One-Shock Versus Three-Shock Defibrillation Protocol Significantly Improves Outcome in a Porcine Model of Prolonged Ventricular Fibrillation Cardiac Arrest

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Background—The success of resuscitation with a 1-shock versus the conventional 3-shock defibrillation protocol was investigated subject to the range of treatment variation imposed by automated external defibrillators (AEDs).

Methods and Results—Ventricular fibrillation was induced in 44 domestic pigs. After 7 minutes of untreated VF, animals were randomized among 4 groups representing all combinations of the 1- versus 3-shock protocol and 2 different AED regimens (AED1, AED2). Because few AEDs support a 1-shock protocol, manual defibrillators were used to replicate the AED treatment regimen: electrical waveform, dose sequence, and cardiopulmonary resuscitation (CPR) interruption intervals. Initial shock(s) were delivered, followed by 60 seconds of CPR, and the treatment was repeated until resuscitation was successful or for 15 minutes. The 1-shock protocol was associated with improved outcome, reducing CPR interruptions from 45% to 34% of total resuscitation time ($P=0.019$) and increasing survival from 64% to 100% ($P=0.004$). Survival was 91% for AED1 versus 36% for AED2 ($P=0.024$) with a 3-shock protocol but was increased to 100% for both by adoption of a 1-shock protocol. Improvements in postresuscitation left ventricular ejection fraction and stroke volume were observed with AED1 compared with AED2 (difference of means, 15% and 28% of baseline respectively, $P<0.001$) regardless of defibrillation protocol.

Conclusions—Adoption of a 1-shock versus a 3-shock resuscitation protocol improved survival and minimized outcome differences imposed by variations in AED design and implementation. When a conventional 3-shock defibrillation protocol was used, however, the choice of AED had a significant impact on resuscitation outcome. (Circulation. 2006;113:2683-2689.)

Key Words: arrhythmias ■ cardiopulmonary resuscitation ■ contractility ■ defibrillation ■ fibrillation ■ hemodynamics ■ resuscitation

Early defibrillation has an overriding impact on outcomes of out-of-hospital sudden cardiac arrest. In specific environments, early defibrillation with automated external defibrillators (AEDs) by lay providers has enabled improvements in the rate of initial resuscitation and survival to hospital discharge after sudden cardiac arrest. Therefore, these successes, however, have not been repeated in all response environments.

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Recent clinical studies have suggested that AED-imposed interruptions of cardiopulmonary resuscitation (CPR) that occur after initial defibrillation shocks may adversely affect patient outcomes. These concerns have been corroborated in laboratory experiments, especially with respect to the interval required for automated rhythm analysis and defibrillator charging between CPR and defibrillation shock. Furthermore, it has been reported that wide variations with respect to this interval exist among commercially available AEDs, and it has been postulated that the survival effect of “hands-off” interval variation among AEDs may far exceed any documented defibrillation efficacy differences.

Certain CPR interruptions (eg, hands-off delay between chest compressions and defibrillation shock) are imposed by the design and implementation of a particular defibrillator. Other interruptions, however, can be minimized by modifications of the resuscitation protocol. In particular, low CPR “duty cycle” (percentage of rescue time devoted to rescue breaths and chest compressions) has been linked to poor resuscitation outcome. Modification of the defibrillation protocol such that a single shock is delivered between each interval of CPR increases the CPR duty cycle by eliminating the need for postshock rhythm analysis and defibrillator charging intervals between multiple shocks. Depending on

Received September 29, 2005; revision received March 3, 2006; accepted April 10, 2006.

