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Pulmonary vein anatomy and its variations in a Turkish atrial fibrillation cohort undergoing cryoballoon-based catheter ablation

Kriyobalon ile atriyum fibrilasyonu ablasyonu yapılan Türk kohortunda pulmoner ven anatomisi ve varyasyonları

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ABSTRACT

Objective: Pulmonary vein (PV) anatomy has drawn attention since assumption that atrial fibrillation (AF) may originate from PVs and that electrical isolation of PVs may be beneficial in eliminating these triggers. The present study aims to investigate PV anatomy and its variations in a sample of Turkish patients undergoing PV isolation (PVI) for AF.

Methods: 250 patients underwent multidetector computed tomography before cryoballoon-based PVI for AF. PV and left atrial (LA) anatomy were evaluated in 3-dimensional epicardial reconstructions.

Results: 980 PVs were observed. All PVs drained into the LA. Mean superoinferior (SI) dimension for each vein was significantly larger than mean anteroposterior (AP) dimension. Accessory PVs were only seen on right side. Accessory veins were significantly smaller in both AP and SI diameter than other veins. Right-sided PV ostia were more round. Expected anatomy of 2 atrial ostia for right upper and lower lobe veins on each side was seen in 94.8% of patients. Remainder had other variant anatomy in right PVs. Conjoined ostium in the LA was seen in 35.6% of patients.

Conclusion: PV variations were common in Turkish AF cohort undergoing PVI, which may be important to know about prior to ablation therapy for procedural success.

ÖZET

Amaç: Atriyum fibrilasyonunun (AF) pulmoner venlerden (PV) köken alabildiği ve bu odakların ablasyon ile ortadan kaldırılabildiğinin öğrenilmesi üzerine PV anatomisine duyulan merak artmıştır. Bu çalışmada, AF için PV izolasyonu (PVI) yapılan Türk hasta popülasyonunda PV anatomisi ve varyasyonlarının gösterilmesi hedeflenmektedir.

Yöntemler: AF için kriyobalon ile PVI yapılması planlanan 250 hastaya, işlem öncesinde çok kesitli bilgisayarlı tomografi yapıldı. PV ve sol atriyum (LA) anatomisi üç boyutlu epikardiyal rekonstrüksiyonlar üzerinde incelendi.

Bulgular: Toplam 980 PV gözlendi, hepsinin sol atriyuma açıldığı görüldü. Venlerin ortalama süperoinferiyor (SI) çapları ortalama ön-arka (AP) çaplarına kıyasla anlamlı olarak daha büyük saptandı. Aksesuvar PV'ler yalnızca sağ tarafta görüldü. Aksesuvar venlerin SI ve AP çapları, diğer venlerinkine kıyasla anlamlı olarak daha küçüktü. Sağ taraflı PV'lerin ostiyumları daha yuvarlaktı. Hastaların %94.8'inde sağ üst ve alt lob venleri beklenildiği üzere iki ayrı ostiyum ile LA'ya açılmaktaydı. Geri kalan hastalarda anatomik varyasyon, sağ PV'lerde gözlendi. LA'ya PV'lerin ortak ostiyum aracılığıyla açılma, hastaların %35.6'sında görüldü.

Sonuç: Türk toplumunda PV anatomisinde çeşitlilikler sıklıkla görüldüğünden, PVI öncesi PV anatomisinin detaylı değerlendirilmesi ablasyon tedavisinin başarısı için önemli olabilir.

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Atrial fibrillation (AF) has been shown to be initiated by triggers originating from ectopic foci located within and/or in close proximity to the pulmonary veins (PVs).[1] Sleeves of atrial myocardium extending into the PVs have been suggested to contribute to arrhythmogenesis.[2,3] This assumption provided the basis for catheter-based ablation strategies. Different ablation technologies use either radiofrequency[4] or cryo-energy[5–7] for electrical isolation of the PVs.[8] Accordingly, understanding both expected and variant PV anatomy has drawn significant interest.[9,10]

In addition to its role in diagnosis of coronary arterial anatomy,[11] multidetector computed tomography (MDCT) angiography has the ability to demonstrate PV drainage pattern and identify variations.[9,12] Therefore, it has gained recognition as a preprocedural imaging tool used to improve periprocedural outcomes in patients scheduled for AF ablation.

