

# THE INFLUENCE OF PULMONARY VEIN ANATOMY ON OUTCOMES AFTER ABLATION OF PAROXYSMAL ATRIAL FIBRILLATION

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The authors declare no potential  
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## Abstract

**Background.** Pulmonary vein isolation is the cornerstone of catheter-based treatment for atrial fibrillation. Cryoballoon ablation offers an effective and reproducible method for pulmonary vein isolation, yet recurrence of arrhythmias remains a challenge. Despite advances in catheter technologies, the role of altered pulmonary vein anatomy as a factor for atrial fibrillation recurrence is poorly studied.

**Materials and Methods.** This prospective study included 465 patients with paroxysmal atrial fibrillation who underwent cryoballoon ablation. Pulmonary vein and left atrial anatomy were evaluated using multislice computed tomography. Patients were followed for 24–48 months to assess atrial fibrillation recurrence and anatomical risk factors. Cox proportional hazard modeling and Kaplan-Meier analysis were used to evaluate predictors of arrhythmia recurrence.

**Results.** Complete Pulmonary vein isolation was achieved in all patients. During follow-up, 38% of patients experienced atrial fibrillation recurrence. Patients with altered pulmonary vein anatomy, particularly a left common pulmonary vein and additional pulmonary veins, showed a higher rate of recurrence. Cox regression analysis identified left atrial volume index >50 mL/m<sup>2</sup> and pathological pulmonary vein anatomy as independent risk factors for atrial fibrillation recurrence.

**Conclusion.** Altered pulmonary vein anatomy is a significant risk factor for atrial fibrillation recurrence following cryoballoon ablation. Comprehensive imaging of the left atrial and pulmonary vein using multislice computed tomography can improve patient selection, reducing the recurrence risk and improving long-term outcomes.

## Introduction

The cornerstone of catheter-based treatment of atrial fibrillation (AF) is pulmonary vein isolation (PVI).<sup>1</sup> Over the last few decades, all catheter technologies have targeted specifically the PVI, standard catheter RFA based on sequential 'point by point' applications and the later developed ('single shot'-technology) cryoballoon ablation (CBA).<sup>1,2</sup> Due to the

fact that arrhythmias initial foci of are often found at the ostium of the pulmonary veins (PV), primary triggers are due to stretching of the cardiac muscle at the level of the pulmonary vein junction with the left atrium (LA).<sup>3</sup>

Cryoballoon pulmonary vein isolation (CBA) is an effective treatment for atrial fibrillation (AF).<sup>4-6</sup> CBA is a competitive alternative to radiofrequency (RFA) abla-

tion with its short procedure time, rapid learning curve, and a high reproducibility of the method. Despite advancements in catheter-based therapies and operator experience, arrhythmia recurrence remains an unsolved problem.

Numerous studies still continue to investigate the prerequisites for the success of catheter-based treatment of AF, such as comorbidities, type of AF, and LA size.<sup>7-9</sup> However, PV anatomy as a potential factor is poorly studied.

Altered PV anatomy is an important factor predisposing to arrhythmia recurrence after successful PV isolation. Consideration of PV anatomy as a prognostic factor for the maintenance of sinus rhythm after ablation would help electrophysiologists determine further patient management, reduce unessential procedures, and minimize costs.

This study aimed to evaluate the significance of selected anatomical features of pulmonary veins in predicting the development of arrhythmia recurrence after cryoballoon ablation of pulmonary veins (CBA-PV) for paroxysmal AF.

#### Materials and Methods

**Study population.** In this prospective, controlled study 465 of whom 61% were male consecutive patients with paroxysmal AF (57±11 years) were included and analyzed. Patients with paroxysmal AF for whom a minimum of 2 class I-III antiarrhythmic drugs were not effective were included in the study. Exclusion criteria were as follows: left atrial (LA) dimensions >5.0 cm, left ventricular ejection fraction <40%, New York Heart Association functional class III or IV heart failure, chronic heart failure requiring intervention, stroke or transient ischemic attack within 6 months, previous LA ablation or surgery for AF, prosthetic heart valve, more than 1 cardioversion within 2 years, or implantable cardiac devices. All patients underwent CBA of PV between 2021 and 2023.

