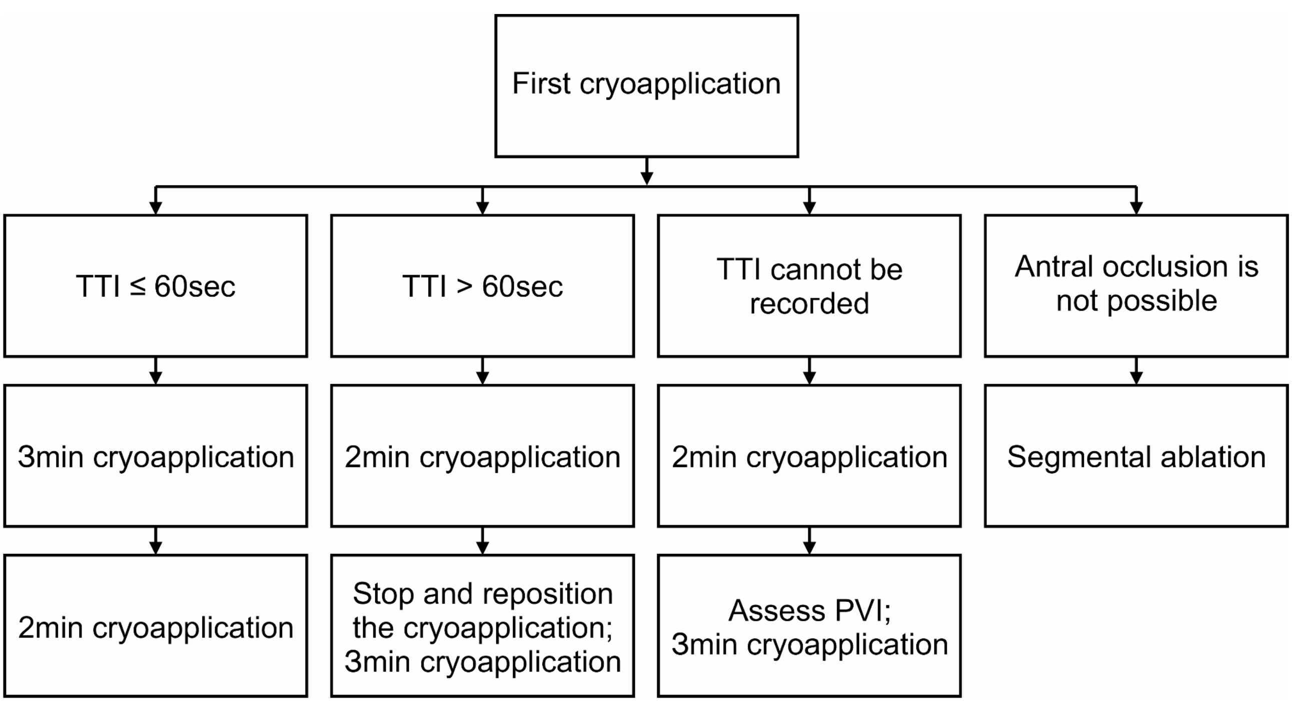


Fig. 1 Cryoballoon Ablation Dosing Strategy. Cryoballoon Ablation Dosing Algorithm. The decision tree was used to guide cryoablation applications during the dosing algorithm study. The protocol required operators to attempt achieving cryoablations with a short duration of time-to-isolation (TTI). TTI: time to isolation, PVI: pulmonary vein isolation

Theory/calculation

The combination of TTI30s and T30s may serve as an effective predictor of PVI durability in second-generation cryoballoons. Therefore, it is recommended to maintain TTI<30 s and T < -31 ℃ at 30 s during cryoablation procedures.

Results

We applied TTIs of <60 and 180 s for the initial ablation and 120 s for the subsequent consolidation ablation. However, when the TTI>60 s during the initial ablation, which was intended to last for 120 s, the procedure was stopped, and adjustments to the balloon position were made. To enhance occlusion effectiveness, left and right anterior oblique positions were used to visualize the contrast agent shunt, guiding further adjustments to the balloon position. In cases where the TTI recording was not feasible, the initial ablation proceeded for 120 s with adequate balloon occlusion. If PVI was achieved following rewarming, the ablation could be repeated once for 180 s. Conversely, if balloon occlusion remained inadequate despite adjustments, segmental isolation was contemplated, with changes in PV potential monitored during the procedure. In this study, there were two cases of PNI, which occurred during freezing of the right upper pulmonary vein and recovered half an hour after stopping freezing. In addition, no pulmonary vein stenosis was not observed in the study. The incidence of serious complications such as pulmonary nerve injury (PNI) or pulmonary vein stenosis was low in this study, and the incidence was less than 1% in the group with a TTI of less than 30 s and T30s of less than 31 °C. Further details are depicted in Fig. 1.

