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Phrenic nerve palsy during right-sided pulmonary veins cryoapplications: new insights from pulmonary vein anatomy addressed by computed tomography

Riccardo Maj[1] · Gianluca Borio[1] · Erwin Ströker[1] · Juan Sieira[1] · Alessandro Rizzo[1] · Alessio Galli[1] · Varnavas Varnavas[1] · Maysam Al Housari[1] · Dimitrios Sofianos[1] · Shuichiro Kazawa[1] · Muryo Terasawa[1] · Gezim Bala[1] · Federico Cecchini[1] · Saverio Iacopino[2] · Thiago Guimarães Osório[1] · Nicoleta Sora[3] · Pedro Brugada[1] · Carlo De Asmundis[1] · Gian Battista Chierchia[1]

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Abstract

Purpose There is still sparse information regarding phrenic nerve palsy (PNP) during the cryoablation of both right-sided pulmonary vein (PV) and its anatomical predictors.

Methods Consecutive patients who had undergone pulmonary vein isolation (PVI) using CB-A and suffered PNP during both right-sided PVs were retrospectively included in our study. Two other groups were then selected among patients who experienced PNP during RIPV application only (group 2) and RSPV application only (group 3).

Results The incidence of PNI during both right-sided PVs cryoapplications was 2.1%, (32 of 1542 patients). There were no significant clinical differences between the 3 groups. Time from basal temperature to −40 °C significantly differed among the groups for both RIPV ($p = 0.0026$) and RSPV applications ($p = 0.0382$). Patients with PNP occurring during RSPV applications had significantly larger RSPV cross-sectional area compared to patients without PNP ($p = 0.0116$), while in patients with PNP during RIPV application, the angle of RIPV ostium on the transverse plane was significantly smaller compared to patients without PNP ($p = 0.0035$). The carina width was significantly smaller in patients with PNP occurring during both right-sided PVs cryoapplications compared to patients in which PNP occurred only during one right-sided PV application ($p < 0.0001$); a cutoff value of 8.5 mm had a sensitivity of 87.3% and a specificity of 75.0%.

Conclusion PNP in both right-sided PVs applications is a complication that occurred in 2.1% of cases during CB-A. Pre-procedural evaluation of right PVs anatomy might be useful in evaluating the risk of PNP.

Keywords Cryoballoon · Phrenic nerve palsy · Atrial fibrillation · Ablation · Right pulmonary vein anatomy

1 Introduction

Phrenic nerve palsy (PNP) is the most frequent complication of cryoballoon ablation (CB-A) performed for atrial fibrillation (AF) [1]. The reported incidence of phrenic nerve injury during CB-A in the early studies varies between 3.5 and 11.2% [2–4], and it mostly involves the right-sided phrenic nerve (PN), due to its close proximity to the right superior pulmonary vein (RSPV) and right inferior pulmonary vein (RIPV). Although during CB-A most phrenic nerve injuries are transient and resolve within minutes; still this complication can be disabling, and in some cases, it can lead to loss of nerve function that can persist for months [5]. Moreover, this procedure can lead to the discontinuation of the procedure when occurring during cryothermal applications delivered to the firstly targeted right-sided pulmonary vein (PV) [6]. Anatomical and procedural predictors of PNP during CB-A have been extensively described [6–9]; still, in case of its occurrence, the management of the procedure is far from being perfectly defined [10]. The aim of this study was to

Riccardo Maj and Gianluca Borio contributed equally to the work as co-first authors

✉ Riccardo Maj
maj.riccardo@gmail.com

[1] Heart Rhythm Management Center, UZ Brussel-VUB, Laarbeeklaan 101, 1090 Brussels, Belgium

[2] Electrophysiology Unit, Villa Maria Cecilia, Via Corriera, 1, 48033 Cotignola, RA, Italy

[3] Thoraxcentrum, Blekingesjukhuset, Karlskrona, Sweden

describe the anatomical characteristics of the patients who experienced right PNP during cryothermal applications according to the right PV or PVs involved.

