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Cryoballoon ablation of atrial fibrillation is effectively feasible without previous imaging of pulmonary vein anatomy: insights from the 1STOP project

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Abstract

Background Pulmonary vein isolation by cryoablation (PVI-C) is a standard therapy for the treatment of atrial fibrillation (AF); however, PVI-C can become a challenging procedure due to the anatomy of the left atrium and pulmonary veins (PVs). Importantly, the utility of imaging before the procedure is still unknown regarding the long-term clinical outcomes following PVI-C. The aim of the analysis is to evaluate the impact of imaging before PVI-C on procedural data and AF recurrence.

Methods Patients with paroxysmal AF underwent an index PVI-C. Data were collected prospectively in the framework of 1STOP ClinicalService® project. Patients were divided into two groups according to the utilization of pre-procedural imaging of PV anatomy (via CT or MRI) or the non-usage of pre-procedural imaging.

Results Out of 912 patients, 461 (50.5%) were evaluated with CT or MRI before the PVI-C and denoted as the imaging group. Accordingly, 451 (49.5%) patients had no pre-procedural imaging and were categorized as the no imaging group. Patient baseline characteristics were comparable between the two cohorts, but the ablation centers that comprised the imaging group had fewer PVI-C cases per year than the no imaging group ($p < 0.001$). The procedure, fluoroscopy, and left atrial dwell times were significantly shorter in the no imaging cohort ($p < 0.001$). The rates of complications were significantly greater in the imaging group compared to the no imaging group (6.9% vs. 2.7%; $p = 0.003$); this difference was attributed to differences in transient diaphragmatic paralysis. The 12-month freedom from AF was 76.2% in the imaging group and 80.0% in the no imaging group ($p = 0.390$).

Conclusions In our analysis, PVI-C was effective regardless of the availability of imaging data on PV anatomy.

Keywords Paroxysmal atrial fibrillation · Cryoballoon · Outcomes · AF recurrences · Cardio imaging

Abbreviations

AAD	Anti-arrhythmic drug
AF	Atrial fibrillation
BMI	Body mass index
CKD	Chronic kidney disease
CBA	Cryoablation
EHRA	European Heart Rhythm Association
LVEF	Left ventricular ejection fraction

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PAF	Paroxysmal atrial fibrillation
PVI-C	Pulmonary vein isolation by cryoablation
TE	Thromboembolic event
TIA	Transient ischemic attack

1 Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, and it is associated with many adverse clinical outcomes, including thromboembolic events, heart failure, dementia, impaired quality-of-life, increased medical costs, and all-cause mortality [1–3]. To date, the electrical isolation of the pulmonary veins (PVs) is a class I indication in patients that are refractory or intolerant to at least one class I or III antiarrhythmic medication with recurrent symptomatic paroxysmal AF (PAF) [4, 5]. Despite the source of energy used for the ablation, the standardized protocols, and the increasing number of procedures, complete PV isolation (PVI) remains arduous to obtain in 20–30% of patients [3–9]. One of the numerous reasons is the complex and variable anatomy of the left atrium (LA) and of the PVs. Cross-sectional imaging (computed tomography (CT) or magnetic resonance imaging (MRI)) can be requested in advance of a PVI procedure to assess the atrial anatomy, to measure the dimensions of the LA and PVs and to identify the presence of a complex/abnormal anatomy [10–12]. However, the utility of imaging (CT or MRI) before PVI by cryoablation (PVI-C) has not been well established. In our analysis, we assess the impact of imaging on the safety, efficacy, and procedural efficiency of PVI-C by reviewing real-world data from patients with PAF being treated by cryoballoon ablation.