Five time nodes, namely TTI30s, TTI35s, TTI40s, TTI45s, and TTI60s, were established based on observations from the initial procedure. The relationships between TTIs and the durability of PVI were analyzed at each time node, while the incidence of reconnected PVs was assessed both before and after each time node. Reconnected PVs were only evident before and after the first time node (TTI30s). Notably, the incidence of reconnected PVs was significantly lower in the group with TTI<30 s compared to those with TTI≥30 s (22.22% vs. 34.34%, P=0.04). The incidences of reconnected PVs at subsequent time nodes (TTI35s, TTI40s, TTI45s, and TTI60s) were comparable. Please refer to Fig. 2 for further details.

Four T30s nodes (-25 °C, -29 °C, -30 °C, and −31 °C) were established based on observations from the initial procedure. The incidence of reconnected PVs was

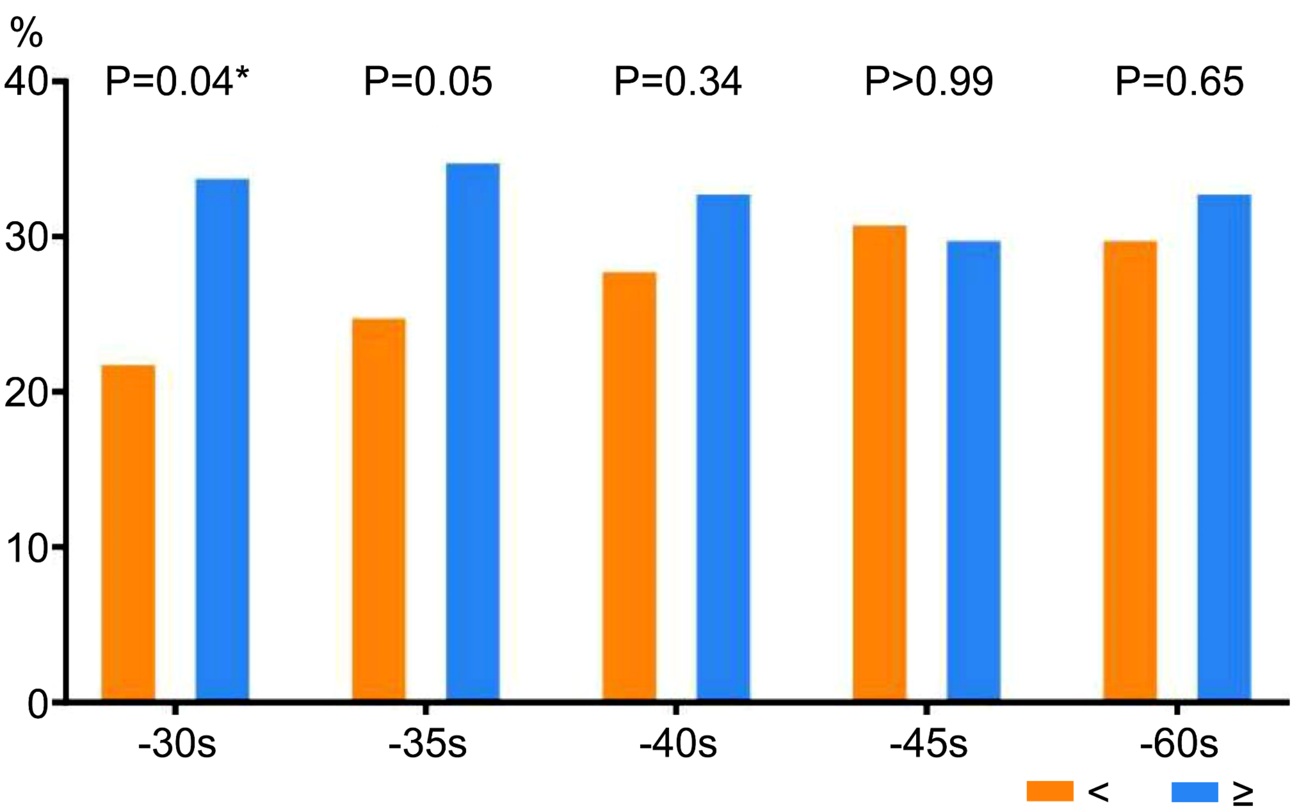


Fig. 2 Incidence of Reconnected PVs in Different TTI Time Nodes. Data are presented as percentages. Five time nodes were established using the first procedure TTI (TTI30s, TTI35s, TTI40s, TTI45s, and TTI60s). The incidences of reconnected PVs were compared before and after each time node. The yellow bar represents TTI, the time node. The blue bar denotes TTI > the time node

significantly lower in the group with T30s < -31 °C compared to those with T30s ≥ -31 ℃ (24.81% vs. 34.96%, $P=0.04$). However, similar incidences were observed at other T30s nodes (T-25 °C, -29 °C, and −30 °C). Please refer to Fig. 3.

Comparisons were made between intraoperative parameters of the TTI<30 s and TTI≥30 s groups. The mean T30s was significantly lower in the TTI<30 s group than in the TTI≥30 s group (-31.74±4.59 vs. -28.39±5.21, $P<0.0001$). The TTI was also significantly shorter in the TTI<30 s group compared to the TTI≥30 s group (21.11±5.28 vs. 52.74±21.09, $P<0.0001$). Please refer to Table 1; Fig. 4 for further details.