2 Methods

2.1 Patient population

Consecutive patients who had undergone PVI using CB-A technology from January 2014 to April 2019 at the Heart Rhythm Management Center, UZ Brussel, and suffered PNP during both RIPV and RSPV cryothermal applications were retrospectively included in our study (group 1). Two other groups were then selected among patients who experienced PNP during RIPV application only (group 2) and during RSPV application only (group 3), respectively. Patients with persistent PNP that determined the discontinuation of the procedure before the last PV were targeted and/or the switch to touch-up radiofrequency (RF) ablation, and patients with right common ostium (RCO) or right middle pulmonary vein (RMPV) documented on computed tomography (CT) scan before the procedure were excluded by the study. Other exclusion criteria were any contraindication for the procedure including the presence of an intracavitary thrombus, uncontrolled heart failure (HF), and contraindications to general anesthesia. The study was approved by our local ethics committee and was carried out in accordance with the ethical principles for medical research involving human subjects established by the Declaration of Helsinki.

2.2 Cryoballoon ablation procedure and phrenic nerve function monitoring

The CB-A procedure has been described in detail previously [11]. All procedures were performed under general anesthesia and using short-acting neuromuscular blocking drugs for endotracheal intubation. Briefly, after obtaining LA access through a single trans-septal puncture, a steerable 15 Fr sheath (FlexCath Advance, Medtronic, Minneapolis, USA) was positioned in the left atrium (LA). Before introducing the CB in the sheath, the inner lumen mapping catheter (ILMC) was inserted in its lumen. Afterwards, the 28 mm CB was advanced through the sheath into the LA, and it was then inflated and positioned close to each PV ostium. Before ablation, for each PVs, the ILMC was positioned at a proximal site in the PV ostium, in order to record the baseline pulmonary vein potentials (PVPs). Once a good occlusion was documented, cryothermal energy was commenced and delivered for 180 s. During the right-side PVs applications, PN function was monitored by positioning a standard decapolar catheter in the superior vena cava (SVC) or in the subclavian vein and by pacing the right PN (20 mA at 1.0 ms pulse width at a cycle length of 1200 msec). Phrenic nerve capture was monitored both via the femoral venous pressure waveform (VPW) analysis [12] and through the right hemidiaphragm contraction, which was monitored by fluoroscopic imaging and manual palpation of the right hemiabdomen.

2.3 Diagnosis and management after phrenic nerve palsy

In case of decrease of more than 50% of the VPW peak-to-peak initial value, and/or if weakening or cessation of right diaphragmatic movement, the cryoapplication was immediately stopped with deflation of the CB [13]. No further balloon application was applied to the culprit PV. Impending palsy was defined as a progressive weakening of diaphragmatic motility without a complete paralysis [14], while transient PNP was defined as the weakening/loss of hemidiaphragmatic motion with a full recovery before the end of the procedure; persistent PNI was diagnosed if the right hemidiaphragm elevation was still present after a waiting time of 30 min at the end of the procedure. Since in our protocol, cryoapplication is performed first in the RIPV and next in the RSPV, in the cases of PNP occurring during RIPV application, cryoablation of the RSPV was attempted only in those cases where the PN function completely recovered. In all cases, the patient was scheduled for a chest X-ray during a sniff maneuver the next day. Diaphragmatic function was then evaluated by a radiologist on the basis of the shape of an elevated hemidiaphragm both in antero-posterior and lateral fluoroscopy projections. Once the diagnosis of PNP was established, the patient was closely monitored with follow-up visits.

2.4 CT scan analysis

The cardiac CT was carried out according to the protocol previously described [15]. Multislice cardiac computed tomographic studies were primarily viewed in the transverse plane, in the coronal plane, and in the coronal oblique plane. CT images were assessed and analyzed by two experienced observers in consensus. The PV ostium was defined by the intersection between the PV wall and the posterior atrium wall. Transverse images were reformatted to have a direct coronal image, which were rotated afterwards to generate an oblique sagittal image at the ostium. The image obtained in this way allowed the best visualization of the ostium (i.e., perpendicular to the long axis of the vessel), and it was used to measure its major and minor diameters and the cross-sectional area (Fig. 1). The spatial pattern of orientation of the PV ostia compared with both frontal and transverse body axis was assessed in the frontal and in the transverse views, respectively; the orientation angle of the right-sided PVs ostia was then assessed as previously described [15] (Fig. 2). The left atrial

