Cardiovascular Topics

The value of measured partial oxygen pressure during pulmonary vein closure and the relationship with the diameter of the closed vein in patients with cryoablation

Enes Çon, Namık Kemal Eryol, Mehmet Tuğrul İnanç, Deniz Elçik

Abstract

Aim: The aim of this study was to investigate the value of partial oxygen pressure (PO_2) changes measured in the left atrium (LA) during transient pulmonary vein (PV) closure in patients undergoing cryoablation and its relationship with the diameter of the closed PV.

Methods: The study was carried out on a total of 25 cases. The grouping of PVs was made separately as the left superior, left inferior, left common, right superior, right inferior, right common and total PVs. PV measurement was made from angiographic images obtained after the cryoablation balloon was inflated and opaque. From the LA, the difference between the PO_2 values in the blood gases obtained before and during the temporary closure of each PV was evaluated as the PO_2 change. The difference of the lowest temperature reached during the closing of each PV from –36°C was termed the heat difference. The relationship of PO_2 change with PV diameter and the heat difference were investigated.

Results: There was no significant relationship between any of the PV diameters and PO_2 changes ($p > 0.05$). There was a significant relationship between heat differences and PO_2 changes in the left superior ($p = 0.011$), right superior ($p = 0.049$), right 'common' ($p = 0.037$) and total PVs ($p = 0.001$), but there was no significant relationship between heat differences and PO_2 changes in the left inferior, left 'common' and right inferior PVs ($p > 0.05$).

Conclusion: In the light of these data, PO_2 change could demonstrate the success of cryoablation, and was related with the cooling degree, but not with the PV diameter.

Keywords: atrial fibrillation, cryoablation, pulmonary vein

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Department of Cardiology, Erciyes University School of Medicine, Kayseri, Turkey

Enes Çon, MD, enes_con@hotmail.com

Namık Kemal Eryol, MD

Mehmet Tuğrul İnanç, MD

Deniz Elçik, MD

Atrial fibrillation (AF) is the most common cardiac arrythmia, characterised by high-rate and non-organised electrical activity originating from the atrium. It is often related to some predisposing factors, including advanced age, hypertension, valvular disease, congestive heart failure, hypertrophic cardiomyopathy, thyrotoxicosis (especially AF without rate control), coronary artery disease, medications, pulmonary embolism, chronic lung disease, caffeine intake, infections, various metabolic disorders, obesity and underlying sleep disturbance.[1,2]

AF is often complicated, with increased risk for ischaemic stroke, congestive heart failure and thromboembolism, and as a result, high rates of hospitalisation and mortality.[3] Echocardiography (ECG) is essential for the definitive diagnosis of AF. Irregular RR intervals are seen in ECG derivations and there is no prominent P wave in AF.[4]

The main methods used in the treatment of this arrhythmia are anticoagulation, rhythm control and heart rate control. Rhythm control can be achieved medically (with amiodarone, dronedarone, vernakalant, ibutilid and propofenon) or by ablation methods.[5] Ablation is an interventional therapeutic approach, aiming to eliminate the arrhythmogenic regions in the myocardial tissue by using heating or cooling energies. Cryoablation causes cell death by forming ice crystals that break down the cell membrane.

Pulmonary vein (PV) isolation is the most common ablation approach for AF. With this method, electrical isolation is provided by creating necrosis between the left atrium (LA) and the PV; the length of the AF loop is progressively extended and formation of AF is prevented.[6]

The aim of this study was to investigate the value of partial oxygen pressure (PO_2) changes measured in the LA during transient PV closure in patients undergoing cryoablation, and to determine the relationship of PO_2 changes in the LA with the diameter of the closed PV and with the heat changes, reflecting the success of cryoablation.

Methods

Twenty-five patients over the age of 18 years who had undergone cryoablation for paroxysmal AF were included in the study. The exclusion criteria were: chronical obstructive lung disease, LA diameter of > 4.5 cm and the need for oxygen support.