We conducted a comparison of intraoperative parameters between the T30s < -31 °C and T30s ≥ -31 °C groups. Significantly lower mean T30s values were observed in the T30s < -31 °C group compared to the T30s ≥ -31 °C group (-35.23 °C±2.95 °C vs. -26.44 °C±4.06 °C, $P<0.0001$). The TTI was significantly shorter in the T30s < -31 °C group compared to the T30s ≥ -31 °C group (36.88±22.88 s vs. 45.89 °C±22.47 s, $P<0.0001$). Please refer to Table 2 for detailed results.

Among the 399 PVs assessed, 126 were identified as reconnected, while 273 exhibited durable PVIs. During the first procedure, TTI<30 s were recorded in 90 PVs. Of these, 70 PVs remained isolated, while 20 PVs reconnected during the subsequent procedure. The sensitivity, specificity, and positive predictive values of TTI<30 s for predicting durable PVI were calculated as 25.64%, 84.13%, and 77.78%, respectively (see Table 3).

Similarly, T30s < -31 °C was identified in 133 PVs during the initial procedure, of which 100 remained isolated and 33 reconnected during the subsequent procedure. The sensitivity, specificity, and positive predictive values of T30s < -31 °C for predicting durable PVI were calculated as 36.63%, 73.81%, and 75.19%, respectively.

We also identified TTI<30 s and T30s < -31 °C in 43 PVs during the first procedure. Among these, 36 PVs remained isolated, while seven reconnected during the subsequent procedure. The sensitivity, specificity, and positive predictive values of TTI<30 s and T30s ≥ -31 °C for predicting durable PVI were calculated as 13.19%, 94.44%, and 83.72%, respectively.

In the COX regression model predicting postoperative PV reconnection, TTI<30 s and T30s ≤ -31 °C were used as variables. Multivariable analysis confirmed that TTI<30 s served as an independent predictor of PV durability (refer to Table 4).

