EDITORIAL COMMENT

Shifting Ventricular Fibrillation Drive Mechanism as Time Progresses
Evidence From Explanted Human Hearts*

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It has been known for 85 years that ventricular fibrillation (VF) is a dynamic process. In a foundational study, Wiggers (1) used high-speed photography to show that VF progresses through a series of stages. Much more has been learned as cardiac mapping technology has progressed. In cardiac mapping, cardiac potentials are sensed from many sites simultaneously using either electrical or optical technology. This information is then used to track cardiac waves moving through the tissue. Using electrical mapping technology, Huang et al. (2) reclassified the stages of VF using a high-density epicardial array and a set of descriptors of the underlying VF patterns. They found that VF rapidly gained complexity in the first minute, followed by a recovery of organization over the next 10 min (2). Although the changing nature of VF has long been appreciated, the bulk of VF mapping studies have focused on the first minute of VF. This is the stage of VF during which implantable defibrillators deliver therapy, and implantable cardioverter-defibrillator and cardiac mapping technologies were developed during roughly the same period. The picture of early VF that has developed from many studies is that VF waves are self-regenerating and arise from functional re-entry, whether the re-entrant circuits are persistent ("mother rotors") or transient (3–5).

In recent years, more attention has been paid to the later stages of VF, often referred to as "long duration ventricular fibrillation" (LDVF). This is the stage of VF that patients undergoing out-of-hospital arrest may be in when defibrillation therapy is delivered. The picture that has emerged from epicardial, endocardial, and intramural mapping studies in animals is that LDVF is not simply a less energetic version of short duration ventricular fibrillation (SDVF). Rather, it is fundamentally different in character. LDVF waves in the bulk myocardium do not seem to self-regenerate through the formation of re-entrant circuits. Rather, waves propagate away from foci arising from the Purkinje system. In hearts with human-like Purkinje networks (i.e., dogs), waves begin near the endocardium and propagate toward the epicardium. Because propagation is tenuous in the ischemic, electrically depressed muscle, waves frequently fail on the way, causing sites on the epicardium to activate with lower frequency than those on the endocardium (6–9).

The primary contribution of the paper by Jackson et al. (10) in this issue of JACC: Clinical Electrophysiology is to extend this picture to human hearts. The investigators studied Langendorff-perfused human hearts explanted from transplant recipients. Perfusion was stopped following VF induction and VF activation patterns were recorded using an epicardial electrode array, an endocardial basket electrode array, and an array of 4-electrode needles inserted into the myocardium. The mapping results were broadly similar to those in animals. During LDVF, waves tended to propagate from the endocardium outward and propagation failure was common; this tendency was not seen in SDVF. During LDVF, activation frequency was faster near the endocardium than at the epicardium; a similar gradient was not seen in SDVF. Re-entry was observed much less frequently during LDVF than

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SDVF. Furthermore, sharp deflections that the investigators attributed to Purkinje activation became more prominent in signals acquired on or near the endocardium as VF progressed. Such potentials were often the initiation site of waves in the working myocardium. To further explore the idea that LDVF waves originate in Purkinje tissue, the investigators employed an additional preparation in which canine hearts were dissected into islands of ventricular myocardium joined by strands of Purkinje tissue. Simulating LDVF using rapid pacing in the absence of perfusion, they showed that the Purkinje strands were more ischemia-resistant than the myocardium islands were. Furthermore, rapid activation potentiated spontaneous Purkinje activations after the cessation of pacing. These findings are consistent with other data in the literature on the behavior of Purkinje tissue (11–13) and may explain why Purkinje tissue that is subjected to rapid drive in early VF generates spontaneous waves after the working muscle has become too depressed to support re-entry.

This study is subject to limitations. The explanted human hearts that were used, although likely the only ones available for such a study, are from a very sick population, and possibly one in which fatal ventricular arrhythmias are relatively uncommon (14). The mapping instrumentation provides a low-resolution picture of activation patterns throughout the ventricles, making it difficult to conclusively rule out the presence of re-entry during LDVF. Furthermore, the identification of Purkinje deflections during VF was by visual inspection, which could be subject to uncertainty. Nevertheless, the findings are in line with animal studies in the literature and provide important insight into the mechanisms of human VF as it persists beyond the first minutes. As the investigators point out, this could lead to new strategies for adjunctive drug therapy for patients in prolonged VF. For example, drugs that target spontaneous Purkinje activation could promote defibrillation or prevent the reinitiation of VF in long-downtime patients.

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REFERENCES


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