

Pressure-Guided Cryoballoon Isolation of the Pulmonary Veins for the Treatment of Paroxysmal Atrial Fibrillation

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Pressure-Guided Cryoballoon Pulmonary Vein Isolation. *Background:* Pulmonary vein (PV) isolation using a balloon-mounted cryoablation system is a new technology for the percutaneous treatment of atrial fibrillation (AF). Complete PV occlusion during balloon ablation has been shown to predict successful electrical isolation. The aim of this study was to correlate mechanical PV occlusion with changes in a pressure curve recorded at the distal tip of the cryoballoon catheter.

Methods and Results: We analyzed 51 PVs in 12 patients (61 ± 6 years old) with paroxysmal AF. At first, PV occlusion via the cryoballoon was documented by changes in the pressure curve. Once the PV is occluded, the pressure curve registered in the vein converts from a left atrial pressure curve to a pulmonary artery pressure curve: the PV wedge curve. Occlusion was then confirmed by transesophageal echocardiography (TEE). Following 2 cryoablation applications, electrical PV isolation was assessed with a circumferential mapping catheter. Under the exclusive guidance of changes in the pressure curve at the tip of the cryoballoon, mechanical occlusion confirmed by TEE was achieved in 47 of 51 PVs (92%). Three PVs required further TEE guidance to achieve occlusion. All 50 occluded veins were electrically isolated after cryoablation. One right inferior vein, which could not be occluded with the balloon, displayed conduction post cryoablation and was isolated by focal ablation.

Conclusions: Occlusion and electrical isolation of PVs during cryoballoon ablation can be predicted by the appearance of a PV wedge curve at the tip of the catheter. This new straightforward parameter may facilitate the procedure. (*J Cardiovasc Electrophysiol*, Vol. pp. 1-6)

atrial fibrillation, cryoballoon, invasive pressure measurement, catheter ablation, transesophageal echocardiography

Introduction

Currently, electrical pulmonary vein (PV) isolation is the cornerstone of atrial fibrillation (AF) ablation procedures.^{1,2} Achieving PV isolation with standard radiofrequency (RF) ablation catheters, however, remains a technically demanding and time-consuming technique, which also frequently requires the use of a 3-dimensional mapping system. In addition, ablation in the left atrium (LA) and the PVs has been associated with significant complications,³ such as thromboembolic events, PV stenosis⁴ or atrioesophageal fistulae.^{5,6} In an effort to overcome these problems, new ablation devices and energy sources, including the cryoballoon catheter, have been developed. The cryoballoon delivers cryoenergy over

an occluding balloon system to create circumferential lesions around the PVs.^{7,8} The clinical success rate using the cryoballoon device is comparable to the results after PV isolation using RF energy.^{9,10}

In a recent study, we demonstrated that complete mechanical occlusion of the PVs during the freeze as documented by transesophageal-Doppler-echocardiography (TEE) predicts electrical PV isolation.¹¹ However, performing TEE-guided cryoballoon PV isolation requires additional well-trained personnel and the use of general anesthesia.

Aiming to find a simpler tool to confirm complete mechanical occlusion of the PV, we hypothesized that occlusion may be predicted by changes in the pressure curve recorded at the tip of the balloon.

Methods

Patients

We included 12 patients with drug-refractory symptomatic paroxysmal AF. Informed consent was obtained from all patients before the procedure.

Ablation Procedure

All patients were anticoagulated at least 1 month prior to the procedure. Two days before ablation, anticoagulation was

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stopped aiming for an international normalized ratio between 1.8 and 2.0. Antiarrhythmic drugs were continued to stabilize sinus rhythm.

The ablation procedure was performed under general anesthesia and continuous TEE assessment. The technique for proper echocardiographic visualization of the PVs and their flow has been previously described.¹²