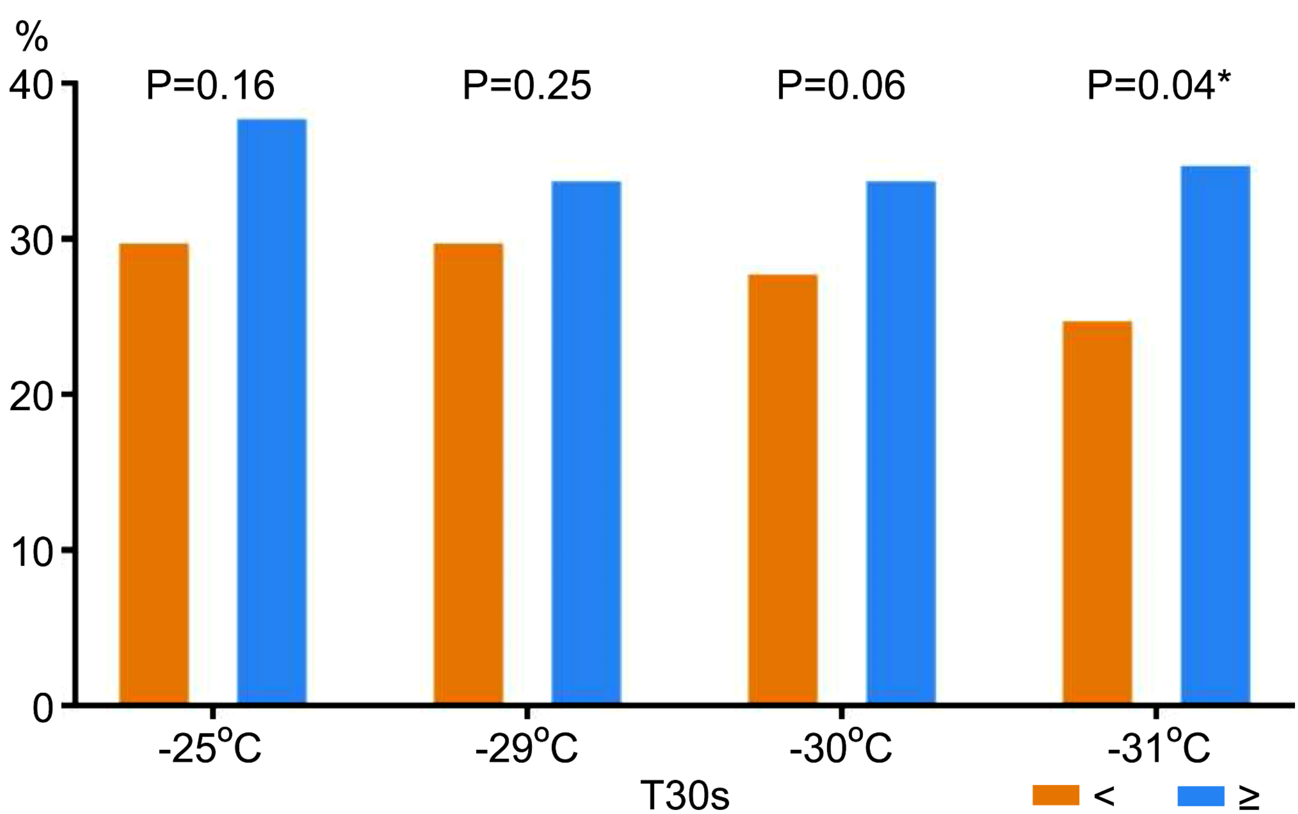


Fig. 3 Incidence of Reconnected PVs in Different T30s. Data are expressed as percentages. Four temperatures at 30 s (T30s) nodes (T-25 ℃, T-29 ℃, T-30 ℃, and T-31 ℃) were established based on the first procedure recording. The incidence of reconnected PVs was compared before and after the initial ablation. The yellow bar represents T30s, a temperature node. The blue bar represents T30s >, the temperature node

Table 1 Index ablation results according to time-to-isolation (TTI)