**Multislice computed tomography.** LV and LA anatomy were evaluated in all patients using multislice computed tomography (MSCT) (Aquilion, Toshiba, Japan) before the CBA of PV. The anatomy of PV and LA were assessed in all patients using multislice computed tomography (MSCT) (Aquilion, Toshiba,

Japan) before the CBA PV procedure. Initially, 3-dimensional images of the anatomical structures of the LA and PV were obtained, followed by a quantitative calculation of the LA volume index of body surface area. The normal anatomical structure of the PV is characterized by two left and two right branches, with no abrupt branching up to 2-3 cm before flowing into the LA. Any deviation from this norm was considered if a common collector of any side (more often on the left) or additional pulmonary veins were identified.<sup>10</sup> Left common collector (LCPV) was typically defined when the left ipsilateral PVs were connected by a common trunk before entering the LA. An additional PV was identified if it flowed into the PV separately from the typical superior and inferior PVs.

**Cryoablation procedure.** Cryoballoon isolation of the PV was carried out with local anesthesia and sedation using propofol and, if needed, fentanyl. First, a diagnostic catheter was guided from the femoral access into the coronary sinus. Then, a transseptal puncture was performed using a BRK-1 needle delivered inside a long Preface introducer. Heparin was administered at a rate of 100 units/kg, ensuring that the activated clotting time reached a value of at least 300 seconds. Subsequently, the entire system was replaced by a 15 Fr FlexCath controlled delivery system. Using this delivery system, a 28-mm cryoballoon catheter and a diagnostic 8-pole circular-tipped catheter were inserted into each PV, achieving electrical isolation of all four main PVs.

During the ablation of the right PV, pacing of the phrenic nerve was performed to prevent phrenic nerve palsy, using a guided diagnostic catheter. The necessary occlusion of the isolated PV was confirmed by contrast accumulation in the corresponding PV, and the cooling temperature was brought down to -50 to -60 degrees below Celsius for 180 to 240 minutes. If good occlusion of the PV and PV isolation was achieved within 30 seconds, the ablation of 180 seconds was sufficient. The endpoint was a confirmation of bidirectional block from the PV to the LA.

**Postablation management and follow-up.** After the ablation procedure, all patients were followed up for 24-48

months to assess the effect of pathological change in LV anatomy on the development of recurrences in the long-term follow-up period. Each patient had regular check-ups at 3, 6, 12, 18 and 24 months, and then twice a year. At each follow-up visit, patients were examined for the presence of any signs of AF and any reported arrhythmia recurrences. Additionally, to reveal any recurrences, whether symptomatic or asymptomatic they underwent 24-hour ambulatory Holter ECG monitoring. Any recorded episode of atrial arrhythmia lasting more than 30 seconds was considered as a recurrence. Episodes of atrial arrhythmia during the blanking period were not included as primary endpoints and were not considered chronic treatment failures.

**Treatment endpoint.** The primary goal of the study was to assess the success of the treatment. This success by the absence of: 1) any detectable arrhythmia after a blinded period, 2) use of an unspecified, antiarrhythmic drug, and 3) any off-protocol intervention for AF (such as cardioversion and ablation). Additionally, maintaining sinus rhythm after ablation with a previously ineffective antiarrhythmic drug at the same or lower dose was considered successful.

**Ethical approval.** Patients will be selected with informed consent. The study protocol was approved by the Local Ethical Commission of the Syzganov National Centre of Surgery with №4 on 10.11.2023.

**Statistical analysis.** The results for continuous variables are present-

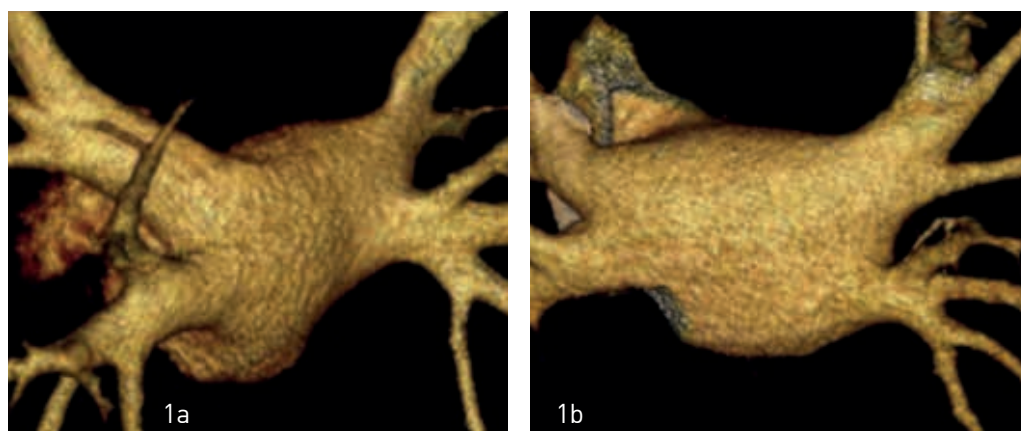
ed as the arithmetic mean  $\pm$  standard deviation. To compare mean values the Mann-Whitney U-test based on the distribution of the values was used. Cox proportional hazard model was used to estimate risk ratios (RR) and their corresponding 95% confidence intervals (CI) for independent predictors of arrhythmia recurrence. Distant outcomes were illustrated using the Kaplan-Meier curve, and the log-rank test was performed to show the significance of differences in values. To establish differences between groups proportional hazard models were used. The primary efficacy endpoint was evaluated using Fisher's two-sided exact criterion of binomial proportions. Statistical analyses were conducted using IBM SPSS Statistics-19 software.