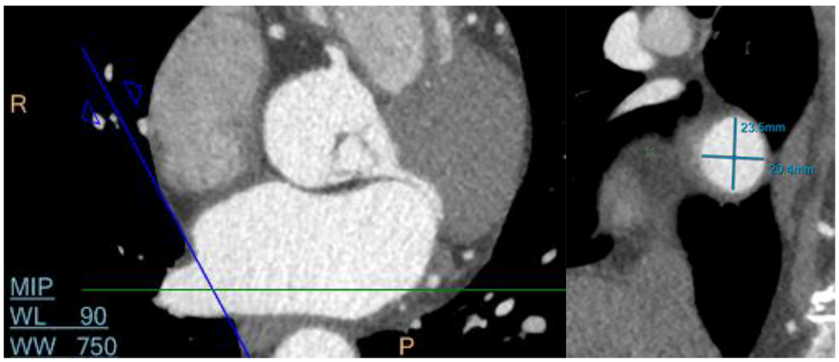

Fig. 1 Computed tomographic scans obtained for assessment of PV ostium dimensions. An oblique coronal image shows the RIPV in cross-section perpendicular to the long axis of the vessel. From this view, both diameters can be measured. RIPV, right inferior pulmonary vein

3D representation was then performed for subsequent analysis using the GE advantage software; this view allowed the visualization of the PV ostia and the various PV orientations and the measurement of the carina width, as previously detailed [16] (Fig. 3).

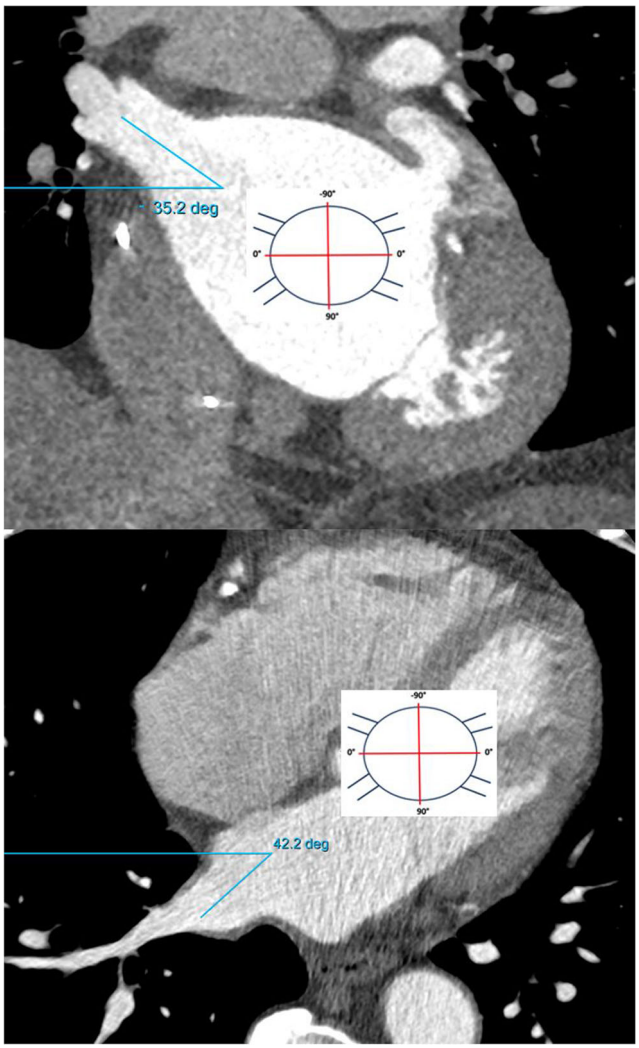

Fig. 2 Computed tomographic scans obtained for assessment of PV ostium orientation. The small graphic shows a schematic explanation of the method by which the angle of orientation of each PV was retrieved from both the frontal (top) and the transverse plane (bottom). PV, pulmonary vein

2.5 Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD). Categorical variables are expressed as percentages. Comparison between groups was made by means of Student's t-test for unpaired data. Chi-square test was performed for nominal data. Logistic regression analysis was used to analyze anatomical predictors of PNP for continuous variables. Receiver operating characteristic (ROC) curve was performed, and the area under the curve (AUC) was used to determine the predictive value and to assess the optimal cutoff points of relevant predictors, based on the coordinates of the curves with associated sensitivity and specificity values. A two-tailed p value of < 0.05 was deemed significant. Statistical analyses were conducted using the SPSS software (SPSS version 24, Chicago, IL, USA).

