Received: 17 January 2020 | Revised: 26 February 2020 | Accepted: 15 April 2020

DOI: 10.1111/jce.14544

ORIGINAL - ELECTROPHYSIOLOGY

WILEY

Differences between gap-related persistent conduction and carina-related persistent conduction during radiofrequency pulmonary vein isolation

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Disclosures: None.

Abstract

Background: During pulmonary vein isolation (PVI), nonisolation after initial encircling of the pulmonary veins (PVs) may be due to gaps in the initial ablation line, or alternatively, earliest PV activation may occur on the intervenous carina and ablation within the wide-area circumferential ablation (WACA) circle is needed to eliminate residual conduction. This study investigated prognostic implications and predictors of gap-related persistent conduction (gap-RPC) and carina-related persistent conduction (carina-RPC) during PVI.

Methods and Results: Two hundred fourteen atrial fibrillation (AF) patients (57% paroxysmal, 61% male, mean age 62 ± 9 years) undergoing first contact force-guided radiofrequency PVI were studied. Preprocedural cardiac computed tomography imaging was used to assess left atrial and PV anatomy. PVI was assessed directly after initial WACA circle creation, after a minimum waiting period of 30 minutes, and after adenosine infusion. Persistent conduction was targeted for additional ablation and classified as gap-RPC or carina-RPC, depending on the earliest activation site. The 1-year AF recurrence rate was higher in patients with gap-RPC (47%) compared to patients without gap-RPC (28%; $P = .003$). No significant difference in 1-year recurrence rate was found between patients with carina-RPC (37%) and patients without carina-RPC (31%; $P = .379$). Multivariate analyses identified paroxysmal AF and WACA circumference as independent predictors of gap-RPC, whereas carina width and WACA circumference correlated with carina-RPC.

Abbreviations: AF, atrial fibrillation; Carina-RPC, carina-related persistent conduction; CF, contact force; CT, computed tomography; Gap-RPC, gap-related persistent conduction; LA, left atrium; PV, pulmonary vein; PVI, pulmonary vein isolation; RF, radiofrequency; WACA, wide-area circumferential ablation.

Conclusions: Gap-RPC is associated with increased AF recurrence risk after PVI, whereas carina-RPC does not predict AF recurrence. Moreover, gap-RPC and carina-RPC have different correlates and may thus have different underlying mechanisms.

KEYWORDS

atrial fibrillation, carina, catheter ablation, persistent conduction, pulmonary vein isolation

1 | INTRODUCTION

Pulmonary vein isolation (PVI) is the cornerstone of catheter ablation in patients with symptomatic paroxysmal and persistent atrial fibrillation (AF).[1] PVI is not always achieved after initial encircling of the pulmonary veins (PVs) and touch-up lesions are frequently required to close residual conduction gaps in the ablation line.[2,3] However, earliest PV activation may also occur on the intervenous carina, i.e. the region between ipsilateral PVs, and several studies identified the carina as a predilection site for persistent left atrial (LA)-PV conduction.[4-7] Additional ablation inside the initial ablation circle, on the carina, is therefore often required, which may be explained by the complex anatomy of this specific region. Crossing myocardial strands have been demonstrated in the carina region, located both on the endocardial and epicardial side, which may function as bridges of electrical connection across ablation lines.[8]

Distinction between gap-related persistent conduction and carina-related persistent conduction (carina-RPC) could be of clinical relevance. Carina-RPC may occur despite sufficient ablation lesion formation and be due to anatomical variabilities, such as epicardially located crossing muscle strands that cannot be reached with endocardial ablation. In contrast, gap-RPC only occurs in the setting of insufficient ablation lesion depth or continuity. Therefore, we hypothesized that gap-RPC and carina-RPC may have a different impact on AF ablation efficacy. The objectives of the current study were to assess prognostic implications of gap-RPC and carina-RPC, and to identify their predictors.

2 | METHODS

2.1 | Patient population

Two hundred and twenty-two consecutive patients with symptomatic AF underwent their first PVI procedure between January 2015 and December 2016 at the VU University Medical Center. Eight patients were excluded for the present analysis due to insufficient computed tomography (CT) imaging quality (n = 7) or incomplete ablation procedure data (n = 1). The remaining 214 patients were included in the present study. AF was classified as paroxysmal if episodes were self-terminating or cardioverted within 7 days of onset. Ablation procedures were preceded by cardiac CT imaging to assess LA anatomy.

All patients provided informed consent and the local medical ethics committee (VU University Medical Center, Amsterdam, The Netherlands) approved collection and management of data. The study conforms with the principles outlined in the Declaration of Helsinki.

2.2 | CT imaging and analysis

All patients underwent preprocedural contrast-enhanced electrocardiogram (ECG)-gated cardiac CT imaging with a dual-source 128-slice (Somatom Definition Flash; Siemens Medical Systems, Erlangen, Germany) or 256-slice (Brilliance iCT; Philips Healthcare, Best, The Netherlands) scanner. Cardiac CT images were obtained after an intravenous bolus of Iobitridol (Xenetix 350) or Iopromid (Ultravist 360) at a rate of 6 mL/s followed by a flush of 45 to 50 mL saline. Non-overlapping images were reconstructed with a 512 × 512 matrix at the early atrial diastolic phase at 60% to 75% of the R-R interval.

Image analysis was performed blinded to clinical parameters and outcomes by a single investigator (MM). Image data were transferred to a commercially available workstation (IntelliSpace Portal, Philips) for three-dimensional (3D) reconstructions and assessment of the LA and PVs (Figure 1A). LA volume was indexed to BSA and was assessed after excluding the PVs at their ostia and the LA appendage (LAA) at its base. The PV ostia were defined as the point of maximum inflection between the PV wall and the LA wall. A common venous trunk was defined as a superior and inferior PV that coalesce before entering the LA.

