Ostial dimensional changes after pulmonary vein isolation: Pulsed field ablation vs radiofrequency ablation

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BACKGROUND Pulmonary vein (PV) stenosis is an important potential complication of PV isolation using thermal modalities such as radiofrequency ablation (RFA). Pulsed field ablation (PFA) is an alternative energy that causes nonthermal myocardial cell death.

OBJECTIVE The purpose of this study was to compare the effect of PFA vs RFA on the incidence and severity of PV narrowing or stenosis.

METHODS Data were analyzed from 4 paroxysmal atrial fibrillation ablation trials using either PFA or RFA; because of absent CT scans or poor computed tomography scan quality, 73 of 153 patients (47.7%) were excluded. Baseline and 3-month cardiac computed tomography scans were reconstructed into 3-dimensional images, and the long and short axes of the PV ostia were quantitatively and qualitatively assessed in a randomized blinded manner by 2 physicians.

RESULTS A total of 299 PVs from 80 patients after either PFA (n = 37) or RFA (n = 43) were enrolled. PV ostial diameters decreased significantly less with PFA than with RFA (% change; long axis: 0.9% ± 8.5% vs −11.9% ± 16.3%; $P < .001$ and short axis: 3.4% ± 12.7% vs −12.9% ± 18.5%; $P < .001$). After a combined quantitative/qualitative analysis, mild (30%–49%), moderate (50%–69%), or severe (70%–100%) PV narrowing was observed, respectively, in 9.0% (15 of 166), 1.8% (3 of 166), and 1.2% (2 of 166) of PVs in the RFA cohort but in none of the PVs after PFA ($P < .001$). Overall, PV narrowing/stenosis was present in 0% and 0% vs 12.0% and 32.5% of PVs and patients who underwent PFA and RFA, respectively.

CONCLUSION This study indicates that unlike after RFA, the incidence and severity of PV narrowing/stenosis after PV isolation is virtually eliminated with PFA.

KEYWORDS Atrial fibrillation; Catheter ablation; Electroporation; Nonthermal ablation; Pulmonary vein stenosis; Pulsed field ablation

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Introduction

In patients who undergo pulmonary vein (PV) isolation as a treatment of atrial fibrillation, complications such as PV stenosis, phrenic nerve palsy, and atrioesophageal fistula have been reported.[1,2] Traditional thermal ablation modalities, such as radiofrequency and cryothermy, rely on thermal extremes that are inherently indiscriminate in tissue destruction and the root of such complications. In contrast, pulsed field ablation (PFA) selectively creates microscopic pores in cell membranes by delivering a pulsed electric field to the target tissue.[3] Cardiomyocytes appear to be particularly vulnerable to PFA compared with other tissues, permitting preferential myocardial ablation.[4–7] Therefore, PFA may avoid complications associated with thermal-based ablation methods.

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In 2 recent multicenter, single-arm studies—IMPULSE (A Safety and Feasibility Study of the IOWA Approach Endocardial Ablation System to Treat Atrial Fibrillation; clinicaltrials.gov identifier NCT03700385) and PEFCAT (A Safety and Feasibility Study of the Farapulse Endocardial Ablation System to Treat Paroxysmal Atrial Fibrillation; clinicaltrials.gov identifier NCT03714178)—a total of 81 patients with paroxysmal atrial fibrillation underwent PFA.[8] There was no observed occurrence of esophageal damage or phrenic nerve injury in any of the patients, nor did any patients manifest symptoms of PV stenosis. Indeed, because of its absence of thermal coagulative necrosis, PFA may be less likely to cause not only PV stenosis but even PV ostial narrowing. Accordingly, in the present study, we compared dimensional PV changes after PFA with those observed after radiofrequency ablation (RFA).

Methods

Patient selection and computed tomography scanning

After the institutional review board's determination that the study was exempt from institutional review board review, data were analyzed from 4 paroxysmal atrial fibrillation ablation trials using either PFA or RFA.

The PFA cohort in the study (Figure 1A) was composed of patients in IMPULSE and PEFCAT enrolled at a single site (Homolka Hospital, Prague, Czech Republic), who had computed tomography (CT) scans at baseline and 3 months after ablation. Patients with scans from either time point with image quality too poor to accurately measure the ostial PV diameter were excluded. The IMPULSE and PEFCAT protocols specified a prospective PV isolation reassessment procedure coincident with the repeat CT scan that, in earlier iterations of PFA therapy, resulted in retreatment of one or more PVs by RFA. Accordingly, for the PFA cohort in this study, PVs that received additional RFA because of PV-left atrium (LA) reconnection during the reassessment procedure and before follow-up CT scanning were excluded from the analysis.

The RFA cohort (Figure 1B) consisted of patients who had CT scans at baseline and 3 months after RFA, at a single institution (Mount Sinai Hospital, NY), in TOCCASTAR[9] (TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation; clinicaltrials.gov identifier NCT01278953) or in the control RFA group of HEARTLIGHT[10] (Pivotal Clinical Study of the CardioFocus Endoscopic Ablation System; clinicaltrials.gov identifier NCT01456000) and before any reablation procedures. Patients from either study with insufficient CT image quality from either time point were also excluded.