3 Results

3.1 Incidence and outcomes of phrenic nerve palsy

Of the total 1542 patients who underwent CB-A during this timespan, 32 (2.1%) patients presented a PNI during both RSPV and RIPV cryoapplication (group 1). This group was then matched with patients who experienced PNP during RIPV application only (23 patients, group 2) or during RSPV application only (35 patients, group 3). Patients with persistent PNP and/or with documented RCO or RMPV were excluded by our analysis. The type of PNP was transient in most cases in all groups (53.1% in group 1, 78.2% in group 2, 62.9% in group 3, $p = 0.1654$). Chest x-ray performed the day after the procedure showed normal diaphragmatic function in all patients. No patient complained of shortness of breath, exertional dyspnea, or any symptom that could be related to PNP.

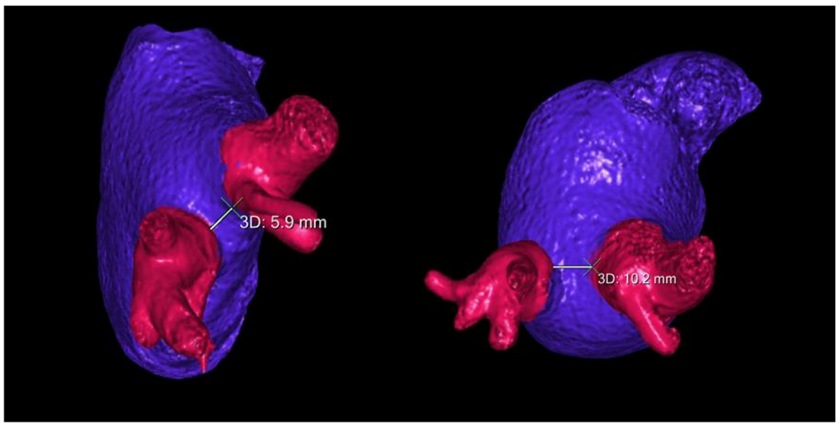

Fig. 3 Reconstructed image for segmentation and analysis in the three-dimensional field of the LA-PV anatomy. The carina width was defined as the shortest possible line through 2 points belonging to the ostia of 2 adjacent right-sided PVs. LA-PV, left atrium-pulmonary vein; PVs, pulmonary veins

3.2 Baseline and procedural characteristics

A total of 90 patients were included in the analysis. The mean age of the population was 59.7 ± 13.9 years (57.8% male). The type of AF was paroxysmal in most cases in all groups (93.8% in group 1, 73.9% in group 2, 85.7% in group 3, $p = 0.1212$). There were no significant differences in other clinical characteristics among the 3 groups (Table 1). The mean procedure time (64.5 ± 12.9 min in group 1, 60.1 ± 9.3 min in group 2, 67.3 ± 15.8 min in group 3, $p = 0.1551$) and the fluoroscopy time (14.0 ± 3.1 min in group 1, 13.8 ± 3.6 min in group 2, 14.6 ± 3.8 min in group 3, $p = 0.6320$) did not differ among the 3 groups. The mean applications time was significantly different for both RIPV (152.8 ± 73.2 s in group 1, 165.0 ± 74.7 s in group 2, 250.6 ± 88.0 s in group 3, $p < 0.0001$) and RSPV applications (151.8 ± 58.1 s in group 1, 206.7 ± 68.7 s in group 2, 144.7 ± 50.2 s in group 3, $p = 0.0006$), due to the early interruption of the freeze for the occurrence of PNP. Temperature drop velocity, as described by time from basal temperature to −40 °C, significantly differed among groups for both RIPV (44.4 ± 9.5 s in group 1, 43.2 ± 9.7 s in group 2, 53.6 ± 15.4 s in group 3, $p = 0.0026$) and RSPV applications (43.4 ± 10.9 s in group 1, 46.3 ± 17.3 s in group 2, 38.4 ± 6.6 s in group 3, $p = 0.0382$). Procedural characteristics are detailed in Table 1.