2 Methods

2.1 Project design

Consecutive patients with PAF who underwent an index PVI-C with the second-generation cryoballoon catheter (Arctic Front Advance; Medtronic, Inc.) from August 2012 until May 2017 in the 43 Italian centers participating to the One Shot TO Pulmonary vein isolation (1STOP) ClinicalService project were included in the analysis. ClinicalService is a national cardiovascular data repository and medical care project designed to describe and improve the quality of diagnostic and therapeutic strategies using technologies and therapies in the Italian clinical practice [13, 14]. The project consists of a shared environment for the prospective collection, management, analysis, and reporting of data from patients in whom Medtronic therapies have been applied. An independent scientific committee of physicians prospectively identifies key clinical questions on a yearly basis for analysis and publication [13, 14]. A charter assigns the ownership of data to the centers and governs the conduct and relationship of the scientific committee and Medtronic. This project was approved by each site's Institutional Review Board and Local Ethics Committees and conforms to the principles outlined in the 1975 Declaration of Helsinki as reflected in the a priori approval by the institution's human research committee. Each patient included in the ClinicalService project provided informed consent for data collection and analysis [13, 14].

The objective of this research was to assess the usage of imaging technologies. Specifically, this analysis evaluated the impact of atrial anatomy awareness before PVI-C by CT or MRI regarding the periprocedural safety and/or long-term efficacy following the index catheter ablation. The primary efficacy endpoint was to determine whether the usage of CT or MRI before PVI-C was associated with higher efficacy (time-to-first AF recurrence). We divided the population into two groups. The imaging group consisted of patients that had a cardiac CT or MRI before the index procedure and the no imaging group included patients who underwent PVI-C without a prior imaging examination. Normal clinical practice standards at each participating center determined when patients were treated by PVI-C and when a patient had a preprocedural CT or MRI. An index score representing the center's level of experience (the ratio between the number of cryoballoon ablation procedures performed and the duration of time (in years) over which the ablations were performed) was calculated to estimate the influence of center experience on procedural data and complications [15].

2.2 Population and procedural characteristics

During the baseline visit, we collected several patient clinical characteristics, including age, sex, date of first AF diagnosis, NYHA and CHA_2DS_2-VASc scores, previous anti-arrhythmic therapy, hypertension, previous thromboembolic events, and atrial geometries measured by echocardiography. During the PVI-C procedure, we collected data on procedure time (skin-to-skin), fluoroscopy time, and the overall time spent in the LA (dwell time). Moreover, we collected the number of target and treated PVs, the number of freeze applications, and the balloon nadir temperature of each freeze. We defined normal anatomy as two right- and two left-sided PVs. Complex anatomy was defined by the presence of accessory and/or supernumerary PVs and /or common ostia. Cardiac imaging tests were performed and interpreted by qualified radiologists and cardiologists in compliance with Italian national standards for performing imaging studies. In order to know the LA anatomy (in patients who underwent ablation without a MRI or CT of the atrium), mapping of LA and PVs was performed during the ablation procedure using different techniques according to the clinical practice of each center, including contrast injection, an inner lumen mapping catheter or stiff guide, and

transesophageal echocardiogram. All information about any adverse events occurring during the procedure or in the following month were recorded and collected, including permanent and transient diaphragmatic paralysis, pericarditis, arteriosus-venous fistula, cardiac tamponade, transient ischemic attack (TIA), stroke, and other minor complications.

2.3 Follow-up and event collection

Follow-up visits were made in accordance with the clinical practice of each center, including clinic visits every 3 months (during the first year after the index PVI-C) and clinic visits every 6 months thereafter. The standard visit consisted of an assessment of the patient's AF-related symptoms, an ECG or Holter monitoring examination, and an assessment of the patient's pharmaceutical medications. Of the entire population, 8% were followed using an implantable loop recorder. The first 90 days after PVI-C were denoted as a landmark "90-day blanking period" whereby no recurrence of AF was counted against the primary efficacy endpoint [4, 5, 8]. Since antiarrhythmic drug (AAD) usage following PVI-C was performed according to each center's practice (rather than a standardized protocol), we analyzed the long-term recurrence of atrial arrhythmia, defined as an electrocardiographically documented episode of AF or atrial tachycardia lasting at least 30 s after an index PVI-C, regardless of AAD usage from the end of the 90-day blanking period [13, 14].