PV diameters were assessed at the level of the PV ostia. To obtain PV diameters, views perpendicular to the centerline of each PV were created using multiplanar formatting (Figure 1B).[9] Carina width was defined as the shortest distance between ipsilateral superior and inferior PV ostia and was measured on the 3D LA reconstruction (Figure 1C). After cutting off left PVs and LAA from the 3D LA reconstruction, the average width of the PV-LAA ridge was calculated by averaging measurements on the level of left superior PV, carina and left inferior PV (Figure 1D).

2.3 | Ablation procedure and analysis

Ablation procedures were performed under conscious sedation, deep sedation, or general anesthesia. After femoral access (modified Seldinger technique), one 8F sheath and two 8.5F long sheaths were introduced and a steerable catheter was placed in the coronary sinus. A bolus of heparin was administered to achieve an activated clotting

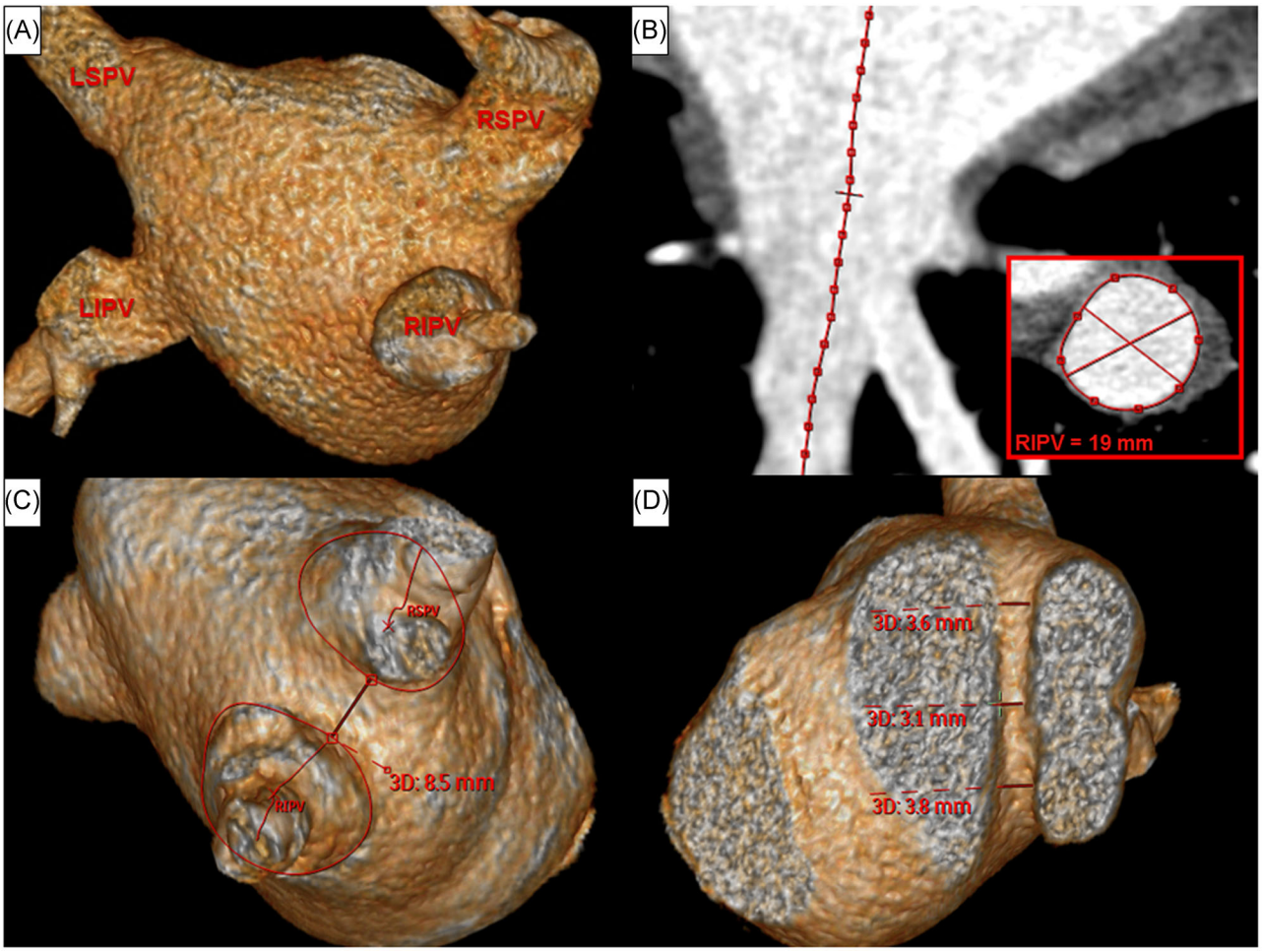

FIGURE 1 CT image analysis. A, Three-dimensional reconstruction of the left atrium (LA) and pulmonary veins (PV) allows for assessment of global PV anatomy. B, PV diameters were obtained after orienting a view perpendicular to the centerline of the PV. C, Carina width, defined as the distance between ipsilateral superior and inferior PV ostia, was measured on the reconstruction of the LA. D, After cutting off left PVs and left atrial appendage (LAA), the average width of the PV-LAA ridge was calculated by averaging measurements on the level of left superior PV, carina and left inferior PV. CT, computed tomography; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein

time of 300 to 400 seconds before transseptal puncture and introduction of catheters into the LA. The atrial septum was punctured under guidance of continuous pressure measurement and fluoroscopy. A circular mapping catheter (Lasso; Biosense Webster, Diamond Bar, CA) and an ablation catheter (Smarttouch; Biosense Webster) were positioned in the LA via long sheaths. Both long sheaths were continuously flushed with heparinized saline.

