Electrode System Influence on Biphasic Waveform Defibrillation Efficacy in Humans

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**Background.** Several clinical studies have demonstrated a general superiority of biphasic waveform defibrillation compared with monophasic waveform defibrillation using epicardial lead systems. To test the breadth of utility of biphasic waveforms in humans, a prospective, randomized evaluation of defibrillation efficacy of monophasic and single capacitor biphasic waveform pulses was performed for two distinct nonthoracotomy lead systems as well as for an epicardial electrode system in 51 cardiac arrest survivors undergoing automatic defibrillator implantation.

**Methods and Results.** The configurations tested consisted of a right ventricular–left ventricular (RV-LV) epicardial patch-patch system, an RV catheter–chest patch (CP) nonthoracotomy system, and a coronary sinus (CS) catheter–RV catheter nonthoracotomy system. For each configuration, the defibrillation current and voltage waveforms were recorded via a digital oscilloscope to measure defibrillation threshold voltage, current, resistance, and stored energy. Biphasic waveform defibrillation proved more efficient than monophasic waveform defibrillation for the epicardial RV-LV system (4.8±4.1 versus 6.7±4.9 J, p=0.047) and the nonthoracotomy RV-CP system (23.4±11.1 versus 34.3±10.4 J, p=0.0042). Biphasic waveform defibrillation thresholds were not significantly lower than monophasic waveform defibrillation thresholds for the CS-RV nonthoracotomy system (15.6±7.2 versus 20.0±11.5 J, p=0.11). Biphasic waveform defibrillation proved more efficacious than monophasic waveform defibrillation in 13 of 20 patients (65%) with RV-LV epicardial patches, 10 of 15 patients (67%) with an RV-CP nonthoracotomy system, and nine of 16 patients (56%) with an RV-CS nonthoracotomy system.

**Conclusions.** Biphasic pulsing was useful with nonthoracotomy lead systems as well as with epicardial lead systems. However, the degree of biphasic waveform defibrillation superiority appeared to be electrode system dependent. Furthermore, for a few individuals, biphasic waveform defibrillation proved less efficient than monophasic waveform defibrillation, regardless of the lead system used. (*Circulation* 1991;84:665–671)

Nonthoracotomy defibrillation in humans has proven to require higher energy levels than epicardial defibrillation.1,2 Any tool that makes defibrillation with a nonthoracotomy lead system easier will improve the likelihood that open-chest surgery can be avoided when implantable defibrilla-


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hospital cardiac arrest immediately before or during implantation of an automatic cardioverter-defibrillator. A total of 51 patients were studied. Fifty-nine patients were initially considered for the study, but eight patients were excluded from the protocol because the additional risk of the protocol was deemed excessive.

In 20 patients, biphasic and monophasic defibrillation pulses were delivered using epicardial patch electrodes (model 0041, CPI) with one over the anterior right ventricle and one over the posterolateral left ventricle (Figure 1, left). In 15 patients, biphasic and monophasic waveform defibrillation was studied using a right ventricular–chest patch (RV-CP) nonthoracotomy system (Figure 1, center). In 16 patients, biphasic and monophasic defibrillation pulses were delivered between a coronary sinus (CS) and an RV catheter electrode system (Figure 1, right). Details of the two nonthoracotomy systems and the epicardial system have been described previously.\(^1\),\(^2\),\(^4\)

All epicardial defibrillation testing was performed when the patient was normothermic and off of cardiopulmonary bypass. All nonthoracotomy testing was performed with the chest closed immediately before performance of the sternotomy or thoracotomy required for standard epicardial defibrillator implantation. Ventricular fibrillation was initiated with 60-Hz alternating current via epicardial pacing/sensing leads for epicardial defibrillation testing and via the RV endocardial catheter for nonthoracotomy defibrillation testing. The initial defibrillation pulse waveform—monophasic or biphasic—was chosen randomly for each patient. Polarity was maintained constant for each configuration throughout the study.\(^5\) During defibrillation pulsing, the voltage and current waveforms were monitored using two Tektronix AM502 differential preamplifiers and two Tektronix 2230 digitizing oscilloscopes, which, in combination with an IBM-AT compatible computer, enabled on-line storage and analysis of waveforms.\(^6\)