2.4 Statistical analysis

Baseline characteristics and clinical data have been summarized and compared between groups using appropriate summary statistics. Variables on a continuous scale have been described as mean, standard deviation, median/interquartile range, and minimum/maximum values. Variables on a categorical scale were presented as counts and percentages. Missing data were not imputed in any of the analysis. Comparisons between groups have been performed using Wilcoxon's test for continuous variables and the chi-square test for categorical variables. The survival analysis was completed by means of the Kaplan-Meier estimation method. Additionally, the differences between groups were tested by log-rank methods, and the proportional hazards models were fitted. The annual rates of complications were reported together with the 95% Poisson confidence intervals. A regression model was used to calculate the incidence rate ratio (IRR), with the d-scale option. An IRR < 1 denoted a lower incidence of the event in the imaging group, while an IRR > 1 denoted a higher incidence of the event in the imaging group. To find predictors for AF recurrence, a Cox regression model was imputed for both univariate and multivariate analyses. Parameters that were found to be significant in the univariable models ($p < 0.10$) were then analyzed in the multivariable analysis. Multivariate analyses were significant at $p < 0.05$.

3 Results

In this analysis, 912 consecutive subjects with PAF underwent an index PVI-C. Of which, 461 (51%) subjects composed the imaging group, and 451 (49%) subjects composed the no imaging group. In the imaging group, 191 (41.4%) subjects underwent MRI evaluation, and 270 (58.6%) subjects had CT evaluation.

3.1 Baseline and procedural characteristics

Baseline patient characteristics and procedural data are listed in Tables 1 and 2, respectively. Except for the pre-imaging procedure, there were few differences between the imaging and no imaging group with regard to baseline characteristics. The no imaging group was more likely to have failed at least 2 AADs, had a higher NYHA class designation, and were less frequently on anticoagulation drug therapy. All other baseline characteristics did not differ, including age, sex, symptoms, LA dimensions, CHA_2D_2-Vasc score, history of stroke/TIA, or hypertension (Table 1).

A measure of center experience is included in Table 2; across all centers, the median number of PVI-C per year was 21.8 (9.1–31.9). The ablation centers that comprised the imaging group had fewer PVI-C cases per year than the no imaging group (17.8 (9.1–21.8) versus 21.8 (9.1–88.8), respectively, $p < 0.001$).

The mean total procedural and fluoroscopy times were 102.1 ± 40.2 min and 26.8 ± 13.9 min, respectively. On average, a reduction in the procedure (Δ 34 min) and fluoroscopy time (Δ 7 min) was observed in the no imaging group ($p < 0.001$). Furthermore, the statistical differences in procedure and fluoroscopy times were preserved when only examining the 816 subjects with normal four-vein anatomy ($N = 415$ in the no imaging group and $N = 401$ in the imaging group). In the imaging group, 60 (13.0%) subjects had complex anatomy. By comparison, the no imaging group had 36 (8.4%) subjects with a complex PV anatomy (denoted as other PV; $p = 0.014$). We repeated the analysis on overall procedural and fluoroscopy time excluding the patients with complex anatomy ($N = 96$ patients excluded) to evaluate the impact of treating complex anatomies. The results showed a reduction across all durations with significantly shorter durations maintained in the no imaging group ($p < 0.001$), as shown in Table 2. Similarly, the LA dwell time was 44.9

Table 1 Baseline characteristics of the total population and statistical comparisons between the two groups of patients: subjects in the no Imaging group versus the imaging group

