Cover Page



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# Chapter 6

Impact of pulmonary vein anatomy and left atrial dimensions on the outcome of circumferential radiofrequency catheter ablation for atrial fibrillation

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# Abstract

Background: Multi-slice computed tomography (MSCT) is commonly acquired prior to radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF) in order to plan and guide the procedure. Importantly, MSCT allows accurate measurement of left atrial (LA) and pulmonary vein (PV) dimensions and classification of PV anatomy. The aim of this study was to investigate the impact of LA dimensions, PV dimensions and PV anatomy on the outcome of circumferential RFCA for AF.

Methods: One hundred consecutive patients undergoing RFCA for AF (paroxysmal 72%, persistent 28%) were studied. Left atrial dimensions, PV dimensions and PV anatomy were evaluated three-dimensionally on MSCT. Pulmonary vein anatomy was classified as normal or atypical based on the absence/presence of a common trunk or additional vein(s).

Results: After a mean follow up of 11.6  $\pm$  2.8 months, 65 patients (65%) maintained sinus rhythm. Enlargement of the LA in anterior-posterior direction on MSCT was related to a higher risk for AF recurrence. No relation was found between PV dimensions and outcome of RFCA. In addition, normal right-sided PV anatomy was related to a higher risk for AF recurrence compared to atypical right-sided PV anatomy. Multivariate analysis showed that anterior-posterior LA diameter on MSCT (OR=1.083, p=0.027) and normal right-sided PV anatomy (OR=6.711, p=0.006) were independent predictors of AF recurrence after RFCA. Conclusion: Enlargement of anterior-posterior LA diameter and presence of normal anatomy of the right PVs are independent risk factors for AF recurrence. No relation was found between PV dimensions and outcome of RFCA.

# Introduction

Multi-slice computed tomography (MSCT) is nowadays commonly acquired prior to radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF). Multislice computed tomography provides important information about the left atrial (LA) and pulmonary vein (PV) anatomy which can be used to plan and quide the RFCA procedure.<sup>1</sup> Moreover, MSCT allows accurate threedimensional assessment of LA and PV dimensions.<sup>2,3</sup> It has been demonstrated that LA dimensions and PV dimensions are enlarged in patients with AF.<sup>4,5</sup> However, whereas LA size is a well-known risk factor for AF recurrence after RFCA,<sup>6-9</sup> little is known about the prognostic importance of PV dilatation. Similarly, the impact of PV anatomy on the outcome of RFCA has not been studied extensively. Potentially, different anatomical drainage patterns could be accompanied by different tissue characteristics of the surrounding myocardium that may increase the resistance of the PV area to electrical isolation. Moreover, certain anatomical variants could pose a technical difficulty to achieve stable catheter position during ablation thereby compromising effective lesion formation. This study describes the impact of LA dimensions, PV dimensions and PV anatomy assessed by MSCT on the outcome of circumferential RFCA for AF.

# Methods

## Patient population and evaluation

The patient population comprised 100 consecutive patients with symptomatic drug-refractory AF, undergoing circumferential RFCA. After RFCA, all patients were evaluated on a regular basis at the outpatient clinic during a 12 months follow-up period. Routine electrocardiograms were recorded each visit and 24-hour Holter registrations were scheduled at 3, 6 and 12 months after the

ablation. Importantly, all patients were encouraged to immediately obtain an electrocardiogram when experiencing palpitations. All medications were continued for at least 3 months. Afterwards, anti-arrhythmic drugs were discontinued at the discretion of the physician. After a post-ablation blanking period of 3 months, recurrence of AF was defined as any recording of AF on electrocardiogram or an episode longer than 30 seconds on 24-hour Holter monitoring.<sup>10</sup> After 12 months follow-up, the study population was divided into two groups: patients with maintenance of AF (recurrence group).