CT scanning was performed using standard-of-care, site-specific protocols not altered for the purposes of this analysis. In general, scans with a slice thickness of ≤1 mm were selected for modeling and measurement. Aforementioned exclusions due to image quality were associated with multi-millimeter slice thickness, leading to insufficient resolution of the PV ostia or to contrast-filling defects during the scan inducing artifacts in the resulting 3-dimensional (3D) model. All scans at the

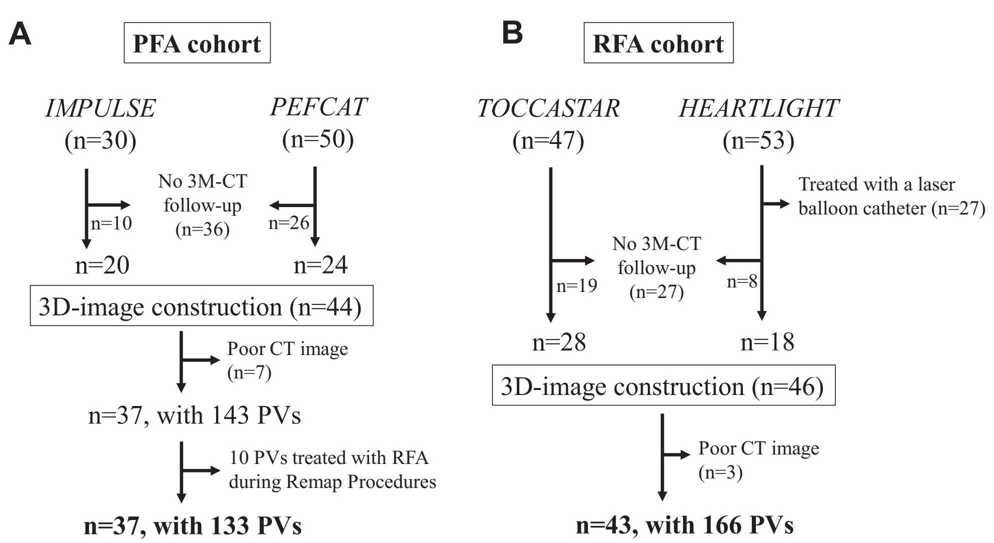

Figure 1 Patient selection for the PFA and RFA cohorts. In both cohorts, patients who had CT scans at baseline and 3 months were included; patients with poor quality 3D CT images were excluded. **A:** In the PFA cohort, 10 PVs were excluded because they received additional RFA because of PV-LA reconnection during the protocol-mandated remapping procedures before follow-up CT scanning at 3 months. **B:** In the RFA cohort, patients in the arm treated with a laser balloon catheter in HEARTLIGHT were excluded. 3D = 3-dimensional; CT = computed tomography; HEARTLIGHT = Pivotal Clinical Study of the CardioFocus Endoscopic Ablation System (clinicaltrials.gov identifier NCT01456000); IMPULSE = A Safety and Feasibility Study of the IOWA Approach Endocardial Ablation System to Treat Atrial Fibrillation (clinicaltrials.gov identifier NCT03700385); LA = left atrial; PEFCAT = A Safety and Feasibility Study of the Farapulse Endocardial Ablation System to Treat Paroxysmal Atrial Fibrillation (clinicaltrials.gov identifier NCT03714178); PFA = pulsed field ablation; PV = pulmonary vein; RFA = radiofrequency ablation; TOCCASTAR = TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (clinicaltrials.gov identifier NCT01278953).

3-month time point were acquired prospectively, by protocol and not driven by the presence of symptoms associated with PV stenosis.

Ablation procedure

All procedures were performed as previously described.[8–10] In brief, intravenous unfractionated heparin was administered to maintain an activated clotting time of 300–400 seconds. After femoral venous access, and transseptal puncture with intracardiac echocardiography guidance, one of the following ablation methods was used for PV isolation, as confirmed with a multielectrode circular mapping catheter:

1. PFA: The monophasic PFA procedures were performed under general anesthesia because of significant muscular contraction. However, biphasic PFA procedures were performed with sedation alone, since the nature of biphasic PFA with this system is such that it recruits minimal or no skeletal muscle during ablation. Through the 13-F deflectable PFA sheath, the 12-F over-the-wire PFA ablation catheter (Farawave, Farapulse, Menlo Park, CA) was deployed in a flower or basket configuration at the PV ostia such that the splines achieved circumferential contact (Figure 2). Catheter placement was guided by fluoroscopy and intracardiac echocardiography. During ablation in a majority of patients who underwent PFA, a standard electrophysiology catheter paced the ventricles to synchronize the pulses to just after QRS onset (5–10 heartbeats); latter patients received largely asynchronous delivery without pacing. The generator outputs of the monophasic and biphasic waveforms ranged from 900 to 1000 V per application and from 1800 to 2000 V per application, respectively. Before and after PFA, phrenic nerve function was evaluated by observing diaphragmatic motion during either patient inspiration or direct phrenic pacing. Neither luminal esophageal temperature monitoring nor mechanical deviation of the esophagus was used.