Baseline characteristics	Total ($N = 912$)	No imaging ($N = 451$)	Imaging ($N = 461$)	p value
Age at index ablation (years)	59.0 ± 11.1	58.9 ± 11.3	59.1 ± 11.0	0.708
Gender (female)	28.8% (263)	30.2% (136)	27.5% (127)	0.385
Body mass index	26.9 ± 4.0	26.9 ± 3.9	26.8 ± 4.1	0.668
Any atrial fibrillation-related symptoms	87.2% (795)	88.2% (398)	86.1% (397)	0.336
Months from first atrial arrhythmia	51.9 ± 94.1	50.8 ± 118.4	52.9 ± 62.4	0.058
Failed ≥ 2 AADs	46.9% (427)	51.2% (231)	42.6% (196)	0.015
New York Heart Association class				0.001*
1	82.1% (748)	76.7% (345)	87.4% (403)	
2	17.0% (155)	22.0% (99)	12.1% (56)	
3	0.8% (7)	1.0% (4)	0.5% (3)	
4	0.1% (1)	0.3% (1)	0.0% (0)	
History of stroke/TIA	5.0% (45)	5.1% (23)	4.8% (22)	0.825
Cardiac insufficiency	2.2% (20)	1.8% (8)	2.6% (12)	0.401
Hypertension	46.0% (416)	43.4% (195)	48.6% (221)	0.121
Any valve disease	4.8% (44)	4.0% (18)	5.7% (26)	0.245
Any other cardiovascular diseases	3.4% (31)	2.7% (12)	4.2% (19)	0.224
Presence of patent foramen ovale	7.4% (67)	5.8% (26)	9.0% (41)	0.066
CHA_2DS_2-VASc				0.113*
0	26.9% (245)	25.7% (116)	28.0% (129)	
1	31.7% (289)	35.5% (160)	28.0% (129)	
2	22.7% (207)	22.5% (101)	22.9% (106)	
3	13.6% (124)	12.0% (54)	15.1% (70)	
4	4.0% (36)	3.0% (13)	5.1% (23)	
≥ 5	1.1% (10)	1.4% (6)	0.9% (4)	
Diabetes	4.7% (43)	5.1% (23)	4.3% (20)	0.584
Chronic renal failure	2.6% (23)	1.8% (8)	3.4% (15)	0.151
Left atrial diameter (mm)	40.8 ± 5.9	40.8 ± 6.4	40.7 ± 5.5	0.462
Left atrial volume (cm^3)	62.7 ± 22.6	67.5 ± 30.8	62.4 ± 22.0	0.711
Anti-arrhythmic drug	72.3% (659)	73.6% (332)	71.2% (327)	0.425
Anti-arrhythmic drug IIIC	34.1% (310)	35.0% (157)	33.2% (153)	0.603
Anti-arrhythmic drug IC	45.3% (413)	46.6% (210)	44.0% (203)	0.489
Beta-blockers	45.6% (415)	42.1% (189)	48.7% (226)	0.062
Anticoagulants	80.2% (731)	77.4% (349)	82.9% (382)	0.046

AAD, anti-arrhythmic drug; *TIA*, transient ischemic attack

*Statistical test conducted between entire no imaging cohort versus imaging group

± 20.7 min in the no imaging group and 65.3 ± 24.2 min in the imaging cohort ($p < 0.001$). Additionally, more freeze applications were utilized (on average) in the imaging cohort when comparing the isolation of the left superior, right superior, and right inferior PVs.

The majority of patients (85.7%) were in sinus rhythm before the procedure (82.7% in the no imaging group versus 88.6% in the imaging group; $p = 0.009$), and 98.0% of the subjects ended the procedure in sinus rhythm (with no difference between groups; $p = 0.399$).

3.2 Complications

Out of 912 subjects, 44 (4.8%) subjects experienced an adverse event related to the PVI-C procedure. The imaging group had a significantly greater overall complication rate than the no imaging group (6.9% vs. 2.7%; $p = 0.003$). The most frequent event was transient diaphragmatic paralysis because of phrenic nerve impairment, which occurred in 24 (2.6%) subjects, including 5 (1.1%) in the no imaging group and 19 (4.1%) in the imaging group ($p = 0.004$). All

Table 2 Procedural characteristics of the total population and comparison between the two groups of patients: subjects in the no imaging group versus the imaging group