A 3D mapping system (Carto3; Biosense Webster) was used to create an electroanatomical map of the LA with integration of the segmented CT scan. Radiofrequency (RF) energy was delivered in a wide-area circumferential ablation (WACA) pattern using either a sequential point-by-point technique or a "dragging" technique. No additional techniques for improvement of catheter stability (eg, pacing-induced heart rate acceleration, high-frequency jet ventilation, automatic catheter contact force [CF] controller) were used. Maximum power limit was set at 30 W for the posterior wall and 35 to 40 W for other segments. A CF of 10 to 20 g was targeted during ablation. Ablation lesions were tagged manually or using an automated lesion tagging system (VisiTag; Biosense Webster), at the operator's discretion. Automatically tagged lesions were only displayed when the following predefined criteria were met: stability maximum range 2 to 3 mm, stability minimum time 8 to 10 seconds, force overtime set at 30% to 50%, and minimum force of 5 g. Ablation lesions were displayed as standard tags or as a grid on the LA shell.

After closing the initial WACA circles, electrical cardioversion was performed if required to achieve sinus rhythm. Isolation of the PVs was assessed by placing the mapping catheter in a stable position in the ostium of the superior and inferior PV. When entrance block could not be confirmed, the earliest bipolar PV potential was identified from the circular mapping catheter and the ablation catheter was advanced in this area. Subsequently, the precise site of residual conduction was localized by carefully dragging the ablation catheter along the ablation line and on the intervenous carina to identify the earliest activation site. The site of persistent connection

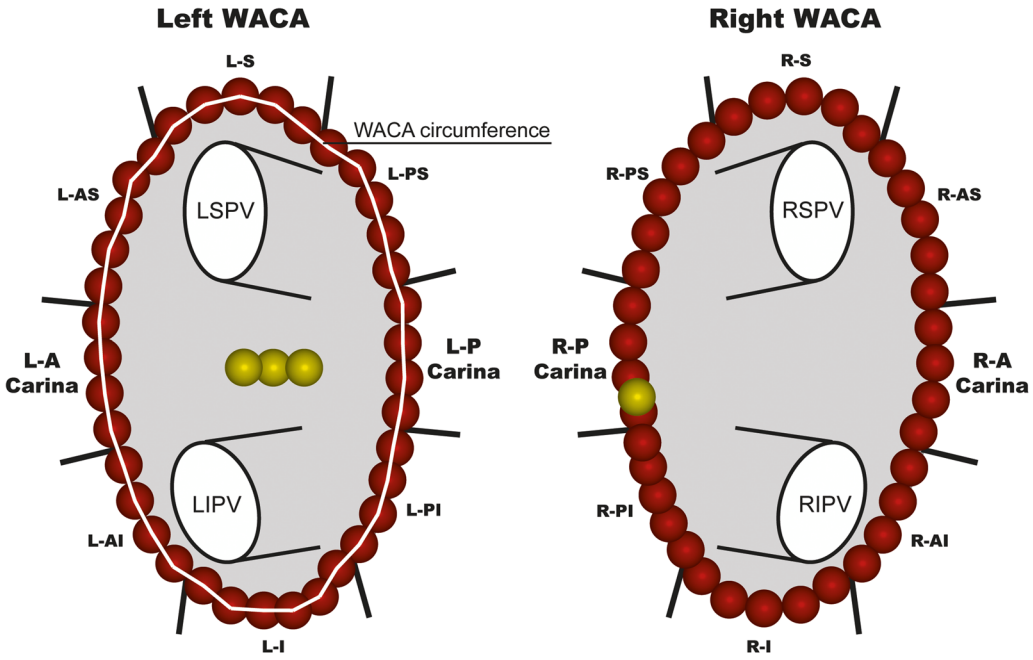

FIGURE 2 Schematic illustration of WACA segments and measurement of WACA circumference. Schematic illustration showing left (L) and right (R) wide-area circumferential ablation (WACA) and measurement of WACA circumference. Yellow tags represent additional ablation of carina-related persistent conduction (carina-RPC) in the left WACA and additional ablation of gap-related persistent conduction (gap-RPC) in the right WACA. Mean/minimum contact force and impedance drop were recorded for each ablation lesion tag and all tags were categorized according to a 16-segment model. A, anterior; AI, anterior inferior; AS, anterior superior; carina-RPC, carina-related persistent conduction; I, inferior; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; P, posterior; PI, posterior inferior; PS, posterior superior; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; S, superior; WACA, wide-area circumferential ablation

was subsequently targeted to achieve PV isolation and to confirm the site of residual conduction. Additional ablation targeting residual conduction was performed using similar ablation settings as used for the initial WACA circles. Ablation power was reduced to 30 W on the intervenous carina. After a waiting period of at least 30 minutes, persistence of PVI was tested through administration of intravenous adenosine. Adenosine was administered initially in a dose of 6 mg and was titrated up with 6 mg increments until atrioventricular block was noted, with a maximum total dosage of 24 mg. If reconnection occurred during the waiting period or after adenosine administration (acute reconnection), additional ablation was performed until complete isolation was achieved. In persistent AF patients, additional LA ablation beyond PVI was performed at the discretion of the operator. Residual conduction after the initial WACA circles was classified as either gap-related or carina-related depending on the site of the earliest activation (Figure 2). Carina-RPC was defined as residual conduction with the earliest activation in the carina region not within 10 mm of the initial WACA circle, as determined by the build-in distance measurement tool in the Carto3 system.

All procedures were exported to a dedicated Carto3 workstation and analyzed offline. Only ablation tags of the initial WACA circle were analyzed, that is, tags on the intervenous carina or additional lesions to close residual gaps were not analyzed. Mean and minimum CF and impedance drop were recorded for each tag and all tags were categorized according to a 16-segment model (Figure 2). Impedance drop was defined as the difference between preablation impedance and the lowest recorded impedance value during ablation. Mean CF was calculated for each segment by dividing the total force-time-interval by the total duration of RF application of the respective segment. Subsequently, for both WACA circles and carina segments mean CF and impedance drop were calculated separately. The circumferences of both WACA circles were measured using the built-in "design line" feature on the 3D electroanatomical map of the LA through all ablation tags of the initial WACA circle.