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Circulation is available at http://www.circulationaha.org DOI: 10.1161/CIRCULATIONAHA.105.592121
the AED model, this translates to ~15 to 75 seconds of hands-off time being removed between each interval of CPR. Such a protocol is now practical thanks to the high first-shock efficacy of biphasic waveforms.5,13–15 This study examined the hypothesis that wide variations in AED design, especially with respect to CPR interruption intervals, have a significant impact on resuscitation success. It also tested the hypothesis that a new 1-shock defibrillation protocol designed to increase the percentage of time devoted to ventilation and circulatory support would improve resuscitation outcomes and minimize the impact of AED design variations. To conduct the tests, 2 AEDs were selected that exemplify the extremes of short versus long CPR interruption intervals as reported by Snyder et al (Figure 1).12 Devices A (fastest) and F (next to slowest, device G being fully automatic) and therefore excluded) from that report were identified in Tables 1 and 2. Manual defibrillators were used in preference to AEDs for the delivery of defibrillation shocks because 1 of the representative AEDs could not be configured to deliver the desired 1-shock protocol. The manual defibrillators were manufactured by the same companies and delivered the same waveforms as the corresponding AEDs. Both waveforms are impedance compensating but differ significantly in other aspects, with AED1 using a low-capacitance, high-tilt waveform typical of low-energy, biphasic defibrillators, and AED2 using a high-capacitance, low-tilt waveform typical of high-energy, biphasic defibrillators (Table 1). For all groups, VF cardiac arrest was induced by application of an initial sequence of either 1 or up to 3 shocks. The shocks were delivered between the right infraclavicular electrode and the cardiac apex. In a controlled setting where the operator was blinded to the shock administration, the 1-shock protocol was delivered to the pigs for 200 J, 200-300-360 J, and 29-35-39 A, respectively, for AED1 and AED2, respectively. The shocks were delivered with a volume-controlled ventilator (model MA-1, Puritan-Bennett, Carlsbad, Calif). End-tidal PCO2 was monitored with an infrared analyzer (model 01R-7101A, Nihon Kohden Corp, Tokyo, Japan). Respiratory frequency was adjusted to maintain an end-tidal PCO2 between 35 and 40 mm Hg. For measurement of aortic pressure, a fluid-filled catheter was advanced from the left femoral artery to the thoracic aorta. For measurement of right atrial pressure, pulmonary arterial pressure, and blood temperature, a 7F, pentalumen, thermodilution catheter was advanced from the left femoral vein, and flow was directed into the pulmonary artery. For inducing ventricular fibrillation (VF), a 5F pacing catheter (EP Technologies, Inc, Mountain View, Calif) was advanced from the right cephalic vein into the right ventricle until an ECG current of injury was recorded. For measurement of left ventricular functions, a 5-MHz, single-plane with 5-MHz continuous-wave Doppler transesophageal echocardiographic transducer with 4-way flexure (model 21363A, Hewlett-Packard Co, Medical Products Group, Andover, Mass) was advanced from the incisor teeth into the esophagus for a distance of ~35 cm.

Animal Preparation
Male domestic pigs weighing between 38 and 42 kg were made to fast overnight with the exception of free access to water. Anesthesia was initiated by injection of ketamine (20 mg/kg IM) and completed by ear vein injection of sodium pentobarbital (30 mg/kg). Additional doses of sodium pentobarbital (8 mg/kg) were injected to maintain anesthesia at intervals of 1 hour. Auffed endotracheal tube was advanced into the trachea. Animals were mechanically ventilated with a volume-controlled ventilator (model MA-1, Puritan-Bennett, Carlsbad, Calif). Respiratory frequency was adjusted to maintain an end-tidal PCO2 between 35 and 40 mm Hg. For measurement of aortic pressure, a fluid-filled catheter was advanced from the left femoral artery to the thoracic aorta. For measurement of right atrial pressure, pulmonary arterial pressure, and blood temperature, a 7F, pentalumen, thermodilution catheter was advanced from the left femoral vein, and flow was directed into the pulmonary artery. For inducing ventricular fibrillation (VF), a 5F pacing catheter (EP Technologies, Inc, Mountain View, Calif) was advanced from the right cephalic vein into the right ventricle until an ECG current of injury was recorded. For measurement of left ventricular functions, a 5-MHz, single-plane with 5-MHz continuous-wave Doppler transesophageal echocardiographic transducer with 4-way flexure (model 21363A, Hewlett-Packard Co, Medical Products Group, Andover, Mass) was advanced from the incisor teeth into the esophagus for a distance of ~35 cm.

