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Relative Efficacy of Monophasic and Biphasic Waveforms for Transthoracic Defibrillation After Short and Long Durations of Ventricular Fibrillation

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Background—Recently, interest has arisen in using biphasic waveforms for external defibrillation. Little work has been done, however, in measuring transthoracic defibrillation efficacy after long periods of ventricular fibrillation. In protocol 1, we compared the efficacy of a quasi-sinusoidal biphasic waveform (QSBW), a truncated exponential biphasic waveform (TEBW), and a critically damped sinusoidal monophasic waveform (CDSMW) after 15 seconds of fibrillation. In protocol 2, we compared the efficacy of the more efficacious biphasic waveform from protocol 1, QSBW, with CDSMW after 15 seconds and 5 minutes of fibrillation.

Methods and Results—In protocol 1, 50% success levels, ED₅₀, were measured after 15 seconds of fibrillation for the 3 waveforms in 6 dogs. In protocol 2, defibrillation thresholds were measured for QSBW and CDSMW after 15 seconds of fibrillation and after 3 minutes of unsupported fibrillation followed by 2 minutes of fibrillation with femoral-femoral cross-circulation. In protocol 1, QSBW had a lower ED₅₀, 16.0±4.9 J, than TEBW, 20.3±4.4 J, or CDSMW, 27.4±6.0 J. In protocol 2, QSBW had a lower defibrillation threshold after 15 seconds, 38±10 J, and after 5 minutes, 41.5±5 J, than CDSMW after 15 seconds, 54±19 J, and 5 minutes, 80±30 J, of fibrillation. The defibrillation threshold remained statistically the same for QSBW for the 2 fibrillation durations but rose significantly for CDSMW.

Conclusions—In this animal model of sudden death and resuscitation, these 2 biphasic waveforms are more efficacious than the CDSMW at short durations of fibrillation. Furthermore, the QSBW is even more efficacious than the CDSMW at longer durations of fibrillation. (*Circulation*. 1998;98:2210-2215.)

Key Words: defibrillation ■ cardiopulmonary resuscitation ■ arrhythmia

Numerous studies, both in animals and in humans, have shown that certain truncated exponential biphasic waveforms with well-chosen phase durations have lower defibrillation thresholds than monophasic truncated exponential waveforms for internal defibrillation.¹⁻⁵ Other studies, in humans or animals, have shown that certain truncated exponential biphasic waveforms have either a lower defibrillation threshold or greater defibrillation efficacy for the same size shock than a monophasic damped sinusoidal waveform for transthoracic defibrillation.^{6,7}

Another type of biphasic waveform exists for external defibrillation in addition to the truncated exponential biphasic waveform, ie, the quasi-sinusoidal waveform.⁸ A study in humans has shown that the probability of success of a 200-J shock was higher for the biphasic quasi-sinusoidal waveform than for the critically damped monophasic waveform.⁹ Although both biphasic waveforms perform better than the monophasic waveform, it is not known which of these 2 biphasic waveforms has the lower defibrillation threshold for transthoracic defibrillation.

Shocks from the implantable cardioverter-defibrillator are given within seconds of the onset of fibrillation. Because most previous studies of biphasic waveforms have focused on internal defibrillation, shocks have been delivered after only 10 to 30 seconds of ventricular fibrillation. In contrast, the first transthoracic defibrillation shock in the prehospital setting is often administered >5 minutes after the patient collapses.^{10,11} The defibrillation efficacy of biphasic waveforms after minutes of fibrillation has not been compared with that of monophasic waveforms.

This study was designed to test the following hypotheses. First, we hypothesized that both biphasic waveforms, the truncated exponential and the quasi-sinusoidal, would defibrillate with a lower delivered energy than the critically damped monophasic waveform after short durations of ventricular fibrillation. Furthermore, we predicted that the quasi-sinusoidal biphasic waveform, with its gradual onset, would defibrillate at a lower delivered energy than the truncated exponential biphasic waveform, with its abrupt onset, and the critically damped monophasic waveform. Second, we hy-

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pothesized that the more efficacious biphasic waveform in protocol 1 would also defibrillate at a lower delivered energy than the critically damped monophasic waveform after 5 minutes of fibrillation.

Methods

This work was approved by the Animal Care and Use Committee at the University of Alabama at Birmingham. It conforms to the "Position of the American Heart Association on Research Animal Use" published in *Circulation* in April 1985.