The first attempt at defibrillation occurred 10 seconds after the onset of ventricular fibrillation regardless of which waveform was tested and regardless of which lead system was used.\(^7\) The external pulse generator used (model 2394, Medtronic) had a 120-\(\mu\)F capacitor and was capable of delivering 65\% tilt, truncated exponential monophasic or biphasic waveform pulses. In the case of biphasic pulsing, the tilt of both the initially positive phase and the subsequent negative phase of the biphasic pulse was 65\%.\(^4\) The monophasic 65\% tilt, 120-\(\mu\)F waveform chosen for study was selected to conform to that available in implantable defibrillators. The biphasic waveform chosen for study was asymmetric and simulated the output available from a single capacitor circuit where the leading edge voltage of the negative phase equaled the trailing edge voltage of the positive phase. The negative phase started 0.2 msec after termination of the positive phase. The single-capacitor biphasic waveform was specifically chosen instead of a double-capacitor biphasic waveform because it could reduce the size of an implantable defibrillator.

In the case of epicardial defibrillation, the defibrillation protocol began with a 400-V leading edge voltage setting on the pulse generator. This voltage resulted in an approximately 10-J stored energy pulse regardless of waveform shape. If the initial 400-V leading edge voltage was unsuccessful, a rescue pulse was delivered quickly to restore normal sinus rhythm. A minimum of 3 minutes elapsed before ventricular fibrillation was reinduced. The pulse amplitude setting was then increased by 100 V to 500 V (approximately 15 J stored energy) for the next ventricular fibrillation episode. If the initial 400-V pulse was successful, then pulse amplitude was decreased by 50 V to 350 V (approximately 7.5 J stored energy). Adjustments in pulse amplitude were made in 100-V increments between pulse generator settings of 400 V to 700 V (the maximum used with our epicardial
patients) and in 50-V steps for pulse generator settings of less than 400 V. The defibrillation threshold was defined as the lowest pulse amplitude that could successfully terminate ventricular fibrillation 10 seconds after its initiation.

For nonthoracotomy defibrillation protocols, the same method for determining the defibrillation threshold was used as described for epicardial defibrillation. However, the initial pulse strength chosen to determine the defibrillation threshold was 600 V (approximately 20 J stored energy). Also, the maximum voltage setting was 800 V. If this proved unsuccessful, the defibrillation threshold was arbitrarily and conservatively set at 900 V for purposes of comparative data analysis but was excluded during calculations of percent efficacy curves. This occurred with one patient in the CS-RV protocol in two patients in the RV-CP protocol, all during monophasic pulsing only. Application of voltages of 900 V or more was avoided because of concerns over tissue injury. As with epicardial defibrillation protocols, a minimum of 3 minutes elapsed between inductions of ventricular fibrillation. Rescue pulses for nonthoracotomy defibrillation studies were provided by a hybrid R2 anteroposterior CP system (Darox Corp.) connected to an independent defibrillator power source (Physio-Control LifePak 5). After defibrillation thresholds were determined with the initial monophasic or biphasic waveform, the defibrillation threshold was determined for the alternate waveform. Each patient served as his or her own control. It should be acknowledged that regardless of the lead system used, defibrillation thresholds could not be measured probabilistically because of the clinical limitations of repetitive ventricular fibrillation induction and termination in patients.

Statistical analysis of the data was performed using paired Student's t tests. Defibrillation efficacies for the monophasic and biphasic waveforms were compared for leading edge voltage, leading edge current, resistance, and stored energy at defibrillation threshold values for each of the current pathways examined. Percent efficacy curves were then calculated for each waveform and for each lead system examined.