Variable	TTI<30s	TTI ≥ 30s	*p*
PVs			
Mean T_{30s} (°C)	-31.74 ± 4.59	-28.39 ± 5.21	<0.0001*
Mean minimal temperature (°C)	-45.88 ± 7.05	-43.36 ± 7.09	0.08
TTI (s)	21.11 ± 5.28	52.74 ± 21.09	<0.0001*
Mean temperature at TTI (°C)	-26.78 ± 11.58	-35.79 ± 5.91	<0.0001*
Total number of applications	2.28 ± 1.12	2.28 + 1.2	0.95
PV reconduction (n, %)	20(22)	68(34)	0.04*
LSPV			
Mean T_{30s} (°C)	-32.18 ± 5.57	-28.38 ± 4.64	0.03*
Mean minimal temp.(°C)	-47 ± 5.01	-45.63 ± 6.17	0.37
TTI (s)	25.91 ± 2.71	57.33 ± 21.25	<0.001*
Mean temperature at TTI (°C)	-32.4 ± 4.98	-37.88 ± 5.79	>0.99
Total number of applications	2.82 ± 1.11	2.35 ± 1.18	0.22
PV reconduction (n, %)	2(18)	25(37)	0.31
LIPV			
Mean T_{30s} (°C)	-29.42 ± 3.86	-26.62 ± 4.41	0.08
Mean minimal temperature (°C)	-42.35 ± 5.93	-38.31 ± 5.92	0.11
TTI (s)	20.65 ± 4.74	51.08 ± 15.44	<0.0001*
Mean temperature at TTI (°C)	-24.98 ± 9.49	-32.57 ± 4.51	0.002*
Total number of applications	1.92 ± 1.03	2.29 ± 1.32	0.42
PV reconduction (n, %)	5(19)	16(33)	0.28
RSPV			
Mean T_{30s} (°C)	-33.5 ± 4.43	-28.40 ± 5.49	0.006*
Mean minimal temperature (°C)	-48.14 ± 7.29	-44.64 ± 7.43	0.07
TTI (s)	20.53 ± 5.69	45.24 ± 15.95	<0.0001*
Mean temperature at TTI (°C)	-23.52 ± 14.85	-35.62 ± 6.37	0.0005*
Total number of applications	2.28 ± 0.88	2.14 ± 1.08	0.20
PV reconduction (n, %)	6(21)	13(31)	0.42
RIPV			
Mean T_{30s} (°C)	-32 ± 3.95	-30.5 ± 5.88	0.98
Mean minimal temperature (°C)	-46.56 ± 7.21	-44.23 ± 6.52	0.17
TTI (s)	20.12 ± 5.07	52.3 ± 23.05	<0.0001*
Mean temperature at TTI (°C)	-30.08 ± 9.36	-36.35 ± 5.38	0.02*
Total number of applications	2.4 ± 1.32	2.28 ± 1.22	0.69
PV reconduction (n, %)	7(28)	14(35)	0.60

Note: Data are expressed as mean ± SD or absolute number (percentage). LIPV: left inferior pulmonary vein; LSPV: left superior pulmonary vein; PV: pulmonary vein; RIPV: right inferior pulmonary vein; RSPV: right superior pulmonary vein; T_{30s}: Temperature at 30 s; TTI: time to isolation