Experimental Procedures
Ten minutes before induction of cardiac arrest, the animals were randomized by the sealed-envelope method to 1 of the 4 groups identified in Tables 1 and 2. Manual defibrillators were used in preference to AEDs for the delivery of defibrillation shocks because 1 of the representative AEDs could not be configured to deliver the desired 1-shock protocol. The manual defibrillators were manufactured by the same companies and delivered the same waveform as the corresponding AEDs. Both waveforms are impedance compensating but differ significantly in other aspects, with AED1 using a low-capacitance, high-tilt waveform typical of low-energy, biphasic defibrillators, and AED2 using a high-capacitance, low-tilt waveform typical of high-energy, biphasic defibrillators (Table 1). For all groups, VF cardiac arrest was induced by application of an increasing AC current (1 to 2 mA) delivered to the right ventricle. Mechanical ventilation was discontinued once VF appeared. Resuscitation was attempted after 7 minutes of untreated VF by delivering an initial sequence of either 1 or up to 3 shocks. The shocks were delivered between the right infraclavicular electrode and the cardiac apex. If VF was not reversed after defibrillation shock(s), precordial compressions were performed for 60 seconds at a rate of 100 compressions per minute with a pneumatic, piston-driven chest compressor (Thumper, model 1000, Michigan Instruments, Grand Rapids, Mich). Although other methods are known to provide better circulation, this device is nonetheless superior to manual compressions and was used to ensure consistency between study groups. Coincident with the initiation of precordial compressions, the animal was mechanically ventilated with a tidal volume of 15 mL/kg and an

![Figure 1. AED-imposed interruption interval between CPR and subsequent defibrillation shock for 7 commercially available AEDs.12 Bar widths represent duration of voice instruction to stop CPR. Devices A–F are semiautomatic; device G is fully automatic.](image-url)
FiO2 of 1.0. Ventilations and precordial compressions were synchronized to provide a compression-ventilation ratio of 15:2 with equal compression-relaxation intervals, ie, a 50% duty cycle. To ensure consistency between the study groups, the compression force was adjusted to decrease the anterior-posterior diameter of the chest by \( \pm 25\% \) to control the coronary perfusion pressure within the range of 15 to 2 mm Hg. After 1 minute of precordial compression, another sequence of either 1 or up to 3 shocks was delivered. For groups assigned to the AED1 regimen, all shocks were delivered at a fixed dose of 150 J. For groups assigned to the AED2 regimen, dose was escalated after failed shocks in the sequence 200 to 300 to 360 J.

CPR interruption intervals were imposed for each group as illustrated in Figure 2 and described in Tables 1 and 2, the intervals being determined according to methods previously reported. The advantage of a 1-shock protocol is that an automated postshock rhythm analysis is not necessary, thereby shortening the hands-off interval after defibrillation shock and before initiation of CPR. This interval could not be measured for 1 of the AEDs because it was not possible to configure it for a 1-shock protocol. Instead, this interval was made equal for both AED1 and AED2, with the knowledge that the interval depends only on the time required to perform patient assessment (airway, breathing, circulation) and not on any other aspect of device design or performance.

Resuscitation was considered successful when an organized cardiac rhythm, accompanied by a mean aortic pressure >60 mm Hg, was restored for an interval of 5 minutes or more. The animal was pronounced dead when resuscitation remained unsuccessful at the end of a 15-minute attempt. Hemodynamic and left ventricular functions were monitored every 60 minutes for a period of 4 hours after resuscitation. After the panel of 4-hour postresuscitation measurements had been completed, the animals were returned to their cages and observed for an additional 68 hours. The animals were then euthanized by injection of 150 mg/kg IV pentobarbital. Autopsy was routinely performed for documentation of significant injuries to the bony thorax and the thoracic and abdominal viscera.

