Monophasic Versus Biphasic Transthoracic Countershock After Prolonged Ventricular Fibrillation in a Swine Model

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OBJECTIVE We sought to compare the defibrillation efficacy of a low-energy biphasic truncated exponential (BTE) waveform and a conventional higher-energy monophasic truncated exponential (MTE) waveform after prolonged ventricular fibrillation (VF).

BACKGROUND Low energy biphasic countershocks have been shown to be effective after brief episodes of VF (15 to 30 s) and to produce few postshock electrocardiogram abnormalities.

METHODS Swine were randomized to MTE (n = 18) or BTE (n = 20) after 5 min of VF. The first MTE shock dose was 200 J, and first BTE dose 150 J. If required, up to two additional shocks were administered (300, 360 J MTE; 150, 150 J BTE). If VF persisted manual cardiopulmonary resuscitation (CPR) was begun, and shocks were administered until VF was terminated. Successful defibrillation was defined as termination of VF regardless of postshock rhythm. If countershock terminated VF but was followed by a nonperfusing rhythm, CPR was performed until a perfusing rhythm developed. Arterial pressure, left ventricular (LV) pressure, first derivative of LV pressure and cardiac output were measured at intervals for 60 min postresuscitation.

RESULTS The odds ratio of first-shock success with BTE versus MTE was 0.67 (p = 0.55). The rate of termination of VF with the second or third shocks was similar between groups, as was the incidence of postshock pulseless electrical activity (15/18 MTE, 18/20 BTE) and CPR time for those animals that were resuscitated. Hemodynamic variables were not significantly different between groups at 15, 30 and 60 min after resuscitation.

CONCLUSIONS Monophasic and biphasic waveforms were equally effective in terminating prolonged VF with the first shock, and there was no apparent clinical disadvantage of subsequent low-energy biphasic shocks compared with progressive energy monophasic shocks. Lower-energy shocks were not associated with less postresuscitation myocardial dysfunction. (J Am Coll Cardiol 2000;36:932–8) © 2000 by the American College of Cardiology

Sudden unexpected cardiac death is most commonly caused by ventricular fibrillation (VF), and immediate and effective treatment of VF is the primary goal of advanced cardiac life support (ACLS). A number of clinical studies indicate that the earlier electrical defibrillation can be performed, the greater the likelihood that countershock will be effective in terminating VF and that resuscitation efforts will be successful (1). However, although countershock may terminate VF, asystole and cardiac rhythms not associated with arterial pressure pulses (pulseless electrical activity [PEA]) follow countershock in approximately 60% of patients receiving out-of-hospital ACLS (2,3). These postcountershock rhythms are almost always fatal. The mechanism for these countershock outcomes is unknown, but it may be related to the duration of cardiac arrest and global myocardial ischemia, the limited coronary flow produced by conventional cardiopulmonary resuscitation (CPR) (which is often performed before countershock) or the effects of countershocks themselves on myocardial ultrastructure and function.

Attempts to improve countershock outcome have largely focused on decreasing the time to initial countershock. Recently, attention has been directed toward assessing the benefit of nontraditional defibrillation waveforms on countershock outcome. Biphasic waveforms, the standard for implantable cardioverter-defibrillators, have been tested in animals and in selected patient populations after extremely brief (<20 s) episodes of induced VF (4–7). Low-energy (150 J) biphasic waveforms have been shown to be as effective as higher-energy (200 J) monophasic waveforms in terminating VF of such short duration. In addition, low-energy biphasic waveforms result in fewer electrocardiographic (ECG) abnormalities, specifically ST segment elevation or depression, when compared with conventional monophasic defibrillation (7,8). These ECG abnormalities have been used as a surrogate marker of myocardial injury.

Transthoracic biphasic countershock has not been well studied in the setting of prolonged VF, the scenario most commonly encountered in clinical practice (9). The purpose of this study was to compare monophasic and biphasic defibrillation waveforms in a swine model of VF of 5-min duration. Four different existing definitions of successful defibrillation were selected as primary outcome variables.
METHODS

This study followed the National Institutes of Health guidelines for the use of laboratory animals in biomedical research and was approved by the Animal Resource Center and Animal Utilization Committee of our institution.

Male and female domestic swine (26 kg to 36 kg) were sedated with a single intramuscular injection of telazol (4 mg/kg) and xylazine (2 mg/kg). After endotracheal intubation, ventilation was performed with 50% oxygen and 50% nitrous oxide, and anesthesia was maintained with inhaled isoflurane (mean alveolar concentration 0.5% to 1.5%). Minute ventilation was adjusted to maintain an arterial pO₂ >200 mm Hg, pCO₂ of 35 mm Hg to 45 mm Hg and an arterial pH of 7.35 to 7.45.