Table 1 Baseline and procedural characteristics (RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; AF, atrial fibrillation; CAD, coronary artery disease; TIA, transient ischemic attack; PNP; phrenic nerve palsy). Categorical variables are expressed as absolute. Continuous variables are expressed as mean ± SD

	RIPV+; RSPV+ ($n = 32$)	RIPV+; RSPV- ($n = 23$)	RIPV-; RSPV+ ($n = 35$)	p value
Age (years)	60.9 ± 14.3	59.1 ± 13.2	59.2 ± 14.2	0.8487
Male gender	22	11	19	0.2674
Paroxysmal AF	30	17	30	0.1212
Hypertension	19	14	18	0.7288
Diabetes mellitus	4	5	5	0.6334
CAD	3	2	4	0.9360
Previous TIA/stroke	2	2	1	0.6311
BMI (kg/mq)	26.6 ± 4.2	26.9 ± 5.0	26.2 ± 4.6	0.8348
Left atrial diameter (mm)	41.4 ± 6.8	39.7 ± 10.2	41.8 ± 5.7	0.5560
Procedure time (min)	64.5 ± 12.9	60.1 ± 9.3	67.3 ± 15.8	0.1551
Fluoroscopy time (min)	14.0 ± 3.1	13.8 ± 3.6	14.6 ± 3.8	0.6320
Transient PNP	17	18	22	0.1654
RIPV application time (sec)	152.8 ± 73.2	165.0 ± 74.7	250.6 ± 88.0	**< 0.0001**
RSPV application time (sec)	151.8 ± 58.1	206.7 ± 68.7	144.7 ± 50.2	**0.0006**
Time to −40 °C in RIPV (sec)	44.4 ± 9.5	43.2 ± 9.7	53.6 ± 15.4	**0.0026**
Time to −40 °C in RSPV (sec)	43.4 ± 10.9	46.3 ± 17.3	38.4 ± 6.6	**0.0382**
Nadir temperature in RIPV (°C)	−51.2 ± 6.7	−50.1 ± 5.2	−48.5 ± 4.1	0.1454
Nadir temperature in RSPV (°C)	−50.0 ± 6.3	−53.9 ± 4.8	−50.5 ± 4.5	**0.0288**

3.3 Anatomical characteristics according to the PV involved

The anatomical characteristics of the right-sided PVs were analyzed according to the PNP occurrence (Table 2). The mean RIPV maximal and minimal diameters and the cross-sectional area were not significantly different among patients with and without PNP. On the other hand, patients with PNP occurring during RSPV applications had significantly larger cross-sectional area of the RSPV compared to patients without PNP (287.6 ± 73.4 mmq in RSPV+ group, 240.6 ± 81.4 mmq in RSPV− group, $p = 0.0116$). The orientation of RSPV ostium in both frontal and transverse planes did not differ among patients with and without PNP, while in patients with PNP during RIPV application, the angle of the RIPV ostium on the transverse plane was significantly smaller compared to patients without PNP (24.7 ± 12.8° in RIPV+ group, 32.8 ± 12.0° in RIPV− group, $p = 0.0035$). In the univariate analysis, both the RSPV area (OR 1.01, 95% CI 1.00–1.02; $p = 0.021$) and the transverse angle of the RIPV ostium (OR 0.95, 95% CI 0.91–0.99, $p = 0.07$) were the only anatomical predictors of the occurrence of PNP during RSPV and RIPV applications, respectively (Table 3). In the multivariate analysis including also the temperature drop velocity in RIPV, both time from basal temperature to −40° ($p = 0.010$) and the RIPV transverse angle ($p = 0.004$) were found to be independent predictors of PNP during RIPV application (Table 3).

3.4 Carina width

The carina width was significantly different among patients with PNP occurring during both RIPV and RSPV cryoapplications compared to patients in which this complication occurred only during one right-sided PV application (7.5 ± 2.1 mm in RIPV+/RSPV+ group, 9.8 ± 2.8 mm in RIPV+/RSPV− plus RIPV+/RSPV− group, $p < 0.0001$) (Fig. 4). The ROC curve analysis of the carina width showed it had a strong predictive value (AUC 0.885) (Fig. 5). A cutoff value of 8.5 mm discriminated the occurrence of PNP in both right-sided PVs applications with a sensitivity of 87.3% and a specificity of 75.0%.