The portions of the experimental procedure common to both protocols will be described first. Each dog was anesthetized with sodium pentobarbital 20 to 30 mg/kg and maintained on a constant infusion of $0.05 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ through an intravenous catheter in a foreleg. ECG lead II was monitored throughout the experiment. The animal was intubated with a cuffed endotracheal tube and ventilated with a volume-controlled respirator (Harvard Apparatus) with an air/oxygen ratio to keep a PO_2 of $\approx 100 \text{ mm Hg}$. A constant infusion (5 to $10 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) of lactated Ringer's solution was delivered. A femoral arterial catheter was placed for hemodynamic monitoring and for vascular access for blood gas and electrolyte analysis. Blood gas analysis was performed every 30 to 60 minutes as indicated by the condition of the animal, and corrections in PO_2 , PCO_2 , Na^+ , K^+ , Ca^{2+} , and bicarbonate were made as necessary to maintain normal values. Body temperature was monitored with an esophageal temperature probe and maintained at 37°C to 38°C with a heating pad placed beneath the animal.

FASTPATCH disposable defibrillation electrodes (Physio-Control Corp) were placed on the left and right chest walls. Fibrillation was induced with 60-Hz current from a quadripolar electrophysiology catheter (EP Technologies) in the right ventricle. After all test shocks were delivered, the animal was euthanized. The heart was removed from the animal, weighed, and stored in formalin.

Protocol 1

Three waveforms were tested. The monophasic waveform (Edmark) was a critically damped sinusoidal waveform (Figure 1A).¹² One biphasic waveform (Gurvich) was a quasi-sinusoidal biphasic waveform (Figure 1B).⁸ Both sinusoidal waveforms were delivered from a modified LIFEPAK 7 external defibrillator (Physio-Control Corp). The second biphasic waveform was a truncated exponential waveform delivered from a single 280- μF capacitor bank in which each phase had a 35% tilt (Figure 1C) delivered from an HVS-02 external defibrillator (Ventritex Co) modified to accept an external capacitor bank of arbitrary size and to deliver shocks of leading-edge voltage up to 1300 V. The capacitor size was made large relative to the capacitor size used in internal defibrillators to lower the leading-edge voltage of the shock necessary to defibrillate the animal.¹³ Phase 1 duration was chosen to be optimal for a 75- Ω impedance with a parallel resistor-capacitor network used to represent the heart.¹⁴ The second phase of the biphasic waveform was chosen to be equal to the first phase.¹ Shocks were given after 15 seconds of fibrillation. If the test shock failed, the heart was rescued with a shock of the same shape but approximately twice the energy.

Probability-of-success curves were determined for each waveform in an interleaved fashion. Shocks were delivered in groups of 3, with 1 shock of each waveform shape being delivered in each group. The order of shocks within each group of 3 was randomized. The starting energy for each waveform was 25 J. An up/down protocol was followed until 15 shocks were delivered for each waveform. The 15-shock count did not start until the first reversal from success to failure or failure to success occurred. If the test shock for a particular waveform succeeded, the next shock for that waveform was decreased in energy by 10%. If the test shock failed, the next test shock was increased 10% in energy.

Probability-of-defibrillation-success curves were determined for each waveform by a Probit regression fit method.¹⁵ The 50% effective dose point (ED_{50}) for delivered energy for each waveform was compared by a repeated-measures ANOVA. The null hypothesis that the ED_{50} values were not different for the different waveforms

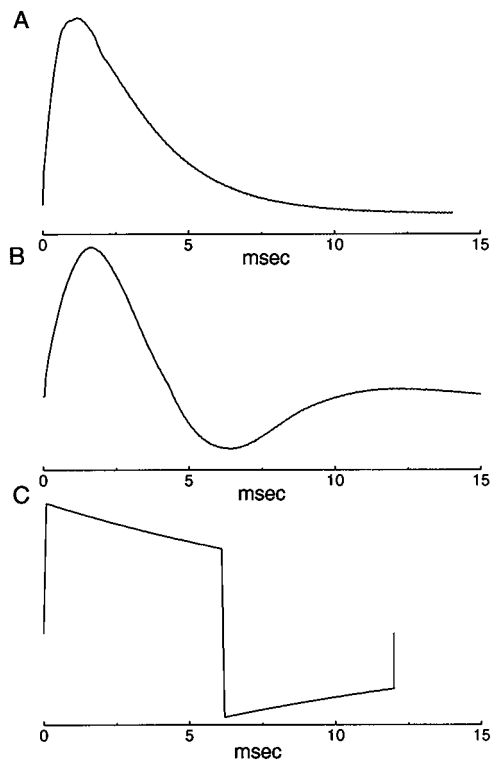


Figure 1. The 3 waveforms: critically damped sinusoidal monophasic (A), quasi-sinusoidal biphasic (B), and truncated exponential biphasic (C).

was rejected at $P < 0.05$. The Student-Newman-Keuls test for multiple comparisons was used to determine differences among the 3 waveforms if the null hypothesis was rejected by the repeated-measures ANOVA.