2.4 | Follow-up

Patients were followed up for 12 months after PVI and underwent mandatory ECG recordings at 1, 3, 6, and 12 months post-PVI. Additional ECG recordings or 24-hour Holter monitoring were obtained when symptoms suggestive of a tachyarrhythmia occurred. Antiarrhythmic drugs were typically discontinued after 3 months in case of no recurrence. Recurrence was defined as any documented episode of AF or atrial flutter lasting more than 30 seconds during follow-up after a blanking period of 3 months. In patients undergoing repeat ablation procedure, each PV was assessed for late reconnection using a circular mapping catheter (Lasso; Biosense Webster) and site of reconnection was noted in a similar fashion as during the index procedure.

2.5 | Statistical analysis

Statistical analyses were performed using SPSS (version 22; IBM Corporation, Armonk, NY). Continuous variables were reported as mean ± standard deviation or as median (interquartile range) where a normal distribution could not be assumed. Categorical variables were expressed as frequency (percentage). Categorical variables were compared using the χ^2 test and continuous variables using the Student *t* test or the Mann-Whitney *U* test when appropriate. A paired *t* test was used to compare imaging and procedural characteristics between left and right PVs. To assess the impact of clinical, imaging, and procedural characteristics on the occurrence of gap-RPC and carina-RPC, univariate logistic regression analyses were separately performed for left and right WACA circles. Univariate predictors with a *P* value of less than .10 were included in multivariate analyses using backward elimination. Kaplan-Meier analyses were performed to assess freedom of atrial tachyarrhythmias for patients with and without gap-RPC and for patients with and without carina-RPC. Differences between subgroups were assessed by the log-rank test. A two-sided *P* value of less than .05 was considered statistically significant.

3 | RESULTS

A total of 214 patients (61% male, mean age 62 ± 9 years) were included for analysis. Paroxysmal AF was present in 121 patients (57%) and PVI was performed 28 (9-65) months after diagnosis of AF. AF was present in 90 patients (42%) at the start of the ablation procedure. Spontaneous AF termination during ablation occurred in 14/90 patients (16%) and organization into (macro-reentrant) atrial tachycardia occurred in 19/90 patients (21%). The mean procedure duration, defined as the time from the first RF application to last RF application, was 95 ± 34 minutes and the mean RF application time was 47 ± 13 minutes. Additional gap or carina ablation was associated with a longer procedure duration (108 ± 31 vs 71 ± 24 minutes; $P < .001$) and RF application time (50 ± 12 vs 40 ± 12 minutes; $P < .001$). Fluoroscopy time was similar for patients with and without additional gap or carina ablation (9 ± 5 vs 10 ± 5 minutes; $P = .586$). Additional LA ablation beyond PVI was performed in 16 patients (7%). Adjuvant ablation of complex fractionated electrograms was performed in six patients (3%), LA roofline was created in eight patients (4%), and a mitral line in three patients (1%). Clinical characteristics, imaging characteristics, and procedural data are depicted in Table 1.

3.1 | Imaging characteristics and ablation procedure analysis

Two separate left-sided PV ostia and two separate right-sided PV ostia were present in 155 patients (72%). A common ostium of the left PVs was found in 35 patients (16%) and an accessory right PV in 29 patients (14%). Left carina width was significantly smaller than right carina width (5.3 ± 2.6 vs 7.0 ± 3.1 mm, respectively; $P < .001$), and the left WACA circumference was shorter than the right WACA circumference (12.3 ± 2.0 vs 13.0 ± 1.9 cm, $P < .001$). Mean CF was 14.0 ± 2.2 g for the left WACA circle and 15.1 ± 2.5 g for the right WACA circle ($P < .001$). Mean CF was not statistically different in left and right carina segments compared to other segments of the WACA circle (left side: 13.7 ± 3.3 vs 14.1 ± 1.8 g; $P = .120$, right side: 15.5 ± 3.4 vs 15.0 ± 2.2 g; $P = .071$).

Table 2 summarizes the prevalence of gap-RPC and carina-RPC after initial encircling of the PVs, during the 30-minute waiting period and after adenosine testing. Concomitant ipsilateral gap-RPC and carina-RPC (either left of right-sided) occurred in 39 patients (18%). Bilateral gap-RPC was noted in 16 patients (7%) and bilateral carina-RPC in 20 patients (9%). Ultimately, the procedural endpoint of complete PVI of all PVs was reached in all 214 patients.

3.2 | Predictors of gap-related and carina-RPC

Table 3 shows the univariate and multivariate analyses of variables associated with left-sided and right-sided touch-up ablation due to gap-RPC. Paroxysmal AF, left WACA circumference, left carina width, and combined LSPV + LIPV diameter were associated with left-sided gap-RPC in univariate analysis. Only paroxysmal AF and the left WACA circumference remained significant in the multivariate analysis. Paroxysmal AF and right WACA circumference were identified as univariate predictors of right-sided gap-RPC, and both remained significant in the multivariate analysis.

Left-sided carina-RPC did not occur in patients with a common left PV ostium. Left-sided first-pass isolation was more common in patients with a common left PV trunk (89% vs 71%; $P = .03$). Table 4 shows the univariate and multivariate analyses for factors associated with necessity of left-sided and right-sided carina ablation due to carina-RPC. In univariate regression analysis, left WACA circumference, combined LSPV + LIPV diameter and left carina width were significantly associated with left-sided carina-RPC. Paroxysmal AF, left WACA circumference, and left carina width were significant predictors of left-sided carina-RPC in the multivariate analysis.

Right WACA circumference, mean CF during ablation on the right carina segments, LA volume, and right carina width were univariate predictors of right-sided carina-RPC. Multivariate logistic regression analysis identified right WACA circumference, mean CF during ablation on the right carina segments and right carina width as independent predictors of right-sided carina-RPC.