Standard forms created for the patients included in the study were filled in and the information [personal history, physical examination, echocardiography, transoesophageal

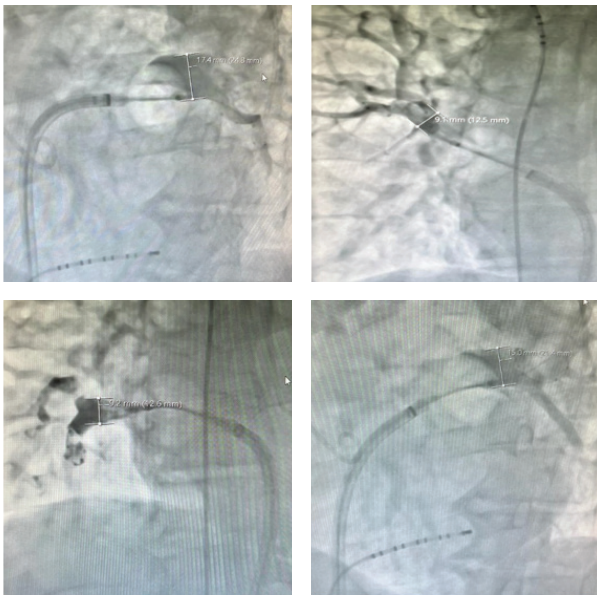

Fig. 1. Pulmonary vein measurement.

echocardiography (TEE), ECG, PV diameters, blood gas results and cryoablation balloon temperature values] were recorded. After ablation, ECG demonstration of PV isolation and a decrease in temperature to at least –36°C were accepted as criteria for success of the cryoablation.

The grouping of PVs was made separately as left superior, left inferior, left 'common' (if any), right superior, right inferior, right 'common' (if any) and total PVs. PV measurement was done from the angiographic images obtained after the cryoablation balloon was inflated and opaque (Fig. 1).

The difference between the PO_2 value in the blood gases obtained from the LA before the PV closure and the PO_2 values in the blood gases obtained from the LA during the temporary closure of each PV was termed the PO_2 change. The difference of the lowest temperature value reached during the closure of each PV from –36°C was termed the heat difference.

Statistical analysis

The Number Cruncher Statistical System 2007 program was used for the statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) for evaluating the data were used. The compatibility of the quantitative data to the normal distribution was tested with the Shapiro–Wilk test and graphical analysis. The Pearson and the Spearman correlation analyses were used to evaluate the relationships between quantitative variables. Significance was assessed at least at a p-value of < 0.05.

Results

Some descriptive information about the patients is shown in Table 1. Accordingly, 44% ($n = 11$) of the patients included in the study were male and 56% ($n = 14$) were female. It was determined that 96% ($n = 24$) of the six-month control ECG findings of patients were in sinus rhythm and 4% ($n = 1$) were in AF. None of the patients had thrombus on the TEE administered before the procedure.

Table 1. Descriptive statistics of the patients

Variables	*Number*	*Percentage*
Gender		
Male	11	44.0
Female	14	56.0
Control ECG 6 months after cryoablation		
Sinus rhythm	24	96.0
Atrial fibrillation	1	4.0
Thrombus in the TEE before the cryoablation		
No	25	100.0

Table 2 demonstrates some descriptive statistics of the patients. The average age of the patients was 56.20 ± 12.774 years, the mean LA diameter in echocardiography was 3.644 ± 0.4908 cm and the ejection fraction was 59.1592 ± 4.53%. The average PV closure times were as follows: superior left PV: 159.20 ± 123.758 s, inferior left PV: 153.60 ± 117.576 s, left common PV: 84.80 ± 115.655 s, right superior PV: 170.40 ± 112.823 s. The mean duration of right inferior PV closure was 178.40 ± 115.603 s and the right common PV closure time was 67.40 ± 114.101 s.

Table 3 shows the variation of measurement results in all PVs. When the PO_2 measurements in the LA during temporary PV closure were examined, the mean was 76.712 ± 10.9533 mmHg for the left superior PV, 67.069 ± 30.0218 mmHg for the left inferior PV and 54.167 ± 22.7513 mmHg for the left common PV, 62.011 ± 23.7394 mmHg for the right superior PV, 56.572 ± 27.3202 mmHg for the right inferior PV and 66.257 ± 9.8651 for the right common PV.