Protocol 2

Two waveforms were tested, the critically damped monophasic waveform (Figure 1A) and the quasi-sinusoidal biphasic waveform (Figure 1B). The defibrillation threshold was first determined for the 2 waveforms after 15 seconds of fibrillation with an interleaved up/down protocol (Figure 2). Shocks were delivered in pairs, with 1 of each shape given before the next pair of tests shocks was delivered. Shock order for each pair was randomized. The initial shock strength was 25 J. If a test shock succeeded for a particular waveform, the next test shock was decreased by 20% in energy. If a test shock failed, the next test shock was increased by 20% in energy. This protocol was followed until a reversal from success to failure or failure to success was recorded for each shock waveform. The lowest shock strength that successfully defibrillated the animal was defined as the defibrillation threshold for that waveform. If the test shock failed, the animal was rescued by a shock of the same shape but approximately twice the energy.

After the defibrillation threshold had been determined for short-duration fibrillation, the animal was given 3000 U heparin. Subsequent doses of 1000 U heparin were given each hour. Cannulas were placed in the right femoral artery and right femoral vein and connected to a perfusion apparatus (Sarns Inc). The perfusion apparatus was primed with 1 L normal saline, 20 mEq KCl, 50 mEq Na_2CO_3 , and 100 mg CaCl_2 . Defibrillation thresholds were then determined for the 2 waveforms after 5 minutes of ventricular fibrillation. During the first 3 minutes, the animal was allowed to fibrillate without external support. Then the perfusion pump was started, and cross-circulation with unoxygenated blood was given at a flow rate of 1 L/min.

After 2 minutes of perfusion, the test shock was administered. The initial shock strength was the defibrillation threshold measured after

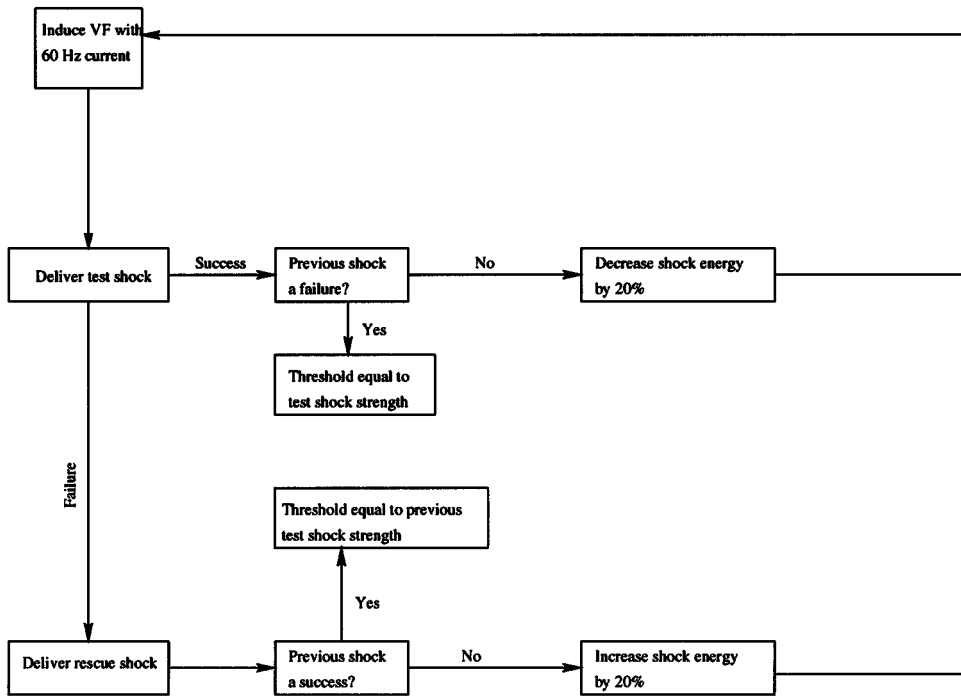


Figure 2. Flow chart describing method used to determine defibrillation threshold in protocol 2.