### Results

The clinical data are summarized in Table 1 for all three sets of patients. Of the 51 patients studied, 35 were men and 16 were women. Mean patient age was 56±12 years. Nineteen patients had coronary artery disease, 20 patients had cardiomyopathies, five had a combination of coronary artery disease and cardiomyopathy, four had primary electrical disease, one had long QT syndrome, and two had a combination of coronary artery disease and valvular disease. Mean ejection fraction was 0.41±0.19. Up to the time of defibrillation testing, amiodarone had been administered chronically to three patients, disopyramide to two patients, and flecainide to one patient. There were no statistical differences in sex, age, body weight, structural heart disease, or ejection fraction among the three groups studied. The defibrillation threshold voltage, current, resistance, and stored energy data are detailed in Table 2.

In the case of epicardial defibrillation with the RV-LV patch-patch system, 13 of 20 patients (65%) had a lower defibrillation threshold when the biphasic pulse was used. Mean leading edge defibrillation

### Table 1. Clinical Data

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients (n)</th>
<th>Sex (M/F)</th>
<th>Body weight (kg)</th>
<th>Age (mean±SEM years (range))</th>
<th>CAD/ non-CAD disease</th>
<th>Clinical arrhythmia (VF/VT)</th>
<th>LV ejection fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epi: RV-LV</td>
<td>20</td>
<td>15/5</td>
<td>77±10</td>
<td>57±15 (30-74)</td>
<td>11/9</td>
<td>19/2</td>
<td>0.39±0.18</td>
</tr>
<tr>
<td>NT: RV-CP</td>
<td>15</td>
<td>11/4</td>
<td>83±18</td>
<td>54±12 (24-73)</td>
<td>7/8</td>
<td>14/1</td>
<td>0.45±0.20</td>
</tr>
<tr>
<td>NT: CS-RV</td>
<td>16</td>
<td>9/7</td>
<td>77±11</td>
<td>55±11 (30-81)</td>
<td>6/10</td>
<td>14/2</td>
<td>0.41±0.20</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>35/16</td>
<td>79±14</td>
<td>56±12 (24-81)</td>
<td>24/27</td>
<td>47/4</td>
<td>0.41±0.19</td>
</tr>
</tbody>
</table>

CAD, coronary artery disease; VF, ventricular fibrillation; LV, left ventricular; Epi, epicardial; RV, right ventricular; VT, ventricular tachycardia; NT, nonthoracotomy; CP, chest patch; CS, coronary sinus.

### Table 2. Defibrillation Threshold Data

<table>
<thead>
<tr>
<th>Current pathway</th>
<th>Voltage (V) MP</th>
<th>Current (A) MP</th>
<th>Resistance (Ω) MP</th>
<th>Stored energy (J) MP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BP</td>
<td>BP</td>
<td>BP</td>
<td>BP</td>
</tr>
<tr>
<td>Epicardial: RV-LV</td>
<td>316±110</td>
<td>262±107</td>
<td>8.2±3.7</td>
<td>41±11</td>
</tr>
<tr>
<td></td>
<td>0.022</td>
<td>0.069</td>
<td>0.35</td>
<td>34.3±10.4</td>
</tr>
<tr>
<td>Nonthoracotomy: RV-CP</td>
<td>74±124</td>
<td>608±148</td>
<td>10.9±3.8</td>
<td>73±16</td>
</tr>
<tr>
<td></td>
<td>0.0051</td>
<td>0.062</td>
<td>0.62</td>
<td>0.0042</td>
</tr>
<tr>
<td>Nonthoracotomy: CS-RV</td>
<td>556±162</td>
<td>495±124</td>
<td>9.5±3.2</td>
<td>59±8</td>
</tr>
<tr>
<td></td>
<td>0.11</td>
<td>0.092</td>
<td>0.52</td>
<td>0.11</td>
</tr>
</tbody>
</table>

