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Pulmonary vein reconnection following cryo-ablation: Mind the “Gap” in the carinae and the left atrial appendage ridge

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A B S T R A C T

Pulmonary vein (PV) isolation (PVI) remains cornerstone to ablation of atrial fibrillation (AF). For effective and durable PVI and thus fewer AF recurrences, lesion gaps in transmurality and contiguity responsible for PV reconnection (PVR) could only be addressed when one is cognizant of the potential location and sites where these lesion characteristics may be more prevalent and responsible for PVR. In the case of RF ablation, newer technologies incorporating contact force, time and power with automated monitoring of lesion formation, paying attention to difficult areas (carinae, left superior PV-LAA ridge, right inferior PV) and measuring inter-lesion distance may provide the tools to reduce PVR. On the other hand, the improved thermodynamic characteristics of the latest generation of cryoballloons and operator dexterity to achieve better PV occlusion, may be crucial determinants towards the direction of reduced PVR. Whether newer visualization tools, more vigilant testing during the index ablation procedure in these particular regions, prolonging or adding cryothermic applications, waiting longer to test for entrance and exit block, and/or use of provocative drug testing (isoproterenol/adenosine challenge) might help prevent future PVRs awaits further studies.

1. Introduction

Arrhythmia recurrences after catheter ablation of atrial fibrillation (AF) are frequent necessitating a repeat ablation procedure in approximately 30% of cases submitted to pulmonary vein (PV) isolation (PVI) effected either via point-by-point radiofrequency (RF) ablation or with use of single-shot techniques, like cryoballoon ablation [1,2]. The majority, albeit not all, of recurrences are due to PV reconnection (PVR), especially when PVR is wide and involves multiple PVs [3,4]. The introduction of newer technologies, such as contact force-sensing catheters during RF ablation and latest-generation cryoballoon catheters have reduced AF recurrences and PVR and thus the need for redo procedures [5,6]. Furthermore, these technologies have reduced PVR as a finding during second procedures. In the past, during repeat procedures, the reported PVR rate was very high reaching rates of 65–95% [7,8]. These PVR rates have now dropped to ~22–38% [5,6,8–10], although exceptions have been reported where PVR rate remains high (62.5%) despite use of newer technology (contact-force RF ablation) [11].

2. Pulmonary vein reconnection sites

An important issue during redo procedures remains the identification of PV sites where PVR has occurred. The means employed to locate these PVR sites include the use of the lasso mapping catheter when RF ablation is intended or the use of the Achieve mapping catheter when cryoablation is planned. Guidance has also been proposed with use of intracardiac echocardiography (ICE) to locate the PVR site [4]. PVR is confirmed during signal (PV potential) recording and during pacing within the PV with resultant atrial capture, thus identifying the lack of entrance and exit block, respectively.

In the study of [3] the *Indian Pacing and Electrophysiology Journal*, PVR after cryoablation was methodically characterized in a small patient sample of 15 patients [3]. Interestingly, the Authors demonstrated that multiple PVs had been reconnected, with both carinae and PV-left atrial appendage (LAA) ridge being common sites of PVR. Furthermore, the Achieve mapping catheter was able to identify PVR with high positive and negative predictive values, but still trailing behind the method of ICE-guided pacing. Surprisingly, the most commonly reconnected PV was the left superior PV (LSPV) which is known to be the easiest PV to isolate during the index procedure. The authors suggested that the carina area between PVs and the thicker tissue in the LAA ridge could be responsible for suboptimal creation of transmural lesions in these sites accounting for the higher PVR occurrence in these regions [3]. Other investigators have also pointed to the LSPV as the most common site of PVR regardless of the method employed during the index procedure, and have attributed it to the specific anatomy of the ridge between the LSPV and the LAA [6,12,13]. During point-by-point RF ablation it is often difficult to achieve and maintain stable catheter position and apply adequate contact force in this region. Similarly, during cryoballoon ablation, adequate balloon coverage

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of this ridge area to achieve satisfactory freezing remains problematic. Apparently similar issues and anatomic variables may pertain to the carinae between the superior and inferior pulmonary veins on both sides [14,15]. Earlier studies using RF ablation have also pointed to the carinae and PV-LAA ridge as the sites of acute and chronic PVR [15,16].

