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GUEST EDITOR'S PAGE

Seeking Better Understanding of Cardiac Arrhythmias and Discovery of Novel Electrophysiological Therapeutic Targets

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The beginning of the year is usually a period when it is natural to express positive intentions that can make life better and the future brighter. When I was asked to write this Guest Editor's Page for *JACC: Case Reports* in January 2021, I immediately thought to use this space with that intention in mind, by advocating for a gentle change in research endeavors in the field to which I belong and deeply love: cardiac electrophysiology.

Cardiac electrophysiology is one of the branches of cardiology that has grown the most in the last 3 decades, thanks to its natural propensity to innovation (1). Nowadays, pretty much all cardiac arrhythmias, including ventricular fibrillation (2,3), have been the objects of research projects, with very encouraging and, more importantly, concrete results. Taking a look at clinical research on cardiac arrhythmias done in the last few years, a great amount of effort has been devoted to mapping complex arrhythmias, such as atrial fibrillation and ventricular arrhythmias. In the majority of these studies, the final goal is cure of the arrhythmia by means of a nonpharmacological treatment known as ablation.

The advent of radiofrequency ablation in the late 1980s and early 1990s (4) progressively shifted the attention of clinicians away from antiarrhythmic drugs, which currently are often considered second-line options or used in those patients who are unsuitable candidates for an invasive procedure. The possibility to eliminate a supraventricular arrhythmia definitively by means of a small thermal injury (today ablation can be obtained either by heating or by freezing) puts antiarrhythmic drugs in a very disadvantageous position, not taking into account their side effects. Antiarrhythmic drugs are increasingly discarded, and consequently, so are all the research efforts made over the years to develop these drugs. I am referring to those studies performed to discover the mechanisms of the arrhythmias. Electrophysiologists have learned that some antiarrhythmic agents are better than others to treat re-entry or triggered activity, just to cite 2 of the most common mechanisms, for example. However, does it still make sense today to teach our students and fellows in training about the mechanism of atrial tachycardia? Does it really matter whether we know that a type of tachycardia is generated by abnormal automaticity or by triggered activity if both types of tachycardia can be eliminated in a few seconds with the stroke of an ablation catheter? Is it still worthwhile to map extensively a scar located in a post-infarct left ventricle to look for channels or gaps of conduction if extensive ablation of the scar is faster and ensures a better outcome? Is there a risk that ablation will homogenize the minds of contemporary cardiac electrophysiologists?

All these questions and other similar ones are rhetorical. It should be clear that there is no

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intention to bring back an old medical practice that is based on administration of antiarrhythmic drugs. Nevertheless, clinical research should be diverted from the sole investigation of outcomes of an ablation procedure (i.e., atrial or ventricular arrhythmia recurrence rate) to favor more proof-of-concept studies, which are less common than in the past. Peer-reviewed international publications with their editorial boards and clinical cardiological societies should embrace more favorably papers that can shed light on the mechanisms of arrhythmias and consequently propose new therapeutic targets. Having a look at the most recent yearly review papers in cardiac electrophysiology (5,6), I am impressed by the number of discoveries made by basic scientists. Unfortunately, many of these discoveries remain limited to nonclinical scenarios and do not translate to clinically applicable therapeutic targets. We should all attempt to favor this transition, and that is the reason I increasingly favor the emergence of cardiologists who are "translational." As Dr. Mark Josephson, one of the founding fathers of the modern cardiac electrophysiology, often used to say in his academic seminars, a winning therapeutic target in cardiac electrophysiology would be that one able to delay or block the fibrotic processes of the myocardium, usually related to ischemic injury or aging. Seconding this wish, hopefully, in the ongoing decade, cardiac electrophysiologists will talk more of new techniques able to reverse fibrosis processes rather than of ablation modalities and related outcomes.

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