MP, monophasic; BP, biphasic; RV, right ventricular; LV, left ventricular; CP, chest patch; CS, coronary sinus; ↓, decrease; ↑, increase; NC, no change.
threshold voltage was significantly lower with the biphasic pulse than with the monophasic pulse (262±107 versus 316±110 V). This represents a 17% decrease in voltage with the biphasic pulse ($p=0.022$; Figure 2, top panel). Mean leading edge defibrillation threshold current was 8.2±3.7 A with the monophasic pulse and 6.9±3.8 A with the biphasic pulse, a 16% decrease in current with the biphasic pulse ($p=0.069$). The leading edge resistance at the defibrillation threshold was 41±11 Ω for the monophasic pulse and was unchanged at 41±10 Ω for the biphasic pulse ($p=0.35$). The stored energy defibrillation threshold for epicardial defibrillation was 6.7±4.9 J when the monophasic pulse was used and 4.8±4.1 J (28% less) when the biphasic pulse was used ($p=0.047$; Figure 3, top panel). The pulse width for the monophasic 65% tilt waveforms was 5.9±1.5 msec. The pulse width for the biphasic 65% tilt waveforms was 5.9±1.4 msec for the first phase and 5.7±1.3 msec for the second phase.

For the RV-CP nonthoracotomy lead system, 10 of the 15 patients (67%) had a lower defibrillation threshold with the biphasic phase. Mean leading edge defibrillation threshold voltage was significantly lower with the biphasic pulse than with the monophasic pulse (608±148 versus 746±124 V, an 18% decrease; $p=0.0051$; Figure 2, middle panel). Mean leading edge defibrillation threshold current was 10.9±3.8 A with the monophasic pulse and 8.9±4.0 A (18% less) with the biphasic pulse ($p=0.0062$). Resistance was 73±16 and 74±17 Ω for the monophasic and biphasic pulses, respectively ($p=0.62$). The stored energy defibrillation threshold for the RV-CP nonthoracotomy system was

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**FIGURE 2.** Plots of delivered leading edge voltage at defibrillation threshold for both monophasic (MP) and biphasic (BP) pulses for three electrode configurations examined. Top, middle, and bottom panels: Paired data for epicardial right ventricular–left ventricular (RV-LV), nonthoracotomy RV–chest patch (RV-CP), and nonthoracotomy coronary sinus–RV (CS-RV) systems, respectively.

**FIGURE 3.** Plots of stored energy at defibrillation threshold for both monophasic (MP) and biphasic (BP) pulses for three electrode configurations examined. Top, middle, and bottom panels: Paired data for epicardial right ventricular–left ventricular (RV-LV), nonthoracotomy RV–chest patch (RV-CP), and nonthoracotomy coronary sinus–RV (CS-RV) systems, respectively.
34.3±10.4 J with the monophasic pulse and 23.4±11.1 J with the biphasic pulse, a 32% decrease (p=0.0042; Figure 3, middle panel). The pulse width for the monophasic 65% tilt waveforms was 10.3±2.0 msec. The pulse width for the biphasic 65% tilt waveforms was 10.2±2.0 msec for the first phase and 10.4±2.0 msec for the second phase.

For the CS-RV nonthoracotomy system, nine of the 16 patients (56%) had a lower defibrillation threshold with the biphasic pulse. There was no statistically significant difference in defibrillation efficacy with the two waveforms for this particular lead system. However, a trend in favor of biphasic waveform pulsing was evident. The mean leading edge defibrillation threshold voltage was 556±162 V when the monophasic pulse was used and 495±124 V (11% less) when the biphasic pulse was used (p=0.11; Figure 2, bottom panel). The mean leading edge defibrillation threshold current was 9.5±3.2 A when the monophasic pulse was used and 8.5±2.8 A (11% less) when the biphasic pulse was used (p=0.092).

Resistance for the monophasic pulse was 59±8 Ω and was essentially unchanged at 60±8 Ω for the biphasic pulse (p=0.52). The stored energy defibrillation threshold for the CS-RV nonthoracotomy lead system was 20.0±11.5 J when the monophasic pulse was used and 15.6±7.2 J (22% less) when the biphasic pulse was used (p=0.11; Figure 3, bottom panel). The pulse width for the monophasic 65% tilt waveforms was 8.6±1.2 msec. The pulse width for the biphasic 65% tilt waveforms was 8.6±1.2 msec for the first phase and 9.0±1.1 msec for the second phase.

