EDITORIAL

Time, Space, and Frequency in Ventricular Fibrillation

José Jalife

Departament of Pharmacology, SUNY Upstate Medical University, Syracuse, New York, USA.

Ventricular fibrillation (VF) is the main immediate cause of sudden, unexpected cardiac death. It appears in the electrocardiogram (ECG) as an aperiodic, irregular rhythm, giving the impression that electrical activation of the ventricles is highly complex and disordered. Unfortunately, despite many years of research and speculation, it has still not been possible to confirm or reject that idea, and therefore, the mechanism underlying VF continues to be a highly debated subject.

During the second half of the 20th century, the predominant hypothesis to explain both VF and atrial fibrillation (AF) was based on multiple wavefronts that propagated in a random and disorganized manner.[1] In 1994, Authur T. Winfree[2] introduced in the Western literature a new alternative theory involving "three-dimensional electrical rotors" that would become unstable when the thickness of the ventricular wall exceeded a critical value. Winfree believed that in some cases various rotors could be "anchored" in the ventricles to collectively maintain activity similar to fibrillation, even when recording electrodes revealed apparently periodic electrical activity. That hypothesis was consistent with experimental findings showing that the heart could sustain reentrant activity around a functional obstacle,[3] and led to the suggestion that rotors could be the organizing centers for VF. Since then, a large number of studies have addressed the involvement of rotors and spiral waves, either stable or unstable, in VF.[4-6] This has led to the development of new analytic techniques that allow quantification of the dynamics of VF, as well as analysis of spatial and temporal changes.

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The technique of mapping dominant frequencies (DF), based on spectral analysis of the signal, was introduced some years ago to quantify the spatial distribution of electrical excitation frequencies in both VF and AF.[7,8] In both cases, that technique, combined with phase maps,[9] allowed identification of relatively stable high-frequency rotors that generate fibrillatory activity in various mammalian species. In the case of the guinea pig, VF is maintained by a high-frequency rotor that in more than 90% of cases is located in the anterior wall of the left ventricle.[10,11] Since the frequency of the rotor is extremely high, the waves that emanate from around it break up recurrently and give rise to fibrillatory conduction. Likewise, in the sheep heart, during AF the highest DF is confined in the majority of cases to the posterior wall of the left atrium,[12,13] a finding that has recently been confirmed in humans.[14] In 1995, Gray et al[15] presented the first images of rotors on the ventricular surface of the isolated rabbit heart under conditions of continuous perfusion. The authors demonstrated the direct relationship that exists between the dynamics of the rotors and the apparent turbulence that accompanies VF in the ECG. Using a high-resolution video camera and a fluorescent dye that allows the membrane potential at the epicardial surface to be recorded, they demonstrated that in the ventricles of the rabbit heart the rotors that generate polymorphic tachycardias by reentry and fibrillation are not stationary but, rather, move continually, following highly intertwined trajectories. Consequently, the obvious conclusion of the study was that even the presence of a single moving rotor is able to generate irregular and apparently chaotic activity that presents in the ECG as VF or even as torsades de pointes.

In an effort to analyze in detail the temporal evolution of DF during VF in an isolated rabbit heart, Chorro et al[16] undertook epicardial recordings on the anterolateral wall of the left ventricle with 240 unipolar electrodes, employing spectral analysis and time-frequency analysis methods. The article, published in this issue of REVISTA ESPAÑOLA DE

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Correspondence: Dr J. Jalife.
Department of Pharmacology, SUNY Upstate Medical University,
766 Irving Avenue, Syracuse, NY 13210, USA.
E-mail: jalifej@upstate.edu

CARDIOLOGÍA, eloquently describes results showing that in the large majority of cases DF varies significantly in time and space over short timescales, even under stable conditions of continuous perfusion.