When the PO_2 changes were examined, the mean was 14.456 ± 9.4267 mmHg for the left superior PV, 9.475 ± 7.4388 mmHg for the left inferior PV, 18.80 ± 7.5612 mmHg for the left common PV. For the superior right PV, the mean was 15.883 ± 11.1720 mmHg, 19.322 ± 9.9646 mmHg for the right inferior PV and 21.50 ± 13.3671 mmHg for the right common PV.

The superior left PV temperature measurements averaged –44.50 ± 15.7438°C, the inferior left PV was –43 ± 11.0272°C, the left common PV was –39.778 ± 20.6774°C, the superior right PV was –46.833 ± 15.9494°C, the inferior right PV was –40.944 ± 20.0249°C and the right common PV was –46.143 ± 19.0388°C.

The superior left PV heat difference measurements averaged 12.938 ± 5.4829°C, the inferior left PV averaged 8.125 ± 4.8010°C, the left common PV averaged 10.778 ± 6.571°C, the superior right PV averaged 14.833 ± 7.2457°C, the inferior right

Table 2. Descriptive statistics of patients and PV closure times

Variables	*Number*	*Minimum*	*Maximum*	*Mean*	*SD*	*Median*
Age	25	18	73	56.20	12.774	54.00
LA diameter (cm)	25	3.0	4.5	3.644	0.4908	3.5
Ejection fraction (%)		46.00	69.00	59.1592	4.53884	57.5
Left superior PV closure time	25	0	300	159.20	123.758	240.00
Left inferior PV closure time	25	0	240	153.60	117.576	240.00
Left common PV closure time	25	0	240	84.80	115.655	0.00
Right superior PV closure time	25	0	300	170.40	112.823	240.00
Right inferior PV closure time	25	0	300	178.40	115.603	240.00
Right common PV closure time	25	0	300	67.40	114.101	0.00
Valid *n* (listwise)	25					

Table 3. Variation in measurement results in all the PVs

Variables	*No.*	*Mean*	*SD*	*Mean rank*
Left				
PV diameter (mm)				
Superior	16	13.681	3.7561	18.88
Inferior	16	12.531	5.9864	17.38
Common	9	18.022	4.0871	31.22
Total	41	14.185	5.1555	
PO_2 after PV closure (mmHg)				
Superior	16	76.712	10.9533	24.22
Inferior	16	67.069	30.0218	23.34
Common	9	54.167	22.7513	11.11
Total	41	68.000	23.6700	
Differentiation of PO_2 after PV closure compared to basal PO_2 (mmHg)				
Superior	16	14.456	9.4267	21.91
Inferior	16	9.475	7.4388	15.50
Common	9	18.800	7.5612	29.17
Total	41	13.466	8.8698	
Closure heat of PV				
Superior	16	–44.500	15.7438	17.47
Inferior	16	–43.000	11.0272	24.66
Common	9	–39.778	20.6747	20.78
Total	41	–42.878	15.0751	
Difference of closure heat from basal heat				
Superior	16	12.938	5.4829	25.78
Inferior	16	8.125	4.8010	16.09
Common	9	10.778	6.4571	21.22
Total	41	10.585	5.7357	
Right				
PV diameter (mm)				
Superior	18	15.906	2.5152	26.53
Inferior	18	13.878	3.2580	17.97
Common	7	13.914	5.7571	20.71
Total	43	14.733	3.5506	
PO_2 after PV closure (mmHg)				
Superior	18	62.011	23.7394	23.17
Inferior	18	56.572	27.3202	20.44
Common	7	66.257	9.8651	23.00
Total	43	60.426	23.6058	
Differentiation of PO_2 after PV closure compared to basal PO_2 (mmHg)				
Superior	18	15.883	11.1720	18.92
Inferior	18	19.322	9.9646	23.47
Common	7	21.500	13.3671	26.14
Total	43	18.237	10.9949	
PV closure heat				
Superior	18	–46.833	15.9494	19.92
Inferior	18	–40.944	20.0249	25.06
Common	7	–46.143	19.0388	19.50
Total	43	–44.256	18.0332	
Difference of closure heat from basal heat				
Superior	18	14.833	7.2457	25.53
Inferior	18	12.944	6.5572	20.22
Common	7	10.143	7.9042	17.50
Total	43	13.279	7.0923	

Kruskal–Wallis test, $p < 0.05$.

PV was 12.944 ± 6.5572°C and the right common PV was 10.143 ± 7.9042°C.