Vascular access was obtained through the right femoral vein. One single transeptal puncture was performed under TEE guidance and a steerable sheath (Flexcath[®], Cryocath, Montreal, Canada) was placed in the LA. After transeptal puncture, heparin was infused to maintain an ACT > 300 during the whole procedure. Ablation was performed using a double-coated cryoballoon (Arctic front[®], Cryocath). Balloon size was selected in accordance with the diameter of the PVs, as measured by TEE. If all PVs presented a diameter < 20 mm, the procedure was performed using a 23-mm diameter cryoballoon; if any PV was > 20 mm, we chose a 28-mm balloon. The balloon has an inner lumen that is usually used to inject contrast fluid through the distal tip of the balloon. For the purposes of the study, this lumen was connected to a continuous pressure monitoring system. The deflated cryoballoon was then advanced over an extra-rigid 0.032-mm guidewire placed inside of each PV (GuideRight[®] Superstiff, St. Jude Medical, St. Paul, MN, USA), and inflated in front of the vein. After inflation, the balloon was advanced to achieve occlusion of the PV. The vein was considered occluded when the initial LA pressure curve recorded at the tip of the balloon changed to a pulmonary artery pressure curve with complete disappearance of the venous A wave (Fig. 1). If PV occlusion was not achieved by simply pushing the balloon into the PV, the device was turned clockwise and counterclockwise or even slightly withdrawn. Once the above-mentioned criteria of occlusion were met or if pressure-guided occlusion could not be attained, the presence or absence of proximal flow was verified with color-Doppler TEE. If leakage was detected, we attempted to occlude the vein under TEE guidance. If necessary, the balloon size was switched. Finally, each PV was frozen twice over 5 minutes in its best occlusion position. During ablation of right-sided PVs, we performed phrenic nerve pacing from a catheter located in the superior vena cava in order to promptly detect phrenic nerve injury.

After cryoablation, every PV was mapped using a 20-pole circular mapping catheter with variable diameter (Optima[®], St. Jude Medical). If remnant ostial potentials were still recorded, differential pacing of the atrium near the vein was performed to prove entrance block in the PV.^{13,14} In case of persistent conduction, electrical isolation was segmentally completed using a 8-mm cryoablation catheter (Freezor Max[®], Cryocath). The endpoint of the procedure was complete electrical PV isolation, documented at least 30 minutes after the last application.

Postablation Care

After the procedure, warfarin was restarted and intravenous heparin was administered until the international normalized ratio was ≥ 2.5 . Warfarin was continued for at least 3 months. On the first postprocedural day, all patients underwent surface ECG, transthoracic echocardiography, and 24-hour Holter monitoring.

Statistical Analysis

Continuous variables are expressed as the mean \pm SD and compared by the Student *t*-test.

Results

Patients

We analyzed 51 PVs (including 3 right-sided supplementary PVs) in 12 patients (61 \pm 6 years old, 4 females). The patients had a history of paroxysmal AF of 5.6 \pm 3.8 years and had tried 3 \pm 1 antiarrhythmic drugs. Four of them had a history of organic heart disease. The mean diameter of the left atrium was 43 \pm 7 mm. The mean diameter of the veins was 19.5 mm and 18 mm for the superior and the inferior ones, respectively.

Pressure-Guided PV Occlusion

All patients were in sinus rhythm during the procedure. The procedure was initiated with a 28-mm balloon in 8 patients and a 23-mm balloon in 4 patients in accordance with the ostial diameter of the PVs. Using the first selected balloon, a PV wedge curve could be obtained in 44 of 51 PVs (Fig. 2). In 3 additional lower PVs with a diameter < 18 mm a wedge position was obtained only after exchanging the 28-mm balloon for a 23-mm balloon. Consequently, a pulmonary artery pressure curve could be obtained in 47 of 51 veins (92%). All pressure curves were analyzed off phrenic nerve pacing, as its introduction produced minor perturbations of the curve that could simulate the persistence of an A curve (Fig. 3). Doppler-TEE confirmed occlusion in all cases except for 1 left lower PV that could not be visualized after inflation of the balloon.

In the remaining 4 veins where no wedge position could be attained, TEE-guided occlusion was attempted:

- Three upper PVs presented an asymmetric off axis ostium morphology that prevented correct positioning of the balloon. The mean diameter of these 3 veins tended to be bigger than the 1 of the veins successfully isolated with a 28-mm balloon (20.5 mm vs 19.5 mm, $P = 0.54$). They were successfully occluded only by first freezing the balloon at the cranial part of the PV antrum, and then pulling it gently back after approximately 45 seconds under attentive TEE guidance in order to close the caudal gap (Fig. 4). This “pull-back” maneuver performed during cryoablation can only be documented under echocardiographic control, as the fluid in the pressure line freezes once the temperature falls below 0°C.
- One right lower PV of 17 mm could not be occluded and presented a persisting jet in the caudal part of the antrum despite all maneuvers.

