Noninvasive Assessment of Cardiac Electrophysiology for Predicting Arrhythmogenic Risk
Are We Getting Closer?

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Identification of patients at significant risk of arrhythmia and sudden cardiac death is one of today’s major cardiology challenges. Although tremendous progress has been made in detecting and characterizing cardiac disease and its progression, largely through imaging modalities, progress in detecting and monitoring changes in arrhythmogenic states has been incremental and has not resulted in robust, reliable methods of assessment. In this issue of Circulation, Ghosh et al1 demonstrate the application of an evolving technology, electrocardiographic imaging (ECGI), for noninvasive assessment of cardiac electrophysiology. They provide convincing data documenting the success of the method for localizing preexcitation (accessory) pathways in Wolff-Parkinson-White patients as well as for assessing short-term remodeling of ventricular repolarization after pathway ablation. The method requires detailed, high-resolution 3-dimensional computed tomographic imaging of the patient’s torso, body surface potential mapping of the torso with the use of hundreds of leads during any rhythms and conditions of interest, and mathematical modeling of the 3-dimensional electric fields to yield “inverse” estimates of epicardial potential distributions and electrograms. Once the 1-time anatomic imaging and modeling are completed (presumed constant for each patient), the body surface potential mapping recorded during any rhythm or cardiac condition can be transformed to the level of the epicardium to visualize epicardial isopotential map sequences, electrograms, and consequently activation and repolarization sequences.

Localization of accessory pathways in Wolff-Parkinson-White syndrome presents an interesting test of the ECGI technology, and the examples provided suggest a practical level of accuracy. Clearly, preablation assessment of pathway location is important in that it reduces the time required to confirm pathway location during invasive assessment in the electrophysiology laboratory. However, conventional 12-lead ECGI likely provides reasonable estimates of pathway location in perhaps 80% of cases. Thus, in its present form, the ECGI technology is not practical for widespread use for this limited application. However, the examples showing epicardial depolarization and repolarization sequences, as well as estimates of action potential duration distributions via activation-recovery intervals derived from the estimated epicardial electrograms, suggest a far more important use. The larger significance of this work is the obvious implication of a more generally applicable electrophysiological imaging modality2 that might offer the opportunity to better observe, characterize, and track the changes in cardiac electrophysiology known to contribute to increased arrhythmogenic risk or progression of disease. Functional, noninvasive imaging associated with magnetic resonance imaging, computed tomography, and ultrasound provides not only anatomic images of tissues and structures but also blood flow, physiological characteristics, and viability of tissue. Analogously, ECGI offers the potential capability of noninvasively imaging cardiac electrophysiology and its dynamics.

The seminal work of Durrer et al3 in mapping the complete activation sequence of human hearts stimulated thinking and research efforts directed toward improved understanding and characterization of cardiac electrophysiology in normal hearts as well as those compromised by disease. The subsequent work during the 1970s and 1980s in the animal laboratories of Madison Spach, Bruno Taccardi, J.A. Abildskov, Neal Moore, Andrew Wit, and many others focused on the use of direct cardiac mapping to provide detailed distributions of depolarization and/or repolarization that would provide the means to reveal arrhythmogenic mechanisms as well as to improve detection, localization, and characterization of disease. The development of body surface potential mapping coupled with the development of robust inverse mathematical estimation methods culminated in the technology presented by Ghosh and his collaborators in this issue of Circulation.

Part of the dilemma is that even with invasive assessment, detection of proarrhythmic states and prediction of arrhythmogenic risk are not within reach. Despite broad understanding and acceptance of the “macro-level” factors contributing to the arrhythmogenic state, namely, presence of regional, slow, or blocked conduction, repolarization gradients, and their rate dependencies and heterogeneities, the paradigm for anticipating or predicting arrhythmic events with any certainty remains elusive. Even in the laboratory, under carefully controlled conditions, and with arrays of measurements available for retrospectively analyzing changes and trends leading to arrhythmias, there are no definitive markers that reliably predict the time or likelihood of an arrhythmic event.

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At the one extreme, laboratory study of acute coronary occlusion results in rapid and dramatic elevation of ST segments in cardiac electrograms over a wide region of myocardium that portends an impending run of ventricular tachycardia that degenerates into ventricular fibrillation. At the other extreme are the subtle but specific changes in electrophysiology that go unmeasured or undetected that lead to significant arrhythmias and sudden cardiac death in a large number of patients suffering from disorders such as channelopathies (long-QT, Brugada, and Andersen-Twll syndromes), congestive heart failure, coronary artery disease, cardiomyopathy, or hypertrophy.

The noninvasive tools available for assessing arrhythmogenic risk, eg, heart rate variability, repolarization indices of QTc, QT:RR (restitution), and many others all show promise but are far from definitive or reliable. Importantly, most of these indices are global and 1 dimensional, meaning that they do not provide local or regional information and do not adequately detect or characterize the subtle changes in electrophysiology that likely portend the dangerous trends leading to likelihood of an impending arrhythmic event. Moreover, they suffer from poor diagnostic and prognostic performance arising from low sensitivity or specificity. Although these indices are promising and of continued interest, they do not address the construct that arrhythmogenic onset does not arise globally but via regional, localized aberrations in electrophysiology. On the other hand, the work of Ghosh et al suggests that detailed, noninvasive regional assessment of the myocardium is possible. Ability to measure depolarization and repolarization sequences would provide information on static and dynamic changes in regional conduction and repolarization. Such a capability would offer the possibility of detecting and tracking regional changes in electrophysiology known to contribute to increased arrhythmogenic risk.

At present, the ECGI method is limited to assessing the epicardial surface, which precludes a more complete assessment of the heart. In turn, this limits investigation of arrhythmogenic mechanisms that certainly involve the electrophysiology of the septum and ventricular walls. Furthermore, the accuracy and resolution of the method have not been validated with robust, independent measurements across different patient populations. Nevertheless, the demonstration of noninvasive assessment of cardiac electrophysiology underlying potentially complex arrhythmogenic states or conditions is exciting and worthy of exploration. Application of this technology to research investigations may provide new insight and knowledge that potentially could be translated to simpler, more conventional ECG analyses. Although we are not close to an ultimate, widely applicable noninvasive means to assess the electrophysiology of the heart, we are, indeed, much closer than we were.

Disclosures

None.

References


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