The aim of the present study was to investigate PV anatomy and its variations in a sample of Turkish patients undergoing PV isolation (PVI) for AF.

METHODS

Study population

Data of 250 patients with drug-refractory AF who underwent MDCT angiography to evaluate PV and left atrial (LA) anatomy before undergoing cryoballoon-based catheter ablation between September 2009 and June 2014 were retrospectively analyzed.

All patients had symptomatic paroxysmal or persistent AF, and failed antiarrhythmic drug therapy. Patients who had episodes of AF lasting longer than 7 days were defined as persistent, and those whose episodes terminated within 7 days were defined as paroxysmal AF.[13]

Patients who had moderate to severe valvular disease, LA anteroposterior (AP) diameter >55 mm, thrombus in LA, contraindication to anticoagulation or abnormal thyroid function were excluded. Furthermore, patients with known allergy to iodinated contrast agent or renal failure (defined as glomerular filtration rate <30 mL/min) were not included.

Detailed medical history regarding AF and related cardiovascular conditions was taken from all patients. Symptomatic severity was recorded according to European Heart Rhythm Association score.[13]

The study was conducted in compliance with the principles outlined in the Declaration of Helsinki and approved by Hacettepe University Non-Interventional Clinical Research Ethics Board.

Abbreviations:

AF	*Atrial fibrillation*
AP	*Anteroposterior*
LA	*Left atrium*
OI	*Ostium index*
PV	*Pulmonary vein*
PVI	*Pulmonary vein isolation*
MDCT	*Multidetector computed tomography*
SI	*Superoinferior*

Image acquisition

All patients underwent MDCT imaging using dual-source, 64-slice scanner (SOMATOM Definition AS, Siemens Healthcare, Erlangen, Germany) as previously described.[14]

Image analysis

Images were retrieved from the hospital picture archiving and communication system and retrospectively analyzed by an experienced radiologist. Anatomy of the PVs and their insertion to the LA on 3-dimensional epicardial reconstructions [in 3 different orthogonal planes (transverse, sagittal, and coronal) or with angulated multiplanar reformatting] were examined. PV ostial anteroposterior (AP) and superoinferior (SI) dimensions were measured using multiplanar reformatting so that each measurement was taken as the vein entered LA in perpendicular direction. PV ovality was then assessed using ostium index (OI), which is calculated as AP dimension divided by SI

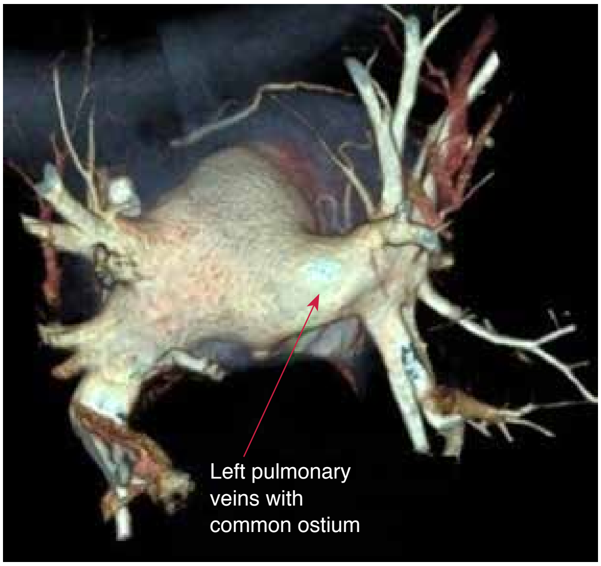

Figure 1. Anatomical variation of left pulmonary veins demonstrating a common ostium.

dimension. A ratio closer to 1.0 indicated a more circular vein.

Common (conjoined) ostium was defined as single atriopulmonary venous junction due to combination of superior and inferior veins proximally at distance ≥5 mm to the LA (Figure 1). Accessory PV was characterized as additional vein other than upper or lower lobe vein that entered the atrium via separate ostium. Accessory PVs were labeled according to the pulmonary lobe into which they drained (Figure 2).