PV Electrical Isolation

All 47 veins in which occlusion of the vein was indicated by the appearance of a PV wedge pressure curve showed no PV potentials after cryoablation. The 3 veins that were finally occluded under TEE guidance were also electrically isolated. Only the right inferior PV where no occlusion could be achieved presented persistent electrical conduction in the caudal part of the ostium, corresponding to the persisting

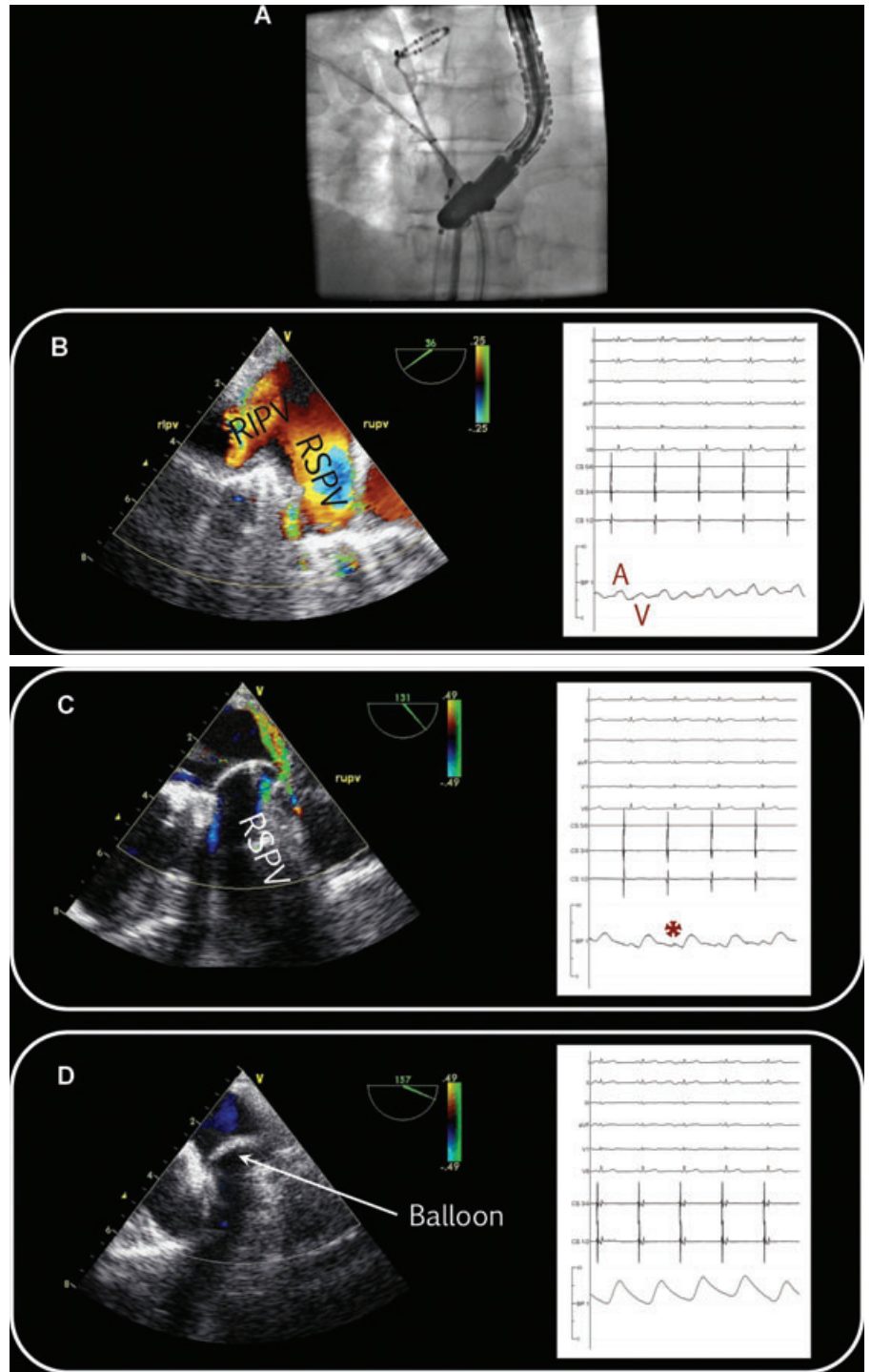


Figure 1. Pressure-guided cryoballoon PV occlusion. (A) Anteroposterior fluoroscopic view of the chest showing the cryoballoon already inflated and placed in front of the right superior PV. The TEE-probe has already been turned to the right side, to allow an optimal visualization of the PV's antrum (shadow). A circular mapping catheter has been placed in the superior vena cava, in order to allow phrenic nerve pacing during the application. (B) Left: echocardiographic view of the RSPV antrum, with the deflated balloon placed in front of it. Right: the matching left atrial pressure curve, with the venous A and V waves, corresponding to the atrial mechanical contraction and the atrial venous filling, respectively. (C) Incomplete occlusion of the RSPV. TEE (on the left) shows a clear leakage. The pressure curve (on the right) shows a much higher V wave approaching a pulmonary artery pressure curve, but with a persistent A curve (*). (D) Complete occlusion of the RSPV. TEE shows the absence of flow in the PV (left) and the pressure curve displays a characteristic pulmonary artery pressure curve (right). PV = pulmonary vein; RSPV = right superior pulmonary vein; TEE = transesophageal echocardiography.