#### Multi-Slice Computed Tomography

#### Image acquisition

Prior to RFCA, all patients underwent an MSCT examination in order to guide the procedure.<sup>1</sup> The MSCT scan was performed with a 64-slice Toshiba Aquilion 64 system (Toshiba Medical Systems, Otawara, Japan). A bolus of 70 ml nonionic contrast material (lomeron 400, Bracco, Milan, Italy) was infused through the antecubital vein at a rate of 5 ml/s followed by 50 ml saline solution flush. Automatic detection of the contrast bolus in the descending aorta was used to time the start of the scan. Craniocaudal scanning was performed during breath-hold, without electrocardiogram-gating. Collimation was 64 x 0.5 mm, rotation time 400 ms and the tube voltage 100 kV at 250 mA. After acquisition, the raw MSCT data were exported, post-processed and analyzed on a dedicated workstation (Vitrea 2, Vital Images, Minnetonka, Minnesota, USA).

#### Quantitative measurements

Pulmonary vein ostium dimensions were evaluated using a 2-dimensional viewing mode. To allow accurate assessment, multiplanar reformatting was

used to place two orthogonal planes parallel to the course of the vein (Figure 1, panel A and B). The third orthogonal plane, oriented perpendicular to the course of the vein, was then used to measure the diameter of the PV ostium in anterior-posterior and superior-inferior direction (Figure 1, panel C). The ratio between the largest and smallest diameter was calculated in order to obtain information on the oval shape of the ostium. Similarly, multiplanar reformatting was used to assess LA dimensions in 3 orthogonal directions: anterior-posterior, longitudinal and transversal direction (Figure 2). Left atrial volume was calculated using the biplane dimension-length formula: LA volume =  $4/3\pi \times (anterior-posterior diameter/2) \times (longitudinal diameter/2).^{11}$ 



Figure 1. Assessment of pulmonary vein diameters. To assess pulmonary vein diameters, two orthogonal planes were placed parallel to the course of the vein (panel A and B). A third orthogonal plane (panel C), oriented perpendicular to the course of the vein, was then used to measure the anterior-posterior (AP) and superior-inferior (SI) pulmonary vein diameter (white arrows).

# Pulmonary vein anatomy

Pulmonary vein anatomy was analyzed from an external view using a threedimensional volume-rendered reconstruction. Pulmonary vein classification was based on the presence or absence of a common trunk and/or additional vein(s) (Figure 3). A common trunk was defined when the superior and the inferior PV joined more than 5 mm before entering in the LA. An additional vein was defined as a supranumerary vein directly entering the LA.



Figure 2. Assessment of left atrial dimensions. The left atrial (LA) dimensions (white arrows) were assessed in three orthogonal directions by using multiplanar reformatting. Panel A: LA dimensions in anterior-posterior (AP) (red line) and longitudinal direction (green line). Panel B: LA dimension in transversal direction (green line). Panel B is a cross-section of panel A at the level of the crosshair and parallel to the red line.

To evaluate the impact of PV anatomy on the outcome of RFCA for AF, left- and right-sided anatomy was additionally classified as normal or atypical. Atypical anatomy was defined as the presence of a common trunk or an additional PV.

#### Radiofrequency catheter ablation

The RFCA procedure was aimed at creating two circumferential lesions around the left- and right-sided ipsilateral PVs approximately 1 cm outside the ostia. All patients received intravenous heparin to maintain an activated clotting time of 300-400 s. Intracardiac echocardiography was used to guide the transseptal puncture. To guide the ablation, a non-fluoroscopic electroanatomical mapping system with MSCT integration was used (CARTO XP<sup>™</sup> with Cartomerge<sup>™</sup>, Biosense Webster, Diamond Bar, California, USA). Contact mapping and ablation was performed using a 4-mm quadripolar open-loop irrigated mapping/ablation catheter (7Fr Navistar<sup>™</sup>, Biosense Webster). A 6Fr quadripolar diagnostic catheter placed inside the right atrium served as a temporal reference. Radiofrequency current was applied at 30-35 W with a maximum temperature of 45°C and an irrigation flow of 20 ml/min until a bipolar voltage of <0.1 mV was achieved, with a maximum of 60 s per point. The end-point of the procedure was PV isolation as confirmed by recording entrance block during sinus rhythm or pacing from inside the coronary sinus.<sup>10</sup>

## Statistical analysis

Statistical analyses were performed with SPSS software (version 16.0, SPSS Inc., Chicago, Illinois, USA). A p-value of <0.05 was considered statistically significant. Data are presented as mean ± SD or as number (percentage). Statistical comparisons for continuous variables were performed with the two **tailed Student's t**-test, paired or unpaired as appropriate. Statistical comparisons for categorical variables were performed with the Chi-square test. Univariate and multivariate logistic regression analyses were performed to study the impact of clinical characteristics, LA dimensions and PV dimensions and anatomy on the incidence of AF recurrence after RFCA. Variables with a p-value <0.05 in the univariate analyses were included into the multivariate **analysis. Multivariate analysis was performed using an 'enter' method**.