A carotid artery, both external jugular veins and a femoral artery were surgically exposed, and micromanometer-tipped catheters (Millar Instruments, Houston, Texas) were inserted and positioned in the right atrium, left ventricle (LV) and aortic arch for pressure monitoring and blood withdrawal. The tip of a bipolar pacing catheter was positioned in contact with the right ventricular endocardium for induction of VF. A thermistor-tipped thermodilution cardiac output catheter was positioned in a branch of the pulmonary artery. Catheter tip positions were confirmed fluoroscopically. Standard lead II of the surface ECG was monitored during instrumentation and throughout the study protocol. Self-adhesive, nonpolarized, defibrillation electrodes, each with an active surface area of 108 ± 2 cm², were applied to the shaved thorax in an anterior-anterior position.

Study protocol. After instrumentation, control heart rate, mean arterial pressure, peak LV pressure, first derivative of left ventricular pressure (LV dP/dt) and cardiac output (CO) were recorded, and arterial blood was analyzed (I-Stat EG7+, I-Stat Corp, Princeton, New Jersey). Animals were randomized to one of two treatment groups via permuted block design. For group 1 animals, countershocks were performed using a monophasic truncated exponential waveform. This waveform was defined by the discharge of a 200 μF capacitor and was designed to operate across a range of resistance values. The 360 J waveform has a leading-edge voltage of 2,000 V to 2,400 V and a duration of 5 ms to 15 ms of the range of resistance values. A schematic representation of the voltage/time curve for the monophasic waveform is shown in Figure 1. Group 2 animals received countershocks with a commercially available, low-energy (150 J) biphasic truncated exponential waveform (ForeRunner, HeartStream Corporation, Seattle, Washington). This defibrillator dynamically adjusts the shock pulse width (duration) based on the impedance measured at the time of the shock. Current is determined passively by Ohm’s law. A schematic representation of the biphasic waveform is presented in Figure 2.

The countershock sequence was designed to follow current guidelines that call for an initial sequence of three “stacked” shocks. The energy doses for group 1 animals were 200 J, then 300 J, followed by 360 J, if VF persisted. Group 2 animals were shocked three times, if necessary, at a fixed energy of 150 J.

After instrumentation and randomization, a 60 Hz AC current pulse was delivered via the pacing catheter to induce VF. After 5 min of VF without CPR, countershock was performed in sequence to a maximum number of three if VF persisted. The postshock rhythm and arterial pressure were recorded and analyzed for a minimum 10 s after each shock.

If countershock terminated VF but resulted in a nonperfusing spontaneous cardiac rhythm defined as systolic arterial

![Figure 1. Voltage versus time plot for monophasic waveform.](image1)

![Figure 2. Voltage versus time plot for biphasic waveform.](image2)
pressure <50 mm Hg, or, if VF persisted after the first three shocks, manual CPR was begun with the animal in the supine position. Chest compressions were performed at a rate of 80 to 100 compressions/min with force sufficient to depress the sternum 1.5 to 2.0 inches. Ventilations were performed at a rate of 15/min using a tidal volume equal to the biphasic waveform; MAP = mean arterial pressure (mm Hg); MTE = monophasic truncated exponential waveform; PLVP = peak left ventricular pressure (mm Hg); wt = weight in kilograms.

Outcome measurements. The following variables were compared between groups: 1) first shock success, defined as termination of VF regardless of postshock rhythm, 2) defibrillation success (termination of VF) with three or fewer countershocks, 3) frequency of a sustained perfusing rhythm (systolic arterial pressure >50 mm Hg) observed within 10 min of the first countershock, the animal was considered a resuscitation failure, and the experiment was terminated.

Statistical analysis. Data analysis was performed using SAS version 6.12 (SAS Institute Inc., Cary, North Carolina) and Planning and Evaluation of Sequential Trials (10). The primary end point of the study, first shock defibrillation success, was designed to be analyzed using the sequential method of Whitehead (11,12). This method allows a reduction in the expected sample size for a trial while yielding well-defined risks for both type I and type II errors.

The study was designed to have a statistical power of 0.80 to detect a 25% absolute change in first shock success rate with the biphasic waveform, with a two-tailed alpha of 0.05. The odds ratio (OR) with the associated 95% confidence interval, adjusted for the bias introduced by the sequential stopping rule (13), was used as the measure of treatment efficacy. Data were analyzed at intervals (after every four animals), and the study stopped when the defined stopping boundary was crossed.