2. RFA: Patients underwent RFA under general anesthesia using either the EnSite NavX (St. Jude Medical, St. Paul, MN) or CARTO (Biosense Webster, Irvine, CA) electroanatomic mapping system. After transseptal puncture and using an 8.5-F deflectable sheath (St. Jude Medical), 1 of 2 RFA catheters were used for catheter ablation: (a) the contact force–sensing TactiCath catheter (St. Jude Medical) in the experimental arm of TOCCASTAR or (b) the ThermoCool NaviStar catheter (Biosense Webster) in the control arm of

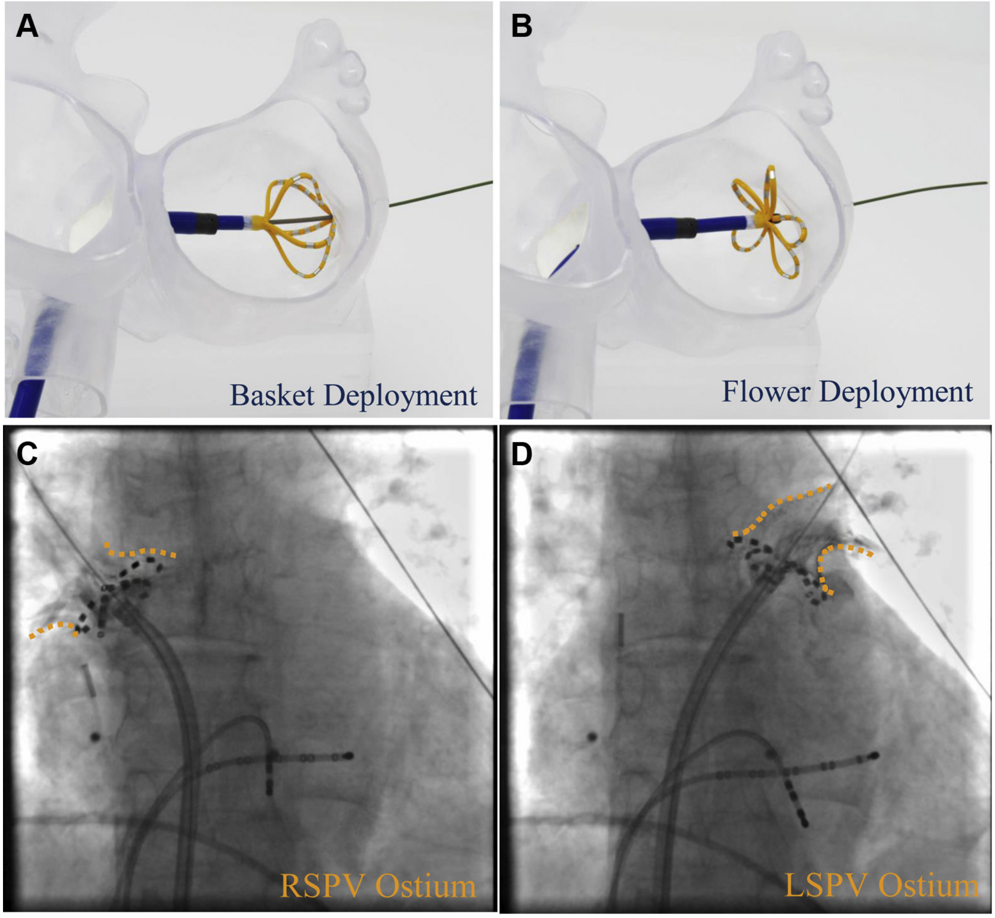

Figure 2 Deployments of the PFA catheter. **A and B:** PFA catheters in silicon models of the left atrium (panel A, basket deployment; panel B, flower deployment). **C and D:** Fluoroscopy of the PFA catheter in a flower petal configuration at the ostia of the RSPV (panel C) and LSPV (panel D). LSPV = left superior pulmonary vein; PFA = pulsed field ablation; RSPV = right superior pulmonary vein.

TOCCASTAR and HEARTLIGHT. Circumferential ablation was performed to achieve PV isolation. Either esophageal temperature monitoring or mechanical esophageal deviation was used in all patients. Isoproterenol-induced latent PV reconnection and non-PV triggers were also targeted if present.