Figure 3. Classification of pulmonary vein anatomy. Panel A: Separate ostia of the left-sided pulmonary veins; Panel B: Separate ostia of the right-sided pulmonary veins; Panel C: Common trunk of the left-sided pulmonary veins (defined as a joint part of the superior and the inferior pulmonary veins of more than 5 mm, before entering the left entering); Panel D: Additional right-sided pulmonary vein (defined as a supranumerary vein directly entering the left atrium). Add = additional pulmonary vein, LIPV = left inferior pulmonary vein, LSPV = left superior pulmonary vein, RIPV = right inferior pulmonary vein, RSPV = right superior pulmonary vein.

#### Results

#### Patient characteristics

One hundred consecutive patients were included (77 men, mean age 56  $\pm$  9 years), from an ongoing clinical registry.<sup>12</sup> Atrial fibrillation was paroxysmal in 72 patients and persistent in 28 patients according to the American College of Cardiology/American Heart Association/European Society of Cardiology guidelines definitions.<sup>13</sup> None of the patients had previously undergone RFCA for AF. Median duration of AF was 48 months (interquartile range: 24-84) and the mean number of anti-arrhythmic drugs used was 3.1  $\pm$  1.3 per patient. The mean anterior-posterior diameter of the LA was 43  $\pm$  6 mm and the mean left ventricular ejection fraction was 58  $\pm$  8% on transthoracic echocardiography (Table 1). The procedural end-point of PV isolation was achieved in all patients. In 11 patients a repeat procedure was performed due to early recurrence of AF.

After a mean follow-up of 11.6  $\pm$  2.8 months, 65 patients (65%) had maintained sinus rhythm (non-recurrence group), whereas 35 patients (35%) had recurrence of AF (recurrence group). Anti-arrhythmic drug treatment had been discontinued in 16 patients (25%) who had maintained sinus rhythm and in 12 patients (34%) with AF recurrence (p=0.30). In the recurrence group a higher prevalence of persistent AF was found compared to the non-recurrence group (14 [22%] vs. 14 [40%], p=0.049).

#### Left atrial dimensions

Left atrial dimensions were measured in three orthogonal directions on MSCT: anterior-posterior, longitudinal and transversal (Figure 2). Mean anterior-posterior diameter was  $41 \pm 7$  mm, mean longitudinal diameter was  $65 \pm 8$  mm and mean transversal diameter was  $59 \pm 7$  mm. Anterior-posterior LA diameter was significantly larger in the recurrence group than in the non-recurrence group ( $43 \pm 6$  mm vs.  $39 \pm 7$  mm, p=0.02). Interestingly, no differences were

found between the recurrence group and non-recurrence group in longitudinal ( $64 \pm 7 \text{ mm vs.} 65 \pm 9 \text{ mm}$ , p=0.45) and transversal ( $59 \pm 7 \text{ mm vs.} 60 \pm 7 \text{ mm}$ , p=0.57) LA diameter. Mean LA volume was  $82 \pm 23 \text{ ml}$ . Left atrial volume was larger in the recurrence group than in the non-recurrence group ( $88 \pm 26 \text{ ml vs.} 78 \pm 21 \text{ ml}$ , p=0.04).

