Electrophysiology of ventricular fibrillation and defibrillation

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The survival rate from ventricular fibrillation is very high for short-duration fibrillation (<30 secs) but decreases to ~3% to 30% in out-of-hospital conditions. During short-duration fibrillation, action potentials occur rapidly with no intervening period of electrical diastole; a shock defibrillates by interacting with the fibrillation action potential to produce a uniformly long postshock extension of refractoriness. In contrast, during long-duration fibrillation, ischemia-induced degradation of cellular electrophysiology occurs, which causes intervening periods of electrical diastole between fibrillation action potentials and, thus, slowing of fibrillation frequency. A successful defibrillation shock must now not only prolong refractoriness when delivered during the action potential but must also excite cells during the periods of depolarized diastole. Biphasic waveforms enhance both effects by causing premature membrane repolarization with the first pulse, thereby allowing sodium channel recovery from inactivation so that the second pulse produces better-formed responses both during the cellular action potential and during the depolarized diastole. Therefore, biphasic waveforms remain superior to monophasic waveforms for treatment of long-duration fibrillation. Improved understanding of the ischemia-induced changes in cellular electrophysiology will suggest further improvements in both defibrillator waveforms and resuscitation techniques. (Crit Care Med 2000; 28[Suppl.]:N219–N221)

Key Words: ventricular fibrillation; defibrillation; out-of-hospital resuscitation; extension of refractoriness hypothesis; ischemia; fibrillation frequency; electrophysiology; isolated rabbit heart

Sudden cardiac death from ventricular fibrillation is responsible for >350,000 deaths per year in the United States (1). Many patients who are susceptible to this fatal arrhythmia are now treated by implantation of an internal defibrillator. For internal ventricular defibrillation, where fibrillation duration is short (usually <20 secs), the probability that the shock will successfully defibrillate is very high, and internal defibrillators are successfully reducing mortality in cardiac patents. In contrast, the survival rate from out-of-hospital cardiac arrest, where fibrillation durations are longer, is very low (~3% to 33%) (2). The probability of successful resuscitation decreases by 10% for each minute of ventricular fibrillation (2). This decrease is due, in part, to the degradation of fibrillation characteristics as global cardiac ischemia develops (3).

DEFIBRILLATION MECHANISMS FOR SHORT DURATIONS OF FIBRILLATION

During short-duration fibrillation in both humans and experimental animals, fibrillation action potentials usually immediately follow each other with little or no intervening periods of electrical diastole. Figure 1 shows monophasic action potentials after 10 secs of ventricular fibrillation in both humans (Fig. 1A) and isolated rabbit hearts (Fig. 1B). Fibrillation cycle length is ~200 msecs in humans (4), 100 msecs in dogs (5) and rabbits (6), and ~120 msecs in pigs (7). Although the actual cycle length varies in different experimental models and in humans, the refractory period of the fibrillation action potential seems to control the local fibrillation cycle length.

Because there is no intervening period of electrical diastole (resting potential between fibrillation action potentials), the shock interacts with cardiac cells during some phase of the action potential rather than during electrical diastole. During fibrillation, cells in different regions of the heart are in different phases of the action potential at the time of shock delivery. Therefore, the shock will be delivered early in the action potential in some regions and late in the action potential in other regions. When the shock is delivered early in the fibrillation action potential, the postshock response is naturally long, regardless of the effectiveness of the shock (6). When delivered late in the action potential, a successful shock must act to prolong the postshock response, as shown in Figure 2A. A shock that fails to produce action potential prolongation when it is delivered late in the fibrillation action potential fails to defibrillate as shown in Figure 2B. To be successful, the shock must produce relatively uniformly prolonged postshock responses throughout the heart regardless of the timing of the shock within individual fibrillation action potentials (6). One potential clinical benefit of this “extension of refractoriness” hypothesis is a decreased defibrillation threshold for shocks that are delivered while cells in low-gradient regions of the ventricle are early in their fibrillation action potentials (8). This occurs because the shock does not need to prolong the postshock response in these low-gradient regions.

THRESHOLD REDUCTION WITH BIPHASIC WAVEFORMS

Biphasic waveforms lower defibrillation threshold (improve the efficacy of defibrillation at low shock intensities) because they produce the required refractory period extension for shocks delivered
late in the action potential, at lower shock intensities. Figure 3 shows monophasic (Fig. 3A) and biphasic (Fig. 3B) waveform shocks delivered late in action potentials from isolated myocytes (9). At a low intensity of 1.5 times the excitation threshold (9), the monophasic shock does not extend the refractory period, although it does produce refractory period extension at three and five times the excitation threshold. Therefore, a low-intensity shock, which produces a local intensity of only 1.5 times the excitation threshold in the low gradient regions of the heart, fails to extend the refractory period at three and five times the excitation threshold. Consequently, a low-intensity shock is not effective in producing refractory period extension at three and five times the excitation threshold.

DEFIBRILLATION MECHANISMS CHANGE AFTER LONG FIBRILLATION DURATIONS

As fibrillation duration increases, the heart is subjected to developing global ischemia, and both postrepolarization refractoriness and conduction delay are produced (12). The rate of development varies throughout the ventricle but, for a given ischemic duration, is most severe in epicardial regions. Therefore, intervals of electrical diastole develop between fibrillation action potentials (3). In the isolated rabbit heart, irregular intervals of electrical diastole (periods between fibrillation action potentials) appear as early as 30 secs; they occur after almost each fibrillation action potential within 2 mins of ischemic fibrillation as shown in Figure 4 (13).

The defibrillation mechanism in ventricular regions that are in electrical diastole at the time of the shock is not refractory period extension, as it was after short fibrillation durations, but rather excitation of depolarized, ischemic cells. As shown in Figure 5 (14), biphasic waveforms are able to stimulate these cells at a lower intensity than monophasic waveforms because the first phase “hyperpolarizes” the resting potential from its ischemic depolarized value, thereby allowing sodium channel recovery and decreasing excitation threshold.

IMPLICATIONS FOR OUT-OF-HOSPITAL DEFIBRILLATION

During long-duration ischemic fibrillation, cellular electrophysiology deteriorates (3). Changes include, for example, slowing of fibrillation frequency (15, 16) owing to postrepolarization refactoriness and conduction failure (12) leading to diastolic intervals between fibrillation action potentials (3, 13), increased tissue resistance as cellular uncoupling takes place, altered membrane resistance as $K_{ATP}$ channels open, intracellular cal-
cium overload (17), and developing contracture (18) and contractile failure. Although our understanding of mechanisms underlying improved defibrillation efficacy with biphasic waveforms suggests that they remain superior to monophasic waveforms at long fibrillation durations, altered cellular characteristics produced by the resulting ischemia suggest that new biphasic waveforms, which better address these altered characteristics, may further improve defibrillation efficacy.

**REFERENCES**

16. Tovar O, Noe W, Jones J: At long fibrillation durations action potentials are more frequent and fractionated in the right ventricle than in the left ventricle. *PACE* 1998; 21:931

**Figure 5.** Transmembrane potentials recorded from isolated myocytes during stimulation with monophasic (A, C) and biphasic (B, D) waveforms with intensities just below (A, B) and above (C, D) the monophasic waveform excitation threshold (reproduced with permission from Jones et al. [14]).