3D measurement method of the PV ostium

Two-dimensional CT images were imported to ITK-SNAP 3.8.0[11] and reconstructed to 3D models. The LA and PVs were segmented and saved as stereolithography (.STL) files. *Common PVs* were conventionally defined as ≥2 veins that joined before entering the LA. Before their provision to blinded measurers, baseline and 3-month images were first displayed side by side to ensure they were from the same patient by examining the baseline and repeat scan for each patient. The files were then opened in Meshlab[12] for measurement. The ostial PV diameters (long and short axes) were measured by rotating both images, assisted by both interior and exterior views of the chamber.

Two cardiologists independently performed measurements on the de-identified image files in a randomized sequence by using a 2-step process. They were blinded to the ablation method. They measured all veins in all scans, not informed of any veins that would ultimately be excluded from the analysis because of additional RFA in the PFA cohort during remapping procedures. In the first quantitative step, 2 measurements for each ostial dimension were averaged to create the final dimension for each PV. In alignment with guidelines and a previous study, *PV narrowing* was defined as a dimensional reduction in either the long or the short axis and graded as mild (30%–49%), moderate (50%–69%), or severe (70%–100%).[13,14]

In the second step, any cases of quantified narrowing were subsequently assessed in a qualitative morphological fashion and categorized as either (1) presence of a waist-like tapering consistent with ablation-related damage or (2) without any tapering, where narrowing could potentially be attributable to factors such as atrial chamber remodeling, volume changes, or shifted extracardiac anatomy between the 2 scan time points.

Statistical analysis

Continuous variables are expressed as mean ± SD and compared using the Student *t* test or the paired *t* test. Categorical variables are expressed as count and percentage and compared using the χ^2 test or the Fisher test, as appropriate. A *P* value of <.05 was considered significant. Statistical analyses were performed with SPSS version 26.0 (IBM Corporation, Armonk, NY).

Results

Patient selection and demographic characteristics

In the PFA cohort (Figure 1A), among a total of 80 patients from IMPULSE and PEFCAT, 3D image reconstruction was performed in 44 patients; 36 other patients were excluded because of absent 3-month CT scans. PV diameters were ultimately measured in 37 patients (143 PVs) since 7 patients were excluded because of poor image quality. Ten of 143 PVs had received RFA during remapping procedures and were thus excluded. Ultimately, 37 patients with 133 PVs were included in the present analysis. The majority of these patients (27 of 37 [73%]) were treated with biphasic PFA, which resulted in 93.3% durable PV isolation at the time of reassessment (92 ± 32 days).

In the RFA cohort (Figure 1B), among a total of 100 patients from TOCCASTAR and HEARTLIGHT, 3D image reconstruction was performed in 46 patients. We excluded 27 other patients who received a laser balloon, and not RFA, in HEARTLIGHT, as well as 27 other patients who did not undergo 3-month CT scanning. Three patients were excluded for poor CT image quality, so ultimately, 43 patients with 166 PVs were included. Of these 43 patients, 14 were treated with a contact force–sensing catheter. All analyzed PVs were successfully isolated during the index procedure.

The baseline patient characteristics are summarized in Table 1. In the entire cohort of 80 patients with paroxysmal atrial fibrillation, the mean age was 60.5 ± 9.8 years and 73.8% were male. Hypertension and diabetes were present in 53.8% and 7.5% of the total cohort. The mean left ventricular ejection fraction (LVEF) and LA diameter were 61.6% ± 5.0% and 39.5 ± 6.0 mm, respectively. Follow-up CT scanning was performed an average of 105 ± 38 days postablation. Coronary artery disease was more frequent in the PFA cohort, and LVEF and LA diameters were slightly higher in the PFA cohort.

Table 1 Baseline patient characteristics

Characteristic	Total cohort (N = 80)	PFA (n = 37)	RFA (n = 43)	*P*
Age (y)	60.5 ± 9.8	58.9 ± 10.1	61.9 ± 9.4	.171
Male sex	59 (73.8)	28 (75.7)	31 (72.1)	.717
Hypertension	43 (53.8)	23 (62.2)	20 (46.5)	.162
Diabetes	6 (7.5)	4 (10.8)	2 (4.7)	.269
Stroke or TIA	5 (6.3)	2 (5.4)	3 (7.0)	.572
CAD (MI or CABG)	6 (7.5)	0 (0.0)	6 (14.0)	.020
LVEF (%)	61.6 ± 5.0	63.0 ± 3.4	60.4 ± 5.8	.017
LA diameter (mm)	39.5 ± 6.0	41.2 ± 3.9	37.9 ± 7.0	.010
Days to CT scan	105 ± 38	108 ± 48	101 ± 27	.436

Values are presented as mean ± SD or n (%).

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CT = computed tomography; LA = left atrial; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PFA = pulsed field ablation; RFA = radiofrequency ablation; TIA = transient ischemic attack.

