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Editorial

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Virtual Ablation of Atrial Fibrillation in Patients With Persistent Atrial Fibrillation: An Unexplored Niche

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▸ See the article "Clinical Usefulness of Virtual Ablation Guided Catheter Ablation of Atrial Fibrillation Targeting Restitution Parameter-Guided Catheter Ablation: CUVIA-REGAB Prospective Randomized Study" in volume 52 on page 699.

This editorial passage focuses on the article "Clinical usefulness of virtual ablation guided catheter ablation of atrial fibrillation targeting restitution parameter-guided catheter ablation: CUVIA-REGAB prospective randomized study," published in volume 52.

Catheter ablation of atrial fibrillation (AF) is one of the treatment options for patients with symptomatic AF, which could modulate the risk of stroke, dementia, heart failure, and mortality.[1)2)] Several trigger factors play a significant role in the onset of paroxysmal AF; however, the mechanisms maintaining persistent AF are still poorly understood. The gold standard of AF ablation techniques is pulmonary vein antral isolation (PVAI). Durable pulmonary vein isolation (PVI) has improved significantly with increasing operator experience, technology, and ablation tools. However, PVAI alone is considerably less effective in patients with persistent AF, compared to those with paroxysmal AF. This may be explained by the formation of the atrial substrate, and the possible role of extra-pulmonary vein (PV) triggers. Several ablation approaches have been developed to modify the atrial substrate, aiming to improve clinical outcomes in patients with persistent AF. The landmark STAR AF II trial demonstrated that the adjunct use of linear and complicated fractionated electrogram ablation with PVAI, did not provide any additional improvement in clinical outcomes, compared to the outcomes associated with PVAI alone.[3)] Several randomized clinical studies that investigated the efficacy of an empirical, adjunctive extra-PV ablation, used with circumferential pulmonary vein isolation (CPVI), have been ineffective. These negative results do not establish the supremacy of the single-treatment strategy with PVAI, in treating patients with persistent AF, and there is a lack of options for improving the outcome in patients with persistent AF. As confirmed by cardiac magnetic resonance imaging (MRI) or invasive contact mapping, the presence of scar or fibrosis in the left atrium is associated with an increased risk of AF recurrence after ablation. Recently, the DECAAF II trial reported that MRI-guided fibrosis ablation in addition to PVI showed no significant difference in atrial arrhythmia recurrence when compared to that associated with PVI catheter ablation alone.[4)] Scar ablation strategies based on cardiac MRI or invasive voltage mapping are inadequate in terms of the accuracy of the measured voltage, which may be influenced by the thinness of the atrial wall, mapping electrodes, and contact between the mapping catheter and

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myocardium tissue. Therefore, the ablation of extra-PV target areas is challenging in patients with persistent AF.

The recent advancements in computer modeling of cardiac electrophysiology provide an integrative framework for addressing the inadequate efficacy of the current approaches. Computational cardiac modeling and simulation incorporate structural and functional elements of experimental and clinical data, with atrial electrical mechanisms and dynamics, thus enhancing our understanding of AF mechanisms and therapy. Simulation studies have demonstrated the efficacy of surgical or catheter-based ablation methods in fibrillation termination of virtual atria.[5)] Likewise, a prospective randomized study demonstrated model-guided selection of preset AF ablation-lesion using customization of computed tomography-derived endocardial-wall anatomy.[6)]

In the current issue of the *Korean Circulation Journal*, Choi et al.[7)] have reported a novel strategy using on-site computational modeling, targeting a high maximal slope of the action potential duration restitution curve (V-Smax), in patients with persistent AF. The specific extra-PV ablation target could be identified by combining the AF wave-dynamics with the chamber map provided by CUVIA AF modeling, which includes histological data such as that pertaining to fibrosis and the orientation of cardiac fibers. Their previously reported CUVIA-I and CUVIA-II trials demonstrated a higher success rate of computational modeling-guided persistent AF ablation than an empirical ablation.[8)9)] In contrast to the previous studies, the CUVIA REGAB prospective randomized study targeted the high V-Smax, and hypothesized its relationship with the perpetuation and wave break vulnerability of AF. However, this high V-Smax targeting strategy exhibited no significant difference in AF recurrence in patients with persistent AF when compared to an empirical ablation (E-ABL) group (25.6% vs. 23.9%, p=0.880). The V-Smax group tended to have higher atrial tachycardia (AT) recurrence rates than the E-ABL group (43.5% vs. 23.8%, p=0.169), resulting in its significantly higher rate of post-RFCA cardioversion (14.4% vs. 5.7%, p=0.027). Considering the additional computational modeling analysis, the total procedure time was significantly longer in the V-Smax group (205.2±56.5 vs. 184.2±45.8 minutes, p=0.008). In contrast, major post-procedural complication rates were not significantly different between the 2 groups (6.7% vs. 3.4%, p=0.498).

However, several concerns remain. First, the hypothesis that high V-Smax would be the candidate for extra-PV ablation needs more scientific evidence. High dominant frequency corresponding to atrial regions with rapid electrical activation rates, may be connected to the remodeled atrial substrate, and thus rendering them as ablation targets. Though the Smax could indicate the wave break vulnerability, whether the high V-Smax ablation affects the AF sustainability is unclear. The effect of V-Smax ablation on AF perpetuation and wave break in real patients was not evaluated in this study because a substrate map was acquired during sinus rhythm. The rate of AF termination during V-Smax ablation could substantiate their hypothesis. Further, the empirical cutoff value of the highest 10% Smax area was arbitrarily chosen. These could possibly explain the varying results of extra-PV dominant frequency ablation and high V-Smax ablation strategies. Second, the current method to acquire V-Smax is questionable. The computational modeling was based on the electroanatomical map (voltage and local activation time map), which depends on the mapping electrode, and its contact with the myocardial tissue. The high-density mapping electrode and associated tissue-contact techniques might improve the V-Smax map precision. Third, the endpoint of ablation in high V-Smax is unclear. Unlike PVAI, it is difficult to confirm the effectiveness of focal ablation on the area with high V-Smax. Moreover, the proposed location of the V-Smax ablation could vary as per three-dimensional electroanatomic maps. Though the overall recurrence rate was not significantly different between the 2 groups, the V-Smax group tended to have a higher rate of AT recurrence; a significantly higher rate of electrical cardioversion was suggestive of the creation of a secondary source of AT. Lastly, the overall recurrence rate of the empirical ablation group was lower than those reported in previous studies on persistent AF. The meta-analysis of studies using contemporary ablation and mapping techniques has reported a success rate of 43–66% for single-procedure catheter ablation for persistent AF.[10)]

In conclusion, this study on patients with persistent AF, confirmed that a new strategy using computational AF modeling and virtual ablation—targeting a restitution parameter-guided Smax, in addition to CPVI—did not improve the AF recurrence rate, when compared to the empirical ablation. Further investigation and development of novel mapping strategies are needed to improve patient outcomes in those with persistent AF. The journey has begun, but there is still a way to go.

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