Branching pattern of PVs was derived and classification of drainage was made according to previous study conducted by Marom et al.[15] Classification results are presented in Table 1.

Statistical analysis

Continuous variables are expressed as mean (± standard deviation) or median (min-max). Categorical variables are presented as number (percentage). Kolmogorov-Smirnov test was used to assess normality. For continuous variables, Student's t-test and Mann-

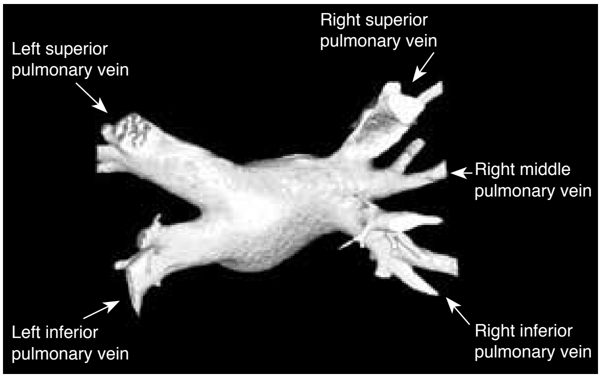

Figure 2. Anatomical variation of right pulmonary veins demonstrating a right-sided accessory pulmonary vein.

Table 1. Pulmonary venous drainage patterns of the study population (n=250)

Type	Definition	n	%
R1	Single common ostium in the left atrium receiving upper, middle, and lower lobe veins	8	3.2
R2a	Two atrial ostia for the upper and lower lobe veins, respectively; the middle lobe vein joins the proximal upper lobe vein less than 1 cm from the ostium	143	57.2
R2b	Two atrial ostia for the upper and lower lobe veins, respectively; the middle lobe vein joins the proximal upper lobe vein more than 1 cm from the ostium	90	36.0
R2c	Two atrial ostia for the upper and lower lobe veins, respectively; the middle lobe vein joins the lower lobe vein	4	1.6
R3a	Three atrial ostia for the upper, middle, and lower lobe veins, respectively	4	1.6
R3b	Three atrial ostia for the upper, superior segment, and lower lobe veins; the middle lobe vein joins the proximal upper lobe vein less than 1 cm from the ostium	0	0
R3c	Three atrial ostia for the upper, a basilar right lower lobe vein, and lower lobe veins; the middle lobe vein joins the proximal upper lobe vein less than 1 cm from the ostium	0	0
R4a	Four atrial ostia for one upper, two middle, and one lower lobe veins, respectively	0	0
R4b	Four atrial ostia for the upper, middle, superior segment, and lower lobe veins, respectively	0	0
R5	Five atrial ostia for one upper, two middle, 1 superior segment, and one lower lobe veins, respectively	1	0.4
L1a	Lower lobe vein joins upper lobe vein to form a common trunk vein less than 1 cm long that drains into the left atrium (one ostium)	63	25.2
L1b	Lower lobe vein joins upper lobe vein to form a common trunk vein more than 1 cm long that drains into the left atrium (one ostium)	26	10.4
L2a	Two atrial ostia for the upper and lower lobe veins, respectively; ostia are separated by left atrial wall	57	22.8
L2b	Two atrial ostia for the upper and lower lobe veins, respectively; ostia are not separated by left atrial wall	104	41.6

Whitney U test were used for inter-group comparisons. Chi-square test and Fisher's exact test were used for comparisons of categorical variables. Fisher's exact test was used in place of a chi-square test when 1 or more cells had an expected frequency of 5 or less. Two-tailed $p<0.05$ was considered statistically significant. Statistical analyses were performed using SPSS software, version 21.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Baseline characteristics of the study population are presented in Table 2. A total of 980 PVs were observed and evaluated (per patient, 4 [range: 3–6]). All PVs drained into the LA. Mean AP dimension, SI dimension, and OI values are provided in Table 3. Mean SI dimension for each type of vein was significantly larger than mean AP dimension ($p<0.001$). Mean AP and SI dimensions for right PVs were 16.20±3.56 mm and 18.61±4.54 mm, respectively. Mean AP and SI dimensions for left PVs were 13.51±3.21 mm and 17.37±4.05 mm, respectively. Accessory pulmonary veins were seen only on right side (n=15). Of those 15 accessory veins, 13 PVs drained right middle lobe and remaining 2 drained superior segment of right lower lobe. AP and SI diameters of accessory veins (AP: 7.31±2.90 mm; SI: 7.69±3.57 mm) were significantly smaller than dimensions of other veins ($p<0.001$). Right-sided PV ostia tended to be more circular (right OI: 0.88±0.12; left OI: 0.80±0.17; $p<0.001$).