Measurements

The primary observations of this study were success of initial resuscitation, 72-hour postresuscitation survival, and postresuscitation myocardial function characterized by left ventricular ejection fraction (EF) and stroke volume (SV). Secondary observations included neurological alertness, shock efficacy, number of shocks required to resuscitate, number of VF episodes, total energy delivered, duration of resuscitation attempt, and percentage of time during which CPR was performed.

Myocardial function was measured by a transesophageal echo-Doppler technique developed by us for this porcine model. These measurements were obtained with the aid of a Hewlett-Packard Sonos 2500 echocardiographic system and a 5-MHz single-plane Doppler transesophageal echocardiographic transducer with 4-way flexure (model 21363A, Hewlett-Packard Co). For the long axis, a 2- or 4-chamber view was obtained. In a blinded review, left ventricular end-systolic and end-diastolic volumes were calculated by the method of disks (acoustic quantification technology, Hewlett-Packard). From these values, EF and SV were computed. These measurements served as quantifiers of myocardial contractile function. Transmural flow velocity was digitized on-screen, and the contour of Doppler spectral decay was traced.

Other measurements were recorded to test for population bias and to assist in consistent performance of the resuscitation protocol. Measurements of aortic and right atrial pressures allowed for estimation of coronary perfusion pressure. End-tidal CO2 was measured continuously to provide an indication of appropriate ventilation and as a quantitative indicator of relative pulmonary blood flow during precordial compression.

Hemodynamic data, including aortic, right atrial, pulmonary artery, and pulmonary occlusive pressures, end-tidal Pco2, and the lead 2 ECG, together with the digital output of the Hewlett-Packard acoustic quantification system, were continuously measured and recorded on a personal computer-based data acquisition system, supported by Computer Data Acquisition System (CODAS) as previously described. A total of 16 channels were provided for continuous recording at appropriate sampling frequencies for the studies proposed. Coronary perfusion pressure was digitally computed from the differences in time-coincident aortic and right atrial pressures and displayed in real time.

A quantitative neurological alertness score developed by our group was used for evaluating neurological recovery at 24-hour intervals for a total of 72 hours. Alertness was scored from 0 (unarousable coma) to 100 (fully alert). The alertness score was based on objective grading of the level of consciousness, respiration, posture, and food and water intakes.

Aortic and mixed venous blood gases, hemoglobin, and oxyhemoglobin were measured with a blood gas analyzer and a cooximeter (models 1306 and 482, Instrumentation Laboratory, Lexington, Mass) adapted for porcine blood. Arterial blood lactate level was measured with a lactic acid analyzer (model 23L, Yellow Springs Instruments, Yellow Springs, Ohio). These measurements were obtained 30 minutes before cardiac arrest and at hourly intervals after resuscitation for a total of 4 hours.

Analysis

All outcome variables were tested first for overall effect, ie, to reject the null hypothesis that all groups were the same. The Fisher-Freeman-Halton test was used for binomial variables, whereas the Kruskal-Wallis analysis of variance was used for continuous variables.

When a significant overall effect was detected \( (P<0.05) \), main factors (ie, AED regimen, choice of shock protocol) were tested for significance, and pairwise tests were performed between all groups. Fisher’s exact test was used for binomial variables, and the Wilcoxon Mann-Whitney test (with repeated measures as appropriate) was
used for continuous variables. All post hoc tests were corrected for multiple comparisons with the method of Bonferroni. All statistics were calculated with StatXact-6 and LogXact-6 software (Cytel Software Corp, Cambridge, Mass).

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

**Results**

A total of 44 experiments were completed. There were no prearrest differences in weight, baseline measurements of hemoglobin and oxyhemoglobin, blood gasses, arterial lactate, end-tidal CO₂, pulmonary arterial pressure, right atrial pressure, heart rate, coronary perfusion pressure, or neurological alertness score among the 4 groups. Similarly, there were no differences in baseline hemodynamic characteristics or myocardial function (Table 3).

