Ablation of Atrial Fibrillation

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Fueled by dissatisfaction with pharmacologic strategies to treat atrial fibrillation (AF), the results of basic and clinical investigation into the understanding of AF initiation and maintenance mechanisms, and the explosive development in catheter-based technologies, AF ablation has matured from a purely investigational technique to a preferred, safe, and effective approach for curing AF, particularly with the circumferential approach. Future insights and developments will help us refine our treatment strategies in patients with permanent AF, making chronic AF ablation safer, faster, and more effective. As the prevalence of AF in the general population continues to increase, the purpose of optimizing our strategy becomes evermore important and more pressing.

Introduction

Atrial fibrillation (AF) is a common clinical problem that is increasing in prevalence. There is evidence that AF may represent a spectrum of atherosclerotic vascular disease, hypertension, systolic and diastolic dysfunction, and metabolic syndromes. According to a time-based clinical classification of AF, there are three basic types of recurrent AF: paroxysmal, persistent, and permanent or chronic. The field of catheter ablation for treating AF continues to evolve [1–6,7•,8••,9–16]. Pathophysiology of AF is complex because there are different mechanisms for paroxysmal, persistent, and permanent AF. Variable progression times from the index episode to recurrent and/or long-lasting or permanent AF within the wide AF population suggest that AF is highly heterogeneous and different mechanisms may account for different progression times. Therefore, the variable success rates reported by different strategies basically depend on the effect that each ablation technique has on all factors triggering and maintaining AF. The best approach would be to individualize the therapy decreasing the duration and the amount of radiofrequency (RF) energy. Recently, Oral et al. [3] proposed a tailored approach in which each patient's ablation strategy is customized to his or her own pathophysiology according to an orderly progression of techniques. They started the ablation procedure by initiating AF and then performed a stepwise approach to cure AF. First they looked for drivers in pulmonary veins (PVs) that were then isolated using one of several techniques [3]. If a PV had potentials but did not appear to be a driver, it was not isolated. Sites of complex fractionated left atrial electrograms were then systematically targeted for ablation. Other potential targets were treated based on noninducibility [3]. In our opinion, such novel approach seems to be a limited approach rather than a tailored one, because the authors found that less than 80% of patients with paroxysmal AF had no recurrent AF after ablation. Such a so-called tailored approach at present appears to be speculative as it implies the knowledge of all mechanisms that are involved in the pathogenesis of AF for each patient. Actually, the lack of knowledge of all factors initiating and maintaining AF has forced us to use standardized techniques with a predefined set of lesions. The first approach by Haissaguerre et al. [1] was based on ablation of PV foci, whereas other strategies mainly targeted substrate by linear or nonlinear lesions. The higher success of circumferential PV ablation (CPVA) suggested that CPVA unlike PV isolation alone affects many AF mechanisms. In the last few years, ablation of fractioned atrial electrograms has been proposed for patients with either persistent or permanent AF. However, fractioned potentials may be a random phenomenon being transient, not reproducible and ubiquitous, and we do not consider them as optimal targets for ablation.