Pulmonary venous drainage classification was performed according to Marom et al.[15] Drainage patterns are summarized in Table 1.

Most patients (n=237; 94.8%) had expected anatomy of 2 atrial ostia for right upper and lower lobe veins. Remaining patients (n=13; 5.2%) had variant

Table 2. **Baseline characteristics of the study population (n=250)**

Variables	n=250
Clinical parameters	
Age, years	55.65±11.07
Male gender	126 (50.40)
Duration of atrial fibrillation history, months	5 (1–36)
Non-paroxysmal atrial fibrillation	50 (20)
European Heart Rhythm Association score	3 (2–4)
Hypertension	115 (46)
Diabetes mellitus	36 (14.40)
History of coronary artery disease[a]	30 (12.0)
Dyslipidemia[b]	66 (26.40)
Chronic obstructive pulmonary disease	9 (3.60)
Current smoker	74 (29.60)
Alcohol consumption[c]	12 (4.80)
Echocardiographic parameters	
Left atrium diameter (mm)	38.6±4.8
Left ventricle end-diastolic diameter (mm)	45.3±2.4
Left ventricle ejection fraction (%)	65.0±2.0
Multidetector computed tomography angiography findings	
Total number of Pulmonary veins (n)	980
Total number of Pulmonary vein ostia (n)	800

Data are median (interquartile range), mean±SD, or n (%).
[a]Defined as previous history for ischemic heart disease.
[b]Dyslipidemia is defined as total cholesterol ≥200 mg/dL or treatment with lipid-lowering agent.
[c]Alcohol intake is defined as having up to 1 drink per day for women and up to 2 drinks per day for men; heavy drinkers and abusers were excluded.

Table 3. Ostial dimensions and index value of pulmonary veins

Pulmonary veins	Antero-posterior diameter (mm)	Supero-inferior diameter (mm)	Ostial index
	Mean±SD	Mean±SD	Mean±SD
Right pulmonary vein			
Upper	16.57±3.30	19.56±4.35	0.86±0.13
Lower	15.83±3.81	17.64±4.58	0.91±0.11
Both	16.20±3.56	18.61±4.54	0.88±0.12
Left pulmonary vein			
Upper	14.10±3.12	18.34±4.27	0.80±0.19
Lower	12.84±3.32	16.41±3.56	0.80±0.18
Both	13.51±3.21	17.37±4.05	0.80±0.17
Common ostium			
Right (n=8)	23.25±3.24	28.13±5.69	0.84±0.13
Left (n=89)	16.53±4.29	28.72±6.40	0.61±0.21
Accessory pulmonary veins			
Right (n=15)	7.31±2.90	7.69±3.57	1.03±0.34
Left (n=0)	–	–	–

SD: Stardard deviation.

anatomy. Four patients (1.6%) had 3 ostia, 1 (0.4%) had 5 ostia, and 8 (3.2%) had common ostium. In 1 case, 2 accessory right middle lobe veins and vein draining superior segment of lower lobe had separate ostia in LA. Otherwise, accessory veins shared common ostium with either right superior PV or right inferior PV. No case differed from Marom's classification of the right pulmonary venous ostium.

There were 161 (64.4%) patients with 2 ostia for left upper and lower lobe veins. Common trunk was seen in 89 (35.6%) patients. No case differed from Marom's classification of the left pulmonary venous ostium.