Resuscitation characteristics and outcome variables are summarized in Table 4, with probability values for overall effect. Shock protocol was significantly associated with successful resuscitation ($P=0.019$), as was the choice of AED ($P=0.046$). The 1-shock protocol reduced CPR interruptions from 45% to 34% of total resuscitation time ($P=0.019$) and increased survival from 64% to 100% ($P=0.004$, 95% confidence interval of difference, 19% to 58%). Similarly, AED1 resulted in better overall survival than AED2: 95% versus 68% (95% confidence interval of difference, 4% to 51%, $P=0.022$). Between-group comparisons (Figure 3) reveal that with a 3-shock protocol, survival was better with AED1 than AED2 (91% versus 36%, $P=0.024$) but was increased to 100% for both by adoption of a 1-shock protocol. All resuscitated animals survived for >72 hours, with no differences in neurological alertness score among the 4 groups of survivors.

Myocardial function was reduced in all animals after successful resuscitation, with the degree of impairment significantly dependent on choice of AED but not shock protocol. For the same shock protocol, AED1 always produced significantly less myocardial dysfunction than did AED2 ($P=0.001$, Figure 4).

### TABLE 3. Baseline Characteristics for Study Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>AED1-1</th>
<th>AED1-3</th>
<th>AED2-1</th>
<th>AED2-3</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass, kg</td>
<td>39 (35-41)</td>
<td>37 (35-39)</td>
<td>35 (34-36)</td>
<td>38 (34-40)</td>
<td>0.31</td>
</tr>
<tr>
<td>Mean aortic pressure, mm Hg</td>
<td>129 (109-131)</td>
<td>120 (102-125)</td>
<td>114 (95-129)</td>
<td>120 (107-145)</td>
<td>0.43</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>6.6 (5.9-8.5)</td>
<td>7.4 (6.6-7.9)</td>
<td>6.9 (6.0-7.9)</td>
<td>8.0 (5.5-9.2)</td>
<td>0.12</td>
</tr>
<tr>
<td>EF, %</td>
<td>63 (62-65)</td>
<td>62 (61-63)</td>
<td>63 (61-64)</td>
<td>63 (63-64)</td>
<td>0.48</td>
</tr>
<tr>
<td>SV, mL</td>
<td>28 (22-30)</td>
<td>27 (25-30)</td>
<td>27 (23-30)</td>
<td>30 (29-30)</td>
<td>0.90</td>
</tr>
</tbody>
</table>

Continuous variables are presented as median with first and third quartiles (Q1–Q3).

