The Long and the Short of Long and Short Duration Ventricular Fibrillation

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The mechanisms behind the complex activation sequences during ventricular fibrillation (VF) have been the topic of intense research over many years. Experimental studies in animal models of VF, as well as clinical studies of human VF, have provided a wealth of data on the nature of electric activity in the fibrillating heart. Supplemented by computer simulations and a theoretical framework of wave propagation in excitable media, our community has amassed significant insights into the mechanisms that lead to the degradation of electric activity into VF and of VF maintenance. However, the majority of these studies have been devoted to VF mechanisms in the short time period after VF onset (short-duration VF, lasting less than 1 minute). In an episode of cardiac arrest outside of the hospital, the median time to delivery of the first defibrillation shock is 4.4 minutes, with VF episodes often lasting as long as 10 minutes (long-duration VF); over this period, the heart becomes ischemic while being subjected to excessively high excitation rates. Changes in the electrophysiological properties of the myocardium take place over these long-duration VF episodes. This is reflected in the altered outcome of a defibrillation shock, with survival rates decreasing rapidly with the increase in minutes spent in VF. Similarly, the guidelines for optimal resuscitation therapy differ depending on VF duration: immediate defibrillation is prescribed if time from VF onset is less than 4 or 5 minutes, whereas giving CPR for up to 3 minutes in advance of the defibrillation shock is believed to improve outcome when VF persists for 4 or 5 to 10 minutes. Because little is known about the mechanisms of VF maintenance over long periods of fibrillatory activity, acquiring such knowledge is expected to contribute significantly to the development of therapies that increase the survival odds as VF persists.

The study by Li et al1 in this issue of Circulation Research is among a very few1,2,3 that have attempted to characterize cardiac electric activity in long-duration VF and certainly the most comprehensive. The authors recorded 10 minutes of electrically induced VF in pigs. A transmural array consisting of 9×9 needles with 6 electrodes per needle was used to map 3D activation sequences in a 3.9-cm³ volume of the anterior left ventricular (LV) free wall (4% of total ventricular volume) near the insertion of the papillary muscles. The close proximity of the electrodes allowed for successful tracking of the complex wavefront dynamics in VF. An impressive array of tools developed for the analysis of activation sequences initially in 2D but extended to 3D for this study was used to analyze the types of wavefronts in the mapped region and to detect reentrant circuits, thus providing a rare glimpse into the spatiotemporal dynamics during long-duration VF in the pig heart.

The study concluded that whereas intramural reentry was present during the early stages of VF (short-duration VF), reaching a maximum incidence of ~11% of all episodes after 30 to 40 seconds of VF, occurrences of reentry were no longer detected after 3 minutes of VF. Instead, intramural foci, manifested with low incidence in early VF (6% in the first 10 seconds of VF), became increasingly represented in the wavefront landscape of VF in its later stages, with 27% of all wavefronts in the recorded region arising from such foci at 10 minutes of VF. This is the first direct evidence of the existence of intramural foci during VF. Although the study by Li et al1 could not provide a direct observation and thus mechanistic explanation of the origin of these intramural foci or of their increased incidence in long-duration VF, the authors speculate that activity from the Purkinje network may be implicated, because Purkinje fibers are more tolerant to long-duration VF than the working myocardium. Microreentry involving the Purkinje fibers and triggered activity or abnormal automaticity arising in the Purkinje network were suggested as possible mechanisms and indirectly supported by the presence of Purkinje–ventricular junctions near the insertion of the anterior lateral papillary muscle into the ventricular wall, the region mapped in the present study. Most importantly, the study by Li et al concluded that intramural foci (and not reentry) play an important role in VF maintenance: the long and the short of long-duration VF in the swine heart.

Because VF was mapped in its early stages as well, the results of the study also offer further insights regarding the maintenance of short-duration VF. Up to date, short-duration VF driven by a mother rotor, a stable rotor associated with the fastest activation rates in the heart and the shortest refractory periods, has been evidenced in small hearts such as guinea pigs and rabbits; these species, it has been found to reside on the anterior LV epicardium, where optical recordings allowed its direct observation. Additional support for the existence of the mother rotor has come from studies of early VF in isolated slabs of sheep ventricle, where a single domain of highest peak frequency in the power spectrum (dominant frequency), ie, of fastest activation rate, was

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documented on the tissue surface as a manifestation of an intramurally located mother rotor. These data18–20 thus suggest that not all reentrant waves are equal in maintaining VF and raise the question regarding the universal nature of the mother rotor finding, and its applicability to large hearts such as the human.

A series of studies from Ideker and colleagues21–26 embarked on an extensive search for the mother rotor in a large heart. In carefully orchestrated consecutive sets of experimental studies, early VF activity in swine hearts was mapped from location to location in a search for the mother rotor, using sock and plunge needle electrodes. These studies were unable to find a region of dominant frequency or a sustained reentry in the mapped portions of the pig heart. Instead, results demonstrated that epicardial and intramural reentry during short-duration VF in the pig was brief, typically lasting less than 2 cycles; wavefronts were most often annihilated, by block or collision, without reentering. However, given that parts of the LV remained unmapped, these series of studies narrowed down the possible location of the mother rotor to the regions where the papillary muscles insert into the ventricular wall, regions also suggested previously as sites of spiral wave anchoring.27 The anterior lateral portion of the pig heart mapped in 3D in the present study by Li et al15 contained one of these regions; however, the authors were unable to find a sustained reentry there during the early stages of VF. Thus, the long and the short of short-duration VF in the swine heart, as deduced from these studies, is that intramural foci are present, although their incidence at that stage of VF is low; reentry is typically short-lived; and the only region where a sustained reentry could reside in the pig heart is the posterior septal region of papillary muscle insertion.

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