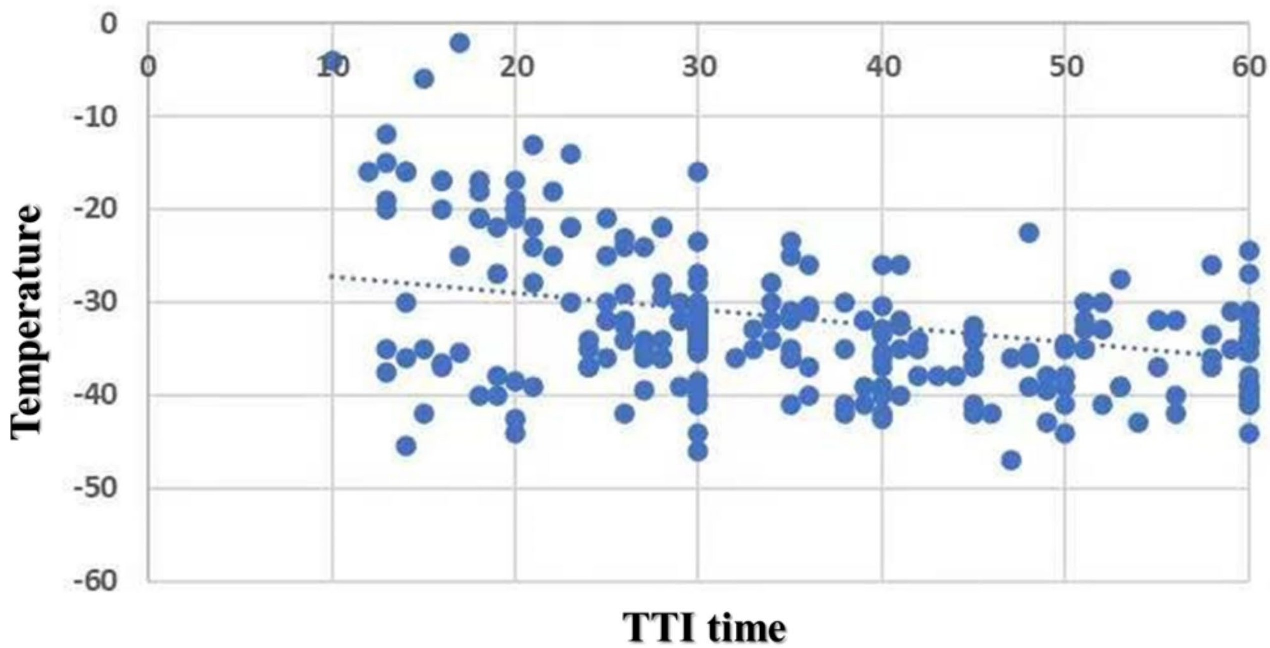
Discussion

The TTI was defined as the duration elapsed from the initiation of cryoablation to the achievement of PVI. With the use of second-generation balloon cryoablation, TTI can be reliably recorded in approximately 80% of PV. This parameter plays a significant role in determining the extent of transmural cryoablation lesion formation and can effectively guide dosing methods [10, 11]. Given its real-time nature, TTI can be monitored during the procedure, providing insights into occlusion efficacy and the durability of PVI. Optimal occlusion conditions allow for the isolation of many PV within 60 s, with durable PVIs observed in up to 96.4% of cases following a 120-second freezing bonus. Notably, a TTI≥60 s has been identified as an independent predictor for PV reconnection [12]. A TTI < 60 s, or a freezing temperature < -40 °C at 60 s, has demonstrated high sensitivity and specificity for achieving postoperative permanent PVI (sensitivity, 86.7%; specificity, 86.2%) during one-year post-procedural follow-up. The attainment of a temperature drop to -40 °C at 60 s indicates complete occlusion of the PV by the CB, serving as an independent predictor for immediate PVI. It is noteworthy that a prolonged TTI is often associated with an increased risk of AF recurrence [12–16].

A previous canine model study has demonstrated that effective PVI can be achieved with a TTI duration of at least 60 s [17]. This finding has served as a foundation for establishing CB dosing protocols in human participants. Two clinical investigations have further emphasized the significance of TTI in guiding the preparation of ablation dose plans [18, 19]. When compared to the use of first-generation balloon cryotherapy involving durations of 240 s–180 s twice, cryotherapy doses guided by TTI + 120 s have revealed superior efficacy in achieving transmural lesions. Additionally, such dosing strategies have been associated with reduced radiation exposure, shortened procedural durations, and minimized risks of collateral tissue damage around the pulmonary vein, including the esophagus and phrenic nerve, due to excessive ablation [10, 20, 21]. Notably, findings from the canine model indicate that TTI + 60 s can achieve complete transmural lesions, with postoperative lesion depths comparable to those observed in the TTI + 120 s group. Based on these insights, the duration of cryoablation performed at our center was 180 s followed by an additional 120 s, indicating the attainment of transmural lesions within this cryoablation timeframe.

The rate of cooling is a critical determinant of cryoablation efficacy, with more rapid cooling rates associated with enhanced outcomes. For instance, a cooling rate of -1.41 °C/s can predict successful PVI, while a rate of < -1.81 °C/s indicates a minimum balloon temperature of < -55 °C [6]. Cooling temperatures exhibit a rapid decline within the initial 30 s, followed by a gradual decrease thereafter. Lower temperatures observed at the 30-second mark correspond to faster cooling rates. This rapid cooling process results in intracellular fluid freezing prior to its extrusion from cells due to osmotic pressure, consequently increasing intracellular freezing and cell death rates. Hence, a faster cooling rate correlates with higher rates of cell death.

This study used TTI intervals of 30 s, 35 s, 40 s, 45 s, and 60 s as temporal markers to assess the relationship between TTI and the durability of PVI. Significantly



Correlation between temperature and time to isolation

lower incidences of reconnected PVs were observed in cases where TTI was <30 s. Multivariable analysis further confirmed TTI<30 s as an independent predictor of PVI.

