Received: 22 September 2019 | Accepted: 28 September 2019

DOI: 10.1002/joa3.12249

EDITORIAL

Journal of Arrhythmia Open Access WILEY

What is the meaning of age-related change in CFAE?

Pulmonary vein (PV) isolation is effective for most patients with paroxysmal atrial fibrillation (AF). However, PV isolation is not enough for the treatment of persistent and long-standing persistent AF. Further modification of atrial substrate maintaining AF seems necessary in those patients. To improve the clinical outcome in patients with persistent AF, extensive ablations have been adopted, including, ablation of complex fractionated atrial electrograms (CFAE), multiple linear lesions, posterior left atrial (LA) box isolation, ganglionated plexi ablation, rotor/driver ablation, and ablation of low-voltage areas (LVA).

The incidence of AF increases with age. Atrial electrical and structural remodeling plays an important role in the progression of AF. However, the relationship between electrophysiological properties of LA and age is unclear. Therefore, Park et al evaluated the effects of age on electroanatomical remodeling in LA which was assessed by the extent of CFAEs, and demonstrated that increasing age was associated with decrease in the extent of CFAE area. Aging is generally associated with slow conduction by fibrosis. CFAE indicates slow conduction or pivot points of wave fronts. Therefore, I have speculated that CFAE extent might increase according to age. The authors explained that the decrease in CFAE extent with age is caused by the reduction of electrical complexity by fibrotic scar change and structural remodeling progression. However, they did not perform the voltage mapping, thereby, it is unknown presence of LVAs or scar regions which are associated with aging. Moreover, the extent of CFAE may be influenced by its definition. Nademanee et al[1] defined CFAEs as low-voltage atrial electrograms (0.04-0.25 mV) and short cycle length (120 ms or less). The original CFAE is not sufficiently expressed in automated CFAE module of NavX system (St. Jude Medical Inc) which employs only cycle length of below 120 ms, but not voltage. Therefore, NavX system may include higher voltage CFAEs, therefore, a wider area of CFAE may be detected in the younger age group. We have performed LA voltage mapping during sinus rhythm in 115 patients with persistent AF (75 long-standing persistent AF).[2] The LVAs (<0.5 mV) were identified in 47% of the patients.[2] The patients with LVAs were significantly older than those without LVAs (65 ± 8 vs 60 ± 10, $P = .003$).[2] We re-analyzed the prevalence of LVAs by age in 321 patients with persistent AF. The prevalence of patients with LVAs increased with increasing age (8% in 30s-40s, 15% in 50s, 33% in 60s, 44% in 70s, 60% in 80s: K. Kumagai, unpublished data). Their results of CFAE are contrary to ours of LVAs. However, there is no correlation between CFAE areas during AF and LVAs during sinus rhythm, and LVAs during sinus rhythm do not always coincide with those during AF. Therefore, the result that significant reduction in CFAE area with increasing age reported by Park et al is an interesting finding and gave us a new insight.

Park et al demonstrated that success the rate after CFAE ablation was similar among all age groups despite differences in the extent of CFAE. However, they did not show the data of control group without CFAE ablation. Therefore, it is unclear whether additional ablation of CFAEs after PV isolation improves clinical outcome. Recent randomized clinical trials, including STAR AF II, etc. demonstrated that the ablation of CFAEs showed no benefit over PV isolation in patients with persistent AF. However, ablation of CFAEs sometimes terminates AF. Among CFAEs, there may be culprit and bystander CFAE. CFAEs where ablation terminates AF may be culprit for AF perpetuation, while CFAEs where ablation does not terminate AF may be bystander. Although it is difficult to distinguish them, antiarrhythmic drugs use or modification of CFAEs module may focus on culprit CFAE. Nademanee et al[1] used intravenous ibutilide to highlight CFAE associated with perpetuating AF after CFAE ablation. They demonstrated that the ablation of CFAE resulted in the termination of AF in 95% of the patients, however, 28% required concomitant ibutilide treatment.[1] We demonstrated that the ablation of only CFAE localized with nifekalant may be sufficient for clinical efficacy in the patients with persistent or long-standing persistent AF.[3] Ohe et al[4] modified the CFAE module of CARTO system to express a high degree of fragmented potentials and showed that defragmentation was effective for persistent AF. Although CFAE and LVA may be associated with rotors or abnormal substrate, they are indirect indicators of AF drivers. A study using a phase mapping system revealed that rotors and multiple wavelets did not always correlate with CFAEs and LVAs.[5] Although efficacy of ablation of CFAEs and LVAs is controversial at the moment, they may attract attention again in future by advance of mapping technology. We may be still in the middle of a journey to cure AF.

CONFLICT OF INTEREST

The author declares no conflict of interests for this article.

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