Left atrial field isolation with pulsed field ablation: a new option for challenging left atrial tachycardias?

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Catheter ablation is a highly effective treatment for most cardiac arrhythmias. It has therefore received high-degree recommendations, including as first-line therapy, in current international guidelines. Introduced into clinical practice more than 30 years ago, radiofrequency (RF) ablation carries several important advantages and remains the cornerstone of catheter ablation. Application of RF current results in discrete lesions due to careful titration of ablation energy. Besides its well-established efficacy, there is a detailed understanding of the biophysiological processes in lesion development with RF ablation. On the other hand, application of RF current may also affect tissues other than the target area and may induce pro-inflammatory processes in and adjacent to the ablated tissue.

It is with this background that the potential detrimental consequences of RF ablation prompted the search for alternative ablation energy sources. Mainly developed for catheter ablation of atrial fibrillation (AF) with a single-shot balloon device, cryo-ablation, laser energy and high-intensity focused ultrasound (HIFU) were introduced into clinical practice over the last 20 years. However, all of these techniques may cause serious collateral damage, especially to the phrenic nerve and the esophagus. The high incidence of fatal complications with the HIFA balloon has led to its withdrawal from the market (1).

An ablation technique specifically targeted at the myocardium, without affecting adjacent extracardiac structures represents the ideal tool for the interventional treatment of cardiac arrhythmias. Recently introduced into clinical practice, pulsed field ablation (PFA) seems to provide these properties. PFA is a non-thermal ablation modality that creates an electrical field via ultra-rapid electrical pulses, ultimately resulting in cardiomyocyte cell death. The only PFA catheter that has received regulatory approval in selected regions is the multielectrode pentaspline catheter (Farawave, Farapulse Inc. / Boston Scientific). However, this catheter is only approved for catheter ablation of AF by means of pulmonary vein isolation. Therefore, data on the use of PFA applied to substrates other than the pulmonary veins are limited (2,3).

In this issue of the journal, *Gunawardene* and co-workers present their early experience with PFA for the treatment of patients with post-AF ablation atrial tachycardia (AT) (4). Their analysis includes 15 patients with a history of multiple AF/AT ablation procedures. In these patients, a total of 19 left atrial (LA) tachycardias were explored using ultra-high-density mapping. Eighteen of the 19 LATs represented macro-reentry tachycardia. There were 7 anterior, 5 perimitral, and 4 roof-dependent ATs, as well as 1 AT originating from each the LA appendage and the posterior LA wall, respectively. Using the pentaspline catheter that was inserted into the LA via a deflectable sheath (13 Fr), the authors performed anterior "line" ablation in 11, LA posterior wall isolation in 10, and roof "line" ablation in 3 patients, and mitral isthmus ablation in 1 patient. Acute success of AT ablation was achieved in all cases. Twelve of the 19 ATs terminated with the first PFA impulse. Of note, a considerable mean number of 38±17 PFA applications was required to achieve bidirectional conduction block along the ablated areas. The mean procedure time was two hours and 20 minutes, and the mean fluoroscopy time was 18 minutes. There were no procedural complications. Done in almost all patients in whom posterior LA isolation had been performed, endoscopy demonstrated the absence of any mucosal lesions in the esophagus. During a limited median follow-up duration of 7.7 months, one of the 15 patients experienced AT recurrence following a 90-day blanking period. Two patients were treated with an antiarrhythmic drug at the end of follow-up.

The authors are to be commended for reporting novel and interesting data on PFA for the treatment of post AF-ablation LAT. Given its promising results in ablation of AF, it seems reasonable to explore the application of PFA to the atrial substrate beyond the pulmonary veins. ATs following complex ablation procedures for persistent AF may represent a challenging target for catheter ablation (5). Although currently used high-density mapping systems provide support in exploring the anatomical und electrophysiological characteristics of AT mechanisms, ablation using conventional techniques can still be difficult. Nayak and co-workers elegantly described the anatomical circuits of complex ATs following AF-ablation which may involve epicardial bridging sites, mainly at Bachmann's and the septopulmonary bundle (6). In their cohort of patients with multiple prior ablation procedures, the prevalence of an epicardial bridge contributing to the AT circuit was as high as 38%. Thus, a combined endo-/epicardial ablation approach has been proposed for use in selected patients (6, 7). Nevertheless, even with the use of a percutaneous epicardial access, ablation at Bachmann's or the septopulmonary bundle can be challenging due to the close proximity to the coronary arteries, the esophagus or epicardial fat. Furthermore, access to the target region may be prevented by pericardial reflections (8). In this context, PFA represents a novel option to reach and ablate in these areas, obviating the need for an epicardial access while potentially overcoming some of the other limitations of epicardial LA ablation. Although the study by *Gunawardene et al.* is limited by its small sample size of only

15 patients and a relatively short follow-up duration, the reported high rate of efficacy of PFA in complex ATs following AF-ablation is encouraging and suggests that PFA may be a promising alternative to RF ablation in this setting.

However, despite all the (justified) enthusiasm about the use of PFA as a novel strategy in the ablation of complex ATs, a few words of caution are warranted.

First, the electrical field that is created by the pentaspline catheter results in lesions that are markedly larger in terms of lesion width as compared to those created with conventional RF ablation. While a conventional ablation line is created by point-by-point application of RF current with a typical inter-lesion diameter of ~5 mm, a PFA application series induces a significantly larger lesion. Thus, using PFA aimed at creating a bidirectional conduction block across a target area creates an ablated field rather than a linear lesion. In the study by *Gunawardene et al.* , "linear" ablation at the anterior wall resulted in ablation of a mean of three-fourths of the entire LA anterior wall. In this study, PFA for roof line ablation resulted in complete posterior wall isolation in the majority of patients; and some patients underwent both anterior ablation and posterior wall isolation. With this in mind, known potentially detrimental consequences of the elimination of anterior and posterior LA wall contractility need to be considered. Impaired LA distensibility may result in increased atrial pressure, with a consecutive rise in pulmonary venous pressure and the clinical presentation of "stiff LA syndrome" characterized by dyspnea and exercise intolerance (9). Furthermore, a higher burden of LA fibrosis may increase the risk of thromboembolic events, even in sinus rhythm and with an electrically activated LA appendage (10).

Second, multiple pre-clinical and clinical studies suggest that PFA may be able to avoid collateral damage to extracardiac tissue because it aims to selectively affect myocardial cells. Although esophageal damage with PFA has never been reported, there is a growing body of evidence on transient phrenic nerve dysfunction and coronary arterial spasm associated with PFA (2, 11). It does not seem unlikely that these observations are a direct result of PFA rather than autonomic responses.

Third, PFA in the LA is often painful and may also cause skeletal muscle contraction. It is intuitive to assume that these effects may be more pronounced when PFA is applied to the posterior wall. This suggests that an intensified sedation protocol with comprehensive monitoring or general anesthesia may be required to ensure a smooth procedure for both patients and operators.

Technical advances and innovations in the interventional treatment of cardiac arrhythmias have moved the field forward, but the search for the ideal ablation energy is still ongoing. Key requirements for a candidate modality include myocardial cell specificity, creation of discrete lesions using titratable energy, proven acute and long-term effectiveness and an insightful understanding of the biophysiological processes in lesion formation. Present-day PFA seems to comply with some of these features, but certainly not all of them. However, further improvements to PFA can be expected. Novel PFA catheters have undergone preliminary clinical testing and several large-scale clinical trials are underway to establish a definitive role for PFA in the treatment of complex cardiac arrhythmias.

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