15 seconds of fibrillation. Defibrillation thresholds were determined in an interleaved fashion according to the same protocol as for 15 seconds of fibrillation (Figure 2). When the defibrillation threshold had been successfully determined for 1 of the waveforms, interleaving stopped (so as to minimize the number of ventricular fibrillation episodes), and all subsequent episodes were shocked with the other waveform. Once defibrillated, the animal was allowed to recover for 45 minutes before fibrillation was reinduced. If the animal was asystolic or had pulseless electrical activity after defibrillation, perfusion was maintained without pacing for 30 seconds. If the animal was still asystolic after 30 seconds of perfusion, pacing was begun from the right ventricular catheter. Perfusion was halted once cardiac mechanical activity was noted. If the blood pressure was <60 mm Hg after 30 seconds with no cross-circulation, perfusion was reinstated and the animal was resuscitated with 1 mg epinephrine.

The defibrillation threshold was defined as the lowest shock energy that successfully converted ventricular fibrillation to a perfusing rhythm after resuscitation of the animal. A 2-level ANOVA with repeated measures was used to compare defibrillation thresholds. The 2 levels were shock waveform and duration of fibrillation. Again, the Student-Newman-Keuls multiple-comparisons test was used to compare means.

Results

Protocol 1

Six dogs weighing 15±4 kg (mean±SD) were studied. The defibrillation threshold was significantly lower for the quasi-sinusoidal biphasic waveform (16.0±4.9 J) than for the truncated exponential biphasic waveform (20.3±4.4 J), which, in turn, was significantly lower than the critically damped sinusoidal monophasic waveform (27.4±6.0 J) (Figure 3).

Protocol 2

The defibrillation threshold for the quasi-sinusoidal biphasic waveform was significantly lower than that for the critically

damped sinusoidal monophasic waveform for both long- and short-duration fibrillation (Figure 4). After 15 seconds of fibrillation, the defibrillation threshold for the quasi-sinusoidal biphasic waveform (38±10 J) was lower than for the monophasic waveform (54±19 J). After 5 minutes of fibrillation, the defibrillation threshold for the quasi-sinusoidal biphasic waveform (41±5 J) was lower than for the monophasic waveform (80±30 J). In addition, the defibrillation threshold for the monophasic waveform was significantly higher at 5 minutes than at 15 seconds. The quasi-sinusoidal biphasic waveform defibrillation threshold did not increase significantly.

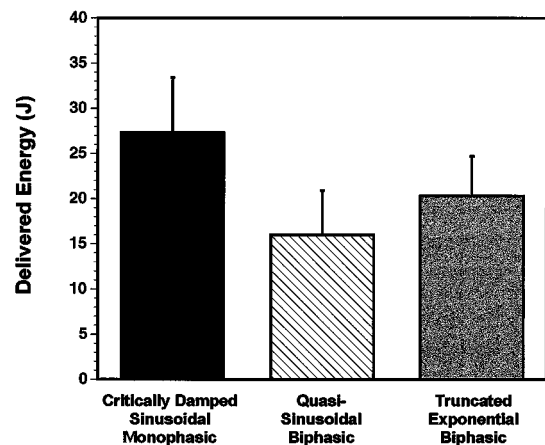


Figure 3. Mean ED₅₀ for 3 waveforms tested in protocol 1. Each bar indicates mean delivered energy for a waveform, with SD indicated by bracket. Defibrillation threshold for critically damped sinusoidal biphasic waveform was significantly different from ED₅₀s for other 2 waveforms. ED₅₀ for truncated exponential biphasic waveform was significantly different from that for critically damped sinusoidal monophasic waveform.

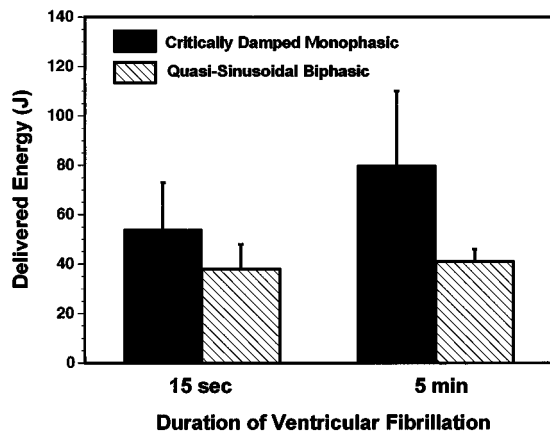


Figure 4. Defibrillation thresholds in terms of energy for quasi-sinusoidal biphasic waveform and critically damped sinusoidal monophasic waveform after 15 seconds and after 5 minutes of fibrillation. Defibrillation threshold for biphasic waveform did not change significantly with duration of fibrillation, whereas defibrillation threshold for monophasic waveform was significantly different after 5 minutes of fibrillation vs after 15 seconds of fibrillation. In both cases, defibrillation threshold for biphasic waveform was significantly different from that of monophasic waveform.