4 Discussion

To the best of our knowledge, this is the first study investigating specifically the anatomical characteristics of the patients who experienced right PNP during cryothermal applications according to the right PV or PVs involved. The main findings of our study are as follows: (i) the incidence of PNI during

Table 2 Anatomical characteristics of right-side PVs according to PNP occurrence (RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein). Continuous variables are expressed as mean ± SD

	RIPV+; RSPV± ($n = 55$)	RIPV-; RSPV+ ($n = 35$)	p value
RIPV maximal diameter (mm)	19.2 ± 2.7	19.0 ± 2.5	0.7254
RIPV minimal diameter (mm)	16.1 ± 2.3	15.7 ± 2.6	0.4389
RIPV area (mmq)	247.1 ± 65.6	239.4 ± 67.4	0.5925
RIPV transverse plane (°)	24.7 ± 12.8	32.8 ± 12.0	0.0035
RIPV frontal plane (°)	9.2 ± 11.6	4.3 ± 15.2	0.0874
RSPV maximal diameter (mm)	20.8 ± 2.7	20.9 ± 2.4	0.8586
RSPV minimal diameter (mm)	16.4 ± 3.1	16.9 ± 2.8	0.4410
RSPV area (mmq)	270.2 ± 78.9	285.6 ± 75.7	0.3617
RSPV transverse plane (°)	−23.5 ± 8.0	−22.3 ± 8.7	0.5043
RSPV frontal plane (°)	−30.1 ± 8.7	−32.8 ± 8.3	0.1476
	RIPV± ; RSPV+ ($n = 67$)	RIPV+; RSPV− (n = 23)	0.4389
RIPV maximal diameter (mm)	19.1 ± 2.7	18.8 ± 2.2	0.6321
RIPV minimal diameter (mm)	15.7 ± 2.5	16.7 ± 2.1	0.0890
RIPV area (mmq)	241.9 ± 68.4	250.3 ± 59.0	0.6007
RIPV transverse plane (°)	28.6 ± 13.5	25.7 ± 11.6	0.3604
RIPV frontal plane (°)	6.8 ± 14.1	8.7 ± 10.7	0.5569
RSPV maximal diameter (mm)	21.1 ± 2.5	19.9 ± 2.7	0.0548
RSPV minimal diameter (mm)	16.9 ± 2.9	15.8 ± 3.3	0.1334
RSPV area (mmq)	287.6 ± 73.4	240.6 ± 81.4	0.0116
RSPV transverse plane (°)	−22.6 ± 8.7	−24.5 ± 6.6	0.3418
RSPV frontal plane (°)	−31.7 ± 9.0	−29.4 ± 7.2	0.2707
	RIPV+; RSPV+ ($n = 32$)	RIPV+/−; RSPV−/+ ($n = 68$)	0.4389
Carina width (mm)	7.5 ± 2.1	9.8 ± 2.8	< 0.0001

Table 3 Univariate and multivariate analysis (OR, hazard ratio; CI, confidence interval; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein)

	Univariate analyses			Multivariate analyses		
	OR	95% IC	*p* value	OR	95% IC	*p* value
Time to −40 °C in RIPV	0.95	0.91–0.99	0.008	1.06	1.02–1.11	0.010
RIPV maximal diameter	1.03	0.87–1.22	0.759			
RIPV minimal diameter	1.06	0.88–1.27	0.552			
RIPV area	1.00	0.99–1.01	0.598			
RIPV transverse plane	0.95	0.91–0.99	0.007	1.07	1.02–1.12	0.004
RIPV frontal plane	1.03	1.00–1.07	0.092			
Time to −40 °C in RSPV	0.96	0.93–1.00	0.080			
RSPV maximal diameter	1.23	0.98–1.53	0.070			
RSPV minimal diameter	1.13	0.95–1.34	0.177			
RSPV area	1.01	1.00–1.02	0.021			
RSPV transverse plane	1.03	0.97–1.09	0.340			
RSPV frontal plane	0.97	0.92–1.02	0.269			

both right-sided PVs was 2.1%; (ii) both RSPV area and the transverse angle of the RIPV ostium were associated with increased risk of PNP during the corresponding PV application; and (iii) a small carina width was a significant predictor of PNP occurrence in both right-sided PVs in our specific cohort of patients (all patients experienced PNP at least during one cryoapplication).

