Catheter ablation of atrial fibrillation: do we know what we are doing?

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Although atrial fibrillation (AF) represents the most common arrhythmia that is seen in every day cardiology practice, the surgeons, and not the cardiologists, were the first to take the initiative for its radical cure. Cox and colleagues developed the Maze procedure and its modifications in the 80s followed by the pioneering attempt of Swartz et al. to ablate the arrhythmia in the electrophysiology laboratory in 1994. Now, catheter ablation is an established therapeutic option for certain patients with AF. Several ablation strategies have emerged which, although extremely diverse, report similar success rates, in the range of 60–80%, with 30–40% of patients followed for a year or two having had two procedures, however, different endpoints and methodology of assessment of AF recurrence make interpretation of success rather difficult. It is of interest that despite the considerable clinical experience and accumulated evidence from experimental data, the exact mechanism of eliminating AF by catheter ablation techniques is still unknown.

Pulmonary vein isolation, substrate modification, or both?

Since the seminal studies by Haissaguerre’s group, the effectiveness of segmental ablation at the ostia of the pulmonary veins (PV) has been demonstrated in several reports. There is substantial evidence that isolation of the PV, either by ostial or circumferential radiofrequency lesions, removes a potential source of arrhythmia that initiates and perpetuates AF. Although re-emergence of AF following PV disconnection procedures is usually due to recurrence of PV conduction, complete electrical isolation of the PVs may not be necessary for a successful outcome. Recurrence of PV conduction following complete PV isolation may occur in up to 98% of PVs and may not indicate a propensity to arrhythmia. Thus, recurrence of AF following ablation indicates recurrence of PV conduction, but the opposite is not always true. Anatomically guided circumferential PV ablation even when performed with a clear endpoint of delivering coalescent lesions that produce a voltage reduction to <0.1 mV and delayed local conduction (>30 ms) between contiguous points across the line cannot achieve complete electrical isolation of PVs in 25–45% of patients. When such clear endpoints are not necessarily achieved, complete isolation of all PVs is present in <20% of patients and does not predict freedom from AF in the long-term. Complete transmural lesions are difficult to obtain with percutaneous ablation techniques, and achievement and verification of complete lines of block may be cumbersome. Nevertheless, the presence of anatomic gaps within linear ablation lesions does not necessarily preclude therapeutic effects.

It seems that not only focal activity within the PVs may act as potential trigger of AF, but anisotropic conduction properties at the PV–left atrial junction may also promote reentry. PV antral ablation, therefore, may be effective by modifying conduction properties of the PV–left atrial junction without achieving permanent PV isolation. Furthermore, nonencircling left atrial lesions created by catheter ablation have been found equally effective with circumferential ablation in eliminating permanent AF. Intraoperative radiofrequency ablation noncircling lesions in the LA have been reported to have a success rate of 90% in the IRAAF study, and surgical ablation of the left posterior atrial wall at the base of the left atrial appendage and at the orifice of the left inferior PV can terminate chronic AF. High success rates have also been reported with tailored catheter approaches that target triggers and drivers of AF through spectral analysis and electrogram-guided ablation during AF or sinus rhythm in the true atrium or the appendage, but the mechanism of eliminating AF appears to be different than that of circumferential ablation, and success rates with electrogram-guided ablation have not always been so favourable. Approaches aiming at non-inducibility of the arrhythmia may also produce...
favourable long-term results with\textsuperscript{15,36} or without\textsuperscript{36,37} verification of PV isolation. It seems, therefore, that conduction delay or substrate modification created by even incomplete ablation lines around the PV ostia may also prevent induction and/or maintenance of AF.