Table 1. Baseline characteristics			
Variable	Total (n = 100)		
Age (years)	56.4 ± 8.6		
Male/female	77/23		
Body Surface Area (m <sup>2</sup> )	2.1 ± 0.2		
Type of atrial fibrillation (paroxysmal/persistent)	72/28		
Duration of atrial fibrillation (months)	64 ± 60		
Anti-arrhythmic drugs used per patient	3.1 ± 1.3		
Hypertension	53 (53%)		
Coronary artery disease	8 (8%)		
Diabetes mellitus 8 (8%)			
Echocardiography			
Anterior-posterior left atrial diameter (mm)	43 ± 6		
Left ventricular ejection fraction (%)	58 ± 8		

#### Pulmonary vein dimensions

Pulmonary vein ostial dimensions were assessed in anterior-posterior and superior-inferior direction on MSCT (Table 2). Pulmonary vein dimensions were larger in superior-inferior direction than in anterior-posterior direction (21.1  $\pm$  2.3 mm vs. 16.3  $\pm$  2.5 mm, p<0.001). Overall, right-sided PVs had a larger

diameter than left-sided PVs (20.0  $\pm$  2.4 mm vs. 16.6  $\pm$  1.6 mm, p<0.001). Similarly, superior PVs had a larger diameter than inferior PVs (19.6  $\pm$  3.8 mm vs. 17.5  $\pm$  3.1 mm, p<0.001). With regard to the shape of the PV ostium, left-sided PVs had a more pronounced oval shape than right-sided PV ostia indicated by a lower ratio between the largest and smallest PV diameter (ratio 0.65  $\pm$  0.09 vs. 0.84  $\pm$  0.09, p<0.001).

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Variable	Anterior-	Superior-	Mean diameter	Ratio	
	posterior	posterior	(mm)		
	diameter (mm)	diameter (mm)			
Right superior pulmonary vein	18.8 ± 4.2	23.3 ± 4.5	21.0 ± 4.0	0.80 ± 0.11	
Right inferior pulmonary vein	17.7 ± 2.9	20.3 ± 3.2	19.0 ± 2.8	0.87 ± 0.10	
Left superior pulmonary vein	14.3 ± 2.6	21.1 ± 3.6	17.7 ± 2.4	$0.67 \pm 0.13$	
Left inferior pulmonary vein	12.1 ± 2.7	18.8 ± 2.5	15.4 ± 2.0	$0.65 \pm 0.15$	
Additional pulmonary vein	8.9 ± 3.1	10.1 ± 2.4	9.5 ± 2.5	$0.82\pm0.11$	
Left common trunk	$19.5\pm4.5$	33.5 ± 4.7	$26.5\pm3.4$	$0.59\pm0.15$	
All right pulmonary veins	18.2 ± 2.5	21.8 ± 2.8	20.0 ± 2.4	$0.83\pm0.08$	
All left pulmonary veins	13.2 ± 2.5	19.9 ± 2.0	16.6 ± 1.6	0.66 ± 0.11	
All pulmonary veins	16.3 ± 2.5	21.1 ± 2.3	18.7 ± 2.2	0.77 ± 0.09	

Table 2. Pulmonary vein measurements on multi-slice computed tomography

Pulmonary vein dimensions were not related to the recurrence of AF during follow-up: no differences were found in mean PV diameter between the recurrence and non-recurrence group (18.8  $\pm$  2.2 mm vs.18.6  $\pm$  2.2 mm, p=0.74). In addition, a similar oval shape of the PV ostia was found in the both groups (non-recurrence group versus recurrence group: ratio 0.77  $\pm$  0.09 vs. 0.77  $\pm$  0.09, p=0.73).

#### Pulmonary vein anatomy

Pulmonary vein anatomy was assessed based on the presence/absence of a common trunk and/or additional PV. A total of 174 left-sided PVs and 226 rightsided PVs were identified on MSCT. Separate ostia of the left superior PV and left inferior PV were present in 74 patients (74%) and a common trunk of the left PVs was present in the remaining 26 patients (26%). In addition, separate ostia of the right superior PV and right inferior PV were observed in 78 patients (78%), an additional right-sided PV in 18 patients (18%) and 2 additional right-sided PVs was present in 26 patients (26%) and atypical anatomy of the left-sided PVs was present in 26 patients (26%) and atypical anatomy of the right-sided PVs was observed in 22 patients (22%).

Normal anatomy of the right-sided PVs was associated with a significantly higher risk for AF recurrence compared to atypical anatomy of the right-sided PVs (unadjusted OR: 7.353, p=0.010). In contrast, the presence of normal or atypical anatomy of the left-sided PVs had no significant impact on the outcome of RFCA (unadjusted OR: 2.145, p=0.14).

