EDITORIAL COMMENT

Pulsed-Field Ablation for Atrial Fibrillation



Meta-Analysis Confirms Expected Initial Outcomes

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trial fibrillation (AF) is one of the most prevalent tachyarrhythmias, and its treatment methods are continuously advancing. Regarding catheter intervention, thermal ablation methods, including radiofrequency ablation (RFA) and cryoballoon ablation (CBA), have traditionally been primary techniques. However, the emergence of a nonthermal ablation method known as pulsedfield ablation (PFA) has the potential to revolutionize AF treatment. PFA delivers high-voltage electric fields in brief pulses to myocardial tissue, creating pores in the cardiomyocyte cell membranes and inducing cell death, known as irreversible electroporation. A noteworthy aspect of this technique is that the myocardial tissue has a higher sensitivity to pulsed fields than the surrounding tissues, allowing for selective ablation of the myocardium. As a result, the risk of collateral damage to critical adjacent structures such as the esophagus and phrenic nerve is reduced. Furthermore, the strength of the electric field is key to reducing the need for direct tissue contact in irreversible electroporation, simplifying the procedural approach. These characteristics suggest that PFA may offer improved safety and efficacy compared with conventional thermal energy ablation.1

In this issue of *JACC: Asia*, Li et al² conducted a comprehensive meta-analysis to evaluate the efficacy and safety of PFA in patients with AF. One of the key strengths of the present meta-analysis by Li et al² is the inclusion of significantly more studies and patients compared with previous analyses.² They systematically searched PubMed, Embase, and the Cochrane Library databases until January 2023,

selecting 46 relevant studies investigating the use of PFA for AF. This meta-analysis included over 11,000 patients across these studies, providing a larger data set and a stronger basis for evaluating PFA outcomes than previous reports.³⁻⁵ Using these data, they compared PFA outcomes with those of conventional thermal-energy ablation. Their analysis revealed that PFA had a higher success rate for acute pulmonary vein isolation and reduced procedure times. Although PFA demonstrated a high first-pass isolation rate in this analysis, reversible electroporation does not necessarily guarantee the long-term durability of pulmonary vein isolation. Nevertheless, the significant reduction in atrial arrhythmia recurrence rates at 3 months postprocedure compared with conventional thermal ablation demonstrated in this study suggests that PFA, under appropriate protocols, may provide sustained lesion formation.

Safety remains the most critical concern of AF ablation. This study confirmed that PFA reduces the incidence of severe complications such as phrenic nerve injury and esophageal damage. Conversely, an increased risk of cardiac tamponade has been reported; however, this risk may be further mitigated through technological advancements and procedural refinement. For example, the incidences of pericardial perforation and cardiac tamponade have been reduced in recent reports. Notably, the transition from rigid straight-tip guidewires to flexible J-tip wires has been reported to decrease this complication. 4,7

However, the inclusion of many non-randomized studies makes it challenging to completely eliminate biases related to patient backgrounds. Atrial arrhythmia recurrence rates vary greatly depending on the follow-up methods used, highlighting the importance of standardized follow-up. These potential biases should be carefully considered regarding their impact on the results, and future research will require randomized controlled trials with long-term follow-up.

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Nevertheless, by aggregating data from multiple studies, this study provided robust evidence supporting the clinical benefits of PFA, thereby guiding practitioners to adopt this emerging technology. Although several similar reports have been published recently, the strength of this study is its comprehensive analysis of a larger number of studies. Therefore, clarifying the efficacy and safety of PFA for AF ablation is crucial.

More importantly, PFA is still a relatively new technology that is undergoing rapid development, with further improvements in outcomes anticipated as clinical experience increases. Innovations in guidewire use are believed to reduce the incidence of cardiac tamponade. Additionally, the optimization of ablation protocols is important for enhancing treatment outcomes. Furthermore, improved PFA catheters are scheduled for future introduction, and further performance enhancements are expected. Therefore, reports on treatment outcomes should be continuously updated using the latest information, and the relevance of these reports may change rapidly over time.

Moreover, many of the studies included in this meta-analysis used Boston Scientific's Farapulse device; however, devices from other manufacturers were also employed, revealing slight differences in outcomes between the devices. With the advent of various PFA devices on the market, further research on the differences in performance and safety between these devices will advance, contributing to the clinical adoption of PFA.

In conclusion, PFA has been considered to have the potential to overcome the traditional challenges of AF ablation, and the safety and efficacy demonstrated in this meta-analysis met these expectations. As PFA technology advances and procedural techniques are further refined, it may soon become the preferred and safer standard for the management of AF. Consequently, more patients are expected to benefit from these advanced treatments. Nevertheless, the possibility of unexpected complications cannot be entirely ruled out, emphasizing the importance of continuous monitoring, rigorous research, and long-term followup to ensure the safety and efficacy of this evolving technology.

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REFERENCES

- **1.** Inoue K. Pulsed-field ablation for atrial fibrillation achieving excellence with a simplified technique. *Circ J.* 2023;87(12):1727–1729.
- **2.** Li R, Zhang X, Liu X, et al. Effectiveness and safety of pulsed field ablation in patients with atrial fibrillation. *JACC Asia*. 2025;5(1):143–157.
- **3.** Aldaas OM, Malladi C, Han FT, Hoffmayer KS, Krummen D, Ho G, et al. Pulsed field ablation versus thermal energy ablation for atrial fibrillation: a systematic review and meta-analysis of procedural efficiency, safety, and efficacy. *J Interv Card Electrophysiol*. 2024;67(3):639–648.
- **4.** de Campos MCAV, Moraes VRY, Daher RF, et al. Pulsed-field ablation versus thermal ablation for atrial fibrillation: a meta-analysis. *Heart Rhythm 02*, 2024;5(6):385-395.
- **5.** Amin AM, Nazir A, Abuelazm MT, Ibrahim AA, Elbenawi H, Aboutaleb A, et al. Efficacy and safety of pulsed-field versus conventional thermal ablation for atrial fibrillation: a systematic review and meta-analysis. *J Arrhythmia*. 2024;40(5):1059-1074.
- **6.** Ekanem E, Neuzil P, Reichlin T, Kautzner J, van der Voort P, Jais P, et al. Safety of pulsed field ablation in more than 17,000 patients with atrial fibrillation in the MANIFEST-17K study. *Nat Med.* 2024;30(7): 2020-2029.
- **7.** Füting A, Reinsch N, Brokkaar L, et al. Bronchial safety after pulsed field ablation for paroxysmal atrial fibrillation. *Circ Arrhythm Electrophysiol*. 2023:16(4):e011547.
- **8.** Reddy VY, Dukkipati SR, Neuzil P, et al. Pulsed field ablation of paroxysmal atrial fibrillation: 1-year outcomes of IMPULSE, PEFCAT, and PEFCAT II. JACC Clin Electrophysiol. 2021;7(5):614-627.
- **9.** De Potter T, Grimaldi M, Duytschaever M, et al, inspIRE Trial Investigators. Predictors of success for pulmonary vein isolation with pulsed-field ablation using a variable-loop catheter with 3D mapping integration: complete 12-month outcomes from inspIRE. Circ Arrhythm Electrophysiol 2024;. 2024;17(5):e012667.

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