3.3 | Follow-up

Two hundred thirteen patients (99.5%) completed 12 months of follow-up; one patient died from a noncardiac cause. Recurrence of atrial tachyarrhythmias was documented in 73 patients (34%) at 12 months follow-up. In 50 patients (68%) with recurrent tachyarrhythmias, AF was observed, whereas in seven patients (10%) only atrial flutter was

TABLE 1 Clinical, imaging, and procedural characteristics

	Total cohort (n = 214)	Initial WACAs only (n = 79)	Extra ablation required (n = 135)	*P* value
Clinical characteristics				
Age, y	62 ± 9	62 ± 10	62 ± 9	.523
Male	130 (61%)	46 (58%)	84 (62%)	.563
Paroxysmal AF	121 (57%)	37 (47%)	84 (62%)	**.028**
AF duration, mo	28 (9-65)	26 (10-62)	29 (9-67)	.854
Body mass index, kg/m^2	28 ± 4	28 ± 4	28 ± 4	.945
Congestive heart failure	31 (14%)	10 (13%)	21 (16%)	.561
Hypertension	95 (44%)	34 (43%)	61 (45%)	.760
Diabetes mellitus	15 (7%)	7 (9%)	8 (6%)	.417
Coronary artery disease	24 (11%)	13 (17%)	11 (8%)	.063
Prior stroke	19 (9%)	10 (13%)	9 (7%)	.137
$CHADS_2VASC$ ≤1	90 (42%)	29 (37%)	61 (45%)	.225
Number of failed AAD	1.4 ± 0.7	1.4 ± 0.6	1.4 ± 0.7	.864
Imaging characteristics				
LA diameter, cm	4.1 ± 0.6	4.1 ± 0.6	4.2 ± 0.6	.501
LA volume, mL	118 ± 34	113 ± 28	121 ± 37	.101
LAVI, mL/m^2	57 ± 16	56 ± 13	58 ± 17	.300
Common ostium left PV	35 (16%)	16 (20%)	19 (14%)	.238
Accessory right PV	29 (14%)	15 (19%)	14 (10%)	.076
Left superior PV diameter, mm	17.8 ± 2.4	17.3 ± 2.3	18.0 ± 2.4	.071
Left inferior PV diameter, mm	15.3 ± 2.6	15.0 ± 2.7	15.5 ± 2.5	.462
Right superior PV diameter, mm	19.7 ± 2.8	19.4 ± 2.9	19.9 ± 2.7	.216
Right inferior PV diameter, mm	17.8 ± 2.8	17.4 ± 2.8	18.1 ± 2.8	.064
Left carina width, mm	5.3 ± 2.6	4.7 ± 2.5	5.7 ± 2.5	**.009**
Right carina width, mm	7.0 ± 3.1	6.3 ± 3.0	7.3 ± 3.1	**.021**
Left PV-LAA ridge width, mm	4.1 ± 1.3	4.1 ± 1.5	4.1 ± 1.2	.776
Procedural characteristics				
Type of anesthesia/sedation				.057
General anesthesia	6 (3%)	5 (6%)	1 (1%)	
Deep sedation	119 (56%)	42 (53%)	77 (57%)	
Conscious sedation	89 (42%)	32 (41%)	57 (42%)	
Dragging ablation performed	105 (49%)	42 (53%)	63 (47%)	.359
Procedure duration, min	95 ± 34	71 ± 24	108 ± 31	**<.001**
Fluoroscopy time, min	10 ± 5	9 ± 5	10 ± 5	.586
Radiation dose, Gy × cm^2	9.1 ± 4.7	8.8 ± 4.7	9.2 ± 4.8	.501
RF application time, min	47 ± 13	40 ± 12	50 ± 12	**<.001**
Left-sided first-pass isolation	158 (74%)	79 (100%)	79 (59%)	**<.001**
Right-sided first-pass isolation	138 (64%)	79 (100%)	59 (44%)	**<.001**
Bilateral first-pass isolation	107 (50%)	79 (100%)	28 (21%)	**<.001**
Left WACA mean CF, g	14.0 ± 2.2	14.3 ± 2.1	13.9 ± 2.3	.141
Right WACA mean CF, g	15.1 ± 2.5	15.5 ± 2.4	14.9 ± 2.5	.100
Left WACA number of segments with mean CF <10 g	1 (0-2)	1 (0-2)	1 (0-2)	.550
Right WACA number of segments with mean CF <10 g	0 (0-1)	0 (0-1)	0 (0-1)	.060
Left carina mean CF, g	13.7 ± 3.3	14.2 ± 3.4	13.4 ± 3.2	.132

(Continues)

TABLE 1 (Continued)

	Total cohort (n = 214)	Initial WACAs only (n = 79)	Extra ablation required (n = 135)	*P* value
Right carina mean CF, g	15.5 ± 3.4	15.9 ± 3.2	15.2 ± 3.5	.168
Mean impedance drop (Ω)	13.0 ± 2.8	12.8 ± 2.7	13.1 ± 2.8	.535
Left WACA circumference, cm	12.3 ± 2.0	11.6 ± 1.7	12.7 ± 2.0	**<.001**
Right WACA circumference, cm	13.0 ± 1.9	12.4 ± 1.8	13.4 ± 1.8	**<.001**
Additional LA ablation beyond PVI	16 (7%)	9 (11%)	7 (5%)	.096
Procedural complications	10 (5%)	5 (6%)	5 (4%)	.380

Note: All values are mean ± standard deviation or median (interquartile range) for continuous variables and number (%) for categorical variables. P values in bold indicate significance (p < 0.05).
Abbreviations: AAD, antiarrhythmic drug; AF, atrial fibrillation; CF, contact force; LA, left atrium; LAVI, left atrial volume index; PV, pulmonary vein; PVI, pulmonary vein isolation; RF, radiofrequency ablation; WACA, wide-area circumferential ablation.

documented. In 16 patients (22%), both AF and atrial flutter were observed during follow-up. Kaplan-Meier survival analyses demonstrated a significantly higher rate of recurrence in patients with gap-RPC (47%) compared to patients without gap-RPC (28%; *P* = .003). Gap-RPC was both a predictor of recurrence in paroxysmal AF patients (41% vs 20%; *P* = .012) and persistent AF patients (59% vs 35%; *P* = .012). Probability of recurrence was similar in patients with carina-RPC (37%) and patients without carina-RPC (31%; *P* = .379), irrespective of AF type. No significant difference in arrhythmia recurrence was found between patients with and without bilateral first-pass isolation (30% vs 38%; *P* = .152). Kaplan-Meier survival analyses of patients with and without gap-RPC and carina-RPC are shown in Figure 3.