4.1 Phrenic nerve injury during right-sided pulmonary vein cryoballoon ablation

Phrenic nerve injury is a well-known complication of CB-A. Although nowadays the incidence of this complication decreased since the first reports after the introduction of the second-generation cryoballoon (Arctic Front Advance, Medtronic, Minneapolis, USA) [17, 18], still this problem is far from being solved. The incidence of PNP in previous studies varies considerably because of the differences in terms of definition, CB use, freezing protocol, and protective maneuvers. The current indications for avoiding PNP include a single 28 mm CB use, short freeze duration, continuous diaphragmatic compound motor action potential (CMAP) monitoring, and active deflation when the CMAP decreases > 30% from the baseline [19, 20]. On the other end, some studies addressed the possibility to predict the occurrence of PNP according to both anatomical and procedural data. In a study from Kühne et al. [7] on 65 patients with paroxysmal AF treated with the first-generation CB, both the short distance between the RSPV and the SVC and a low temperature during

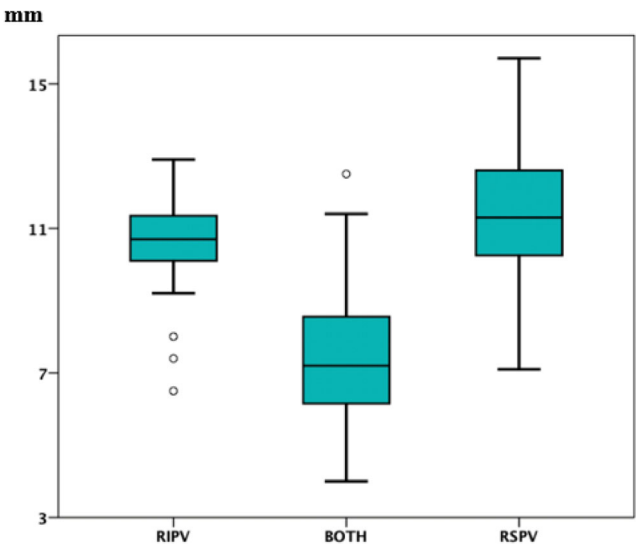

Fig. 4 The carina width (in mm) according to the right PV or PVs involved. PV, pulmonary vein

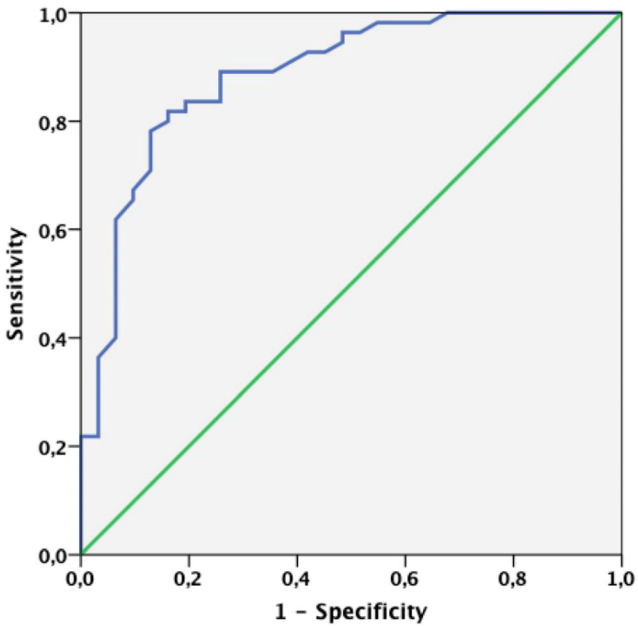

Fig. 5 Receiver operating characteristic curve for carina width (AUC 0.885, $p < 0.001$)

the first 30–40 s of the freezing cycle were associated with PNP. These results were then confirmed by Mugnai et al. [9], who demonstrated that a low temperature during the early phases of the freezing cycle (less than −38 °C at 40 s) in the RSPV predicted PNP with a sensitivity of 80.5%, a specificity of 77%, and a negative predictive value of 97.9%. The role of freezing velocity in PNP occurrence was then also addressed and demonstrated for RIPV [6]. All these observations are consistent with the data presented in our study, where time from basal temperature to −40 °C was significantly shorter for patients who experienced PNP during both RIPV ($p = 0.0026$) or RSPV ($p = 0.0382$) applications.