Table 4 shows the relationship of PO_2 changes with PV diameter and heat difference. There was no significant relationship of PO_2 changes with the left or right superior, inferior and common PV diameters ($p > 0.05$). On the other hand, the heat difference of the left superior ($r = 0.617$; $p = 0.011$), right superior ($r = 0.535$; $p = 0.049$), right common ($r = 0.900$; $p = 0.037$) and total PV ($r = 0.552$; $p = 0.001$) positively correlated with the PO_2 change.

Table 4. Relationship of PO_2 changes with PV diameter and heat difference

	PO_2 change		
Variables	n	r	p-*value*
PV diameter (mm)			
Left superior	16	0.380	0.235
Left inferior	16	–0.024	0.931
Left common	9	0.233	0.546
Right superior	18	–0.161	0.522
Right inferior	18	–0.003	0.992
Right common	7	–0.536	0.215
Total	84	0.231	0.068
Heat difference			
Left superior	16	0.617	0.011*
Left inferior	16	0.081	0.776
Left common	9	0.335	0.379
Right superior	18	0.535	0.049*
Right inferior	18	0.284	0.253
Right common	7	0.900	0.558
Total	84	0.552	0.001*

There was no statistically significant relationship between the PO_2 change and the PV diameter ($r = 0.211$; $p = 0.054$). There was no statistically significant relationship between the heat difference and the PV diameter ($r = 0.131$; $p = 0.23$). According to Fig. 2, a statistically significant positive correlation was found at the 55.8% level between total PV heat differences and PO_2 changes ($r = 0.558$; $p = 0.00$; $p < 0.01$).

The anti-arrhythmic treatment received by the patients and their compliance with the treatment were not followed up. All patients had symptomatic improvement.

Discussion

Paroxysmal AF constitutes 35–40% of patients admitted to hospital with AF and its frequency in the general population is equal to permanent AF and perhaps even more.[7] Although the exact molecular mechanism of paroxysmal AF is poorly understood, some changes in atrial structure and function with the effect of some genetic factors, aging, circulation system or

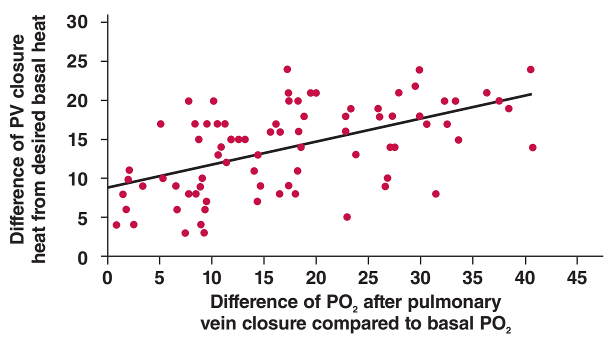

Fig. 2. The relationship between total PV heat differences and PO_2 changes (correlation: $r = 0.558$; $p = 0.00$).

metabolic diseases are thought to form an ectopic activity in the atrium that predisposes to this disorder.[8]

PVs have a strong potential to induce tachyarrhythmias in patients with paroxysmal AF. For this reason, cryoablation results in a prolonged AF cycle length and return to sinus rhythm in patients with paroxysmal AF, which provides comparable results with radiofrequency ablation.[9,10]

Catheter ablation of AF carries a significant risk of major complications.[11] The most common ones are: oesophageal injury (< 0.5%), periprocedural stroke (< 1%), tamponade (1–2%), PV stenosis (< 1%), phrenic nerve palsy (1–2%), vascular complications (2–4%) and asymptomatic cerebral embolism (5–20%).

In a study reporting the results of over 1 000 ablation procedures performed in high-volume centres throughout Europe, the rates of acute severe complications were 0.6% stroke, 1.3% tamponade, 1.3% peripheral vascular complications and around 2% pericarditis.[12] In the current study, no complications developed in the patients. This may have been due to the use of 28-mm balloons, the small number of patients or the experience of the centre.