Success of AF Ablation Strategies

Surgical treatment for AF preceded catheter-based approaches by more than a decade [4]. The initial Maze procedure included linear lesions performed in both atria, and the success of this procedure was reported to be excellent. This procedure has evolved over time, and surgical AF ablation techniques at many centers currently employ RF or cryoablation lesions in the left atrium surrounding each PV extending to the mitral annulus and across posterior wall. These lesions, similar to our approach, aim to create anatomic lines of conduction block, particularly in the posterior left atrium, and prevent the development of reentrant left atrial tachycardias. With the Maze III approach, Cox [4] reported the maintenance of sinus rhythm in 95% of patients, regardless of presence of structural heart disease or persistent AF. However, the morbidity and risks associated with cardiac surgery greatly limited its wide clinical application. The excellent results reported by the surgical approach were not confirmed by initial percutaneous catheter ablation techniques particularly in the right atrium and were terminated prematurely when PVs were found to be the dominant source of triggers initiating AF, and the initial technique for AF ablation was to ablate the culprit focus within the PV [1]. The focal approach was frequently complicated by PV stenosis and initial enthusiasm was also tempered by long procedure times with limited success rates, which frequently required repeat procedures. The focal technique then evolved to electrical disconnection of all PVs by segmental ablation of PV potentials using the LASSO catheter (Biosense Webster, Diamond Bar, CA) positioned within the ostium of the vein representing a further advance in catheter ablation of AF. Based on the observation that substrate modification is indeed important in curing AF simultaneously with PV isolation, we developed for the first time a different strategy for AF ablation. Specifically, we performed circumferential RF lesions around each vein or a single large circumferential lesion including two PVs with the endpoint of ablation being the absence or marked reduction (90%) in the amplitude of electrical signals within the encircling lesions [5]. Ablation was guided by three-dimensional electroanatomic mapping with excellent results in patients with paroxysmal, persistent, and permanent AF. Following our excellent results, there was an initial skepticism, but these results were subsequently confirmed in a randomized study that compared our technique with PV isolation [6]. These data demonstrated that elimination of PV triggers alone is not an optimal strategy and that any AF ablation strategy requires substrate modification as an optimal endpoint. At present, in fact, in patients with persistent AF, PV isolation is frequently associated with additional substrate modification, whereas in those with paroxysmal AF substrate modification is added only in the presence of AF inducibility. The crucial role of substrate modification for much better outcomes in patients undergoing AF ablation constitutes the basis for the development of other techniques. Two years ago, Nademanee et al. [7•] identified different areas of fractioned electrograms and ablating such areas not only in the left atrium but also in the right atrium may result in elimination of AF in most patients with AF. Actually, any ablation strategy which involves substrate modification is probably included into CPVA, which also affects both PV triggers and autonomic substrate [8••]. At present, results from other groups performing RF ablation to eliminate electrophysiologic, anatomic, or autonomic substrates confirm our initial excellent results indicating that substrate modification is indeed crucial for predicting a good outcome after AF ablation. During RF applications around PVs or during additional lesions lines including coronary sinus, we commonly observe a transition from AF to a more organized atrial tachyarrhythmia, which becomes slower and totally organized just before conversion to sinus rhythm. This represents in our opinion a convincing proof that a transient substrate modification is indeed involved in acutely restoring sinus rhythm. We also consider the spontaneous conversion of postablation left atrial tachycardia to sinus rhythm as a result of a late substrate modification after ablation [9]. In such cases, left atrial tachycardia may persist up to 2 months after the procedure, particularly in patients with persistent/permanent AF but, in most of them, atrial tachycardia can resolve spontaneously. Our large experience on more than 10,000 patients undergoing CPVA (59% with permanent AF, 45% with structural heart disease, and 44% with enlarged atria), suggests that fractioned electrograms may be ubiquitous both in the right and left atrium particularly in patients with long-standing AF or permanent AF.

AF Ablation: Role of Autonomic Substrate Modification

RF ablation approaches to treat AF have focused on empirical destrcution of myocardial tissue, but recent studies have reported that selectively ablating autonomic nerves and ganglia may result in AF suppression with little, if any, damage to healthy myocardium. It is known that any AF ablation strategy requires several RF applications in a single patient, which may create gaps, particularly in patients receiving linear lesions. The presence of such gaps provides slow conduction areas for sustaining macroreentrant tachycardias, which may require further RF applications to eliminate them either at the initial ablation procedure or at a later time due to a new arrhythmia development. The inability to achieve the same success for AF ablation as has been attained for Wolff-Parkinson-White syndrome, atrioventricular node reentry tachycardia, and atrial flutter has been thought to be related to the greater electrophysiologic complexity of AF compared with the other syndromes. However, the mechanism for focal firing has not been discerned and there is no rationale for PV isolation as suggested by the limited success rates with PV isolation alone. The initial report and landmark paper by Haissaguerre et al. [1] on identification of PV foci raises several basic questions: How does focal tachycardia in the PV become AF and not atrial tachycardia? How does a single premature depolarization in a PV become AF and not an atrial premature beat? How do PVs develop focal firing in the first place? Our clinical study for the first time addressed these issues attempting to determine whether vagal reflexes during RF ablation may predict long-term success and maintenance of sinus rhythm [8••]. We have recently localized vagal fibers and/or ganglia around all PV ostia at the venoatrial junction by eliciting vagal reflexes [8••]. Elimination of such reflexes by continuous RF applications frequently results in late parasympathetic attenuation up to 6 months after the index procedure, which is associated with no AF recurrences. These observations clearly confirm that PV ectopy and PV isolation are only the tip of the iceberg. Therefore, CPVA has multiple mechanisms of action which also include attenuation of vagal tone, that enhance the long-term benefit of the procedure with success rates approaching 100% [8••]. On the other hand, it is well known that parasympathetic stimulation is involved in AF induction and maintenance, as vagal stimulation dramatically shortens the atrial refractory period, increasing the probability that multiple reentrant circuits can exist simultaneously, further increasing maintenance of AF. A recent study has confirmed our findings by identifying four major autonomic ganglionated plexuses outside the PV ostia in patients with AF [10]. Simultaneously, the Bordeaux group [10] has reported that vagal excitation may enhance PV arrhythmogenicity and maintenance of AF. These observations open new doors for curing AF offering a specific lesion set, which is included in our approach. More recently, 60 patients underwent ablation for paroxysmal and persistent AF [10]; 33 had standard PV isolation plus ganglionated plexi ablation at all PV antra, and 27 received PV isolation alone. The former group showed a 91% freedom from AF recurrence, whereas the latter had a 71% success rate. Of interest, ganglionated plexi ablation prior to antrum isolation eliminated focal firing from PV in 95% of patients [10]. These data clearly suggest that autonomic substrate ablation is indeed crucial in increasing the success rate or freedom from AF recurrence.