Changes in PV diameters

As shown in Table 2, while average ostial diameters were consistently reduced in all PVs in the RFA cohort, none of the average PV diameters was significantly reduced in the PFA cohort. Similarly, expressed as percentage change in diameter (Table 3), PV ostia decreased significantly less

Table 2 Pulmonary vein ostial diameters (mm) before and after ablation

Variable	Axis	PFA N	PFA Pre	PFA Post	P	RFA n	RFA Pre	RFA Post	P
RSPV	Long	32	21.0 ± 3.6	21.0 ± 3.7	.844	43	20.0 ± 2.8	18.8 ± 3.2	.001
	Short		19.2 ± 3.9	19.6 ± 4.0	.216		18.4 ± 3.6	16.3 ± 3.6	<.001
RIPV	Long	36	19.9 ± 2.7	19.7 ± 2.9	.645	43	18.6 ± 3.7	17.6 ± 4.1	.005
	Short		17.6 ± 3.4	18.3 ± 3.3	.046		16.7 ± 3.4	15.3 ± 3.4	<.001
LSPV	Long	28	22.1 ± 2.7	22.4 ± 2.8	.317	37	20.4 ± 3.2	16.8 ± 4.5	<.001
	Short		15.9 ± 2.5	16.1 ± 3.1	.532		13.9 ± 3.2	11.4 ± 3.7	<.001
LIPV	Long	31	17.6 ± 2.8	17.9 ± 2.7	.245	37	17.0 ± 3.1	13.9 ± 4.4	<.001
	Short		14.1 ± 2.9	14.2 ± 3.1	.679		11.6 ± 2.6	9.8 ± 3.4	<.001
LCV	Long	6	30.2 ± 4.0	30.7 ± 4.1	.620	6	32.6 ± 2.7	26.8 ± 3.9	.003
	Short		19.0 ± 3.4	20.6 ± 3.5	.110		15.9 ± 0.9	13.4 ± 2.3	.084
Total	Long	133	20.5 ± 4.0	20.7 ± 4.1	.408	166	19.5 ± 4.3	17.2 ± 4.7	<.001
	Short		16.9 ± 3.7	17.3 ± 4.0	.009		15.3 ± 4.1	13.4 ± 4.4	<.001

Values are presented as mean ± SD unless specified otherwise.

LCV = left common pulmonary vein; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; PFA = pulsed field ablation; RFA = radiofrequency ablation; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

with PFA than with RFA (% change; long axis: 0.9% ± 8.5% vs −11.9% ± 16.3%; $P < .001$ and short axis: 3.4% ± 12.7% vs −12.9% ± 18.5%; $P < .001$).

Using the initial quantitative methodology only, mild (30%–49%), moderate (50%–69%), or severe (70%–100%) PV narrowing/stenosis was observed, respectively, in 0.8% (1 of 133), 0.0% (0 of 133), and 0.0% (0 of 133) of PVs in the PFA cohort and in 11.4% (19 of 166), 1.8% (3 of 166), and 1.2% (2 of 166) of PVs in the RFA cohort ($P < .001$) (Figure 3A). When further analyzed with the second step 3D qualitative morphological methodology, the one instance of mild narrowing in the PFA group demonstrated no evidence of a waist-like tapering (Figure 4). In contrast, the majority of instances of mild narrowing with RFA (15 of 19 PVs [78.9%]) did indeed display a waist-like tapering consistent with ablation-related damage (Figure 5). All 5 PVs with moderate or severe narrowing with RFA displayed a waist-like tapering consistent with ablation-related damage. Thus, using the combined quantitative/qualitative morphological methodologies, mild (30%–49%), moderate (50%–69%), or severe (70%–100%) PV narrowing/stenosis was observed, respectively, in 9.0% (15 of 166), 1.8% (3 of 166), and 1.2% (2 of 166) of PVs in the RFA cohort but in none of the PVs in the PFA cohort ($P < .001$) (Figure 3B).

Overall, PV narrowing/stenosis was observed in 0% (0 of 133) and 12.0% (20 of 166) of PVs in the PFA and RFA cohort, respectively (Figure 3B). On a per-patient basis, this translates to PV narrowing/stenosis in 0% of patients (0 of 37) in the PFA cohort and 32.5% of patients (14 of 43) in the RFA cohort.

Table 3 Percentage change (%) in pulmonary vein ostial diameters

Variable	Axis	PFA	RFA	P
RSPV	Long	0.4 ± 7.4	−5.8 ± 10.4	.005
	Short	3.2 ± 12.1	−11.0 ± 12.7	<.001
RIPV	Long	−0.4 ± 10.7	−5.4 ± 12.4	.065
	Short	5.4 ± 13.0	−8.0 ± 13.2	<.001
LSPV	Long	1.5 ± 7.0	−18.7 ± 16.5	<.001
	Short	1.6 ± 11.1	−16.7 ± 22.8	<.001
LIPV	Long	2.1 ± 8.0	−18.8 ± 20.7	<.001
	Short	2.0 ± 14.5	−16.4 ± 23.7	<.001
LCV	Long	2.2 ± 8.6	−18.0 ± 8.3	.002
	Short	9.0 ± 11.5	−15.3 ± 16.8	.015
Total	Long	0.9 ± 8.5	−11.9 ± 16.3	<.001
	Short	3.4 ± 12.7	−12.9 ± 18.5	<.001

Values are presented as mean ± SD.