Discussion

In terms of delivered energy, both types of biphasic waveforms tested in this study, ie, quasi-sinusoidal and truncated exponential, required less delivered energy to defibrillate than the critically damped sinusoidal monophasic waveform for external defibrillation after 15 seconds of ventricular fibrillation. In addition, the quasi-sinusoidal biphasic waveform required less energy to defibrillate than the truncated exponential biphasic waveform after 15 seconds of fibrillation (protocol 1). After 5 minutes of fibrillation, the quasi-sinusoidal biphasic waveform defibrillated with less energy than the critically damped sinusoidal monophasic waveform (protocol 2).

Effect of Fibrillation Duration on Defibrillation Energy Requirements

Only a few studies have examined the effects of the duration of fibrillation on the defibrillation threshold. Most of these studies deal with internal defibrillation and with fibrillation durations of <1 minute.¹⁶⁻¹⁸ In a dog model of defibrillation, using internal electrodes and bidirectional monophasic defibrillation pulses delivered along 2 pathways, Echt et al¹⁶ showed that the energy necessary to defibrillate rose from 27 ± 13 J at 5 seconds to 41 ± 14 J at 30 seconds of fibrillation. Jones et al¹⁸ showed that in a working rabbit heart model of defibrillation, both monophasic and biphasic waveform defibrillation thresholds increased with duration from 5 to 15 to 30 seconds. At all durations, the biphasic threshold was lower than the monophasic threshold. This difference increased with fibrillation duration. In a study using sequential trapezoidal defibrillation pulses in a pig model of defibrillation, Fujimura et al¹⁹ concluded that a delay in defibrillation therapy of up to 90 seconds has no significant effect on the ability to defibrillate the heart. Bardy et al¹⁷ found no difference between the mean defibrillation thresholds in

humans when fibrillation was allowed to continue for 10 versus 20 seconds (11.5 ± 5.9 versus 12.0 ± 6.9 J, $P=NS$). Winkle et al²⁰ showed that in humans, the probability of successful defibrillation with low-energy shocks (5.9 J) was higher for ventricular fibrillation lasting 5 seconds than for ventricular fibrillation lasting 15 seconds, yet there was no significant difference between the success rates of high-energy shocks (24.2 J) delivered at the same 2 durations. Together, these results suggest that for ventricular fibrillation durations up to 90 seconds, the defibrillation threshold for monophasic waveforms increases with duration, whereas the results are inconclusive for biphasic waveforms.

However, the time before a defibrillation shock is administered to individuals experiencing sudden cardiac arrest without an implantable cardioverter-defibrillator (the vast majority of individuals) is much longer than 90 seconds. Studies have shown that the time from initiation of ventricular fibrillation to delivery of a defibrillation shock is at best 6 to 12 minutes.^{11,21} Very little is known about the effect of several minutes of fibrillation on defibrillation energy requirements. This question becomes important as the concept of "public access defibrillation"²² is implemented and smaller, lighter defibrillators with new waveforms are developed. One way to make defibrillators smaller and lighter is to have their maximum shock size be smaller than the current 360-J standard.²³ An important question is, how much energy need these defibrillators be capable of delivering so as to rapidly defibrillate patients after prolonged intervals of ventricular fibrillation?

This study found that the defibrillation threshold increased markedly with time during fibrillation for the monophasic waveform tested. The defibrillation threshold was $\approx 50\%$ greater after 5 minutes of fibrillation than after 15 seconds of fibrillation (Figure 4). The monophasic waveform tested, the critically damped sinusoidal waveform, is the waveform used in the majority of external defibrillators that are in use today. Conversely, the biphasic waveform tested in this study increased only nonsignificantly between 15 seconds and 5 minutes of fibrillation. In addition, the defibrillation threshold was much smaller for the biphasic than the monophasic waveform at both durations of fibrillation. After 5 minutes of fibrillation, the defibrillation threshold for the monophasic waveform was almost twice that for the biphasic waveform (Figure 4).