According to the recently reported results of the PRAISE study, carina ablation, albeit more commonly on the right side, was required in about half of patients presenting with early or late PVR, indicating that the carinae as the segments with the thickest tissue are the weak links in attaining durable PVI even in the contemporary era of use of newer technologies, such as automated algorithms incorporating contact force monitoring [5]. Indeed, lack of complete lesion transmurality (depth) and contiguity within the ablation area can explain PVR, as indicated in studies of contact-force guided PVI [17,18] and cryoballoon ablation [15].

3. Durable PVI

Recently, among the ways proposed by investigators to achieve durable PVI via cryoablation is prolonging ablation duration after achieving isolation indicating that such an approach can decrease PVR and repeat procedures [19]; the apparent benefit of such prolongation might well be related to achieving lesion transmurality in these difficult to ablate areas. One way to circumvent the need to pay particular attention to establish an effective carina and/or LSPV-LAA ridge ablation is the approach of encircling PVI, where both ipsilateral PVs (PV pair) are isolated in a circumferential fashion. When the results of this encircling approach alone were compared with adjunctive carina ablation, PVR between the superior and inferior PVs (along the inter-PV isthmus) could not be demonstrated in 88% of cases [20]. However, AF recurrences were similar in the two groups indicating that carina ablation may not be necessary in patients having the encircling PVI approach. Nevertheless, other studies have indicated that carina ablation is necessary in about half of these cases (40–56%) to achieve durable PVI, even when using the circumferential/encircling PVI method [21–23].

In general, the aim is to achieve *durable PVI*. With contemporary technologies (contact force RF ablation and latest generation cryoballoons), this seems to be an attainable target [1,2,5,8,24] (Table 1). Identifying the weak links in this endeavor should help focus on these areas and thus further enhance the success rates of the index procedures and curtail the need for redo procedures [3,5]. With older technologies, it was the rule to find PVR as the cause of AF recurrences. However, using current technologies, investigators have reported significantly higher (62–79%) than previously reported rates (0–41%) of finding all 4 PVs still isolated at repeat procedures for AF recurrence [10,25]. Of course, non-PV ablation for non-PV triggers will be needed in cases of non-PVR. However, the prevalence of non-PV triggers remains low at least for patients with paroxysmal AF; non-PV triggers more commonly characterize patients with non-paroxysmal AF [26]. Although investigators have claimed that single-shot techniques, such as those using circular multielectrode catheters [27], or cryoballoons afford fewer scar gaps compared to point-by-point RF ablation method [13,28], this needs to be further confirmed in comparative studies. Others have reported fewer reconnection gaps in the left or both-sided PVs with use of newer generation balloons compared with old-generation balloons [6,29].

Table 1
Technologies and techniques promising to reduce pulmonary vein reconnection (PVR) and arrhythmia recurrences after pulmonary vein isolation (PVI) in patients with atrial fibrillation.

RF ablation
• contact force monitoring
• automated algorithms of real-time adjustment of contact force, power and time of RF application
• visualization of lesion formation
• controlling inter-lesion distance/ablation line contiguity/catheter stability
Cryothermic ablation
• Second/third generation cryoballoons with improved thermodynamic features
• Complete balloon occlusion of the PV
• Real-time monitoring of PVI (PV potential elimination)
Both RF- and Cryo-ablation
• Inter-PV carina and PV-LAA ridge ablation