LCV = left common pulmonary vein; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; PFA = pulsed field ablation; RFA = radiofrequency ablation; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

Discussion

In this study, 3-month follow-up CT scanning after ablation of paroxysmal atrial fibrillation demonstrated significantly lower average reductions in PV ostial diameters with PFA than with RFA. *PV narrowing/stenosis*, defined by a reduction in ostial diameter of ≥30% combined with the morphological absence of a waist-like tapering, was significantly less frequent in the PFA cohort than in the RFA cohort (0% vs 12.0% of PVs and 0% vs 32.5% of patients).

PV narrowing and PFA

The incidence of PV stenosis with RFA reported in the literature decreased significantly between the period 1999–2004 (median 5.4%) and the period 2005–2013 (median 3.1%).[13] However, in most of these studies, *ostial PV narrowing* was defined as >50% and varying imaging modalities were used. More recently, Teunissen et al[14] systematically examined the incidence of PV stenosis using 3D magnetic resonance imaging and CT images in 976 patients who underwent PV isolation. They graded PV stenosis as mild (30%–49%), moderate (50%–69%), and severe (70%–100% diameter reduction) in accordance with society consensus statements.[15] They observed a similar incidence of PV stenosis with RFA as in our analysis: total 13.7%

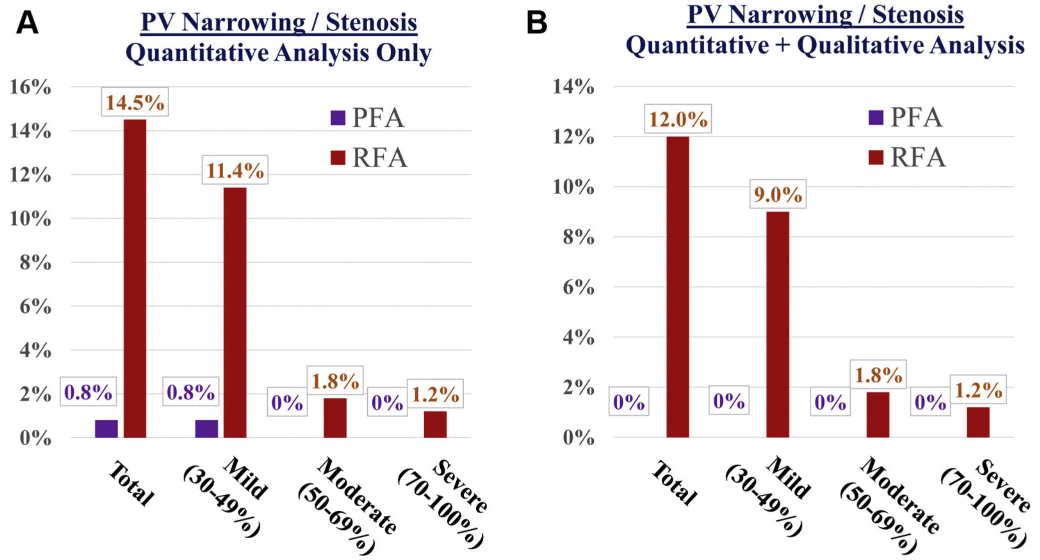

Figure 3 Rates of PV narrowing/stenosis after PFA or RFA. The PFA cohort demonstrated significantly lower rates of PV narrowing/stenosis than the RFA cohort ($P < .001$), whether analyzed only on a quantitative basis (**A**) or using the combined quantitative plus qualitative morphological methodology (**B**). No moderate or severe narrowing/stenosis was observed with either analysis in the PFA cohort. PFA = pulsed field ablation; PV = pulmonary vein; RFA = radiofrequency ablation.

(572 of 4171 PVs); mild 12.3% (514 of 4171 PVs); moderate 1.2% (50 of 4171 PVs); severe 0.2% (7 of 4171 PVs).

To our knowledge, there have been no reports of PV stenotic change caused by PFA in the clinical setting. In our previous experimental study where thoracic vein isolation was performed with PFA (n = 14) and RFA (n = 3) in swine, venous angiography at 2 months follow-up did not reveal any luminal transitions to suggest vein stenosis in all swine. However, PFA lesions were histologically composed of more organized, homogeneous fibrosis replacing the myocardium