#### Predictors of AF recurrence

Univariate logistic regression analyses were performed to study the impact of LA dimensions, PV dimensions and PV anatomy, as well as clinical risk factors (e.g. type AF, hypertension) on the outcome of RFCA for AF (Table 3). A large anterior-posterior LA diameter (unadjusted OR: 1.082, p=0.021) and a large LA volume (unadjusted OR: 1.019, p=0.045) were related to a higher risk for recurrent AF after RFCA. Similarly, patients with persistent AF had a higher risk for AF recurrence (unadjusted OR: 2.429, p=0.049). The presence of normal right-sided PV anatomy was related to a higher risk for AF recurrence (unadjusted OR: 7.353, p=0.010). Subsequent multivariate analyses demonstrated that anterior-posterior LA diameter (OR: 1.083, p=0.027),

# persistent AF (OR: 3.004, p=0.035) and normal right-sided PV anatomy (OR: 6.711, p=0.006) were independent predictors of AF recurrence (Table 4).

Table 3. Univariate logistic regression analysis of clinical and anatomical characteristics on multi-slice computed tomography as risk factors for recurrence of atrial fibrillation after radiofrequency catheter ablation

Variable	e	OR	95% CI	P-value
Clinical	and echocardiographic characteristics			
Age (pe	r years)	1.027	0.978-1.079	0.28
Male ge	nder	1.012	0.381-2.691	0.98
AF dura	tion (per months)	1.032	0.952-1.118	0.45
Failed a	nti-arrhythmic drugs (per drug)	1.109	0.802-1.532	0.53
Persiste	nt atrial fibrillation	2.429	0.989-5.963	0.049*
Hyperte	nsion	0.908	0.399-2.067	0.82
Left ven	tricular ejection fraction (per %)	0.971	0.920-1.026	0.30
Multi-slice computed tomography characteristics				
Normal	right-sided pulmonary vein anatomy	7.353	1.603-33.333	0.010*
Normal	left-sided pulmonary vein anatomy	2.146	0.771-5.988	0.14
Mean pi	ulmonary vein diameter (per mm)	1.033	0.856-1.247	0.73
Left atrial diameter				
	Anterior-posterior (per mm)	1.082	1.012-1.156	0.021*
	Longitudinal (per mm)	1.021	0.967-1.078	0.45
	Transversal (per mm)	1.018	0.958-1.082	0.57
Left atria	al volume (per ml)	1.019	1.000-1.038	0.045*

\* included in multivariate logistic regression analysis

Variable	OR	95% CI	P-value
Clinical characteristics			
Persistent atrial fibrillation	3.004	1.082-8.345	0.035
Multi-slice computed tomography characteristics			
Normal right-sided pulmonary vein anatomy	6.711	1.736-26.316	0.006
Left atrial diameter			
Anterior-posterior (per mm)	1.083	1.009-1.162	0.027
Left atrial volume (per ml)	1.000	0.967-1.035	0.98

Table 4. Multivariate logistic regression analysis of clinical and anatomical characteristics on multi-slice computed tomography as risk factors for recurrence of atrial fibrillation after radiofrequency catheter ablation

#### Discussion

The present study investigated the impact of LA dimensions, PV dimensions and PV anatomy on the outcome of circumferential RFCA for AF. The main findings were that enlargement of the LA in direction on MSCT was an independent predictor of AF recurrence after RFCA. In contrast, PV dimensions were not related to the outcome of RFCA. Finally, atypical anatomy of the rightsided PVs was independently associated with less recurrences of AF after RFCA.

#### Left atrial dimensions

Left atrial enlargement is an important risk factor for the development of AF in the general population,<sup>14</sup> and has been identified as an independent predictor of AF recurrence after RFCA.<sup>6-9</sup> Significant dilatation of the LA is thought to be a marker of a large extent of atrial remodeling which may limit the efficacy of RFCA. In the present study, assessment of LA dimensions was performed in three directions on MSCT: anterior-posterior, longitudinal and transversal. Anterior-posterior LA diameter was identified as a predictor of AF recurrence, whereas longitudinal and transversal LA diameters were not. Moreover, anterior-posterior LA diameter was a stronger predictor of AF recurrence than LA volume. Atrial dilatation is thought to be predominantly oriented in longitudinal and transversal direction and not in anterior-posterior direction.<sup>11</sup> A potential explanation for our finding is that the dilatation of the LA in anterior-posterior direction occurs at a more advanced stage of atrial enlargement and reflects a higher extent of atrial remodeling, thereby explaining its prognostic value to predict AF recurrence after RFCA. Importantly, anterior-posterior LA diameter was an independent predictor of AF recurrence even after correction for type of AF.