### Results

Complete isolation of the PV ostium was successful in all patients. Of the 465 patients, 298 (64%) showed normal LA and PV anatomy, while 167 (36%) displayed pathological alterations of PV. Over the 24–48-month follow-up, 178 patients (38%) experienced a recurrence of AF. Those with recurrent AF primarily exhibited enlarged right (RSPV) and left superior (LSPV) PV ( $p < 0.001$ ) as shown in Figure 1. The presence of left common PV (LCPV) ( $n = 126$ , Log-rank  $p < 0.001$ ) and additional right pulmonary veins rPV ( $n = 67$ , Log-rank  $p < 0.001$ ) were associated with early development of sustained arrhythmia recurrences. Table № 1 presents the comparison between the group with recurrence and the group without recurrence.

Figure 1a. LSPV

Figure 1b. RSPV



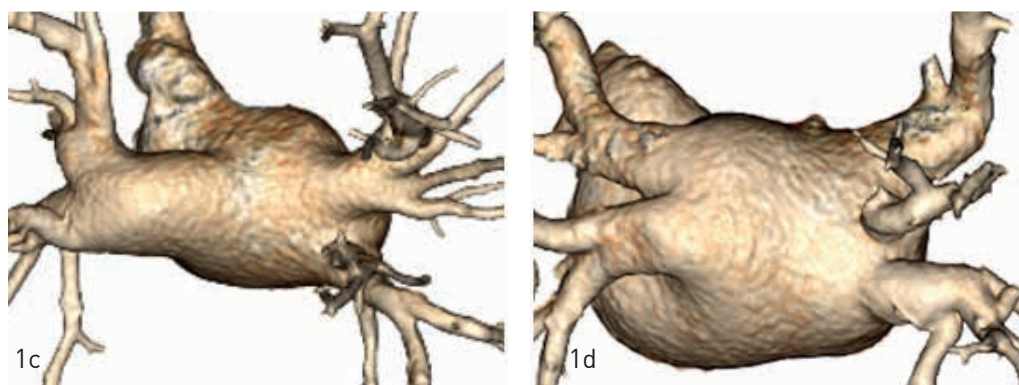


Figure 1c. LCPV

Figure 1d. rPV

Figure №1. MSCT images of the left atrium and pulmonary veins with pathologic changes. 30% of patients had enlarged LSPV – 1a, 20% of patients had enlarged RSPV – 1b, 12% of patients had left common LCPV – 1c, 6% of patients had right accessory rPV – 1d.

Table № 1 presents the comparison between the group with recurrence and the group without recurrence.

№		No recurrence (n=287)	Recurrence (n=178)	p
1	Age (yrs)	56 ± 10,2	58 ± 9,5	0,312
2	Male, n (%)	180 (63%)	104 (59%)	0,572
3	Hypertension, n (%)	138 (48%)	98 (55%)	0,784
4	Diabetes, n (%)	23 (8%)	19 (11%)	0,321
5	Structural heart disease, n (%)	75 (26%)	87 (49%)	0,225
6	Coronary heart disease, n (%)	39 (14%)	27 (15%)	0,741
7	LA diameter (mm)	39 ± 7	42 ± 6	0,02
8	LA volume index (mL/m <sup>2</sup> )	47 ± 9	53 ± 7	0,005
9	Normal PV anatomy, n (%)	238 (83%)	60 (34%)	0,1
10	Patholog PV anatomy, n (%)	49 (17%)	118 (66%)	0,05

Table 1. Clinical characteristics of patients. LA – left atrium, PV – pulmonary vein.