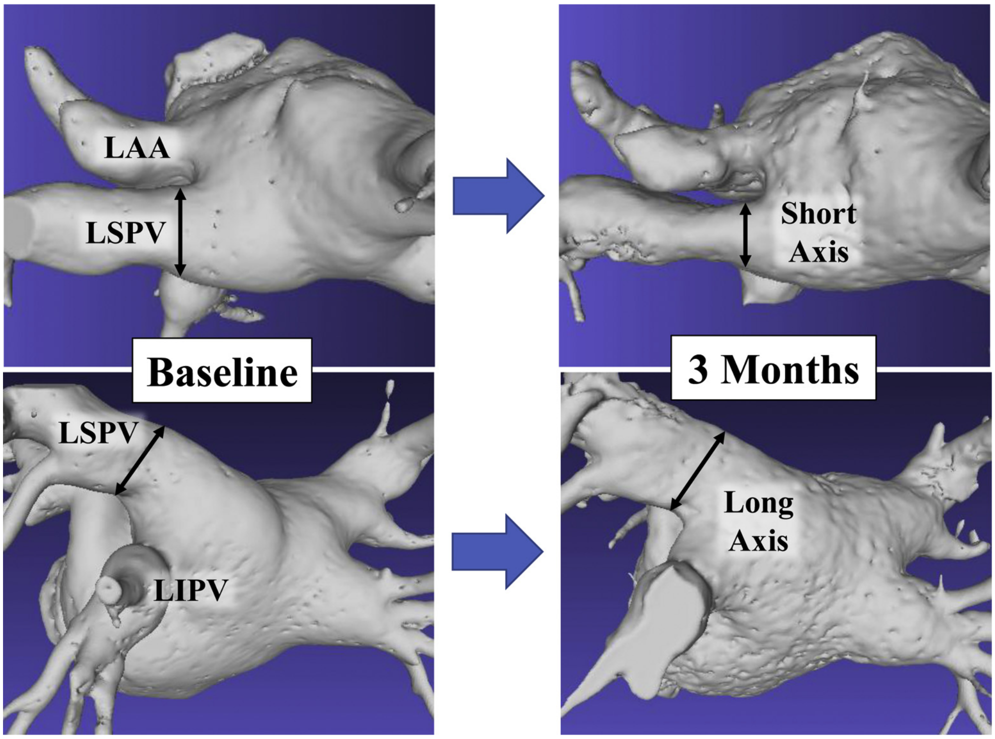

Figure 4 Qualitative morphological analysis after PFA. For each vein on the 3-dimensional CT scan, the long and short axes were measured and qualitatively observed for changes from baseline to 3 months. Compared with the baseline CT scan (**left**), the 3-month CT scan (**right**) of the 1 patient in the PFA group with mild (34%) narrowing in the short axis of the LSPV had no prominent, focal, waist-like change at the vein ostium. Furthermore, the long axis of the LSPV was longer by 10%, suggesting the possibility that the LSPV is compressed in the posterior to anterior direction to a more oval ostial shape. CT = computed tomography; LAA = left atrial appendage; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; PFA = pulsed field ablation.

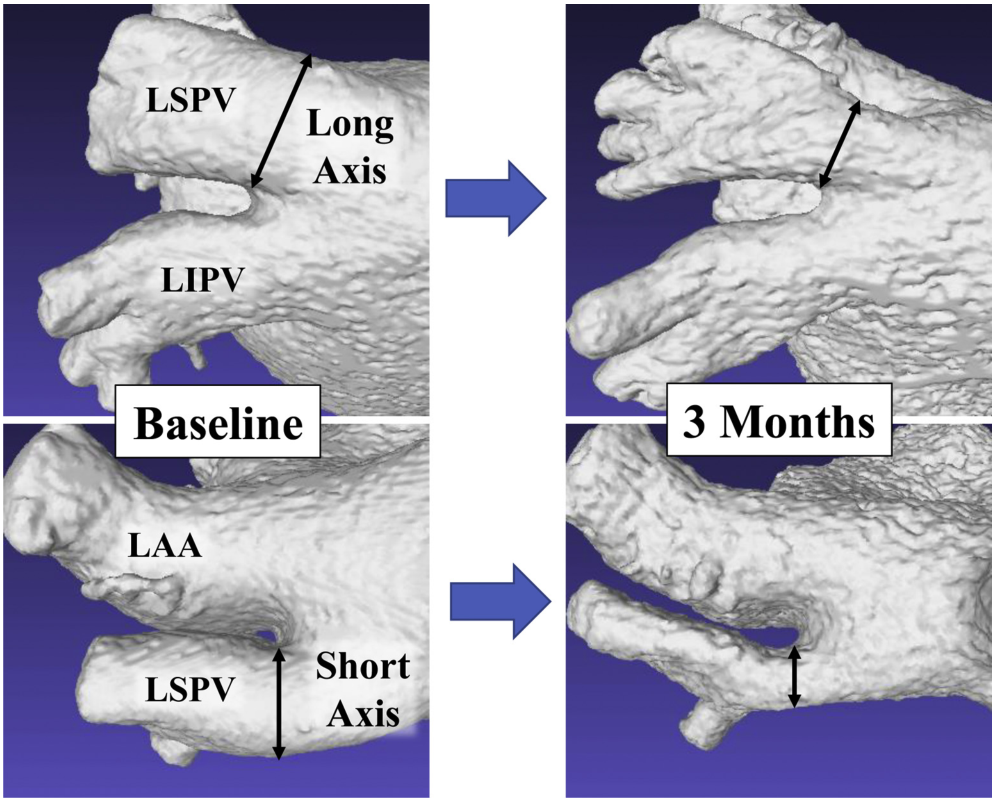

Figure 5 Qualitative morphological analysis after RFA. In this patient treated by RFA, the upper images demonstrated a mild, waist-like narrowing in the long axis of the LSPV. This is most consistent with direct thermally mediated narrowing related to the delivery of radiofrequency energy. LAA = left atrial appendage; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RFA = radiofrequency ablation.

