Journal of Interventional Cardiac Electrophysiology (2024) 67:425–428
https://doi.org/10.1007/s10840-023-01689-4

COMMENTARY

Pulsed field ablation versus thermal energy ablation for atrial fibrillation: the Pulse Era is arriving

Shaojie Chen[1,2]

Received: 28 October 2023 / Accepted: 31 October 2023 / Published online: 22 November 2023

Atrial fibrillation (AF) is a common cardiac arrhythmia associated with increased risks of ischemic stroke, heart failure, and mortality. Catheter ablation–based electrical pulmonary vein isolation (PVI) is an effective rhythm control strategy in treating AF, and to date, the most investigated ablation technologies, i.e., radiofrequency (RF) or cryoballoon (CB), utilize thermal energy [1–3]. Pulsed electric field ablation (PFA), an ablation technology utilizing non-thermal energy, has been developed for catheter ablation of AF in recent years.

The basic mechanism of PFA is the so-called electroporation effect. That is, high-voltage electrical pulses are applied to the phospholipid bilayer of the cell membrane within a very short duration, resulting in the formation of a transmembrane potential and irreversible, micro-pores penetrating damage to the cell membrane, which leads to a change in the permeability of the cell membrane, destroying the homeostasis of the intracellular environment, and ultimately resulting in apoptotic cell death.

The essential characteristic of PFA is the instantaneous pulsed field–generated electroporation effect instead of heating or freezing the tissue. Of note, tissue selectivity is an important characteristic of PFA, and it means that the electroporation effect can only be obtained when the threshold high voltage at the corresponding tissue is reached. These characteristics allow PFA to achieve effective ablation lesion and spare the risk of damage to the neighboring structures such as blood vessels, nerves, or esophagus, which has been demonstrated in preclinical and clinical studies [4].

In this issue of the *Journal of Interventional Cardiac Electrophysiology*, Aldaas and colleagues [5] had their paper "Pulsed field ablation versus thermal energy ablation for atrial fibrillation: a systematic review and meta-analysis of procedural efficiency, safety, and efficacy" published.

In this meta-analysis, six comparative studies characterizing 1012 AF patients who underwent ablation were included. Among them, 43.6% ($n=441$) of the patients were treated with PFA whereas 56.4% ($n=571$) of the patients were treated with thermal energy sources (using RF or CB). The main finding of the meta-analysis was that PFA was associated with significantly shorter procedural time and longer fluoroscopy time, without difference in procedural complications or rate of recurrent AF as compared to thermal ablation energy sources. The significance and limitations were well discussed in the paper [5].

The authors should be congratulated for conducting a timely meta-analysis on a topic with great interest. The PFA technology used in the studied group was the Farapulse System (Boston Scientific) which has been until now the most investigated PFA system. In the control group, the ablation catheters were either contact force–sensing irrigated RF catheters (Thermocool Smarttouch, Biosense Webster, or TactiCath, St. Jude Medical) or cryoballoon catheter (2nd generation, Arctic Front Advance, Medtronic); both RF or CB ablation systems have been the established thermal ablation modalities. Moreover, all included studies appeared to be conducted in experienced centers. Thus, this meta-analysis represented a contemporary comparison between non-thermal and thermal ablation energy sources.

This comment refers to the article available at https://doi.org/10.1007/s10840-023-01660-3.

✉ Shaojie Chen
drsjchen@126.com; s.chen@ccb.de

[1] Cardioangiologisches Centrum Bethanien (CCB), Kardiologie, Medizinische Klinik III, Agaplesion Markus Krankenhaus, Akademisches Lehrkrankenhaus Der Goethe-Universität Frankfurt Am Main, Frankfurt Am Main, Germany

[2] Die Sektion Medizin, Universität Zu Lübeck, Lübeck, Germany

1 Ablation efficiency

It is known that PFA offers a very short ablation time and a very high rate of single-shot PVI. As expected, the presented meta-analysis demonstrated that PFA has consistently shown an extremely high ablation efficiency, which was represented by a substantially shorter procedural time as compared to thermal ablation energy sources, despite the mandated 20-min left atrial dwell time in the PFA group. An efficient ablation means a fast and successful procedure without increasing potential risk associated with gap searching and repeated ablation, and this is remarkable for both patients and medical staff.

2 Fluoroscopy time

In this meta-analysis, PFA seemed to be associated with increased fluoroscopy time as compared to thermal ablation energy sources (> 20 min in the PFA group, > 10 min in the thermal ablation group) [5]. However, it should be mentioned that RF in combination with 3D mapping or CB ablation is a well-established routine practice in the majority of the centers. And it is understandable that the practical approach for an emerging technology, here PFA, requires time for its workflow optimization. As a single-shot ablation system, unlike CB, PFA based on current (first-generation) design needs not only catheter-tissue proximity/contact but also additional catheter manipulations (e.g., rotation, different configurations) to achieve optimal lesion consolidation. Thus, from inexperience to familiarity, the fluoroscopy time should be significantly decreased after a learning curve, in particular along with an incorporation of a 3D mapping system in the future. After the learning curve, the fluoroscopic time for a PFA AF ablation can be reduced to 3.9 min even in relatively complicated cases [6, 7].

