Pulmonary Vein Stenosis after Catheter Ablation for Atrial Fibrillation

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Editorial Comment

Tree randomized trials (PIAF, AFFIRM, and RACE)[1-3] recently showed that rate control was not inferior compared to rhythm control for treatment of patients with atrial fibrillation (AF). However, it should be noted that frequent recurrences of AF and adverse effects of drugs decrease the potential benefits of rhythm control, prompting discontinuation of failed drugs in up to 40% of patients.[2] In addition, the beneficial effects of rhythm control may be nullified by life-threatening cardiovascular events. Such events may be related not to the rhythm but rather to severe adverse effects of antiarrhythmic drugs, especially if they are used in the long term. In this case, these trials emphasize the need for safer and more effective methods for maintaining sinus rhythm. The quest for better drugs and techniques to achieve this goal will, and should, continue in the future.

The relative ineffectiveness of pharmacologic approaches to AF, the risks of antiarrhythmic treatment, and the growing recognition of deleterious AF health effects[4] have helped catalyze the development of curative nonpharmacologic approaches to maintenance of sinus rhythm. The management of AF has become more aggressive, with a shift toward nonpharmacologic therapies, including controlled destruction of the substrate generating and maintaining arrhythmia, so-called ablation therapy.[5-8]

The important new discovery that some episodes of AF are initiated by rapid repetitive firing of atrial myocytes in muscle sleeves located in the pulmonary veins (PVs) has led to the use of catheter-based approaches to isolate these structures electrically, in some cases curing AF.[9-11] Mapping and selective ablation of these rapidly firing arrhythmogenic foci have the potential to cure AF. Although theoretically intriguing, the focal ablation approach is extremely arduous and is associated with prolonged procedure and fluoroscopy times, frequent need for second ablation, insufficient atrial ectopy, and development of a major complication—*PV stenosis.*[9] The incidence of this complication is unclear. PV stenosis has been reported in <2% of patients treated but in >20% of PVs treated with ablation. The risk of PV stenosis during long-term follow-up is not known.[12]

As a typical complication of techniques delivering radiofrequency (RF) energy within PV tissue, PV stenosis can be partly explained by the anatomic and histologic characteristics of the junction between the pulmonary venous vasculature and the left atrium (LA). Myocardial sleeves are always found in the outer layer of PVs, with myocardial cells embedded in a dense collagenous matrix, along with fibrocytes and smooth muscular cells. These cellular types are well known to have the potential for a strong proliferative response to injury, including RF energy-related injury.[13] No histopathophysiologic studies of PV stenosis in humans have been reported; however, in dogs, the pathophysiologic mechanisms of PV stenosis produced by RF delivery include fibrocellular intimal proliferation, endoluminal thrombus formation, endocardial contraction, and proliferation of elastic lamina.[14] Intimal proliferation is observed in all stenotic PVs and is responsible for much of the narrowing.[14]

As a result of the poor clinical outcome of focal ablation, modifications of PV ablation procedures have been introduced, i.e., electrophysiologic-guided segmental PV disconnection. It has been suggested that, although PV muscle covers a large extent of the PV perimeter, there are specific breakthroughs from the *LA* that allow ostial PV disconnection with minimal ablation.[15] With this approach, the risk of PV stenosis can be minimized, provided a conservative approach to ablation is used to minimize the risk. In turn, this may explain the inability to isolate a small percentage of PVs. Fascicles often are too thick to be ablated with conventional RF energy limited to 35 W.[16] This would explain why a saline-irrigated ablation catheter, which creates deeper lesions than a conventional ablation catheter, was needed to isolate 10% of PVs in a recent experience by the Ann Arbor group.[16] Outcomes of systematic irrigated-tip ablation of all four PVs has been reported by the Bordeaux group. Only 1 (0.7%) case of PV stenosis was acutely detected, but the authors did not provide late follow-up assessment of this complication. The low PV stenosis rate was likely due to a number of procedural factors, including the delivery of lesions as proximal as possible and the power limitation to 25 W for the left inferior PV (the most vulnerable to PV stenosis) and 30 W for the other veins.[17]

In this issue of the *Journal,* Pürerfellner et al.[18] report the impact of PV ostial ablation using an irrigated-tip catheter on the incidence, time course, and prediction of PV stenosis. In particular, they assessed the clinical value of serial computed tomography (CT) scanning in detecting PV stenosis. Ablation 2 to 5 mm within PVs resulted in 6% and 2% of mild (20%–50% of luminal narrowing) and severe (>70%) PV stenosis rates at a distance between 0 and 1.5 cm ab ostio, as detected by serial CT scanning, despite an overall success rate of 49%. Interestingly, analysis of delivered energy showed no significant correlation with the degree of stenosis overall (although a trend was detected), and more energy was delivered in the superior segment of stenosed left inferior PV, likely due to difficult manipulation of the mapping catheter in this vein or due to closely located or common ostia of the left-sided PVs, with summation of PV injury effects. However, the small sample size of this report mitigates against drawing sweeping conclusions and emphasizes the technical difficulties in ablating thick bundles in the outer layer of PVs without

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injuring the intervening intima and PV fibromuscular tissue and inducing fibrotic narrowing responses, notwithstanding the size of the irrigated-tip catheter.