Defibrillation Efficacy of Different Types of Biphasic Waveforms

Two different shapes of biphasic waveforms were examined in this study: the truncated exponential waveform, similar to that used in implantable cardioverter-defibrillators,³⁻⁵ and the quasi-sinusoidal waveform suggested by Gurvich and Markarychev.⁸ After 15 seconds of fibrillation, the ED_{50} for each type of biphasic waveform was significantly lower than that for the monophasic waveform (Figure 3). In addition, the ED_{50} for the truncated exponential biphasic waveform was $\approx 25\%$ higher than for the quasi-sinusoidal biphasic waveform.

One major difference between the 2 biphasic waveforms is that the truncated exponential waveform has an abrupt onset,

with the leading edge of the waveform being almost a step function, whereas the quasi-sinusoidal waveform increases more slowly with time after its onset. Several experimental studies have demonstrated that waveforms with a more gradual onset, such as an ascending ramp, have lower defibrillation energy requirements than waveforms with an abrupt onset to the maximum value, such as a square wave or descending ramp.^{24–26}

Modeling studies that represent stimulation or defibrillation by the achievement of a particular minimum voltage across a parallel resistor-capacitor network suggest that an ascending waveform should require less energy than a descending or square waveform if the rate of rise is within a certain range related to the time constant of the resistor-capacitor network.¹⁴ This resistor-capacitor network can also be thought of as a low-pass filter that passes the lower frequencies of the quasi-sinusoidal waveform better than the high frequencies generated by the leading and trailing edges of the truncated exponential biphasic waveform.²⁷

The resistor-capacitor network can be used to choose an “optimal” first-phase duration for a truncated exponential biphasic waveform.²⁸ If we define the optimal truncation point for the first phase of a biphasic waveform as the time at which the voltage across the network is at maximum, then for a 280- μF capacitor delivered into a 75- Ω load, the optimal truncation point should be ≈ 9 ms. A 35% tilt waveform using a 280- μF capacitor and delivered into a 75- Ω load will have a 9-ms duration. As a first approximation, choosing the second phase of a biphasic waveform to be equal to the first phase of the waveform is a good choice.¹ Therefore, although it has not been rigorously validated, the 35%/35% biphasic waveform delivered from a 280- μF capacitor is probably a reasonable truncated exponential biphasic waveform to test.

One of the reasons to strive for a lower defibrillation energy is to allow the production of new smaller, lighter external defibrillators. A waveform that consistently defibrillates at a lower energy should allow the construction of a smaller defibrillator. With present technology, however, it is easier to make a small, light defibrillator using a truncated exponential biphasic waveform than using the quasi-sinusoidal biphasic waveform, even though defibrillation efficacy is slightly better for the quasi-sinusoidal waveform. Improvements in technology may make this difference less important in the future. These improvements might include the use of new materials that will make inductors smaller or the use of duty-cycle waveforms to shape waveforms in new ways.²⁷

Study Limitations

Two limitations of protocol 2 are that defibrillation thresholds instead of probability-of-success curves were measured and that 1 of the biphasic waveforms tested in protocol 1 was not tested in protocol 2. The reason for these 2 limitations is that it is not possible to give as many test shocks and fibrillation episodes when each fibrillation episode lasts 5 minutes as when each fibrillation episode lasts only 10 or 15 seconds. Because of the possible cumulative effects of a number of 5-minute episodes of fibrillation, it is possible that the defibrillation requirements changed during the course of the experiments in protocol 2. For this reason, shocks for the 2

waveforms were interleaved. However, once the threshold was determined for 1 waveform, all subsequent episodes were used to determine the threshold for the other waveform. This was usually the monophasic waveform.

A limitation of both protocols is that the defibrillation patches were placed on the right and left sides of the thorax instead of in the precordial or anterior-posterior configurations that are more commonly used clinically. This was done because the shape of the thorax differs in dogs and humans. Whereas the chest is relatively flat and broad in humans, it is narrow and V-shaped in dogs.

Clinical Implications

These data show that the energy requirements for defibrillation do not change significantly during the first 5 minutes of fibrillation for the quasi-sinusoidal biphasic waveform tested in this study. These results suggest that to be useful in the prehospital setting, a clinical device using such a waveform may not need the ability to deliver significantly more energy than is necessary to defibrillate after a short period of ventricular fibrillation. Studies are necessary to test whether these animal model results carry over for prehospital cardiac arrest in humans before we will know whether biphasic external defibrillators may have a maximum energy capability below the 360-J level currently indicated in AHA guidelines.²³ Furthermore, it is unknown whether the advantage shown for the quasi-sinusoidal biphasic waveform would also apply to the biphasic truncated exponential waveforms.

Acknowledgments

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