A repeat ablation procedure was performed in 40 of 73 (55%) patients with documented tachyarrhythmia recurrence, after a median of 7 (6-10) months. The overall median number of reconnected PVs was 2 (0-2). Persistent isolation of all PVs was demonstrated in 12 patients (30%). Left-sided PV reconnection rate at repeat procedure was higher in patients with left-sided gap-RPC during index procedure (56% vs 19%; *P* = .033). Right-sided PV reconnection rate at repeat procedure was similar for patients with and without right-sided gap-RPC during index procedure (60% vs 60%; *P* = 1.000). Neither left-sided nor right-sided carina-RPC during the index procedure was predictive of ipsilateral PV reconnection during repeat procedure. The majority (71%) of reconnected segments during repeat procedure did not correspond to the site of residual conduction during the index procedure.

4 | DISCUSSION

The present analysis of gap-RPC and carina-RPC during CF-guided PVI yielded the following findings: (a) additional ablation lesions beyond the initial WACA circles were frequently required to achieve PVI; (b) gap-RPC was associated with a higher AF recurrence rate after PVI, whereas carina-RPC was not associated with AF recurrence; (c) WACA circumference was an independent predictor of both gap-RPC and carina-RPC and (d) carina width was independently associated with carina-RPC.

4.1 | Carina-related persistent conduction

The intervenous carina has been extensively reported as a predilection site for persistent PV-LA conduction.[4,5,10] Several factors may explain the crucial role of the carina region in achieving PVI. Anatomical reports showed that the thickest myocardial sleeves

TABLE 2 Prevalence of gap-RPC and carina-RPC

	After initial encircling	During 30-min waiting period	After adenosine testing	Total
Left WACA (n = 214)				
Gap-RPC	24 (11%)	13 (6%)	3 (1%)	40 in 37 (17%) patients
Carina-RPC	39 (18%)	12 (6%)	6 (3%)	56 in 47 (22%) patients
Right WACA (n = 214)				
Gap-RPC	31 (14%)	8 (4%)	14 (7%)	57 in 52 (24%) patients
Carina-RPC	58 (27%)	18 (8%)	14 (7%)	90 in 78 (36%) patients

Abbreviations: Carina-RPC, carina-related persistent; gap-RPC, gap-related persistent conduction; WACA, wide-area circumferential ablation.

TABLE 3 Univariate and multivariate factors associated with gap-RPC

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Gap-RPC in left WACA (n = 37)						
Paroxysmal AF	2.810	1.254-6.297	.012	3.327	1.387-7.981	**.007**
Age, y	1.017	0.977-1.058	.421			
Hypertension	1.079	0.530-2.197	.834			
AF duration, mo	1.005	0.999-1.011	.129			
Dragging ablation performed	1.661	0.809-3.411	.167			
Procedure under conscious sedation	0.949	0.461-1.952	.887			
WACA circumference, cm	1.320	1.095-1.591	.004	1.345	1.107-1.635	**.003**
WACA mean CF, g	1.069	0.904-1.263	.436			
WACA mean power, W	0.801	0.588-1.090	.158			
Number of segments mean CF <10 g	0.977	0.736-1.296	.871			
WACA mean impedance drop (Ω)	0.966	0.861-1.085	.562			
LA volume, mL	0.993	0.982-1.005	.230			
LSPV + LIPV diameter, mm	1.077	1.002-1.157	.043	**	**	**
Left carina width, mm	1.135	0.990-1.300	.069	**	**	**
Average PV-LAA ridge width, mm	1.211	0.933-1.574	.151			
Gap-RPC in right WACA (n = 52)						
Paroxysmal AF	2.290	1.167-4.496	.016	3.522	1.607-7.719	**.002**
Age, y	1.021	0.986-1.058	.243			
Hypertension	1.348	0.720-2.522	.350			
AF duration, mo	1.001	0.995-1.007	.806			
Dragging ablation performed	0.949	0.508-1.773	.870			
Procedure under conscious sedation	1.279	0.682-2.400	.443			
WACA circumference, cm	1.439	1.196-1.730	<.001	1.572	1.282-1.926	**<.001**
WACA mean CF, g	1.058	0.925-1.210	.410			
WACA mean power, W	0.956	0.781-1.171	.665			
Number of segments mean CF <10 g	0.875	0.607-1.261	.474			
WACA mean impedance drop (Ω)	0.924	0.814-1.049	.221			
LA volume, mL	1.002	0.992-1.011	.741			
Right accessory PV	0.612	0.221-1.694	.344			
Combined right PV diameter, mm	1.055	0.980-1.136	.152			
Right carina width, mm	1.059	0.959-1.169	.259			

Note: "**" indicates that the variable was removed in the final regression equation (ie, nonsignificant). P values in bold indicate significance in multivariate analysis ($p < 0.05$).

Abbreviations: AF, atrial fibrillation; CF, contact force; CI, confidence interval; gap-RPC, gap-related persistent conduction; LAVI, left atrial volume index; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; OR, odds ratio; PV, pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; WACA, wide-area circumferential ablation.

around the PVs are found in the carina region.[11] The increased local atrial wall thickness may contribute to the nontransmurality of ablation lesions, since RF power, CF and ablation duration are not adjusted to local wall thickness. Moreover, crossing myocardial fibers in the carina region, located both on the endocardium and epicardium, could function as a bridge of electrical connection across ablation lines.[8] The incidence of carina-RPC varies widely between studies, from 1% to 57% of PVs.[4,6,7,10,12] This inconsistency may be due to differences in the distance between WACA circle and the PV ostia. In a previous study, the distance between the WACA circle and the PV ostia predicted the requirement of carina ablation and the incidence of carina-RPC was significantly reduced when using a fixed distance of 8 mm from the WACA circle to the PV ostia.[10] Similarly, in this study, a larger WACA circumference, indicating a greater distance to the PV ostia, was independently associated with a higher incidence of carina-RPC.