The mean and standard deviation for interval data were calculated and were compared using the nonparametric Wilcoxon rank-sum test. The Fisher exact test was used to assess differences in postshock rhythms. A maximum p value of 0.05 was considered statistically significant.

RESULTS

Control values for group 1 and group 2 animals are shown in Table 1. There were no statistically significant differences in measured prearrest hemodynamic variables.

As shown in Figure 3, the trial was terminated after 38 animals were randomly allocated to the study groups and equivalance with respect to first shock success (termination of VF) was demonstrated. Countershock after 5 min of VF resulted in termination of VF after the first shock in 61% of group 1 animals and 50% of group 2 animals (Table 2). The number of animals defibrillated after the second, third or more shocks is also shown in Table 2. The OR of terminating VF with the first biphasic shock versus the first

<table>
<thead>
<tr>
<th>WT (group 1)</th>
<th>MAP</th>
<th>PLVP</th>
<th>LVEDP</th>
<th>CO</th>
<th>LV dP/dt</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTE (group 1)</td>
<td>29.2 ± 3.9</td>
<td>76 ± 16</td>
<td>98 ± 17</td>
<td>7 ± 4</td>
<td>2.68 ± 0.65</td>
</tr>
<tr>
<td>BTE (group 2)</td>
<td>29.2 ± 3.7</td>
<td>83 ± 14</td>
<td>104 ± 14</td>
<td>7 ± 4</td>
<td>3.01 ± 0.80</td>
</tr>
</tbody>
</table>

Table 1. Control Hemodynamic Values for Study Groups

Significant differences were not observed between groups.

WT = weight in kilograms; MAP = mean arterial pressure (mm Hg); MTE = monophasic truncated exponential waveform; PLVP = peak left ventricular pressure (mm Hg); LVEDP = left ventricular end-diastolic pressure; CO = cardiac output (L/min); LV dP/dt = first derivative of left ventricular pressure (mm Hg/s); MAP = mean arterial pressure (mm Hg); MTE = monophasic truncated exponential waveform; PLVP = peak left ventricular pressure (mm Hg); wt = weight in kilograms.
monophasic shock was 0.67 (95% confidence interval 0.18–2.49, p = 0.55).

Only two animals (11%) in the monophasic group and one (5%) in the biphasic group developed a spontaneous perfusing rhythm within 30 s of the first countershock and did not require CPR (p = 0.61, Fisher exact). An additional animal in the biphasic waveform group developed a spontaneous perfusing rhythm after the second shock and did not receive CPR. Three animals could not be resuscitated. One animal in the monophasic waveform group could not be defibrillated despite 17 shocks and 10 min of CPR. Two animals in the biphasic group could not be resuscitated. One of these animals developed PEA after the first shock and failed to respond to 10 min of CPR, and one animal developed asystole after the seventh shock and did not develop a spontaneous electrical rhythm during the 10 min CPR period. Thus, the resuscitation success rate (a sustained perfusing rhythm at any time after termination of VF) was not significantly different between groups.

An organized electrical rhythm without arterial pressure pulses (PEA) followed termination of VF in the remaining animals (Table 2). The incidence of PEA was not statistically different between waveform groups in those animals in which defibrillation was successful after one or more countershocks (15/18 group 1 and 18/20 group 2, p = 1.000, Fisher exact). Manual cardiopulmonary resuscitation duration before the appearance of a systolic arterial pressure >50 mm Hg was also not statistically different between groups for those animals that developed a perfusing rhythm (p = 0.79).

Mean arterial pressure, peak developed LV pressure, LV systolic dP/dt and CO for the two groups at 15 min, 30 min and 60 min after termination of VF in resuscitated animals are shown in Figure 4, panels A to D. Statistical differences in these hemodynamic variables were not observed at these time points.

**DISCUSSION**

There is currently no universally accepted definition of “successful defibrillation.” This deficiency, combined with inherent differences in the study populations (time to defibrillation, early CPR, etc.), has hampered comparisons of defibrillation waveforms in the small clinical series that have been reported. This problem has recently been reviewed and highlighted (9). Existing definitions of successful defibrillation include termination of VF with the first shock, termination of VF with three or fewer shocks, return of cardiac electrical activity after one or more shocks and organized electrical activity with a pulse at some time after shock. In this laboratory study, we included each of these definitions as primary outcome variables. We also sought to determine if: 1) there were differences between waveforms in the time required to restore a perfusing rhythm with CPR alone if countershock produced a cardiac rhythm without pulses and 2) the waveform resulted in differences in postresuscitation LV function.