leakage site detected by TEE. Two focal cryoablations resulted in electrical isolation.

Procedural Parameters

Total time procedure from groin access to sheath removal, including the verification of PV isolation, was 150 ± 23 minutes and total fluoroscopy time 26 ± 5 minutes.

Complications

Transient phrenic nerve paralysis was observed in 2 patients during right upper PV cryoablation. The freeze was

then immediately interrupted and phrenic nerve recovered in both cases within 30 minutes. Those 2 PVs were isolated at postablation mapping.

Although animal studies showed that this complication could appear even a week after cryoablation,⁸ no late phrenic nerve paralysis was observed in our patients.

Discussion

Effective mechanical PV occlusion with a cryoballoon can be predicted by a change in the pressure curve recorded at the tip of the balloon catheter from a left atrial pressure curve to

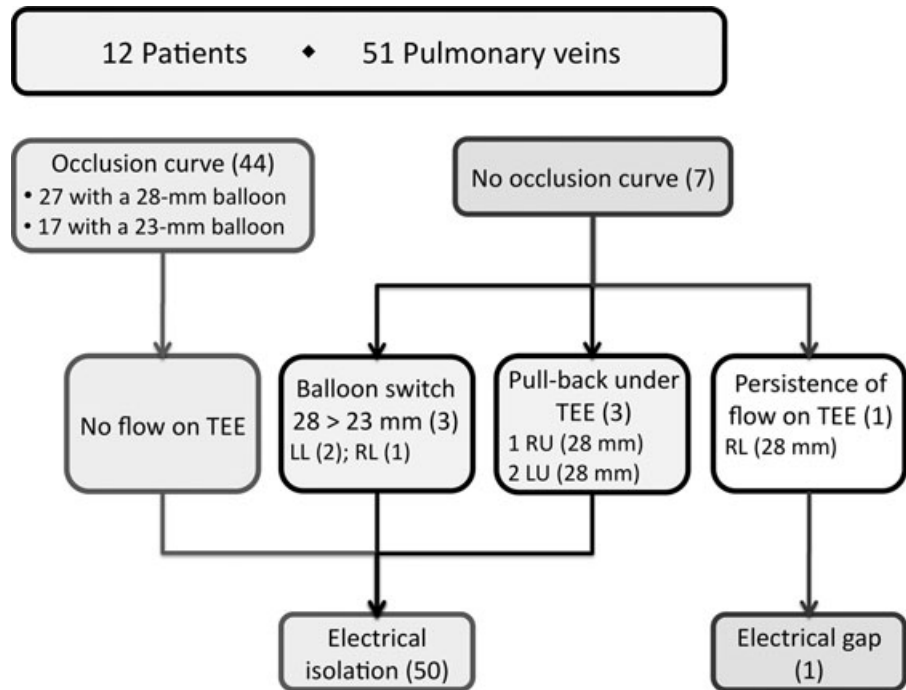


Figure 2. Flowchart showing the technique and size of balloon used to isolate the 51 PVs. LL = left lower; RL = right lower; LU = left upper; RU = right upper.

a pulmonary artery pressure curve. This new predictor allows for prompt and reliable monitoring of the effects of catheter handling and further facilitates optimal occlusion.