### TABLE 4. Resuscitation Characteristics and Outcome Variables

<table>
<thead>
<tr>
<th>Therapy Group</th>
<th>AED1-1</th>
<th>AED1-3</th>
<th>AED2-1</th>
<th>AED2-3</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>First shock efficacy</td>
<td>6/10 [30%–85%]</td>
<td>4/10 [15%–70%]</td>
<td>9/11 [53%–97%]</td>
<td>6/11 [55%–80%]</td>
<td>0.27</td>
</tr>
<tr>
<td>Cumulative 3-shock efficacy</td>
<td>9/10 [61%–100%]</td>
<td>9/10 [61%–100%]</td>
<td>10/11 [64%–100%]</td>
<td>9/11 [53%–97%]</td>
<td>1.00</td>
</tr>
<tr>
<td>Shocks to terminate first episode of VF</td>
<td>1 (1-2)</td>
<td>1 (1-3)</td>
<td>1 (1-2)</td>
<td>1.5 (1-3)</td>
<td>0.29</td>
</tr>
<tr>
<td>No. of VF episodes</td>
<td>2.5 (1-3)</td>
<td>2 (2-3)</td>
<td>2 (1-2)</td>
<td>3 (2-3)</td>
<td>0.38</td>
</tr>
<tr>
<td>No. of shocks per animal</td>
<td>4 (3-5)</td>
<td>3 (2-5)</td>
<td>2 (1-3)</td>
<td>3.5 (2-7)</td>
<td>0.15</td>
</tr>
<tr>
<td>Total delivered energy, J</td>
<td>450 (450-750)</td>
<td>450 (300-750)</td>
<td>400 (200-860)</td>
<td>800 (450-2110)</td>
<td>0.09</td>
</tr>
<tr>
<td>Duration of CPR for survivors, seconds</td>
<td>218 (118-360)</td>
<td>245 (206-308)</td>
<td>260 (235-439)</td>
<td>266 (184-462)</td>
<td>0.60</td>
</tr>
<tr>
<td>Percentage of resuscitation time spent performing CPR, %</td>
<td>65 (55-80)</td>
<td>58 (50-67)</td>
<td>60 (53-73)</td>
<td>44 (38-53)</td>
<td>0.035*</td>
</tr>
<tr>
<td>Postresuscitation ST-segment depression, mV</td>
<td>0.09 (0.04-0.22)</td>
<td>0.25 (0.21-0.29)</td>
<td>0.33 (0.20-0.41)</td>
<td>0.31 (0.21-0.42)</td>
<td>0.007*</td>
</tr>
<tr>
<td>Mean aortic pressure, % of baseline</td>
<td>84 (77-102)</td>
<td>88 (75-99)</td>
<td>81 (79-94)</td>
<td>92 (78-105)</td>
<td>0.96</td>
</tr>
<tr>
<td>Cardiac output, % of baseline</td>
<td>64 (54-97)</td>
<td>70 (59-79)</td>
<td>69 (61-92)</td>
<td>69 (61-96)</td>
<td>0.94</td>
</tr>
<tr>
<td>Heart rate, % of baseline</td>
<td>125 (113-146)</td>
<td>130 (118-134)</td>
<td>124 (109-132)</td>
<td>156 (138-171)</td>
<td>0.13</td>
</tr>
<tr>
<td>Left ventricular EF, % of baseline</td>
<td>85 (82-89)</td>
<td>84 (83-90)</td>
<td>77 (67-83)</td>
<td>69 (62-75)</td>
<td>0.003*</td>
</tr>
<tr>
<td>Left ventricular SV, % of baseline</td>
<td>87 (75-118)</td>
<td>86 (82-89)</td>
<td>76 (70-77)</td>
<td>58 (56-81)</td>
<td>0.015*</td>
</tr>
<tr>
<td>Resuscitated</td>
<td>11/11 [76%–100%]</td>
<td>10/11 [64%–100%]</td>
<td>11/11 [76%–100%]</td>
<td>4/11 [14%–65%]</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Seventy-two–hour survival</td>
<td>11/11 [76%–100%]</td>
<td>10/11 [64%–100%]</td>
<td>11/11 [76%–100%]</td>
<td>4/11 [14%–65%]</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Continuous variables are presented as median with first and third quartiles (Q1–Q3) and proportions with [95% CI]. Descriptive statistics for left ventricular EF, SV, and hemodynamic variables are at 60 minutes after resuscitation. $P$ value is for overall effect.

*Statistically significant with $P<0.05$. 
Both left ventricular EF and SV were better after treatment with AED1 compared with AED2 (difference of means, 15% and 28% respectively, \(P<0.001\)), but neither was significantly affected by shock protocol. SV continuously improved over time, but substantial deficits were still apparent at the conclusion of the 4-hour observation period in animals treated with AED2 combined with a 3-shock protocol. These persistent deficits were not apparent in the other treatment groups. EF, on the other hand, demonstrated little improvement over the 4-hour observation period, with both AED2 and a 3-shock protocol contributing to the deficits. Mean aortic pressure and cardiac output did not differ significantly between groups, being compensated for by higher observed heart rates in the groups with decreased left ventricular volumes (Table 4). Myocardial function for all surviving animals returned to baseline by the end of the 72-hour observation period.