However, even with newer technology (point-by-point RF ablation guided by contact force or latest generation cryoballoons), PVRs do occur. In cases of contact-force guided RF ablation, the majority of PVRs (80%) have been observed on the anterior PV ostia due to inadequate contact force or due to long inter-lesion distances; investigators have proposed that higher mean contact force (15–20 g) in this region can improve durability of PVI [30]. Others have suggested that ablation guided by algorithms of automated control of contact force could effectively reduce early or acute, or even late PVR [9,31,32]. Cardiac magnetic resonance imaging has also been suggested to guide RF ablation and identify and localize gaps [33]. Further studies are needed to better investigate late PVR using these latest technologies. On the other hand, using second-generation cryoballoon technology, PVRs are still observed with more conduction gaps noted in inferior PVs compared to superior PVs [34]. The right inferior PV (RIPV) and minimum balloon temperature may be independent predictors of PVR [25,34,35]. Importantly, reconnected PVs usually have poorer occlusion at the index ablation procedure than PVs that maintain durable PVI [25]. Some investigators have suggested that PVI lesions after cryoballoon ablation are characterized by wider and more continuous lesions than those after RF ablation [36]. However, the carina (saddle) region remains an important, albeit demanding and resistant to ablation, target [37].

4. Persistent AF

Patients with persistent AF constitute a demanding patient group where ablation is less successful compared to patients with paroxysmal AF. Adjuvant substrate modification in addition to PVI has been suggested to enhance the ablation success in this group but has not panned out in randomized controlled trials, while dreaded complications, such as atrioesophageal fistula, are lurking with this type of additional ablation [38,39]. Thus, the recommendation (class I) remains for PVI alone with demonstration of entrance block into the PV as the initial approach for all types of AF [40]. Posterior wall isolation for initial or repeat ablation of persistent AF has been suggested as a promising extra maneuver achievable with RF or cryothermic ablation [41], albeit with use of reduced RF power and with monitoring of the esophageal temperature; however, this extra step still remains a IIb recommendation [40]. Importantly, even in this demanding group of patients with persistent AF, durable PVI achievable with use of newer technologies encompassing carinae ablation may obviate the need for these extra and riskier ablation steps [5,42].

5. Conclusion/perspective

In ***conclusion***, for effective and durable PVI and thus fewer AF recurrences, lesion gaps in transmurality and contiguity responsible for PVR could only be addressed when one is cognizant of the potential location and sites where these lesion characteristics may be more prevalent and responsible for PVR. In the case of RF ablation, newer technologies incorporating contact force, time and power with automated monitoring of lesion formation, paying attention to difficult areas (carinae) and measuring inter-lesion distance may provide the tools to reduce early and most importantly late PVR. Waiting for a longer (>30 min) period to test for entrance/exit block and/or using isoproterenol/adenosine testing for dormant PVR remain available, albeit non-practical, options that will prolong the index procedure. On the other hand, the improved thermodynamic characteristics of the latest generation of cryoballloons and operator dexterity to achieve better PV occlusion, may be crucial determinants towards the direction of reduced PVR.

Whether newer visualization tools, more vigilant testing during the index ablation procedure in these regions (carinae, LSPV-LAA ridge, RIPV), prolonging or adding cryothermic applications, waiting longer to test for entrance and exit block, and/or use of provocative drug testing (isoproterenol/adenosine challenge) might help prevent future PVRs awaits further studies. Some have suggested that cryoablation obviates the need for adenosine testing as dormant conduction with adenosine is uncommon in this setting [43]. There are also certain clues during cryothermic ablation that are considered predictors of effective and durable ablation with reduced possibility of PVR, such as early PVI as indicated by prompt (within 60 sec) elimination of PV potentials, a minimal temperature of $< -51\,^{\circ}$C, and balloon warming time or interval thaw time at $0\,^{\circ}$C $>$ 10 sec [1]. Finally, above all, safety of the ablation procedure remains the ultimate goal and actions (prolonging the procedure, applying higher catheter pressure, more extensive ablation and possibly harmful maneuvers, etc) that may appear promising in reducing PVR but may have a potential to compromise safety should be avoided.

Conflicts of interest

None to be declared.

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