Cryoballoon Ablation in Today's Practice: Can the Left Common Ostium Be Ablated and Injury to the Right Phrenic Nerve Avoided?

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Abstract

Cryoballoon ablation is rapidly gaining popularity among electrophysiologists in the setting of pulmonary vein isolation for the treatment of AF. The first part of the following review focuses on the feasibility and clinical outcome of this technique in patients exhibiting a left common ostium. In the second part, we discuss how to predict and prevent the most common complication related to cryoballoon ablation: right phrenic nerve palsy.

Keywords

Cryoballoon, second-generation cryoballoon, pulmonary vein isolation, left common ostium, phrenic nerve palsy

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Pulmonary vein (PV) isolation is currently an established treatment for drug-resistant AF.[1] A left common PV (LCPV) is present in 9–83 % of the patients, depending on the definition used,[2,3] and counts as the most frequent PV variation, followed by a right accessory middle vein. In recent years, cryoballoon (CB) ablation has emerged as a valid alternative to traditional point-by-point radiofrequency ablation.[4,5] However, mainly due to its geometrical shape the use of the CB in the setting of LCPVs is still under evaluation. In fact, a successful ablation with the CB is tightly related to an optimal occlusion. In addition, one might advocate that in the setting of a LCPV the CB might create a distal lesion leaving the antrum largely unablated. Although, initial experiences with the first-generation CB (Arctic Front™ Cardiac Cryoballoon, Medtronic, USA) reported deceiving results in patients presenting this anatomical variant[6] if compared with individuals exhibiting a normal PV drainage pattern, clinical outcomes with the current second-generation CB (CB-Adv [Arctic Front Advance Cryoballoon, Medtronic, USA]) might greatly differ. In fact, the CB-Adv has been launched on the market with significant technological improvements if compared with its predecessor.[7] During the cryoablation the refrigerant gas is ejected in the balloon through holes known as 'refrigerant jets'. In the CB-Adv the number of refrigerant jets has been doubled and have been positioned more distally on the catheter's shaft. These modifications have led to more homogeneous and circumferential lesions around the PV antrum if compared with the first-generation device.[8,9] This translated in significantly better clinical outcomes,[10] probably due to a higher rate of permanent PV isolation in the long term.[11]

Recently, Ströker et al.[12] analysed the impact of an LCPV on clinical outcome in patients undergoing CB-Adv ablation as an index procedure. In a total of 476 patients, 146 presenting LCPV (study cohort; LCPV+) and 287 with normal PV drainage pattern (control group; LCPV-), were matched in a 1:1 ratio based on propensity scores, which resulted in two balanced groups of 146 patients each. All patients underwent a pre-procedural CT scan and the presence of a common PV ostium was defined as a coalescence of inferior and superior PV ≥5 mm before the insertion into the left atrium (LA). Furthermore, LCPV were subdivided according to the length of the common trunk. Specifically, a short common PV trunk was defined when the distance from the ostium to the bifurcation was 5–15 mm, and a long common trunk when this distance was >15 mm.[12] During the procedure, full occlusion and acute isolation could be achieved in all LCPVs without additional focal tip ablation. Importantly, no significant difference was noted in terms of AF recurrence rate in LCPV+ versus LCPV- patients (46/146 [31 %] versus 39/146 [27 %], respectively, p=0.4), on a mean follow up of 19 months. Of note, within LCPV+ patients the recurrence rate did not differ between short and long common trunks. Recently, Heeger et al.[13] analysed the same issue in a multicentre trial. In a total cohort of 670 patients having undergone CB-Adv as an index ablation in three German centres between 2012 and 2016, 74 individuals exhibited a LCPV. The latter were matched with a control group presenting with a normal PV drainage pattern and analysed on a mean follow up of 1.9 ± 0.9 years. Interestingly, all procedural parameters such as procedural duration, fluoroscopy exposure, number of freezes per vein, rate of acute isolation and rate of complications, among others, did not differ between both groups. Most importantly, clinical outcome in terms of AF recurrence was not worse in the LCPV group. In fact, a total of 47 of 73 patients (64 %) of LCPV group and 49 of 74 patients (66 %) of the control group remained in sinus rhythm (p=0.820). The slightly lower overall success rate in this study compared with Ströker et al. findings might be explained by the higher proportion of patients presenting with persistent AF. We believe that these promising findings might be due to the wide and homogeneous lesions achieved by the CB-Adv, which might extend proximally and successfully ablate a large portion of the PV antrum.

A recent publication by Kenisberg et al.[14] analysed the extension of the lesions after CB-Adv ablation by means of electroanatomical mapping showing that the lesions extended proximally in the PV antra affecting a large portion of the posterior wall of the LA.

However, although all abovementioned studies seem to confirm the ability of the CB to successfully isolate the LCPV, a recent article by Shigeta et al.[15] concluded that on a midterm follow up of 454 ± 195 days the clinical outcome of ablation of AF with the CB was worse in patients with an LCPV than in those without (77 % versus 89 %; p=0.02). The authors hypothesised this difference was due to a distal lesion in the antrum that left the proximal portion largely unablated proven by electroanatomical mapping. Although we strongly believe that the LCPV can be successfully approached with the CB-Adv, future prospective multicentre trials are needed to shed light on this controversial issue.