Procedural characteristics	Total ($N = 912$)	No imaging ($N = 451$)	Imaging ($N = 461$)	p value
Center experience (PVI-C procedures/year)	21.8 (9.1–31.9)	21.8 (9.1–88.8)	17.8 (9.1–21.8)	< 0.001
Procedure time (min)	102.1 ± 40.2	84.9 ± 30.1	118.5 ± 41.8	< 0.001
Without complex anatomies*	100.6 ± 40.1	84.4 ± 29.9	117.0 ± 42.4	< 0.001
With complex anatomies**	110.4 ± 35.5	92.2 ± 30.2	121.9 ± 34.0	< 0.001
Fluoroscopy time (min)	26.8 ± 13.9	23.3 ± 11.4	30.2 ± 15.2	< 0.001
Without complex anatomies[a]	26.3 ± 13.3	23.4 ± 11.3	29.3 ± 14.4	< 0.001
With complex anatomies[b]	28.5 ± 17.2	18.0 ± 9.1	35.3 ± 17.9	< 0.001
Left atrium dwell time (min)	55.6 ± 24.7	44.9 ± 20.7	65.3 ± 24.2	< 0.001
Pre-procedural imaging				
MRI	20.9% (191)	0.0%	41.4% (191)	< 0.001
CT	29.6% (270)	0.0%	58.6% (270)	< 0.001
Pre-ablation rhythm				
Sinus	85.7% (776)	82.7% (372)	88.6% (404)	0.009
Atrial arrhythmias	14.3% (122)	17.3% (74)	11.4% (48)	0.010
DCCV during procedure	12.0% (109)	10.9% (49)	13.0% (60)	0.317
Post-ablation rhythm				
Sinus	98.0% (893)	97.8% (440)	98.2% (453)	0.399
Atrial arrhythmias	2.0% (18)	2.2% (10)	1.8% (8)	0.777
Left superior pulmonary vein	98.7% (901)	99.1% (447)	98.4% (454)	0.291
Number of applications	1.4 ± 0.8	1.3 ± 0.7	1.5 ± 0.8	< 0.001
Balloon nadir temperature (°C)	− 41.3 ± 13.9	− 39.4 ± 12.0	− 43.0 ± 15.1	< 0.001
Left inferior pulmonary vein	98.6% (900)	98.8% (446)	98.4% (454)	0.604
Number of applications	1.3 ± 0.5	1.3 ± 0.5	1.3 ± 0.6	0.148
Balloon nadir temperature (°C)	− 38.5 ± 14.5	− 36.9 ± 13.2	− 40.0 ± 15.5	< 0.001
Right superior pulmonary vein	98.5% (899)	98.8% (446)	98.2% (453)	0.805
Number of applications	1.2 ± 0.5	1.2 ± 0.5	1.3 ± 0.5	0.006
Balloon nadir temperature (°C)	− 44.5 ± 14.7	− 42.9 ± 14.0	− 45.9 ± 15.1	< 0.001
Right inferior pulmonary vein	96.3% (879)	95.1% (429)	97.6% (450)	0.045
Number of applications	1.2 ± 1.8	1.1 ± 0.4	1.2 ± 2.5	< 0.001
Balloon nadir temperature (°C)	− 43.2 ± 14.8	− 42.1 ± 13.7	− 44.2 ± 15.6	0.002
Other pulmonary veins	10.5% (96)	8.4% (36)	13.0% (60)	0.014
Number of applications	1.5 ± 0.9	1.8 ± 1.0	1.3 ± 0.7	0.011
Balloon nadir temperature (°C)	− 44.8 ± 15.7	− 46.7 ± 8.2	− 43.6 ± 19.1	0.783
Follow-up with implantable loop recorder	8.3% (76)	7.1% (32)	9.5% (44)	0.181

($N = 816$ total; $N = 415$ no imaging group; and $N = 401$ imaging group)

[a] Procedure and fluoroscopy times measured only in patients without complex pulmonary vein anatomies

[b] Procedure and fluoroscopy times measured only in patients with complex pulmonary vein anatomies

periprocedural complications are summarized in Table 3. Of note, there were no instances of stroke or PV stenosis in this study.