As regard to the latter, it has been proposed that the unique lesion size and geometry of irrigated-tip ablation reduces the risk of PV stenosis.[19] The lesion configuration would be wider beneath the surface and is deeper, thus reaching epicardial PV muscular sleeves with relatively less damage to the intima. Furthermore, irrigated-tip ablation limits the temperature at the catheter tip-tissue interface, reducing the risk of charring and thrombus formation.[19]

Finally, the fact that PV stenosis tended not to progress during follow-up emphasizes the need for careful and safer ablation procedure. If progression of stenosis is unlikely, the use of on-line imaging techniques, such as intracardiac echocardiography, may better serve the purpose without increasing the patient's exposure to ionizing radiation and the repeated use of dye.[20]

What Are the Implications of These Issues for the Clinical Application of PV Catheter Ablation of AF?

On the one side, it has been shown that RF catheter ablation for AF has relatively low risk, although the initial data usually are reported from highly experienced centers and the risk-to-benefit profile of the same procedure may be different in other institutions.[12] However, the risk of PV injury can be prevented by delivering RF energy at a safe distance around each PV ostia.

On the other side, simple electrical disarticulation of PVs has resulted in cure rates of paroxysmal AF of 70%.[9,15,16,21-23] As AF now is clearly recognized as a disease of the LA, more extensive ablation strategies in the region of the crucial LA posterior wall have proved successful in both paroxysmal and chronic AF.[24,25] Modification of the atrial arrhythmogenic substrate seems to be a rational part of the curative ablation strategy for patients with longer AF duration and larger atria.[26] To summarize, the distinction between a PV origin and a posterior LA origin is crucial. Ablation procedures designed to cure chronic AF must include a portion of the posterior LA wall, thus representing a possible and fruitful melding of the two approaches, linear ablation and PV isolation. In contrast, very limited ablative approaches without excluding any atrial myocardium, such as segmental PV isolation, shows several limitations and may not be adequate to cure chronic AF.[26] High success rates and low complication rates have been reported for PV ablation procedures and in association with the application of linear lesion lines encircling the PVs,[24,25] and it is likely that PV isolation plus substrate modification will be important in the future strategy of catheter ablation for AF.

RF catheter ablation currently is used widely and successfully to treat a variety of arrhythmias. Given the relative dissatisfaction with pharmacologic therapy and the encouraging results seen with ablation in selected patients, it is understandable why so much energy is being focused on identifying a feasible methodology that can be widely applied with a good degree of safety. RF ablation for AF represents the frontier of arrhythmia research and thus far has been considered an investigational technique, but large experience in several centers suggests that it is ready to become a routine clinical tool.[27,28]

Future research to improve the feasibility of the technique must include the development of newer lesion paradigms for PV ablation and simplification of techniques for validation of the design of catheters to ensure stable electrode-tissue contact. One hope is that better understanding of the fundamental mechanisms underlying AF will lead to safer and more effective mechanism-based therapeutic approaches. In addition, more precise location techniques and use of temperature-guided devices or other energy sources should improve the safety of this procedure. In this regard, the use of irrigated-tip catheters has been associated with greater lesion volumes and deeper tissue penetration, with increased therapeutic efficacy, in case of recovery of conduction through PV breakthroughs to LA. However, irrigated-tip ablation may be more useful for ablation of periostial foci or for other approaches involving intra-atrial periostial circumferential RF ablation, as also suggested in the report by Pürerfellner et al.[18] Finally, long-term prospective and randomized surveillance of patients undergoing catheter ablation is needed to assess long-term safety and efficacy and to finally overcome the challenge of AF, so aptly termed "the last big hurdle in treating supraventricular tachycardia."[28]

In summary, catheter ablation procedures to cure patients of AF are in a continuing phase of development. The electrophysiologic community must confront the warning trend toward a higher risk of death in the rhythm control groups in both the RACE and AFFIRM studies.[2,3]

Because it is intrinsically unlikely that sinus rhythm is per se harmful to the patient's life, we believe that the quest for safer and more effective catheter ablation techniques for curing AF will, and should, continue.

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