Right phrenic nerve paralysis (PNP) is the most frequent complication occurring during CB[16–18] when ablating the right sided PVs, specifically the right superior PV (RSPV). This is due to the proximity of the phrenic nerve (PN) to this anatomical structure. Although this adverse effect is usually transient and virtually always resumes within weeks after the procedure, persistence of PNP has been described in the literature.[19] Traditionally, PN function is evaluated by manual palpation of the patient’s abdomen to monitor the excursion of the right hemidiaphragm. Furthermore, albeit the use of increasingly sophisticated monitoring strategies aiming at the prevention of this complication, PNP still seems to occur in a small but non-negligible number of patients. Therefore, pre- and intraprocedural indicators helping to identify patients being potentially more at risk for this complication are warranted.

A recent publication by Mugnai et al.[20] analysed the temperature drop behaviour in the setting of phrenic nerve injury (PNI). In a large cohort of 550 patients with an incidence of PNI, 40 individuals (7.3 %) experienced PNI during ablation in the RSPV. Fortunately, only four (0.7 %) did not resolve until discharge and one (0.2 %) still persisted at 23 months. Interestingly patients with PNI exhibited significantly lower temperatures at 20, 30 and 40 s after the beginning of the cryoapplication in the RSPV (p=0.006, p=0.003 and p=0.003, respectively). Also, the temperature drop expressed as delta temperature/delta time was also significantly higher in patients with PNI. Importantly, a low temperature during the early phases of the freezing cycle (less than -38°C at 40 s) predicted PNI with a sensitivity of 80.5 %, a specificity of 77 % and a negative predictive value of 97.9 %.

Another factor predicting PNI is the position of the CB in the RSPV. In this setting, Saitoh et al.[21] analysed the position of the CB in relation to the cardiac silhouette in the anteroposterior (AP) projection. Anatomical studies conducted on human cadavers consistently showed that after descending almost vertically along the right brachiocephalic vein, the PN continues along the right anterolateral surface of the superior vena cava (SVC). It then progresses inferiorly along the pericardium overlying the right aspect of the right atrial wall.[12] Therefore, in this setting the AP projection might be the ideal fluoroscopic view to delineate the right lateral border of the cardiac silhouette and consequently the right PN course. The authors retrospectively analysed the fluoroscopic position of the CB in AP in a cohort of 165 patients having undergone AF ablation. They concluded that the incidence of PNI in the RSPV significantly increased in case of more distal positioning of the CB relative to the cardiac shadow and that such a simple and straightforward intraprocedural indicator might encourage the operators to attempt occluding this vein more proximally to avoid PNI.

Pre-procedural anatomical evaluation by the means of a CT scan might also play an important role in predicting PNI. In a recent article Ströker et al.[22] meticulously analysed the influence of the RSPV size and its drainage angle in the setting of this complication. The authors concluded that pre-procedural anatomic assessment of right PVs is useful in evaluating the risk of PNI and that ostial vein area and external RSPV–LA angle measurement showed excellent predictive value for PNI at the RSPV.

Given these considerations it seems mandatory to avoid ablating the RSPV with the CB distally positioned in the vessel. An easy and straightforward technique that guarantees a more proximal lesion in the antrum was first described by Casado-Arroyo et al. in 2012.[23] The ‘proximal seal’ manoeuvre consists in initially obtaining a complete occlusion of the vein demonstrated by dye injection. Then, while injecting contrast, the CB-Adv is retrieved slowly to a more proximal position until a small leak is observed. Cryoenergy application is then started, and dye injection is continued in the very first seconds of the application when it is still possible. During freezing, the balloon volume increases (up to 5 % of the initially inflated balloon—from 26.5 to 28 mm) and the internal pressure grows from 2.0–3.0 psi to a maximum of 17.7 psi, resulting in a ‘stiffer’ and less compliant balloon. In some cases, this is sufficient to eliminate the leak and obtain full occlusion without further repositioning. If a residual leak remains, small pressure to the balloon is applied in the early stages of cryoenergy delivery to eliminate it and occlude the vein. In this setting, a larger and less compliant balloon and the small pressure applied to the device in the PV ostium bare a significantly lower chance of creating a more distal lesion in the vessel. This manoeuvre led to a dramatic reduction in incidence of PNI as observed by the authors in their study.

Finally, although manual palpation of the diaphragmatic contraction during PN pacing in the SVC is the most common and straightforward method to avoid this complication during ablation in the right-sided veins, other methods such as the compound motor action potential[24–26] or the analysis of the femoral venous pressure waveform[27,28] have been thoroughly described in the literature as techniques aiming at the intensity monitoring of diaphragmatic contractility. Both methods reproducibly showed their capacity in predicting impending PNP in multiple studies available in today’s literature.

Although, significant progress has been achieved in preventing this complication, it still remains the most frequently associated adverse event related to this procedure. Therefore, all efforts should be used to avoid PNP when performing CB ablation. Ultimately, a more proximal lesion in the PV antrum might also reduce other complications related to distal positioning of the balloon, such as bronchial haemorrhage.[29] ■

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