The study findings revealed that the mean TTI was significantly shorter in the TTI<30 s group compared to the TTI≥30 s group (21.11±5.28 s vs. 52.74±21.09 s, P<0.0001). Notably, the average TTI in the TTI≥30 s group was 52 s. It is noteworthy that a TTI>43 s has been identified as an independent predictor of AF recurrence, indicating a higher likelihood of PV reconnection in this group [6]. Conversely, a mean TTI of 21 s was observed in the TTI<30 s group, indicating a probable absence of recurrence when TTI≥40 s (sensitivity: 90%; specificity: 81%) [14]. Also, each additional 10-second increment required for achieving PVI was associated with a 1.3-fold increase in the risk of recurrence. These findings collectively indicate a high durability of PVI in the TTI<30 s group.

Additionally, four temperature (T30s) nodes (-25 °C, -29 °C, -30 °C, and −31 °C) were established based on data obtained from the initial procedure to assess the relationship between T30s and PVI durability. The incidence of reconnected PVs was notably lower in the T30s < -31 °C group compared to the T30s ≥ -31 °C group (24.81% vs. 34.96%, P=0.04). The TTI was significantly shorter in the T30s < -31 °C group compared to the T30s ≥ -31 °C group (36.88±22.88 s vs. 45.89±22.47 s, P<0.0001). The mean TTI and T30s were recorded as 36.88±22.88 s and −35.23 °C±2.95 °C, respectively, in the T30s < -31 °C group.

The present findings revealed a significantly lower T30s value in the TTI<30 s group compared to the TTI≥30 s group (-31.74 °C±4.59 °C vs. -28.39 °C±5.21 °C, P<0.0001). Notably, our results indicated that T30s < -31 °C may be associated with a reduced incidence of reconnected PVs. The mean T30s value observed in the TTI<30 s group was recorded as -31.74 °C±4.59 °C, revealing that T30s = -31 °C could potentially serve as a significant threshold for achieving durable PVI.

The combination of TTI<30 s and T30s < -31 °C exhibited enhanced predictive capability for PVI durability, due to a higher specificity and a superior positive predictive value compared to TTI<30 s or T30s < -31 °C alone.

Our findings underscored that the presence of TTI<30 s and T30s < -31 °C may correlate with a lower incidence of reconnected PVs. Also, combining TTI<30 s and T30s ≤ -31 °C demonstrated superior predictive performance for durable PVI, characterized by heightened specificity and positive predictive value compared to TTI<30 s or T30s < -31 °C alone. These results advocate for CB operators to meticulously regulate TTI to be <30 s and ensure that the temperature drops to < -31 °C within 30 s during the initial cryoablation procedure.

Limitations

The present observational study is subject to certain limitations. Our analysis focused on the follow-up outcomes of patients who underwent procedures exclusively at a single center, conducted by multiple operators. Consequently, the generalizability of our findings may be constrained when compared to those derived from

Table 2 Index ablation results according to T_{30s}

Variable	T_{30s}<-31℃	T_{30s}≥-31℃	*p*
PVs			
Mean T_{30s} (℃)	-35.23±2.95	-26.44±4.06	<0.0001*
Mean minimal temperature (℃)	-48.18±6.18	-41.00±6.95	<0.0001*
Recorded TTIv (n)	97(133)	191(266)	/
Mean TTIv (s)	36.88±22.88	45.89±22.47	<0.0001*
Mean temperature at TTI (℃)	-32.74±12.19	-33.08±7.09	0.99
Total number of applications	2.47±1.52	2.41±1.33	0.56
PV reconduction	35(133)	91(266)	0.04*
LSPV			
Mean T_{30s} (℃)	-34.77±2.39	-25.94±4.35	<0.0001*
Mean minimal temperature (℃)	-47.93±6.12	-43.37±7.41	0.0007*
Recorded TTI (n)	24(30)	55(70)	/
Mean TTI (s)	51.04±27.41	53.80±20.00	0.92
Mean temperature at TTI (℃)	-39.17±5.98	-36.07±5.95	0.0017*
Total number of applications	2.97±1.83	2.43±1.25	0.05
PV reconduction	7(30)	27(70)	0.17
LIPV			
Mean T_{30s} (℃)	-33.76±1.77	-25.87±4.00	<0.0001*
Mean minimal temperature (℃)	-47.53±3.31	-37.88±5.83	<0.0001*
Recorded TTI (n)	14(17)	60(82)	/
Mean TTI (s)	28.64±14.81	43.13±19.23	0.02*
Mean temperature at TTI (℃)	-27±10.52	-30.59±6.59	0.64
Total number of applications	1.71±0.89	2.56±1.42	0.005*
PV reconduction	3(17)	26(82)	0.38
RSPV			
Mean T_{30s} (℃)	-35.47±2.58	-27.03±3.91	<0.0001*
Mean minimal temperature (℃)	-49.03±6.25	-42.76±6.95	<0.0001*
Recorded TTI (n)	29(38)	41(62)	/
Mean TTI (s)	31.97±19.22	40.17±23.86	0.08
Mean temperature at TTI (℃)	-29.36±16.25	-31.70±7.85	0.41
Total number of applications	2.21±0.95	2.31±1.16	0.91
PV reconduction	5(38)	23(62)	0.01*
RIPV			
Mean T_{30s} (℃)	-35.85±3.59	-27.31±3.68	<0.0001*
Mean minimal temperature (℃)	-47.90±6.83	-40.62±5.94	<0.0001*
Recorded TTI (n)	30(52)	35(52)	/
Mean TTI (s)	34.13±20.25	44.89±26.00	0.05
Mean temp. at TTI (℃)	-33.53±8.94	-34.29±6.65	0.83
Total no. of applications	2.63±1.70	2.40±1.46	0.56
PV reconduction	18(48)	17(52)	0.68