3.3 AF recurrence

During the follow-up period of 694 patient years, no subject was lost to follow-up. AF recurrence was found in 158 (17.3%) subjects. The annual rate of AF recurrence was 19.43% (95% CI, 14.7–25.6%) in the no imaging group versus 23.59% (95% CI, 19.4–28.6%) in the imaging group. Also, the unadjusted survival analysis for freedom from AF recurrence showed no statistical difference between the groups (Fig. 1). The 1-year survival probability was 80.0% ± 5.1 in the no imaging group compared with 76.2% ± 3.9 in the imaging group ($p = 0.390$). Univariate analysis identified age, chronic renal failure, left atrial volume > 61 cm^3, and CHA_2DS_2-VASc ≥ 2 to be associated with AF recurrence

Table 3 Periprocedural complications of the total population and comparison between the two groups of patients: subjects in the no imaging group versus the imaging group

Complications	Total ($N = 912$)	No imaging ($N = 451$)	Imaging ($N = 461$)	p value
Patients with ≥ 1 complication	4.8% (44)	2.7% (12)	6.9% (32)	0.003
Permanent diaphragmatic paralysis	0.1% (1)	0.0% (0)	0.2% (1)	0.322
Transient diaphragmatic paralysis	2.6% (24)	1.1% (5)	4.1% (19)	0.004
Pericardiac effusion	0.4% (4)	0.2% (1)	0.7% (3)	0.327
Cardiac tamponade	0.3% (3)	0.0% (0)	0.7% (3)	0.086
Pneumothorax/hemothorax	0.0% (0)	0.0% (0)	0.0% (0)	0.086
Femoral pseudo-aneurism	0.1% (1)	0.2% (1)	0.0% (0)	0.312
Stroke	0.0% (0)	0.0% (0)	0.0% (0)	0.312
Transient ischemic attack	0.1% (1)	0.2% (1)	0.0% (0)	0.312
Pulmonary vein stenosis	0.0% (0)	0.0% (0)	0.0% (0)	0.312
Hematoma	0.2% (2)	0.0% (0)	0.4% (2)	0.161
Other complications	0.9% (8)	0.9% (4)	0.9% (4)	0.975

(Table 4). CHA_2DS_2-VASc ≥ 2 was the only variable that remained a predictor of an increased risk of AF recurrence using the multivariate model analysis. Lastly, after adjustment for factors associated with AF recurrence and center experience, the usage of pre-procedural imaging (imaging group) was not associated with less frequent post-ablation AF recurrence.

4 Discussion

4.1 Main results

Despite the standardization of the procedure, the source of energy, and the high success on short-term follow-up, complete PVI remains a challenging procedure in the 20–30% of patients with PAF. Some of these challenges include anatomical characteristics (variations in LA and PV anatomy), which can confound balloon-to-PV contact and ultimately lay the foundation for AF recurrences because of poor PVI-C. Here, we report on a real-world clinical setting experience to assess the impact of pre-procedure imaging on the success of the one-shot cryoablation technique for PVI in patients with symptomatic PAF.

The main findings of our study demonstrated that even though more than half of analyzed patients underwent cardiac imaging before the ablation procedure (via CT or MRI), there was no difference in survival analysis on freedom from AF recurrence between the two groups of patients (imaging versus no imaging). Cardiac imaging was more common in centers with less PVI-C volume, and the imaging group had a higher rate of transient diaphragmatic paralysis. On multivariate analysis, the only predictor of AF recurrence was CHA_2DS_2-VASc.