Aetiology of atrial fibrillation

These rather conflicting findings can be interpreted within the context of the multi-factorial aetiology of AF.\textsuperscript{38} There is substantial evidence that, apart from PV firing, additional mechanisms may initiate and perpetuate AF. Other cardiac veins\textsuperscript{39–41} and certain areas of the posterior left atrial wall\textsuperscript{42–44} may have a profibrillatory role. Multiple re-entrant wavelets\textsuperscript{45} and anisotropic reentry leading to rotors with a high dominant frequency\textsuperscript{46,47} have been proposed as potential mechanisms of AF. Elimination of these rotors and AF nests may be one of the mechanisms for the efficacy of real-time frequency analysis or complex fractionated electrogram-guided ablation.\textsuperscript{31,48}

Areas rich in sympathetic innervation may be the source of activity that triggers AF.\textsuperscript{49,50} Ablation of the adjacent area of the ligament of Marshall has yielded moderate success in eliminating episodes of PAF.\textsuperscript{51,52} Vagal reflexes from ganglionated plexi that can be identified by high-frequency stimulation at sites around the circumference of the left atrial–PV junction may also induce and perpetuate AF through spatial heterogeneity of refractoriness.\textsuperscript{53,54} Damage to ganglionated plexi that are usually located 1–2 cm outside the PV ostia\textsuperscript{55} has been proposed as a potential mechanism of antral PV ablation.\textsuperscript{56,57} Partial vagal denervation by catheter ablation has been found efficacious in several studies.\textsuperscript{54,58,59} It, and seems that sympathetic stimulation may be much less effective than vagal stimulation in promoting AF. Parasympathetic denervation through epicardial fat pad ablation has also been reported to have a temporary only effect\textsuperscript{60} or even to increase vulnerability of vagally mediated AF.\textsuperscript{61} Of course, since both sympathetic and parasympathetic elements reside in all four major left atrial ganglionated plexi,\textsuperscript{62,63} denervation lesions may unavoidably affect both components of the autonomic nervous system. Furthermore, nerve sprouting and sympathetic hyperinnervation may also occur early after catheter ablation.\textsuperscript{64,65}

It seems that the more extensive the ablation-induced damage, the higher the possibility of intervening with these mechanisms. Pappone et al.\textsuperscript{18} have suggested that the extent of left atrial ablation (average 30%) is a marker of success rather than PV isolation, although the addition of linear lesions to circumferential ablation by the same group did not affect recurrence rates of AF.\textsuperscript{66} Mere elimination of the left atrial tissue below the critical amount required for reentry\textsuperscript{67} may theoretically affect clinical outcomes. However, increased areas of scar with low voltage and slowed conduction in the left atrium following catheter ablation have also been identified as the underlying substrate for AF recurrence,\textsuperscript{68} and atrial fibrosis may constitute a vulnerable substrate for AF.\textsuperscript{69,70} Even the effect of ablation on left atrial transport function is debatable.\textsuperscript{71–73} The increased risk of complications with extensive ablation procedures should be always kept in mind. According to real-life data, catheter ablation for AF is a procedure that carries a very small but not negligible risk for serious complications.

In a recent worldwide survey on catheter ablation procedures for AF in clinical practice, the incidence of procedure-related stroke and mortality was 0.05 and 0.28%, respectively,\textsuperscript{74} whereas in the recent report by the Hospital Corporation of America’s Casemix Database, in-hospital mortality was 0.69%.\textsuperscript{75} It is not surprising, therefore, that for such a multifactorial disease, no single ablation technique may be universally curative in the long-term. Indeed, true long-term efficacy data for these procedures is limited with most published studies having reported follow-up data for 6–12 months. In the worldwide survey,\textsuperscript{74} follow-up varied widely from <6 months (20 centres), 7–12 months (29 centres), and 1–2 years (25 centres). Only 6 centres had follow-up data beyond 2 years. In patients with heart disease, in particular, long-term follow-up data following ablation for AF is virtually lacking.\textsuperscript{76,77} However, this particular patient subset is of particular interest, especially after recent evidence suggesting that catheter ablation of AF and restoration of sinus rhythm might eventually result in improvement of left ventricular function.\textsuperscript{77}

In conclusion, various ablation techniques are now used for the ablative treatment of AF with a similar long-term success rate. Still, however, the exact mechanism(s) of eliminating AF by catheter ablation techniques is not known. Current ablation techniques appear to target different mechanisms that all contribute to the genesis and perpetuation of AF. PV isolation or modification of PV–left atrial conduction, elimination of rotors and drivers of AF within the left atrial myocardium and autonomic denervation, and, perhaps, elimination of electrically active myocardium beyond a critical threshold appear to constitute potential antiarrhythmic effects of catheter ablation. Further experimental and clinical evidence is certainly needed for the elucidation of these important issues.

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References