The LA volume index was remarkably greater in the group with recurrence than in the group without recurrence. For a more accurate assessment of the risk of AF recurrence, we calculated a cut-off value of 50 (mL/m<sup>2</sup>) for the LA volume index.

In terms of PV anatomy, the number of patients with pathologic anatomy was notably greater in the recurrence

group compared to the non-recurrence group [75 patients, 42.1% vs. 48 patients, 16.7%; p = 0.05].

As it can be seen in Kaplan-Meier analysis, the arrhythmia recurrence following the primary successful catheter ablation was remarkably higher in patients with pathologic PV anatomy (p = 0.001; see Figure 2).

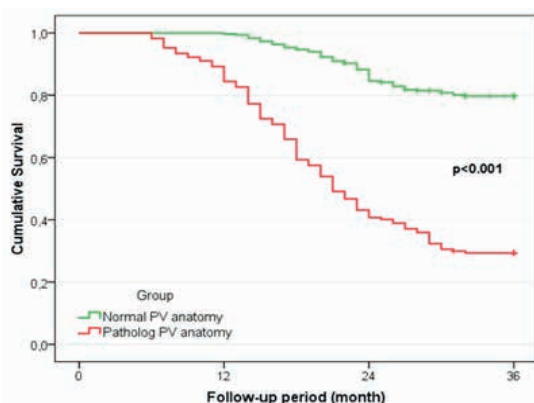


Figure 2. Kaplan-Meier analysis of freedom from AF recurrence in patients after ablation (pathologic PV vs. normal PV)



Figure №2. Kaplan–Meier analysis of freedom from AF recurrence in patients after ablation (pathologic PV vs. normal PV) during the 36-month follow-up period. Patients with pathologic PV anatomy 118 (66%) had more recurrences than those with normal PV anatomy 60 (34%). P-value <0.001.

In our study, Cox regression analysis was used to identify patterns associated with the risk of arrhythmia recurrence. In our initial analysis, we found statistically significant correlations with certain factors, such as left atrial (LA) volume index

greater than 50 (mL/m<sup>2</sup>) and pathological changes of PV anatomy. These factors were then used to create multiple models through multivariate analysis. We observed that arrhythmia recurrence (p < 0.001) was more common in patients with an LA volume index greater than 50 (mL/m<sup>2</sup>). While all the variables were highly correlated, PV pathological anatomy and increased LA volume showed the strongest correlation (see Table 2). Importantly, we found that both of these factors are independent risk factors for arrhythmia recurrence

**Table 2.**  
Multivariate analysis for arrhythmia recurrence. The most consistent patterns included: pathological PV anatomy and high LA volume index.

Patterns	B	P	HR	95% CI for HR
<b>Pathologic PV anatomy</b>	0,75	0,04	1,8	0,97 – 3,95
<b>LA volume index (ml/m<sup>2</sup>)</b>	1,29	0,005	3,15	1,39 – 5,97

**Complications.** In our study, phrenic nerve palsy (PNP) was also the most common complication with an incidence of 2.9%. PNP is reversible to some extent, and can usually recover within the procedure or a few days afterwards, and in some cases within a few months. Additionally, the incidence of PNP decreases with experience gain.

Hemopericardium was noted in 9 (1.9%) patients, which was immediately resolved by pericardiocentesis and evacuation of blood from the pericardial cavity. There were no fatal complications such as stroke, atrio-esophageal fistula or death. The incidence of complications related to the access site during femoral puncture was 2.7. No other unforeseen complications were identified during the entire follow-up period.

#### Discussion

In recent years, catheter-based ablation (CBA) has become a well-deserved treatment option for patients with symptomatic AF. As previously reported, depending on the CBA approach, efficacy rates range from 60 to 80% for paroxysmal AF.<sup>11</sup> This study demonstrated an efficacy rate of 62% for paroxysmal AF. Persistent forms of CBA showed efficacy rates of 50–60% in the long term.<sup>5,12</sup>