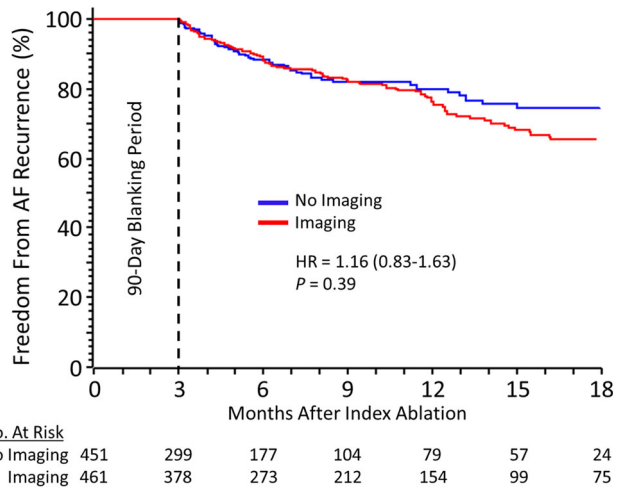

Fig. 1 Freedom from AF recurrence by the Kaplan-Meier estimate

4.2 Cardiac imaging

Electrophysiologists are increasingly requesting cross-sectional imaging (CT or MRI) in advance of many procedures, especially in the case of complex procedures [10–12, 16–19]. The main benefits of cardiac imaging on radiofrequency ablation or complex electrophysiological procedures are well described, i.e., (1) visualizing the anatomy and dimensions of the LA and PVs; (2) identifying any variant anatomy that may interfere with the procedure (e.g., accessory PVs or shared PV ostia); (3) assessing the superior vena cava and inferior vena cava for anatomical approach when variants are present; (4) excluding the presence of thrombus in the left atrial appendage by MRI; (5) identifying the location and course of the esophagus; and (6) identifying the fossa ovalis and any anomalies that may interfere with the trans-septal puncture (e.g., lipomatous hypertrophy of the interatrial septum) [12, 16–19]. Moreover, in procedures using 3D mapping systems, both CT and MRI can be used to merge into electro-anatomical maps and/or overlap onto real-time fluoroscopic

Table 4 Univariate analysis of clinical outcomes against baseline characteristics and multivariable analysis of outcomes against characteristics with significant univariate association

Baseline characteristics	All patients ($N = 912$)			
	Univariable model		Multivariable model	
	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
Group	1.16 (0.83–1.63)	0.394		
Center experience	0.91 (0.49–1.69)	0.775		
Age (continuous)	1.02 (1.00–1.03)	0.034*		
Gender (male)	0.88 (0.63–1.24)	0.471		
Body mass index (continuous)	0.98 (0.94–1.03)	0.459		
History of flutter	1.18 (0.76–1.83)	0.469		
Other previous arrhythmias	0.31 (0.08–1.27)	0.103		
Months from first atrial arrhythmia	1.00 (1.00–1.00)	0.577		
Number of tested AAD ≥ 2	1.10 (0.79–1.54)	0.568		
History of stroke/TIA	1.50 (0.76–2.94)	0.242		
Cardiac insufficiency	0.69 (0.17–2.77)	0.597		
Hypertension	1.15 (0.83–1.58)	0.403		
Diabetes	0.77 (0.28–2.07)	0.599		
Patent foramen ovale	0.96 (0.53–1.73)	0.886		
CHA_2DS_2-VASc ≥ 2	1.48 (1.07–2.05)	0.017*	1.59 (1.10–2.31)	0.014**
Chronic renal failure	2.10 (1.03–4.29)	0.041*		
Left atrial diameter ≥ 41 mm	1.15 (0.75–1.76)	0.529		
Left atrial area ≥ 21 cm^2	1.25 (0.80–1.97)	0.331		
Left atrial volume ≥ 61 cm^3	1.85 (0.99–3.45)	0.052*		

*Significant p value for univariate test allowing a multivariable test

**Significant p value in the multivariable test

AAD, anti-arrhythmic drug; *TIA*, transient ischemic attack

images [12, 18, 19]. Also, CT or MRI scans could be used in post-procedural assessments to recognize and define adverse events, including esophageal injury and acute PV stenosis.

In our research, more than half of PVI-C patients had an imaging examination before the procedure, indicating that the usage of CT and MRI is standardized in current clinical practice during single-shot PVI. Similarly, in the ESC-EHRA long-term registry, 43% of point-by-point RF ablation procedure was done under the guidance of 3D mapping systems fused with CT or MRI images [7]. However, the prevalence of complex PV anatomy differs among published studies; reports vary from 5 to 40% [16–18]. We identified a complex PV pattern in 11% of total patients, which included 8.4% in the no imaging group versus 13.0% in the imaging group. This difference in the rate of non-normal PV presentation between cohorts may reflect the analyzed populations, the difficulty in defining the true PV ostium, and/or the difference in the imaging modalities that were used to denote PV anatomy (CT and MRI versus electro-anatomical mapping and echocardiography). Our analysis showed that the cardiac imaging in the settings of one-shot PVI ablation seemed not to add value to acute- or long-term clinical outcomes. Potentially, CT/MRI could be much more useful in case(s) of repeated ablation or when a more extensive ablation strategy is required in addition to PVI. Moreover, added costs, adequate image acquisitions, expertise in interpretation of 3-D spatial data, and dedicated software could be some limitations in using cardiac imaging.