As shown by the results of Chorro et al,[16] time-frequency analysis is a valuable tool with which to study temporal variations in the electrical signal and to examine the spatial distribution of activation frequencies during VF. This analysis allowed them to demonstrate that although there are significant regional differences in DF, the highest frequency values are located in the apical and anterior zones of the ventricles. The last result is new and interesting since it contrasts with previous studies in rabbit heart in which the authors did not find, or perhaps did not look for, preferential localization. For instance, while Choi et al[17] observed that the frequencies and grouping were spatially and temporally unstable, they did not report preferential localization. These authors concluded that VF consists of highly short-lived areas of unstable frequency whose form changes in space from one moment to the next. The findings indicated to the authors that fibrillation is not the result of rotors but is rather sustained by multiple waves in the two ventricles that randomly change their form. It is important to note, however, that if the spatial distribution of the fibrillatory waves were truly random then the distribution of the DF would also be random. Nevertheless, as clearly shown in the new study by Chorro et al,[16] the highest frequencies tend to be grouped in the apical and anterior zones of the ventricles.

Dr Chorro and coworkers were careful not to introduce speculations to explain the frequency distribution observed in their study. Although the analysis of their data was very detailed, the authors also gave no clear idea regarding the possible mechanisms underlying the variability seen in the DF. However, there is well-known data in the literature on the subject that could help to shed light on the results.[4-6,18] As mentioned, the dynamics of the rotors associated with VF are somewhat species dependent, and the rotors in guinea pig and sheep are more stable than those in rabbit. Nevertheless, the study of Chen et al,[18] which was published several years ago and used phase mapping in an isolated rabbit heart preparation very similar to that of Chorro et al,[16] demonstrated that in that species VF also displays a high degree of organization in the sequences of propagated waves that activate the ventricles similarly both temporally and spatially. In fact, in the study of Chen et al[18] the frequency of the periodic activity was strongly correlated with the DF of the overall bipolar electrogram, indicating that the sources of that activity maintain the VF and may correspond to rotors whose movement is restricted to a particular area of the ventricles. It is also important to note that the lifetime of most of the waves that maintain the VF was quite limited; 98% of the waves lasted less then the mean duration of the activation period.[18] This was part of a general pattern indicating that the recurrent interruption of the waves observed on the surface of the ventricles was not the mechanism that generated the fibrillatory activity or maintained it over time. The results were more consistent with the idea that the three-dimensional rotors and their consequences following propagation were responsible for most of the spectrum of frequencies during VF and, therefore, were crucial to the maintenance of the arrhythmia.[18]

The results described in the previous paragraph are also consistent with data from the Ross group,[19] who recently investigated the way in which activation is organized during VF induced in the presence of a previous infarct in the anterior left ventricular wall of the sheep. Those researchers used 20 needles carrying multiple monopolar electrodes to record the transmural activity of the left ventricle and demonstrated that the regions with the highest activation frequency displayed less variable cycle lengths and were generally hidden within the ventricular myocardium. In some experiments they were able to demonstrate the presence of regions deep in the myocardium whose activity was stable and extremely rapid but highly regular. In other words, while the characteristics of VF in the epicardium were constantly changing in space and time, the activity within the myocardium had a higher frequency and was also highly periodic and organized, a finding that is clearly compatible with the hypothesis that fibrillatory activity is maintained by a three-dimensional rotor in this experimental model.

The results of Ross´s group highlight the substantial limitations that researchers in the field are currently faced with in interpreting recordings of fibrillatory this occurs, whether they are obtained by optical or electrical mapping, since they are necessarily limited to the surface or a portion of the ventricles, even when the analytic methods used are highly reliable, as in the case of Chorro et al.[16] In my opinion, this is an example in which technology has been unable to provide the means or procedures to satisfy the needs of science, the objective of which is to attempt to extend and deepen the understanding of real phenomena. In order to advance our understanding of the mechanisms of VF it will be essential for novel methods, both for recording and for the analysis of cardiac electrical activity, to be generated through the application of new technology. It is almost certain that the new questions that arise from well-designed studies based on these methods will generate new technological challenges and will in turn lead to other, deeper questions. Some hope may lie in the use of computer simulations alongside the development of new three-dimensional ventricular mapping techniques, a possibility that may not be far from becoming reality.

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