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

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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

Atrial fibrillation (AF) is the most common cardiac arrhythmia, 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 propafenon) 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.4

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: chronic 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
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 PO2 value in the blood gases obtained from the LA before the PV closure and the PO2 values in the blood gases obtained from the LA during the temporary closure of each PV was termed the PO2 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 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 PO2 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 PO2 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 10.774 ± 5.671°C, the superior right PV averaged 14.833 ± 7.2457°C, the inferior right

![Fig. 1. Pulmonary vein measurement.](image)
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.

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 ($r = 0.558; p = 0.00; p < 0.01$).

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. 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: $r = 0.558; p = 0.00$).](image-url)
metabolic diseases are thought to form an ectopic activity in the atrium that predisposes to this disorder.1

PVs have a strong potential to induce tachyarrhythmias in patients with paroxysmal AF. For this reason, cryoballoon ablation results in a prolonged AF cycle length and return to sinus rhythm in patients with paroxysmal AF, which provides comparable results with radiofrequency ablation.18

Catheter ablation of AF carries a significant risk of major complications.1 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.2 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.

Reurrence has been reported with a frequency of 20–30% after AF treatment with the cryoablation technique.1 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.3 The most common cause of recurrence of AF after cryoablation is reconnection of atrial tissue with PV potentials, especially in the inferior veins.4

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 were 65.6% after cryoablation and 60.01% with radiofrequency ablation.5 The visual evaluation of PV occlusion quality after positioning the cryoballoon is a criterion for the success of the operation.6 Siklody et al. reported that complete vein occlusion, as assessed by TEE performed during the procedure, was associated with acute procedure success.7 PV occlusion can also be detected by intracardiac echocardiography,7 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.8 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.9

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.10 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.11 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 PO2 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 PO2 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 PO2 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 PO2 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 PO2 change, but no significant correlation was found between the PV diameter and PO2 change.

Our study is the first study to investigate the relationship between PO2 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 PO2 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 PO2 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 PO2 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 PO2 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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References