4.3 Procedure and complications

Overall procedure time, fluoroscopy time, and LA dwell time were significantly lower in the no imaging group, even when considering only patients with typical 4-PV anatomy. This may be explained by (1) the influence of center experience on procedural and fluoroscopic times (15) and/or (2) utilization of a one-shot technology allows the user to isolate the PVs regardless of visualizing details of cardiac anatomy. Simply, the physician needs only to find the correct position to obtain balloon-to-PV occlusion, which may minimize the need for details of individual cardiac anatomy.

A previous study identified a non-significant trend for reduced complication rates in more experienced centers [15]. Here, we found a higher percentage of transient diaphragmatic paralysis in the imaging group compared to the no imaging group, which may be attributed to (1) less center experience,

(2) the increased number of freeze applications in the right-sided PVs, (3) or a combination of factors. However, all other periprocedural complications were infrequent in both groups, with values comparable to other published experiences [7, 15, 16, 20, 21].

4.4 Efficacy outcome

Consistent with previously published studies, our 12-month freedom from AF probability was 80.0% (95% CI, 73.2–85.4%) and 76.2% (95% CI, 72.2–80.6%) in the no imaging and imaging group, respectively. Our data were comparable with those presented in an extensive meta-analysis on 2413 patients that showed that the 1-year clinical success rate of PVI using cryoballoon was 81% (95% confidence interval, 78–84%) [7–9, 22]. These results indicate that cardiac imaging does not impact the efficacy of PVI-C. This could be explained by the fact that the single-shot technologies (e.g., cryoballoon) were designed to be used without a mapping system and without anatomical imaging guidance. In our population, on multivariate analysis, the only baseline characteristics that predicted AF recurrence was high CHA_2DS_2-VASc score. CHA_2DS_2-VASc is well established to be a useful parameter for predicting adverse events after catheter ablation of AF [23, 24]. Moreover, Letsas et al. demonstrated that the CHA_2DS_2-VASc scoring system is an independent predictor of AF recurrence following a single-catheter ablation procedure [25]. These published results agree with our general research findings.

5 Limitations

This analysis presents some limitations, i.e., (1) it was a non-randomized project, so bias could be present in the patient selection and treatment; (2) data of first recurrence of AF after the ablation procedure were collected during in-hospital follow-up visits or remote visits, but we may have missed some earlier AF events; (3) there was not a standardized protocol for the follow-up; only a minority of patents were followed with an implantable loop recorder; and (4) there was not a protocol to perform imaging tests before the procedure. Additionally, the no imaging group had less complex PV anatomy compared to the imaging group; however, we conducted paired-group analyses with only typical 4-PV cohorts and found similar findings. The imaging cohort had a lower PVI-C volume by center than the no imaging cohort, which may influence the procedural results between the imaging and no imaging cohorts. Lastly, the data were based on the clinical practice of several participating centers with different standard-of-care procedures. No recommendations were provided to the participating centers in terms of pharmacological treatment following PVI-C. Thus, it is unknown whether AADs were simply continued after the blanking period as per center practice. However, the strength of this data set resides in the large volume of real-world clinical patient treatment across a wide geographical range of Italian cardiac centers.

6 Conclusions

In our real-world experience, PV anatomy was described by pre-procedure CT or MRI in 51% of the PVI-C index ablations. However, PVI-C seemed to be effective regardless of pre-procedural imaging data on PV anatomy. Cardiac imaging was more common in centers with less experience. Our data demonstrated that pre-procedural imaging may not be necessary in all procedures when using a one-shot balloon ablation catheter to treat patients with symptomatic PAF.

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Compliance with ethical standards

All procedures performed in this project involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Ethical approval This project was approved by each site's Institutional Review Board and Local Ethics Committees.

Informed consent Each patient included in the ClinicalService project provided informed consent for data collection and analysis.

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