The wall of unintended consequences: is the main benefit of posterior LA wall isolation simply more durable pulmonary vein isolation?

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May 16, 2022

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Funding: None

Conflict of Interest: None

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Medicine is rife with therapies originally developed for a specific purpose, yet after some time, the true benefit is determined to lie elsewhere - examples of the "law of unintended consequences". One egregious example is aspirin, where the "true" benefit has shifted several times over decades of use, from analgesic, to anti-inflammatory, to anti-platelet, to anti-malignancy. In fact, our regulatory agencies, including the FDA, allow off-label use of pharmaceuticals and devices in large part to account for adaptation to changing indications based on physician discretion. Invasive electrophysiology is no exception, particularly with ablative approaches employed to treat atrial fibrillation.

Durable pulmonary vein isolation (PVI) remains the primary goal of effective catheter ablation for atrial fibrillation (AF), as multiple high-quality studies over many years have demonstrated that PVI is one of the strongest predictors of freedom from AF after ablation [1]. However, despite our understanding of this seemingly straightforward goal, we continue to struggle to achieve durable PVI. Unacceptably high rates of PV electrical reconnection are seen in patients who return to the EP lab for repeat AF ablation, driving clinical AF recurrence in many patients after PVI [1]. Therefore, there is an ongoing need to improve the ability to durably achieve PVI.

Today, we are in fact able to achieve acute PV isolation in most procedures, highlighting a shortfall in the ability to predict long-term durability of PVI [2]. Acute electrical isolation ideally corresponds to permanent myocardial ablative injury, resulting in permanent fibrosis, and as a result, permanent electrical block.

However, a subset of ablated tissues may appear acutely well-ablated by intraprocedural measures but then eventually recover conduction, as permanent myocardial injury is not achieved. Over time, multiple strategies have been proposed and utilized to both better predict and achieve lesion durability. Achieving transmural lesions likely remains an important component of these strategies, but there remains an ongoing concern for excessive ablation beyond the myocardium, with concern for thermal injury to adjacent extracardiac structures including nerve tissue and the esophagus.

Ablation guided by index estimates of energy delivery, such as Surpoint Ablation Index (AI, Biosense Webster, Inc.) or lesion index (LSI, Abbott), appears to result in improved durability of PVI without increased risks of extra-cardiac collateral injury [3]. These indices are an integration of multiple electrical and mechanical input variables known to improve lesion formation predictability. With these strategies, higher index values are typically targeted along the thicker anterior segments, with lower target values along the thinner posterior aspects of the PV wide-area circumferential ablation (WACA) lesion set. Various strategies to create more shallow lesions along the thin posterior aspects of the LA have been advocated. High-power/short-duration (HPSD) ablation leverages the biophysical principle that with shorter duration, higher power RF delivery, tissue heating and injury occurs primarily through resistive heating, resulting in more shallow and broad lesions [4]. In contrast, longer RF delivery times allow the generation of conductive heating, resulting in ablation lesions that are deeper. In the end, no matter what strategy for RF delivery is employed, there remains inability to precisely tailor ablation energy

delivery to the needs of the specific target tissue. In particular, the posterior aspects of the PVI WACA set remain problematic, where the thinner tissues reduce the margin of error between adequate transmural ablation vs. excessive ablation that risks injury to extracardiac structures.

Therefore, much focus has been centered on optimizing energy delivery along the posterior aspects of the WACA. In this context, Li et al report in this issue of the Journal of Cardiovascular Electrophysiology their experience with targeting LA posterior wall isolation (PWI) in the setting of AF catheter ablation and pulmonary vein isolation PVI utilizing a specific technique of low-flow, medium power, short duration (LFMPSD) ablation in a distributed fashion [5]. There is a fair amount of information to unpack in this approach. The rationale for this approach is that due to the presumed higher likelihood of electrical reconnection along the posterior aspects of the WACA set, additional ablation with a goal to electrically isolate the LA posterior wall may improve the durability of PVI by broadly blocking posterior wall electrical conduction. The authors utilize a distributive or "peppering" approach to RF lesions across the posterior wall to both maintain chances of durable electrical block while minimizing risk of injury to the

esophagus by decreasing chances of over-concentrated ablative energy. In addition, the authors utilize a LFMPSD ablation strategy, which based on preclinical data previously reported by the authors [6], may result in more shallow lesions, as reduced catheter irrigant rate may reduce conductive heating.

In this study, consecutive patients with mostly persistent AF (79.6%) at a single center undergoing firsttime catheter ablation for AF were included, with 137 out of 463 total patients undergoing LFMPSD PWI in addition to PVI, with the remaining undergoing PVI alone. In all but 3 patients in the LFMPSD cohort, PW isolation was achieved acutely, with atrial arrhythmia recurrence in 30.2% of those followed up by 14 months. In the subset of patients who underwent repeat ablation in the +PWI group, 16/18 (88.9%) demonstrated durable PVI while in the PVI alone group only 10/45 (23.9%) patients demonstrated durable PVI. Interestingly, in the +PWI group undergoing repeat ablation, only 7/18 (38.9%) demonstrated durable posterior wall isolation. There are several important caveats to this data, specifically potential patient selection biases at the point of index ablation, the decision to perform PWI (which was not predetermined), and the decision to perform repeat ablation. Despite these caveats, these findings at face value suggest that the addition of PWI increases the likelihood of durable PVI.

Interestingly, durable PWI is apparently not required to achieve this increased rate of durable PVI. Hence, it can be concluded that additional ablation along the PW specifically increases the durability electrical block along the posterior segments of the WACA.

One wonders if these data may in part underpin the findings in several studies demonstrating improved freedom from AF with the addition of PWI to PVI [7]. The conventional wisdom is that PWI helps to exclude additional AF drivers within the PW itself; but could it be that rather, the primary effect of PWI is improving the likelihood of durable PVI? This question clearly needs to be explored further. However, it remains unclear whether the authors' approach is indeed the best strategy to improve durable PVI rates. As the authors show, rates of durable isolation of the PW itself are low, as these reconnections may increase risk of PW-dependent atrial flutters. Moreover, additional ablation along the PW may expose the esophagus to more risk of thermal injury despite the LFMPSD approach employed here.

The described LFMPSD ablation approach remains squarely in the minority of left atrial ablation approaches described and anecdotally utilized in the community, as the ever more popular HPSD approach is quickly becoming the dominant RF ablation strategy [8]. These two diametrically opposite biophysical approaches have the same goal of minimizing risk to adjacent extracardiac structures. It would therefore stand to reason that evaluating whether PWI using an HPSD strategy bolsters PVI durability is a clinically important. In the end, the ultimate goal remains tailoring ablation energy to the appropriate tissue characteristics, that is ablating "just enough" to achieve durable PVI without increased risk of collateral injury. A missing ingredient in this and other approaches remains accounting for tissue-specific characteristics that may impact the ablation biophysical characteristics. In the meantime, the findings in this paper suggest that the commonly applied approach of PWI in addition to PVI, particularly in persistent AF patients, may have the added, if not primary benefit, of improving the durability of PVI. This perhaps unintended consequence of posterior wall isolation may end up benefitting AF ablation outcomes after all.

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