3 Safety

Although the meta-analysis showed no difference in overall procedural complications, PFA seemed to be associated with a trend towards less ablation-related complications, e.g., PV stenosis, PNP, or esophageal lesion [5]. In another recent meta-analysis of non-comparative studies, the authors found a significantly lower rate of overall procedural complications in the PFA group than that in thermal ablation groups [8]. Mild PV stenosis or PNP might not raise a dramatic risk of deteriorating the patient's clinical condition. However, the esophageal lesion is an indicator of atrioesophageal fistula (AEF) which is known as a very rare but catastrophic complication associated with thermal ablation. For the PVI-only procedure, using thermal ablation energy without first-pass isolation means repeated gap searching and additional thermal energy delivery which has been recognized to be associated with increased risk of complications. For the selected patient group where left atrial posterior wall isolation (PWI) may increase the ablation success rate [9], the operators are mainly concerned about (1) the achievability of successful and durable PWI and (2) AEF if they use thermal energy (typically RF). However, this should not be the case if using PFA because of its unique ablation characteristic. Moreover, the "flower pose" of the FARAWAVE PFA catheter offers an ideal configuration for PWI. Recent cohort study has shown good clinical outcome and durable PWI after using PFA [10].

4 Clinical success

Expected as a more powerful ablation technology, PFA of AF appeared to offer a similar clinical success rate as compared to established thermal ablation based on current evidence, and this result seemed to be consistent in randomized and nonrandomized studies. This may be explained by (1) the still non-100% PVI durability; (2) the current PFA (FARAPULSE) system is designed for PVI, whereas RF plus 3D mapping is also an established technology for focal, linear or non-PV ablation; (3) unlike thermal ablation, PFA has little effect on GP denervation as GP may play a role for AF development and maintenance.

5 Current/future perspectives

Figure 1 summarizes the comparison of current thermal energy ablation vs. pulsed field ablation. Figure 2 outlines the possible future development of pulsed field ablation. Using PFA in treating cardiac arrhythmias remains at the beginning stage although initial experience and existing data have shown very promising results. For the technical aspect, future studies for further improvement in catheter/system design, ablation parameters/dosing, and procedural workflow are still needed. For the clinical study aspect, only one randomized trial was included in the meta-analysis, multicenter, powered, randomized controlled studies with continuous rhythm monitoring and long-term follow-up in terms of efficacy and safety for patients with different types of AF are still warranted.

	Thermal energy RF, CB, LB, RFB, HIFU etc.	Non-thermal energy PFA (current generation)
Mechanisms	Heating or freezing	Pulsed field electroporation
Characteristics	Thermal generated cell damage, tissue nonselective	Non-thermal generated cell damage, tissue selective
Time to ablation effect	Time-needed thermal effect	Instantaneous PFA induced electroporation
Patient preparation	(Deep) sedation or GA	(Deep) sedation or GA
Ablation efficiency	+	++
Procedural/Ablation time	++	+
1-pass/single shot isolation	+	++
Fluoroscopy	Majority needed	Needed
3D mapping	RF: needed, CB: with or without	PFA: with or without
Learning curve	RF+++, CB++	PFA+
Risk of adjacent damage?	Yes: Vessels, nerves, esophagus	No PV stenosis, no persistent PNP, no AE Fistula. Clear lesion border, preserved atrial function
Autonomic response	yes	yes
Coronary artery spasm	Autonomic response, thermal effect, preventable	Autonomic response, PF effect, preventable
Silent cerebral lesion	+	+
AF ablation clinical success	+	+
Autonomic denervation	+	-
Durable PVI	+	++

Fig. 1 Current comparison of thermal energy ablation vs. pulsed field ablation

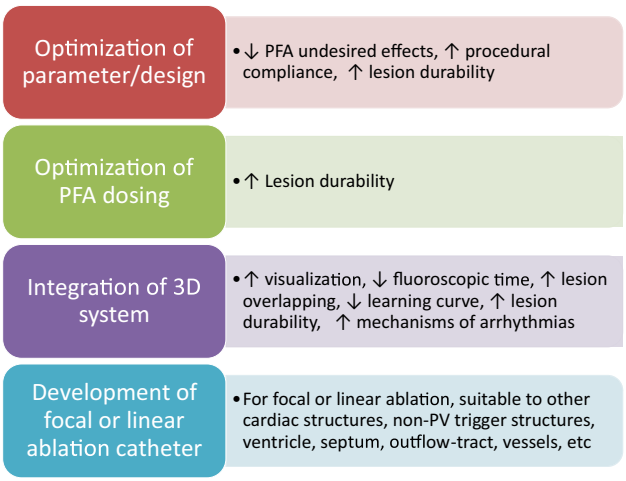

Fig. 2 Potential future developments of pulsed field ablation

Declarations

Conflict of interest The authors declare no competing interests.

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