Circumferential PV Ablation up to 2006

CPVA, which is our current strategy, started at the San Raffaele University-Hospital in Milan, Italy in 1999 [5]. From 1999 to 2006 more than 10,000 patients with paroxysmal, persistent, and permanent AF underwent CPVA with overall success rates of about 90%. Currently, we perform CPVA also by a remote magnetic system with soft catheters by using a video workstation and a CARTO-RMT integration system (Biosense Webster). This remote system is easy and may be safely performed also in less experienced hands [17]. From 1999, CPVA strategy has slightly evolved to a more distal placement of encircling lesion sets, more ablation energy application at sites eliciting a vagal response, more extensive ablation within the encircling lesion sets. At first, the CPVA strategy focused on encircling each PV ostium by circumferential RF lesions performed at least 5 mm from the ostia to prevent PV stenosis. To perform this technique, we use an electroanatomic mapping (CARTO) or the Ensite system (St. Jude Medical, St. Paul, MN), which generate three-dimensional reconstructions of the left atrium and display the spatial locations of the PVs. Four mm-tip catheters were used at first, with maximal energy of 50W and temperature up to 60°C. AF was controlled in 80% of the patients with paroxysmal AF, and no PV stenosis was found during a mean 1-year follow-up. To achieve better results, particularly in patients with persistent AF and associated heart diseases, we have enlarged the encircled area of the periosteal tissue, expanding circumferential lines around the PVs and isolating them two at a time. We have added a posterior line connecting the two encircled areas and another one from the left PVs to the mitral valve annulus, similar to the surgical techniques. In our strategy, RF ablation of the cavotricuspid isthmus has been systematically introduced. For this purpose, we use catheters with 8 mm-tip electrodes and 100W RF power to produce transmural atrial lesions. While performing RF applications in the left atrium, we elicited in about 30% of the patients a vagal reflex, suggestive of autonomic ganglia stimulation, which disappeared as the ablation went on. Clinical follow-up of these patients showed that 99% were free of AF without administration of antiarrhythmic drugs. These data suggest that even the partial ablation of ganglia and fibers of the left atrium, autonomic nervous system is crucial to eliminate AF recurrences. On the basis of our large experience, complication rates were as follows: hemopericardium, 0.2%; stroke, 0.23%; atrial-esophageal fistula, 0.03%; PV stenosis, 0%; and incisional left atrial tachycardias, 6%. Our data on success rates are based on an intensive electrocardiographic monitoring (ie, serial 48-h Holter recordings, and daily 60-sec transtelephonic electrocardiograph recordings for at least 1 year after ablation). The benefits of maintaining sinus rhythm have been questioned by the rate versus rhythm debate, with evidence of possible harm from a pharmacologically based rhythm control strategy [11]. However, there is growing evidence that maintenance of sinus rhythm after catheter ablation without the use of antiarrhythmic drugs is more desirable than AF providing clinical and prognostic benefits. A nonrandomized study [12] in a large cohort of patients with AF has shown a significant clinical improvement with return to baseline community mortality rates after CPVA (589 patients) as compared with drug therapy (582 patients).

Conclusions

In the years since percutaneous RF catheter ablation of AF was first reported, CPVA has remained substantially unmodified [13,14], whereas PV isolation has undergone rapid evolution toward substrate modification with corresponding improvement in success rates minimizing complications [15,16]. Although the increasing knowledge of the mechanisms of AF has been paralleled by the development of different interventional electrophysiology techniques, we still need to learn more about the mechanisms of AF; we also have much to learn about the progression times of the various forms of AF and how to apply this information to ablation timing as well as to tailor ablation strategy to each individual case. The excellent clinical success of our standardized strategy on more than 10,000 cases has addressed several important questions that suggest that catheter ablation of AF may soon become more broadly performed, even by a remote magnetic system. In our experience to achieve the maximum clinical success while minimizing risks any ablation technique should include 1) triggers isolation as we document by elimination of all atrial potentials on ablation lines and within encircled areas to be sure of a true distal disconnection of all four PVs; 2) substrate modification by encircling lesions and additional lines; and 3) local vagal denervation by eliciting and eliminating vagal reflexes. Many prior AF ablation strategies have focused their attention on one of these targets. Recent strategies are focusing on substrate modification and include ablation of low-amplitude and fragmented electrograms or ablation of autonomic ganglia with initial high success rates even in patients with persistent and permanent AF. These data confirm the excellent results first reported by CPVA and clearly emphasize the critical role of substrate modification indicating that AF may be a curable condition.

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