as compared with RFA lesions, which demonstrated greater inflammatory response.[15] Another study using a different PFA catheter design and pulse sequence to ablate atrial tissues in swine reported similar findings.[16] Interestingly, in our preclinical study, we observed that PFA lesions were thinner at their center than at the adjacent nonablated myocardium.[17] While PFA is a newer ablation modality, the chronicity of lesions created by the catheter-based system in this study is well documented. The system's observed rates of durable PV isolation in a published study[8] and as documented in the patients analyzed herein remove the possibility that a subtherapeutic dose may be linked with the observed absence of PV narrowing.

Different patterns of narrowing in mild PV stenosis

Mild PV narrowing/stenosis without a waist-like tapering was defined as "smooth transition narrowing" in the study by Teunissen et al,[14] where among 514 PVs with mild stenosis, 430 (83.7%) revealed a waist-like tapering and only 84 (16.3%) demonstrated a smooth transition narrowing.[14] Similarly in our study, 4 of 19 instances of mild PV stenosis (21.1%) in the RFA cohort had a smooth transition narrowing. A waist-like tapering is thought to be related to fibrosis at the ablation site, but a decrease in lumen size with a smooth transition to the atrium may be explained by reasons such as atrial remodeling, volume changes, or shifted extracardiac anatomy between the 2 CT scan time points.

We examined the characteristics of mild PV stenosis with a smooth transition to the atrium in the 4 affected PVs in the RF cohort and in the 1 PV in the PFA cohort. All these PVs were narrowed in the short axis ($-34.8\% \pm 3.8\%$). In the long axis, the 4 PVs in the RFA cohort had decreased diameters (-27.8%, -26.9%, -25.8%, and -16.0%) at follow-up while the affected PV in the PFA cohort had increased (10.4%). The number of PVs is small, so this divergence in short-long axis dimensions between RFA and PFA may not be significant. But it is interesting to speculate that the PFA vein assumed this more oval cross-sectional shape (ie, an increased long axis and a decreased short axis) because the histological tissue volume loss observed with PFA[17] resulted in more anterior-posterior PV compression by the surrounding tissue (Figure 4). It has been reported that the LA volume decreases after PV isolation, regardless of atrial fibrillation recurrence,[18] and it is likely not only due to reverse remodeling from a decreased atrial fibrillation burden but also due to tissue shrinkage attributable to ablation-induced fibrosis. The rarity of PV narrowing with a smooth transition to the atrium in the PFA cohort may be explained by its nonthermal mechanism of ablation resulting in less global shrinkage of the atria related to fibrotic change.

Limitations

First, this was a retrospective observational study, not a direct randomized comparison of RFA and PFA, and thus subject to potential bias. There were statistically significant differences in some of the baseline characteristics (history of coronary artery disease, LVEF, and LA diameter) between the groups. However, the effect of these differences on our analyses would be expected to be small; note that we compared not the absolute value but the interval changes in PV diameters of each group. Second, in control patients, a contact force–sensing catheter was used in only 32.6% of patients (14 of 43) because TOCCASTAR and HEARTLIGHT were performed between 2011 and 2013. However, in TOCCASTAR, the randomized comparison of contact force–sensing and non-contact force–sensing catheters did not demonstrate any difference in PV stenosis.[9] Furthermore, a study showed that the likelihood of PV stenosis increased along with the advent of contact force–sensing catheters,[14] consistent with the relationship between contact and no contact with respect to thermal lesion efficacy. Third, the location where the PV dimension was measured could be more distal than the actual ablation line in the RFA cohort, because the RFA line was created circumferentially at the ostia of the superior and inferior veins while PFA was performed individually to each vein. In this study, to reduce bias, CT images were deidentified before measurement, so the readers were blinded to the ablation method; accordingly, the same depth level of the PV was measured regardless of the groups. Fourth, in the process of patient selection, only 37 of 80 patients in the PFA cohort and only 43 of 73 patients in the RFA cohort were selected because of the poor image quality or non-availability of follow-up CT scans. This could be a selection bias that cannot be compensated by statistical means.

Conclusion

This analysis indicates that the incidence and severity of PV narrowing or stenosis are significantly reduced with PFA compared with RFA. This may reflect fundamental mechanistic differences in either or both ablation and healing between PFA and RFA.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2020.04.040.

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