Recurrence has been reported with a frequency of 20–30% after AF treatment with the cryoablation technique.[13] In the meta-analysis of 23 studies, it was found that 98% of the patients had complete PV isolation. Disregarding the first three-month period, a one-year success rate was observed in 73% of patients with paroxysmal AF and 45.1% in the persistent AF group.[14] The most common cause of recurrence of AF after cryoablation is reconnection of atrial tissue with PV potentials, especially in the inferior veins.[15]

There are few acknowledged criteria for determining the success of cryoablation. The best known is the length of the period without any relapse. Studies demonstrated that with a follow up of 12 months, the rate of relapse-free cases was 65.6% after cryoablation and 60.01% with radiofrequency ablation.[10]

The visual evaluation of PV occlusion quality after positioning the cryoballoon is a criterion for the success of the operation.[16] Siklody *et al*. reported that complete vein occlusion, as assessed by TEE performed during the procedure, was associated with acute procedure success.[11] PV occlusion can also be detected by intracardiac echocardiography,[17] but it is more expensive and has more complications. Although angiography is the commonly used method to show complete tissue contact and complete occlusion, complete occlusion may not continue during cooling, and this cannot be evaluated by angiography.

In previous studies, the relationship between temperature parameters and acute or late reconnection was evaluated and determined as effective parameters in predicting the success of the procedure. Dorwarth *et al*. investigated real-time recordings and reported a relationship between time of cooling and reconnection.[18] In the study, PV isolation time over 83 seconds was found to be associated with early reconnection and they reported that achieving rapid PV isolation predicted a permanent isolation. On the other hand, in the study of Ghosh *et al.*, a relationship was found between the cooling rate and late reconnection, but it was not reported as an independent predictor.[19]

Fürnkranz *et al.* demonstrated that the minimum temperature reached of –39°C and above for the inferior veins and –42°C and above for the superior veins were associated with acute reconnection.[20] The cryoballoon temperature parameters are automatically recorded during cooling. This is affected by the occlusion of the balloon of the treated PV, because the retention of blood flow in the PV causes a warming effect in the cryoballoon. This situation can be observed with a decrease in temperature after closing the inferior space with the pull-down manoeuvre. In this context, cryoballoon temperature parameters can provide information about balloon–tissue contact.

Deubner *et al*. investigated the relationship between the rapidity of temperature drop in PVs during cryoballoon use and the success of rapid PV isolation.[21] They reported that the –1.41°C/s or higher steepness of the slope of the temperature–time curve was the parameter for a successful cryo-application.

In our study, we aimed to investigate two parameters: the occluded PV diameters and the heat difference from the threshold temperature (–36°C) that can be effective on PO_2 values measured in the LA during PV isolation, which are thought to reflect cryoablation success and AF recurrence after the procedure. The basis of the study was the knowledge that the better the PV is closed, the more successful the process is, and the decrease in the PO_2 value noted in the LA reflects the success of closure of the PV.

We determined that none of the occluded PV diameters were significantly related to the PO_2 decrease in the LA during the procedure. However the heat difference in some of the PVs (superior left, superior right, common right and total PVs) were significantly related to the PO_2 decrease in the LA during the procedure. In addition, when each patient was evaluated separately, a significant and positive correlation was found between temperature difference and PO_2 change, but no significant correlation was found between the PV diameter and PO_2 change.

Our study is the first study to investigate the relationship between PO_2 change measured in the LA during the procedure as a parameter that can predict the cryoablation success and post-procedure AF recurrence, and the temperature difference (high cooling temperatures), which is another parameter accepted as an indicator of success. We showed for the first time that the change in PO_2 values can be used as a parameter to determine the success of the cryoablation procedure, since high cooling temperatures indicate the success of the procedure. However, large-scale supportive studies are needed to support this theory more clearly.

There were two limitations to the study. We did not determine a cut-off value for PO_2 changes to indicate successful ablation. The anti-arrhythmic treatment received by the patients and their compliance with the treatment were not followed up.

Conclusions

This study is the first to investigate the relationship between PO_2 change, measured in the LA during the procedure, as a parameter that can predict the cryoablation success and post-procedure AF recurrence, and the temperature difference, which is another parameter accepted as an indicator of success.

We showed that the change in PO_2 can be used as a parameter to indicate the success of the cryoablation procedure, since high cooling temperatures indicate the success of the procedure. With this blood gas study, we indicated complete closure of the PVs by partial reduction in the contrast ratio. Larger studies are needed to confirm the results of this study.

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