**Table 2. Countershock Success After Five Minutes of Ventricular Fibrillation**

<table>
<thead>
<tr>
<th></th>
<th>CS 1</th>
<th>CS 2</th>
<th>CS 3</th>
<th>&gt;3 CS</th>
<th>PEA</th>
<th>CPR Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTE</td>
<td>11 (61%)</td>
<td>4 (22%)</td>
<td>0</td>
<td>2 (11%)</td>
<td>15 (83%)</td>
<td>186 ± 126</td>
</tr>
<tr>
<td>BTE</td>
<td>10 (50%)</td>
<td>6 (30%)</td>
<td>1 (5%)</td>
<td>3 (15%)</td>
<td>18 (90%)</td>
<td>182 ± 130</td>
</tr>
</tbody>
</table>

Differences between groups were not statistically significant. Countershock success was defined as termination of VF regardless of the resulting rhythm and the presence or absence of spontaneous perfusion.

BTE = biphasic truncated exponential waveform; CPR time = duration (s) of conventional manual CPR before perfusion restored; CS = countershock number; MTE = monophasic truncated exponential waveform; PEA = pulseless electrical activity after VF termination; VF = ventricular fibrillation.

**Figure 4. Hemodynamic values after resuscitation.** Mean arterial pressure (MAP) (Panel A), peak left ventricular pressure (PLVP) (Panel B), left ventricular dP/dt (Panel C) and thermodilution cardiac output (CO) (Panel D) during the 60 min postresuscitation observation period are depicted. Significant differences were not observed between defibrillation waveforms (monophasic n = 18 animals; biphasic n = 20 animals).
Countershock success. The findings of this study indicate that the first shock with a standard “high energy” (200 J) monophasic defibrillation waveform and a “low energy” (150 J) biphasic waveform are equivalent with respect to first shock success (termination of VF). Success with one of the first three defibrillation attempts and the likelihood of immediate return of a spontaneous perfusing rhythm were also similar. In addition, the rate of “failed” resuscitation (terminal PEA or VF) and degree of LV dysfunction over the 1 h immediately after restoration of spontaneous circulation were not different.

A spontaneous cardiac rhythm with arterial pressure fluctuations was infrequently encountered after the first shock in both study groups. The most common outcome, if the first shock terminated VF, was an escape rhythm not associated with arterial pressure fluctuations, so-called PEA. Such an outcome has been previously described with even briefer episodes of VF (3 min) (14,15). Successful defibrillation, if defined as termination of VF and immediate return of a perfusing rhythm, was observed in only 11% of monophasic shocks and 10% of biphasic shocks.

Nearly all animals in both groups required CPR before return of a spontaneous perfusing rhythm. Mean CPR times for the groups were not significantly different. These data suggest that immediate postcountershock contractile dysfunction was similar between groups and that lower-energy shocks did not offer an obvious advantage.

Postresuscitation ventricular function. The degree of ventricular dysfunction after return of circulation was not different between groups. Both groups demonstrated a nadir in developed peak LV pressure and LV dP/dt 30 min after the first countershock, which gradually improved but did not return to prearrest values. Inotropic agents were not administered during the recovery period. Similar degrees of postresuscitation LV contractile function suggest that the higher energy monophasic waveform did not produce greater thermal injury to the myocardium.

The potential benefits of the low-energy biphasic waveform were not observed in this study. Such benefits appear to be related to both the lower energy required for termination of VF as well as the morphology of the defibrillation waveform. In myocardial cell cultures, biphasic shock waveforms produce less membrane disruption (electroporation) and are followed by more rapid recovery of normal cell conductance (16–18). Lower energy biphasic shocks have been shown to produce less ST-segment elevation immediately after countershock and restoration of a spontaneous rhythm in patients with VF of short duration (<20 s) when compared with higher energy monophasic shocks with a damped-sine or truncated exponential waveforms (7,8). However, these ECG changes are transient in duration, and their significance is questionable (19). We did not specifically evaluate ST-segment changes after countershock and resuscitation in our 5-min VF model. It would have been difficult to differentiate ST-segment changes caused by global myocardial ischemia and low-flow myocardial perfusion produced by conventional CPR from those caused by countershock induced injury alone.

It has been suggested that biphasic shocks have fewer effects on myocardial oxidative metabolism and, therefore, result in less postshock cardiac mechanical dysfunction (20,21). The degree of cardiac dysfunction after biphasic shocks in this study, as well as the rate of recovery, was similar to that observed after monophasic defibrillation. In addition, the frequency of postcountershock PEA was similar in both groups, suggesting that low-energy shocks are not protective after prolonged VF.