#### Pulmonary vein dimensions and anatomy

The observations by Haïssaguerre et al. that ectopic beats originating from the PVs can initiate AF, have led to an increasing interest in the PVs as target for RFCA.<sup>15</sup> Nowadays, isolation of the PV region is the cornerstone for most ablation strategies.<sup>10</sup> However, little is known about the impact of PV dimensions and PV anatomy on the efficacy of RFCA for AF.

Similar to LA enlargement, PV dimensions are enlarged in patients with AF.<sup>3-5</sup> Previous series have demonstrated that superior PVs have a larger diameter compared to inferior PVs.<sup>3,16</sup> This finding has been related to a higher incidence of ectopic foci initiating AF originating from the superior PVs than from the inferior PVs.<sup>15,16</sup> In addition, it is suggested that PV dilatation is accompanied by different electrophysiological tissue characteristics in a way that AF is more likely to persist.<sup>4</sup> However, little is known about the prognostic significance of PV dilatation in patients undergoing RFCA to predict AF recurrence.

The present study evaluated the impact of PV ostial dimensions assessed by MSCT on AF recurrence after RFCA. No differences were found in PV ostial dimensions or shape between patients with AF recurrence and patients without AF recurrence during follow-up. These results suggest that PV dilatation has no prognostic value to predict AF recurrence after circumferential RFCA. Most likely, PV dilatation is caused by the presence of AF and can be best considered an epiphenomenon.

The relation between the anatomy of the PV region and the efficacy RFCA for AF has not been studied extensively. Several studies have shown that large variations in pulmonary venous drainage pattern into the LA exist.<sup>3,17-20</sup> Potentially, certain anatomical variants could pose a technical challenge to achieve stable catheter position thereby influencing the outcome of RFCA. Moreover, different venous drainage patterns could be accompanied by different tissue characteristics of the surrounding myocardium that may increase the resistance of the PV area to electrical isolation.

In the present study, the relation between PV anatomy and AF recurrence after RFCA was studied. Pulmonary vein anatomy was analyzed on MSCT and classified according to the presence or absence of a common trunk and/or additional PV as either normal or atypical. Normal anatomy of the right-sided PVs was associated with an increased risk for AF recurrence after RFCA. After correction for anterior-posterior LA diameter and type of AF, normal right-sided PV anatomy remained as independent predictor of AF recurrence after RFCA. These findings may indicate that an atypical PV drainage pattern may be accompanied by an increased susceptibility of the surrounding myocardial tissue for electrical isolation or a lower likelihood for PV ectopy originating from the right-sided PVs. Furthermore an atypical PV drainage pattern may pose less technical difficulty to achieve stable catheter position, resulting in a more effective lesion formation and a lower risk for electrical reconnection.

Recently, Hof et al reported on the impact of PV anatomy on the efficacy of RFCA in 146 patients.<sup>7</sup> Interestingly, no relation was found between PV anatomy and AF recurrence after RFCA. However, the definition of outcome

used by Hof et al included three categories (failure, improvement of AF burden and complete success),<sup>7</sup> and may have precluded from obtaining statistically significant differences among the different groups. The use of this definition may also explain why type of AF, which is a commonly accepted risk factor for AF recurrence,<sup>10</sup> was not related to AF recurrence after RFCA in their study.<sup>7</sup>

# Limitations

Some limitations should be acknowledged. The applicability of MSCT as a preprocedural patient selection tool is limited by the radiation exposure inherited to this technique. However, since MSCT is commonly acquired prior to RFCA to plan and guide the procedure, the present results may help determine whether additional ablation is needed in patients who are scheduled for circumferential RFCA. Furthermore, this study comprised a relatively small group of patients and present findings should be validated in a larger population.

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