Pathologically altered anatomy of the PV has a significant impact on the development of atrial fibrillation pathophysiology. Past studies have confirmed this association.<sup>13,14</sup> In our study, 64.1%

of patients had the classic anatomy with four PVs, which is consistent with recent research findings. The most common abnormalities in PV anatomy were a common left PV manifold (12.1%) and a variant involving an accessory right middle pulmonary vein (5.8%), making up 35.9% of the total cases. An article by Anselmino et al. also emphasized the common left PV manifold as the most prevalent variant in patients with atrial fibrillation.<sup>15</sup> However, another study reported that the typical four PV anatomy was only found in a minority of atrial fibrillation patients (30%). This discrepancy might be due to variations in sample sizes, as a study with 40 patients reported one outcome, while another study with 473 patients found that the typical anatomy was present in no more than 39% of cases, with most patients exhibiting altered PV anatomy.<sup>16</sup>

The pathological changes in the PV and how often they occur in patients with and without AF have been the subject of numerous studies. The findings indicate that atypical pulmonary vein anatomy is remarkably associated with the AF development.<sup>17,18</sup>

Our study revealed that patients with altered PV anatomy had a higher risk of AF recurrence compared to patients with normal LV anatomy. These findings have significant implications for the long-term outcome of cryoballoon ablation. In a recent follow-up, it was found that

patients with normal PV anatomy had a similar AF recurrence rate as those with a left common PV (67% vs. 50%). Another study, which used radiofrequency ablation, reported similar results. It demonstrated a significantly higher recurrence rate of AF in patients with abnormal PV anatomy compared to those with normal PV anatomy.<sup>19</sup>

Additionally, altered PV anatomy seemed to have prognostic significance for arrhythmia recurrence, regardless of the ablation system used. This effect was more noticeable in paroxysmal atrial fibrillation (AF). However, in the recent STOP-AF study, it was found that the variation in PV anatomy did not affect the absence of arrhythmia recurrence after cryoballoon ablation (CBA).<sup>20</sup> Furthermore, two recent studies also indicated that the presence of a common PV manifold was not prognostically significant for arrhythmia recurrence.<sup>21,22</sup>

Despite the extensive research on the outcomes of catheter ablation, identifying new predictors of arrhythmia recurrence is crucial for better patient selection and long-term outcome prediction. It is particularly important to carefully monitor patients with altered PV and LA anatomy and schedule them for repeat catheter ablation as necessary. This approach can help predict the maintenance of normal sinus rhythm without recurrence of arrhythmias for many years.

All studies show that phrenic nerve palsy is the major complication associated with CBA, occurring in the range of 2.7-12.7%.<sup>23,24</sup> In this study, using a 24-hour Holter recording for rhythm monitoring in patients may have been a major limitation. This method of monitoring might not detect symptom-free episodes of paroxysmal atrial fibrillation. We had to use this method because many patients could not be given long-term ECG recording devices.

**Limitations:** The study used 24-hour Holter ECG monitoring, which may not be sufficient to capture asymptomatic short paroxysms, but is more accessible and convenient for a large cohort of patients. Also, this study describes the experience of one center and we can't generalize the findings of this research. Future research with a larger number of

studies and more standardized methodologies would be beneficial to confirm and extend these findings.

**What's known?** Pulmonary vein isolation is a well-established treatment for atrial fibrillation, with catheter-based methods like radiofrequency ablation and cryoballoon ablation being widely used. CBA, in particular, is known for its shorter procedure time, ease of use, and reproducibility. Despite advancements in these techniques, arrhythmia recurrence remains a significant issue for many patients. Previous studies have investigated various factors, such as comorbidities, AF type, and left atrial size, which contribute to the recurrence risk after ablation. However, the impact of anatomical variations in the pulmonary veins on AF recurrence has been less thoroughly examined.

**What's new?** This study provides new insights into the role of altered pulmonary vein anatomy as a predictor of AF recurrence following cryoballoon ablation. It highlights that specific anatomical features, such as the presence of a left common pulmonary vein and additional pulmonary veins, significantly increase the likelihood of AF recurrence. By identifying these anatomical variations through multislice computed tomography, arrhythmologists can better assess the risk of recurrence and tailor post-ablation management strategies. This study emphasizes the importance of incorporating PV anatomy as a prognostic factor in the treatment of AF to improve long-term outcomes.

#### **Conclusion**

Altered PV anatomy is a risk factor for arrhythmia recurrence after CBA of PV. Mandatory imaging of the LA and PV with MSCT improves patient selection for effective catheter-based treatment of atrial fibrillation.

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U.A.: Statistical analysis, methodology. B.K., O.N.: Data curation. S.A.: Supervision. B.N.: Investigation. Y.A.: Conceptualization. M.Zh.: Visualization. All authors approved the final version of the manuscript

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