DISCUSSION

Knowing details of PV anatomy before catheter ablation may be helpful to facilitate anatomically based ablation procedure and improve outcomes.[10,15] Results of the present study demonstrate significant heterogeneity in PV anatomy of Turkish AF cohort undergoing cryoballoon-based PVI.

Anatomical variations in PVs occur due to under-incorporation or over-incorporation of the common PV into the left dorsal atrium during gestation.[16] Approximately 70% of the general population is known to have 4 PVs: right superior and inferior PVs and left superior and inferior PVs, and 4 independent ostia.[15,16] Variation of PV drainage and ostia has been reported to be more common on right side than left.[12,15] In our study, most patients (94.8%) had 2 ostia on right side for upper and lower lobe veins, while 64.4% of patients had 2 ostial patterns on the left. Wannasopha et al.[17] and Marom et al.[15] also reported most common drainage pattern of 2 ostia for right-sided PVs (90.3% and 71%, respectively).

Conjoined veins with common ostia have been reported to occur in 2.4% to 25% of the population[18,19] and are generally more common on the left than on the right. In our study, common ostia were also more common in left-sided PVs. However, 2 ostia on the left- side was still more common than common ostia in our study, in contrast to findings of Wannasopha et al.[17] In our study, prevalence of common ostium on the right side was 16%. Prevalence of common ostium on the right side was reported as 2% and 39% by Marom et al.[15] and Jongbloed et al.,[20] respectively.

Accessory veins have been encountered in 1.6% to 19% of the population.[10,21] Accessory PVs are reported to be separate veins often draining the right middle lobe or the superior segment of the right lower lobe. 28% of the population is known to have 3 to 5 pulmonary venous ostia on the right, usually due to 1 or 2 separate middle lobe vein ostia.[15,22] Right middle lobe vein has direct drainage into the LA in 23% of people, whereas it shares common ostium with the right superior PV or right inferior PV in 69% and 8% of people, respectively.[10] Superior segmental vein of the right lower lobe can also have separate ostium draining into the LA. In our study, accessory PVs were only seen on the right side, with a prevalence of 6%, and they predominantly drained the right middle lobe.

In the present study, right PV ostia were significantly more round than those on left, a finding consistent with results of previous studies.[12,20,23] Furthermore, SI dimensions of the veins were significantly larger than AP measurements, as reported in other studies.[12] Ostial diameter of accessory veins was significantly smaller than that of upper and lower veins.

Veno-atrial junction is electrically active and is regarded as site of arrhythmogenic foci responsible for initiation and maintenance of AF.[24] Left superior PV alone is believed to contribute to half of all ectopic beats leading to AF.[18] Marom et al.[15] reported that patients with separate ostia for the right middle lobe pulmonary vein (s) tended to have a higher frequency of atrial arrhythmia than those with other patterns.[15] Current ablation treatment for AF is focused on electrical isolation of these foci from the LA using either radiofrequency or cryoballoon techniques. In order to eliminate ostial remnants that contribute to AF, it is essential to know the number and branching pattern of PVs.

Variant PV anatomy has been associated with lower single-procedure efficacy.[25] In patients undergoing cryoballoon-based PV isolation for AF, presence of normal PV anatomy pattern was found to be associated with better AF-free survival compared with atypical PV anatomy with common left PV.[26] Furthermore, knowledge of ostial orientation and distance of branches from the ostia may help avoid complications, such as branch vessel stenosis.[27]

This study has some limitations. First, this study reflects those scheduled for PVI with cryoballoon and cannot be generalized to the general population. Second, further studies with larger study population are necessary to make more definitive statements. Lastly, impact of PV anatomical variation on long-term ablation outcomes should be investigated in large-scale studies with different ablation techniques.

In conclusion, MDCT angiography before AF ablation procedure is a useful non-invasive tool for assessment of PV anatomy. Pre-procedural knowledge of PV variations may help electrophysiologists facilitate ablation procedure and prevent periprocedural complications.

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Keywords: Atrial fibrillation ablation; computed tomography; pulmonary vein anatomy.

Anahtar sözcükler: Atrial fibrilasyon ablasyonu; bilgisaraylı tomografi; pulmoner venler anatomisi.