Moreover, the present study demonstrated an independent association between carina-RPC and a greater carina width, that is, the distance between ipsilateral superior and inferior PV ostia. Increased carina dimensions may be associated with the presence of more complex myocardial architecture such as epicardially located crossing strands, which could explain the requirement for ablation inside the WACA circle to achieve complete isolation of the PVs. The complex anatomy of the carina region may also hamper ablation catheter stability. Lower CF values have been found in carina segments during PVI when operators were blinded to CF data.[13] In the current study,

TABLE 4 Univariate and multivariate factors associated with carina-RPC

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Carina-RPC in left WACA (n = 47)						
Paroxysmal AF	1.950	0.986-3.858	.055	2.204	1.036-4.686	**.040**
Age, y	0.978	0.944-1.012	.197			
Hypertension	0.967	0.506-1.847	.919			
AF duration, mo	0.998	0.991-1.005	.590			
Dragging ablation performed	0.681	0.356-1.303	.246			
Procedure under conscious sedation	1.250	0.655-2.388	.499			
WACA circumference, cm	1.391	1.164-1.661	<.001	1.298	1.059-1.592	**.012**
Mean CF carina segments, g	0.989	0.891-1.097	.836			
Mean impedance drop carina segments (Ω)	0.979	0.903-1.062	.607			
LA volume, mL	0.997	0.987-1.007	.539			
LSPV + LIPV diameter, mm	1.072	1.006-1.142	.033	**	**	**
Left carina width, mm	1.281	1.123-1.462	<.001	1.180	1.012-1.375	**.035**
Average PV-LAA ridge width, mm	1.168	0.920-1.482	.203			
Carina-RPC in right WACA (n = 78)						
Paroxysmal AF	1.270	0.722-2.236	.407			
Age, y	0.992	0.962-1.022	.581			
Hypertension	1.214	0.694-2.124	.498			
AF duration, mo	0.999	0.994-1.005	.827			
Dragging ablation performed	0.978	0.561-1.707	.939			
Procedure under conscious sedation	1.048	0.595-1.842	.872			
WACA circumference, cm	1.477	1.237-1.762	<.001	1.349	1.102-1.651	**.004**
Mean CF carina segments, g	0.881	0.799-0.970	.010	0.882	0.796-0.978	**.017**
Mean impedance drop carina segments (Ω)	1.017	0.935-1.105	.702			
LA volume, mL	1.009	1.001-1.018	.030	**	**	**
Right accessory PV	0.626	0.263-1.489	.289			
Combined right PV diameter, mm	1.054	0.986-1.127	.120			
Right carina width, mm	1.198	1.087-1.321	<.001	1.129	1.001-1.273	**.048**

Note: "**" indicates that the variable was removed in the final regression equation (ie, nonsignificant). P values in bold indicate significance in multivariate analysis ($p < 0.05$).

Abbreviations: AF, atrial fibrillation; CF, contact force; CI, confidence interval; gap-RPC, gap-related persistent conduction; LAVI, left atrial volume index; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; OR, odds ratio; PV, pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; WACA, wide-area circumferential ablation.

lower mean CF at the right carina segments was independently associated with ipsilateral carina-RPC.

4.2 | Gap-related persistent conduction

Previous studies have shown that lesions/segments with gaps are characterized by lower impedance drop, lower FTI, lower Ablation Index (AI), and greater interlesion distance compared to lesions/segments without gaps.[14-16] However, cutoffs for these parameters to predict the occurrence of gaps demonstrated poor positive predictive value, indicating the difficulty to reliably identify lesions/segments that lead to gap occurrence. The present study aimed to identify predictors of gap-RPC per WACA circle and demonstrated that neither mean CF, number of segments with CF less than 10 g, nor mean impedance drop was associated with gap-RPC.

A larger WACA circumference correlated with a higher incidence of gap-RPC. This association was independent of clinical and anatomical characteristics and may be explained by the fact that a larger WACA circumference requires a higher number of individual ablation lesions, which increases the likelihood that any of the lesions is either nontransmural or does not connect properly to an adjacent lesion. Whereas PV antral isolation proved to be significantly superior to segmental PVI in reducing the risk of AF recurrence, previous studies are not conclusive about the optimal distance of the circumferential ablation lesions to the PV ostia.[17-19] The findings of the present study may provide a possible explanation for previous conflicting results regarding the optimal distance of the ablation line to the PVI ostia. Although an advantage of wider antral ablation may be that it simultaneously targets additional pathological AF substrate,[19] this study suggests that the consequent larger WACA lesion set results in an increased risk of conduction gaps. Further