Occlusion of the PV seems to be the best predictor of electrical isolation, as it indicates optimal circumferential contact with the PV ostium and avoids the warming effect of persistent flow. Other predictors of occlusion and therefore

electrical isolation of the PVs with a cryoballoon have already been studied:

- The minimal temperature achieved during cryoballoon ablation and the slope of rewarming are correlated with electrical isolation,⁸ but no precise cut-off value has been correlated with effective PV isolation. Besides, the temperature registered during cryoablation depends also on the size of the cryoballoon. In our study, the only vein that could not be isolated with the balloon displayed a minimal temperature of -40°C , compared with a mean temperature of -51°C achieved in the other veins isolated with a 28-mm balloon.
- The degree of occlusion determined by contrast injection at the tip of the inflated balloon has also been correlated with electrical isolation.¹⁵ Individual contrast injection, however, provides no continuous feedback on the effect of maneuvers attempted to occlude the PV. Furthermore, contrast may be contraindicated in patients with known allergic reaction, or renal or thyroid disease.
- As we have recently shown, TEE-guided assessment of PV mechanical occlusion during cryoballoon PV isolation is feasible and effective: it predicts effective electrical isolation with a positive predictive value of 98%.¹¹ However, this technique requires the presence of a trained echocardiographer during the whole procedure and the use of general anesthesia. The use of intracardiac echocardiography instead of TEE would increase the costs of the procedure. However, 1 advantage of the echo-guided method over the pressure-guided approach is that the “pull back” maneuver of the balloon can be monitored during the cryo application.

In our small study, all occluded veins were electrically isolated. In our previous work, using TEE to verify occlusion, 109 of 111 occluded PVs (98%) showed postablation electrical isolation.¹¹ With conventional RF techniques, the PV isolation rate ranges from 80 to 98%. Accordingly, verification of electrical isolation might be superfluous if complete

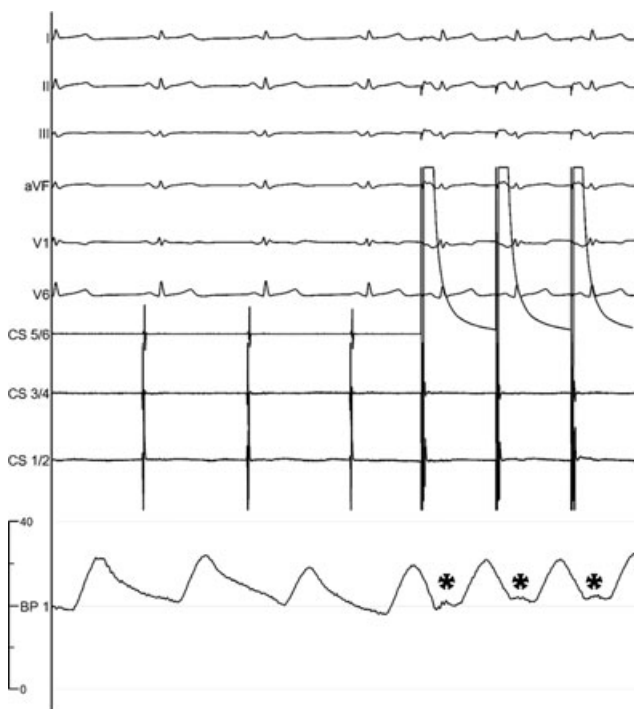


Figure 3. Perturbation of the pressure curve during phrenic nerve pacing. During the first 3 sinus beats, a clear occlusion curve can be observed. The introduction of pacing in the last 3 beats produces an artifact in the pressure that simulates the persistence of a venous A wave of atrial contraction (*).