Percent defibrillation efficacy as a function of stored energy for each of the three lead systems used for both monophasic and biphasic pulses is shown in Figure 4. In this figure, percent efficacy for each lead system was referenced to a 15-J stored energy value.

A 15-J reference value was chosen because it marks a 2:1 safety margin for a 30-J device. At the 15-J limit for monophasic pulses, the epicardial RV-LV patch-patch system was efficacious in 95% of patients, the RV-CP nonthoracotomy system was efficacious in 7% of patients, and the CS-RV nonthoracotomy system was efficacious in 44% of patients. For biphasic pulses at the 15-J stored energy level, the epicardial patch-patch system was 90% efficacious, the RV-CP nonthoracotomy system was 20% efficacious, and the CS-RV nonthoracotomy system was 44% efficacious. If either waveform was considered, percent efficacy at 15 J for the epicardial RV-LV patch-patch lead system, RV-CP nonthoracotomy lead system, and CS-RV nonthoracotomy system would increase to 95%, 27%, and 60%, respectively. Percent efficacy curves for defibrillation as a function of leading edge voltage are shown in Figure 5.

It is important to note that several patients had actual defibrillation thresholds measured between 800 and 900 V even though the defibrillator was maximally set to 800 V. These cases all occurred in the RV-CP protocol—four during monophasic pulsing and two during biphasic pulsing. Although the pulse generator was set at 800 V, voltage values of 850, 822, 826, and 844 V were measured during monophasic pulsing, and values of 860 and 854 V were measured during biphasic pulsing. Intrinsic variances in pulse generator output caused leading edge voltage values to vary from the setting value of 800 V. These findings confirm the need to record the voltage and current waveforms oscilloscopically. Three patients did not defibrillate with the 800-V defibrillator setting. Two were in the RV-CP protocol during monophasic testing only, and one was in the CS-RV protocol during monophasic testing only. An arbitrary defibrillation threshold value of 900 V was used in Figure 2 (and the corresponding energy values in Figure 3) for illustrative purposes to show the minimum deviation from biphasic waveform defibrillation thresholds observed for these three indi-
Discussion

The results of the present study indicate that biphasic pulse defibrillation is useful for nonthoracotomy lead systems as well as for epicardial lead systems. However, biphasic pulse defibrillation is not more efficacious than monophasic pulse defibrillation for every lead configuration or for every patient. In earlier research, we demonstrated substantial patient-to-patient variability in defibrillation efficacy when examining four distinct nonthoracotomy pulsing techniques, including monophasic, biphasic, sequential, and simultaneous dual-pathway pulsing in each of 12 patients receiving implantable defibrillators. Both of these studies infer that improvements in defibrillation efficacy from the use of any particular lead system, waveform, or pulsing technique cannot be assumed as a matter of course. Nevertheless, biphasic waveform defibrillation provides options for improving defibrillation, particularly with some forms of transvenous defibrillation and in some patients with high defibrillation thresholds, that would not be present if only monophasic pulses were used.

The first clinical study to examine biphasic waveform defibrillation was undertaken by Winkle et al. In their study, the lead system was restricted to two epicardial patches, and the biphasic waveform had a second phase substantially smaller in amplitude than that used in our study. In the 21 patients examined, biphasic epicardial defibrillation proved only moderately superior to monophasic waveform defibrillation with the advantage manifest at low pulsing energies rather than at high. This is in contrast with our study in which biphasic pulsing could be superior to monophasic pulsing over a wide range of energies. The lack of improved efficacy with biphasic pulsing at the higher energies in the study of Winkle et al may have been a result of the waveform shape selected. In animal studies using epicardial patches or nonthoracotomy RV-CP lead systems, lower defibrillation thresholds have consistently been shown to occur with biphasic pulses that have negative phases containing approximately 10% of the energy of the positive phase. The choice of waveform in our study conforms with these findings and may explain the differences in outcome between our study and that of Winkle et al, at least with regard to epicardial defibrillation. On the other hand, it must be acknowledged that the differences in outcome may simply reflect differences in patient populations given that both study groups were relatively small.