Note: Data are expressed in mean±SD or absolute number (percentage). PV: pulmonary vein; LSPV: left superior pulmonary vein; LIPV: left inferior pulmonary vein; RIPV: right inferior pulmonary vein; RSPV: right superior pulmonary vein; TTI: time-to-isolation; T_{30s}: Temperature at 30s

prospective multicenter randomized controlled trials. Therefore, the necessity for a randomized trial involving a larger patient group becomes apparent to validate our conclusion regarding the predictive use of combining TTI at 30 s with T30s in assessing PVI durability during second-generation CB procedures.

Our study findings underscore the potential effectiveness of controlling TTI to <30 s and achieving a temperature reduction to < -31 °C within 30 s during the initial cryoablation phase.

Table 3 Predictors of the PVI durability: TTI < 30 s, T_{30s} ≤ -31℃, TTI < 30 s, and T_{30s} ≤ -31 ℃ as predictors of PVI durability

	Sensitivity	Specificity	positive predictive value
TTI<30 s	25.64	84.13	77.78
T_{30s}<-31 ℃	36.63	73.81	75.19
TTI<30 s and T_{30s}<-31 ℃	13.19	94.44	83.72

Note: PVI: pulmonary vein isolation; TTI: time-to-isolation; T_{30s}: Temperature at 30 s

Table 4 Multivariable Cox regression analysis indicating factors predicting late PV reconnection

Variables	β Coefficient	Hazard Ratio (95% CI)	*P* Value
TTI<30 s	0.52	1.69(1.00–2.83)	0.04*
T_{30s}<-31 ℃	0.46	1.57(0.98–2.54)	0.06
Recorded TTI	0.11	1.12(0.69–1.82)	0.65

Note: CI: confidence interval; PVI: pulmonary vein isolation

Conclusions

The combined assessment of TTI<30 s and T30s<31 °C may serve as a predictive indicator for assessing the durability of pulmonary vein isolation following second-generation CB procedures.

Abbreviations

AF	Atrial fibrillation
ATa	Atrial tachyarrhythmia
CB	Cryoballoon
LA	Left atrium
LIPV	Left inferior pulmonary vein
PVI	Pulmonary vein isolation
RSPV	Right superior pulmonary vein
T_{30s}	Temperature at 30 s
TTI	Time-to-isolation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13019-024-03168-x.

Supplementary Material 1

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Author contributions

Obtaining financing and Administrative support: Lin YZ; Conception and design of the research: Zhang JC, Chen L and Wu MQ; Analysis and interpretation of the data: Chen JQ and Wu MQ; Collection and assembly of data: Lian LL, and Wu MQ; Data analysis and Statistical analysis: Peng YM, Liao XW and and Wu MQ; Manuscript writing and Critical revision of the manuscript for intellectual content: Zhang JC and Wu MQ; Final approval of manuscript: All authors.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study has been performed with the approval of the Ethics Committee of Fujian Provincial Hospital (Approval number: K2023-09-005) and with appropriate participant written informed consent in compliance with the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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