Low energy countershocks. Although these potential advantages of biphasic waveform defibrillation were not observed in this study, neither was the potential disadvantage of a fixed-out, low-energy waveform, namely, the inability to increase energy, demonstrated to be a problem. The first shock defibrillation success rate was similar between the two study groups, and the number of animals successfully defibrillated with the second or third low-energy shock was not statistically different from the monophasic group in which shock energy was increased for subsequent rescue shocks. This finding supports the observations of others who have evaluated monophasic and biphasic waveforms in other animal models of prolonged VF. Walcott and co-workers (22) measured defibrillation threshold in canines after 180 s of VF followed by 2 min of femoral-femoral cross-circulation at a flow rate approaching that reported for conventional closed-chest CPR. The threshold was significantly lower for the biphasic waveform being evaluated. Although the biphasic waveform evaluated by Walcott was slightly different from the one used in this study, it is likely that the defibrillation threshold in our animal preparation was substantially below the 150 J output of the biphasic defibrillation device used in our study. Halperin et al. (23) observed a similarly lower defibrillation threshold in swine subjected to multiple shocks during resuscitation studies. Animals used in the Halperin study were approximately the same body weight as the swine used in our study. It can be assumed that transthoracic impedance was also similar. The concern about energy reserve may be more theoretical than real in models of prolonged VF.

Study limitations. The 5-min VF duration and resuscitation method used in this study was selected to replicate a clinical scenario likely to be encountered in bystander (public access) defibrillation. Recognition and confirmation of cardiac arrest, emergency medical services activation via 911 access, locating an automated defibrillation device and transporting it to the patient, applying the defibrillation electrodes, activating the defibrillator and eventual countershock may require up to 5 min (24). If automated defibrillation results in a nonperfusing rhythm, as was almost always observed in this study, only basic life support with conventional cardiopulmonary resuscitation will be available to the lay rescuer after countershock. Although epinephrine, if given before or after countershock, would probably have decreased the time required to restore a perfusing rhythm, it
would not be available to the lay rescuer. Epinephrine has also been shown to adversely affect ventricular function after resuscitation (25). It was anticipated that epinephrine therapy during resuscitative efforts would have confounded the assessment of LV function during the 1-h postresuscitation observation period and would also have increased the likelihood of spontaneous refibrillation, necessitating additional countershocks after the first rescue shocks.

Although we observed no differences between the monophasic and biphasic waveforms with respect to the selected outcome variables, some differences are apparent at shorter VF duration (15 to 90 s). However, VF of such short duration is infrequently encountered in the setting of out-of-hospital sudden cardiac death. The methods used in this study to assess cardiac function after countershock provide only global, but clinically relevant, measures of myocardial contractile function. Segmental function was not evaluated, nor were histologic comparisons made for the study waveforms. Regarding the size of the treatment effect sought by the study design, reducing the treatment effect sought—from 25% to 10%—would require a sample size approximately six times the current design. Considering the accepted utility of the monophasic waveforms, we felt that the use of additional animals could not be justified, because there is no need to demonstrate that the two waveforms are exactly equivalent, only that there is not a substantial difference in efficacy between them. If, by contrast to the results actually obtained, there had been a trend toward improved efficacy with the biphasic waveform, a larger study designed to obtain adequate power to detect a smaller difference in efficacy (e.g., 10%) would be indicated (26). A monophasic truncated exponential waveform was compared with the biphasic truncated exponential waveform. It is uncertain whether similar findings would be observed if a monophasic damped sine waveform, used most frequently in clinical care, had been used. The shock strengths used in this study were those recommended for adult patients and may have accentuated the observed changes in postresuscitation ventricular function.

Conclusions. Whether there are important differences between defibrillation waveforms for VF durations >5 min in animal cardiac arrest models and the clinical population remain to be determined. A single animal study assessing 1 h outcome after 8 min of unsupported VF has demonstrated no significant difference between a monophasic and biphasic waveform (27). Defining defibrillation success in meaningful terms acceptable to the medical community should precede studies of more prolonged VF. Considering the frequency with which countershock with either waveform was followed by a nonperfusing rhythm after VF termination, it would seem prudent that the lay bystander with access to an automated defibrillator using either waveform be well trained in basic CPR to facilitate resuscitation from postcountershock PEA. A recent clinical study suggests that CPR preceding countershock of prolonged VF may decrease the likelihood of a nonperfusing rhythm after countershock (28).

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