The influence of waveform shape on defibrillation efficacy, whether biphasic or monophasic, is not well understood. One possible explanation is that cellular excitation is dependent on the frequency content of the exciting pulse. Frequency-dependent characteristics of transmembrane ionic transmission have been identified. For example, at very high voltages, static direct current fields can force depolarization. However, at low voltages, cellular depolarization becomes more dependent on the exciting pulse’s frequency content. Frequency-dependent cellular excitation may vary from heart to heart, reflecting variations in cellular diseased processes or in anatomic substrate. These considerations may account for certain waveforms defibrillating better than others in the same patient.

There are other possible explanations for the improved defibrillation efficacy often seen with biphasic pulses. Biphasic shocks may be able to excite a greater mass of tissue given the observation that biphasic pulses have a lower excitation threshold for myocardial cells that are exposed to a high extracellular potassium concentration, which may occur during ventricular fibrillation. The ability to excite greater quantities of tissue may also increase the excitable gap during which biphasic pulses can interrupt the reentrant or “wavelet” pathways responsible for sustenance of fibrillation. A lower excitation threshold would lower the defibrillation threshold under either the “critical mass” or the “upper limit of vulnerability” hypothesis of defibrillation.

Another explanation for the superiority of biphasic shocks is the suppression of postshock ectopic beats after unsuccessful defibrillation. Zhou et al reported that in approximately 80% of their unsuccessful episodes, the first postshock activation is an ectopic beat in the region of low-voltage gradient. Because biphasic shocks have a much greater stabilizing effect on the transmembrane potential gradient, their likelihood of inducing postshock-triggered ectopic activity may be less. The stabilizing effect of biphasic pulses has been demonstrated in the form of lower mechanical dysfunction after shock, less transient conduction block in the region of high-voltage gradient, and better defibrillation efficacy after long episodes of ventricular fibrillation.

Assessment of the results of this study extends beyond analysis of the mechanism of monophasic and biphasic waveform pulsing. Several limitations to this study, foremost of which is the small population size, might have influenced our findings. Relatively small patient numbers could have affected, in particular, the statistical significance of the monophasic-biphasic comparison for the CS-RV lead system. For this lead system, a few more patients may have resulted in a statistical outcome favoring biphasic pulsing. Furthermore, larger patient numbers might have revealed that the process of defibrillation was influenced by factors other than waveform or lead system (e.g., cardiac anatomy or disease process). The relatively small population size should not, however, negate the observation that individual response to defibrillation pulses varied significantly from the response of the group regardless of the lead system used.
A second possible limitation in this study was that the patients do not represent the population of cardiac arrest patients at large. The underlying structural heart disease in our patients was coronary artery disease in a minority of cases (24 of 27 patients). This reflects a conscious bias in the patient selection process that excluded individuals with borderline coronary artery perfusion from a rigorous research protocol. Thus, the defibrillation threshold data from this study, regardless of waveform or lead system used, may underestimate the energy requirements for defibrillation in the general population, who may more often be prone to the effects of concomitant ischemia than patients in the present study.

Additional study limitations are that only a single biphasic waveform was selected and only a limited number of lead systems could be examined. The vagaries of defibrillation are only likely to increase if one were to consider all of the waveform and lead system options available. Consequently, our findings can be expected to apply only to the waveforms and lead systems used in the present study.

Summary

Biphasic shocks often reduce defibrillation thresholds with nothoracotomy as well as epicardial lead systems. However, patient cardiothoracic anatomy, disease process, arrhythmogenic substrate, and lead system may affect biphasic pulsing efficacy in ways that are not understood. In individual patients, biphasic pulsing with certain lead systems can be equal to or inferior to monophasic waveform pulses. However, as a rule, the ability to use biphasic waveform defibrillation makes it more likely that a patient can be spared an open thoracic surgical procedure for placement of an implantable defibrillator and improve defibrillation in some patients who require epicardial lead systems.

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References


KEY WORDS • ventricular fibrillation • biphasic waveform • automatic cardioverter-defibrillator • sudden death
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