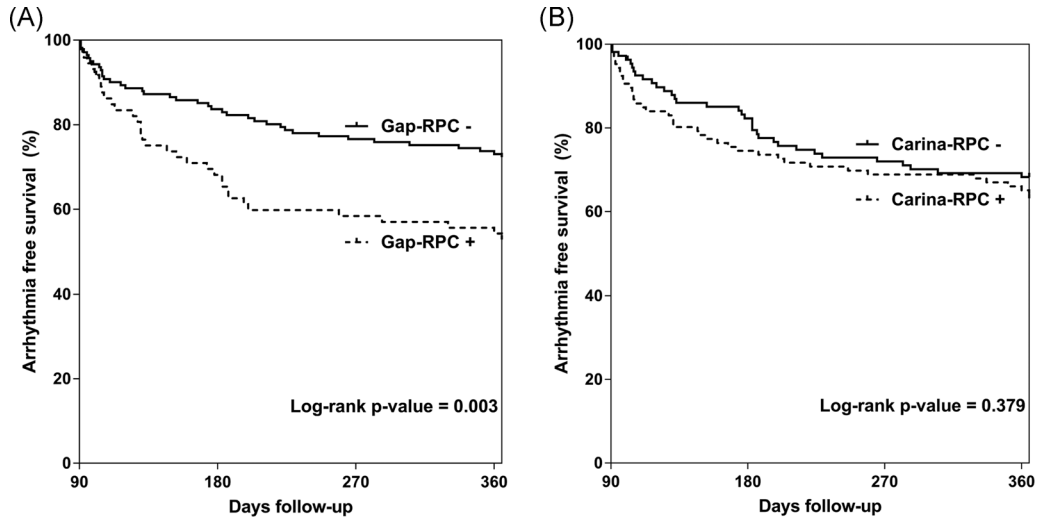

FIGURE 3 Kaplan-Meier survival analyses for freedom of atrial tachyarrhythmias. Kaplan-Meier survival analyses for freedom of atrial tachyarrhythmias divided by occurrence of (A) gap-related persistent conduction (gap-RPC) and (B) carina-related persistent conduction (carina-RPC)

prospective studies are warranted to elucidate the optimal distance of the WACA circle to the PV ostia.

Interestingly, gap-RPC was more frequent in paroxysmal AF patients compared to persistent AF patients. Previous research showed that paroxysmal AF patients have a thicker LA wall compared to persistent AF patients, which implies that deeper and longer ablation is required to create transmural lesions.[20] Since identical ablation strategies were employed for patients with paroxysmal and persistent AF in our study, different atrial wall thicknesses might explain the observed association between gap-RPC and AF type.

4.3 | Impact on AF ablation efficacy

During AF ablation, reversible myocardial injury may lead to nontransmural and noncontinuous chronic ablation lesions.[21,22] Creation of persistent, transmural, and continuous lesions is crucial to achieve durable PVI and is dependent on multiple factors, such as ablation duration, power, catheter-tissue contact, and catheter stability.[23,24] Several markers of effective lesion formation have been described and use of these markers to guide AF ablation hold the potential to improve durability of PVI.[4,25] Moreover, the necessity of additional ablation beyond the initial WACA circles is generally considered to indicate inadequate lesion formation, and could, therefore, provide predictive value for arrhythmia recurrence after PVI.[26] Complete PVI is frequently not achieved after the initial WACA circles and resumption of electrical conduction after obtaining PVI is often seen in these patients.[3,27,28] Hussein et al[5] recently reported on the results of a prospective study in which 40 persistent AF patients underwent PVI guided by a novel marker of ablation quality (AI, Carto3; Biosense Webster). The authors found that despite the use of strict criteria for lesion depth, interlesion distance and catheter stability, carina-RPC was frequently observed.

In the present study, gap-RPC was associated with increased AF recurrence risk after PVI whereas carina-RPC did not impact AF recurrence risk. This may result from touch-up lesions in the WACA circle being ineffective due to edema caused by the initial ablation. However, this is contradicted by Das et al,[15] who demonstrated durable isolation during repeat electrophysiology study in the WACA segments that exhibited gap-RPC during index PVI. Accordingly, in the present study reconnected segments during repeat procedure did not match with the sites requiring additional ablation during index procedure. Another explanation may be that gap-RPC and carina-RPC represent different underlying mechanisms. Gap-RPC indicates the presence of nontransmural or noncontinuous ablation lesions, which may go partly undetected in the setting of transient PVI due to reversible ablation injury. Ultimately, this results in late PV reconnection and AF recurrence. In contrast, carina-RPC can be the result of anatomical variability and might be inevitable, despite adequate WACA circle ablation. In a WACA circle entirely consisting of contiguous ablation lesions of sufficient depth carina-RPC may still occur, possibly due to partly epicardially located myocardial crossing fibers. Although eliminating carina-RPC is required to achieve PVI, its occurrence is not necessarily indicative of insufficient lesion formation and, as such, does not predict late PV reconnection and AF recurrence.

4.4 | Limitations

Some limitations need to be acknowledged. First, the present study was observational and the ablation protocol was not standardized. Both point-by-point ablation and RF ablation by the catheter dragging technique were performed in the study population. Although the occurrence of gap-RPC and carina-RPC was similar for both techniques, additional thorough evaluation of individual lesion data, such as

the force-time-integral, time of RF application per lesion and AI, was hampered by using the catheter dragging technique. Guidance of RF ablation by lesion quality markers, such as AI and Lesion Size Index (LSI), might reduce the risk of gap-RPC and carina-RPC.[4] Moreover, (very) high power and short duration (HPSD) ablation was recently shown to improve lesion contiguity and transmurality.[29,30] These technologies were not used in the current study as these were not available during the study period. Although our results cannot be directly extrapolated to patients undergoing AI/LSI-guided ablation or ablation using other technologies, this study suggests that multiple mechanisms may underlie persistent PV-LA conduction during PVI.

Repeat electrophysiology study during follow-up was not part of the study protocol. Although PV reconnection is generally considered the main mechanism underlying AF recurrence following PVI, the exact mechanisms of AF recurrences in the present study could not be determined.

A further limitation of the present study is the lack of left and right atrial activation mapping to detect potential connections between the right PV carina region and the right atrium,[31] or between the left PV antrum and Marshall bundle or coronary sinus. A recent study showed that activation mapping could aid in delineating mechanisms underlying the need for carina ablation. Moreover, high-density electroanatomic mapping and assessment of pace capture on the ablation line may improve the accuracy and sensitivity for localizing residual conduction and were not performed in the present study.

5 | CONCLUSIONS

Gap-RPC is associated with increased AF recurrence risk after RF-PVI, whereas carina-RPC does not predict AF recurrence. Moreover, different correlates were found for gap-RPC and carina-RPC, suggesting different underlying mechanisms of gap-RPC and carina-RPC.

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How to cite this article: Mulder MJ, Kemme MJB, Götte MJW, et al. Differences between gap-related persistent conduction and carina-related persistent conduction during radiofrequency pulmonary vein isolation. *J Cardiovasc Electrophysiol*. 2020;31:1616–1627. https://doi.org/10.1111/jce.14544