4.2 Anatomical predictors of phrenic nerve palsy

The right PN normally descends vertically from its origin and continues along the lateral aspect of the SVC and then, while descending down, it turns posteriorly as it approaches the superior cavo-atrial junction and follows in close proximity to the right-sided PVs [21]. Its course is generally anterior to the RSPV and then it tends to deviate laterally as it descends toward the right hemidiaphragm. Although some degree of anatomical variability in the course of the right PN might be expected [22], still anatomical factors of both LA and PVs were analyzed in previous studies in order to predict PNP occurrence. In a study conducted in our center by Ströker et al. [8] on 41 patients who experienced PNP during CB-A, both RSPV-LA angle (OR 1.03, $p < 0.001$) and RSPV area (OR 1.2, $p < 0.001$) were found to be independent predictor of PNP during RSPV applications. These results are in line with the data from Miyazaki et al. [20], and with our present data, since in our cohort of patients, PNP occurred more frequently during RSPV applications in case of larger cross-sectional area of the RSPV (287.6 ± 73.4 mmq vs 240.6 ± 81.4 mmq, $p = 0.0116$). Indeed, a large PV ostium might favor a more distal placement of the CB, taking it closer to the course of the right PN [23]. For the RIPV, we found that the transverse angle of the RIPV ostium was associated with increased risk of PNP during RIPV application (24.7 ± 12.8° vs 32.8 ± 12.0°, $p = 0.0035$). As shown in Fig. 2, this angle describes the position of the RIPV ostium in relation to the front and the rear of the body. A smaller angle therefore implies a more anterior position of the PV ostium, and it was found to be associated with the increase of risk of PNP during RIPV applications, as the CB-A might be located in a more lateral position and eventually closer to the PN trajectory.

4.3 Carina width

In previous studies from our group [6, 8], RCO was found to be predictive of PNP. Therefore, in this study we choose to exclude patients with this PV variant documented on CT scan. Still, we found that patients who suffered PNP during both RIPV and RSPV cryothermal applications had a smaller carina width when compared to patients who experienced PNP only in one right-side PV (7.5 ± 2.1 mm vs 9.8 ± 2.8 mm, $p < 0.0001$). In particular, a cutoff value of 8.5 mm discriminated the occurrence of PNP in both right-sided PVs applications with a sensitivity of 87.3% and a specificity of 75.0%. This observation may find its explanation in the wide area covered by the CB [24]: in case of a small carina between the 2 PVs, as the lesions created by the CB might be overlapping; also the eventual injury of the right PN might be favored by a short distance between the 2 ostia. In case of PNP during the firstly targeted right-sided PV then, careful evaluation of the carina width before delivering cryothermal applications to the second right-side PV might be reasonable. In case of documented small carina width, extreme caution should be taken on monitoring the PN function also during the secondly targeted right-sided PV ablation.

5 Limitations

Our study has some important limitations. First, a major limitation of our study is its nature (i.e., non-randomized, single-center, retrospective). In addition, due to infrequent documentation of PNP during both right-sided PVs applications, the sample size is still small, and a prospective validation group could not be included. Third, we could not reproducibly locate on the CT scans the course of the right phrenic artery and right PN, as recently described [22, 25, 26]. Fourth, we did not use a diaphragmatic CMAP to assess diaphragmatic contraction neither three-dimensional reconstruction through electroanatomical map [27] to locate the right PN course. Future prospective studies are needed to better define the clinical impact of PV anatomy on the occurrence of PNP during CB-A.

6 Conclusions

PNP in both right-sided PVs applications is a complication that might occur in around 2.1% of cases during CB-A. Pre-procedural evaluation of right PVs anatomy might be useful in evaluating the risk of PNP; in particular the assessment of dimensions and orientation of PV ostia and the carina width might suggest be able to adapt a more careful monitoring of the PN function during cryoapplications.

Compliance with ethical standards

Conflict of interest Prof. de Asmundis, Prof Brugada, and Prof Chierchia have received consulting fees and speaker honoraria from Medtronic. G.B.C. and C. d A. have received compensation for teaching and proctoring purposes from AF solutions Medtronic.

Ethical approval All procedures performed in the studies involving patients 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.

Informed consent Informed consent was obtained from all individual participants included in the present study.

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