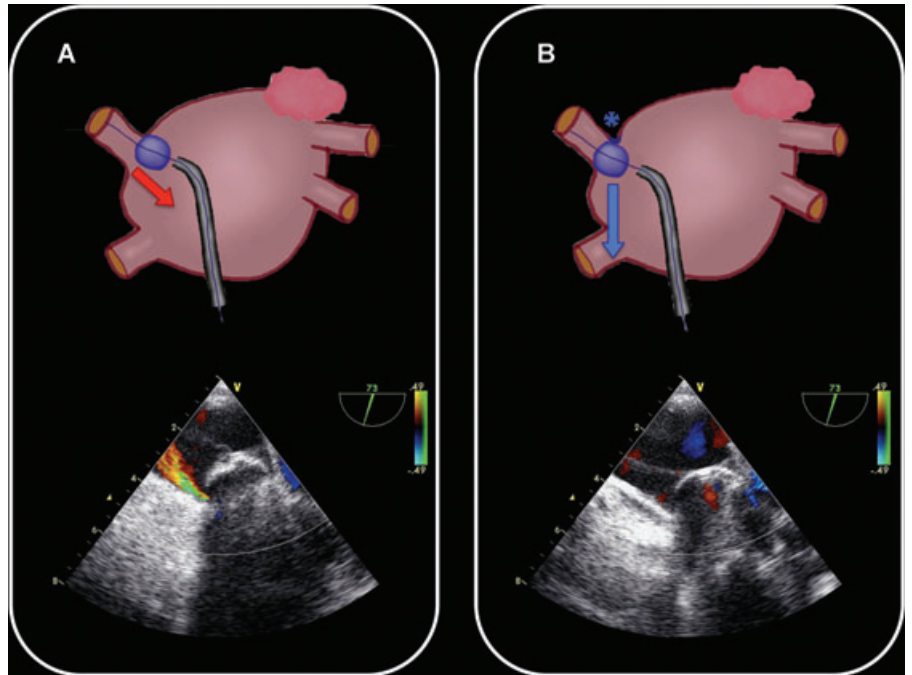


Figure 4. TEE-guided pull-back maneuver. (A) Schematic drawing and corresponding color-Doppler TEE image showing the presence of residual flow in the inferior aspect of the right superior PV (red arrow). (B) A slight withdrawal of the balloon after having frozen it to the superior aspect of the vein (blue arrow) allows then sealing this gap, as shown by the disappearance of flow inside of the PV.

occlusion is documented. Nevertheless, it remains mandatory in those PVs where occlusion cannot be documented in order to complete the circumferential lesion. If PV occlusion had just been assessed using the pressure curve, that would have been necessary in 4 of 12 patients (33%).

With this combined pressure and TEE-guided cryoballoon technique, procedure and fluoroscopy times (including both ablation time and mapping time post ablation) were shorter than in our previously published procedural parameters using RF energy,¹⁶ and also shorter than with the exclusively TEE-guided ablation,¹¹ although this might be also due to the progression of our learning curve.

Our study also underscores certain important aspects of the pathophysiology of pulmonary circulation. The observed change from a left atrial pressure curve to a pulmonary artery one indicates the absence of collateral circulation during acute occlusion. This may account for the severe symptoms (such as drug-resistant pneumonia) appearing in patients with an acute occlusion of a PV post-RF ablation,¹⁷ compared with the mild symptoms observed in patients with chronic stenosis where some collateral circulation had developed.¹⁸

Acute short PV occlusions, however, do not seem to entail any clinical problem, as no lung damage has been reported using the cryoballoon technique.^{9,10}

Study Limitations

No electrical mapping was performed before ablation. Pressure-guided assessment of PV occlusion was not compared to the injection of contrast fluid, as the high viscosity precluded obtaining a neat pressure curve when the inner lumen of the balloon was filled with contrast. Also, as no pressure curve can be registered beneath 0°C, exclusive pressure monitoring would fail to detect late balloon dislocations occurring during cryoablation.

All patients were in sinus rhythm during evaluation of pressure guided PV occlusion. Thus, we couldn't assess the utility of this parameter during AF. No patients with common ostium were included in the study. The continuation of an-

tiarrhythmic drugs around the procedure could have affected PV mapping and the acute outcome.

Conclusion

Occlusion and electrical isolation of the PVs during cryoballoon ablation can be predicted by a PV wedge pressure curve recorded at the tip of the catheter. This straightforward parameter can be used to complement other occlusion criteria such as contrast injection, minimal temperature, and the slope of rewarming, facilitating effective PV occlusion.

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