ECG recordings for 1 animal in the AED1-1 group and 1 in the AED1-3 group could not be retrieved. Based on the remaining 42 recordings, first-shock and cumulative 3-shock defibrillation efficacies (termination of VF at 5 seconds after shock) were examined. Owing to large animal size, efficacy was relatively low for both waveforms but did not differ among the treatment groups (Table 4, \(P=0.27\)). Cumulative 3-shock efficacy was nearly identical among the groups: 90% for each of the AED1 groups, 91% for AED2-1, and 82% for AED2-3 (\(P=1.00\)). No significant differences were detected in the number of shocks required to resuscitate or the number of VF episodes per resuscitation attempt.

**Discussion**

The present study found that adoption of a 1-shock defibrillation protocol successfully increased the percentage of time during which subjects received CPR during a resuscitation attempt compared with a conventional 3-shock protocol, thereby reducing postresuscitation myocardial dysfunction and increasing survival. It was also demonstrated that with a conventional 3-shock protocol, design variations among currently available AEDs have a significant impact on resuscitation success, despite similar defibrillation efficacy. Importantly, the 1-shock protocol was also found to minimize the impact of AED-imposed treatment variations.

**Efficacy of Shocks**

Escalation of defibrillation dose with higher-energy shocks has been proposed as a means to terminate VF with fewer shocks (with a presumption of higher cumulative efficacy) and thereby minimize interruptions of CPR.\(^{18}\) Such was not the case in this study. AED1 delivered nonescalating 150-J shocks, whereas AED2 delivered escalating shocks of 200 to 300 to 360 J, yet the cumulative 3-shock efficacy was similar and high for all groups. In light of this result, it is important to note that the animal model used is conservative, exhibiting first-shock efficacy for both waveforms lower than has been reported clinically for either (typically 90% or better).\(^{5,13}\) This situation should favor the premise of dose escalation and higher-energy shocks (escalate the dose to more rapidly terminate VF after failed shock), yet no differences in cumulative efficacy, number of shocks required for resuscitation, or postresuscitation myocardial dysfunction were observed.

![Figure 3](image_url)  
**Figure 3.** Seventy-two-hour survival for each study group, with 95% confidence intervals. *\(P=0.004\) vs AED2 with 3-shock protocol. †\(P=0.024\) vs AED2 with 3-shock protocol.

![Figure 4](image_url)  
**Figure 4.** Postresuscitation myocardial function of surviving animals as a percentage of baseline for each study group (mean and SD): A, left ventricular EF; B, SV. All between-group comparisons are statistically significant (Wilcoxon Mann-Whitney test with repeated measures, Bonferroni correction for multiple comparisons) except *AED1-1 vs AED1-3 and †AED1-3 vs AED2-1.
tation, or number of VF episodes were observed between the 2 dose strategies.

Outcome
The observation of different survival outcome despite similar defibrillation efficacy is readily understood in the context of the overall resuscitation process. When the duration of cardiac arrest is prolonged, continuous and good-quality CPR, especially chest compressions, is an extremely important determinant of successful resuscitation. Both experimental and clinical studies have demonstrated that interruption of chest compressions for as little as 10 seconds between each interval of CPR for rhythm analysis, ventilation, or patient assessment significantly reduces the number of chest compressions delivered to a patient. This, in turn, reduces coronary perfusion pressure and myocardial blood flow, decreases successful resuscitation, and increases the severity of postresuscitation myocardial and cerebral dysfunction. This is especially important with regard to AEDs, because most currently available AEDs require significantly longer than 10 seconds for rhythm analysis and charging. CPR interruptions are prolonged even further when the conventional (and recommended) 3-shock protocol is used.

It is clear that the performance of a defibrillator must be viewed in a much larger context than its efficacy at terminating VF. An optimal defibrillator must minimize interruptions of CPR for voice prompts, rhythm analysis, and capacitor charging. In addition, the electrical therapy must provide high efficacy while simultaneously minimizing postresuscitation myocardial dysfunction.

Limitations
The protocol used in this study followed current recommendations of the American Heart Association and International Liaison Committee on Resuscitation by delivering immediate defibrillation on availability of the AED, ie, before CPR. Although some evidence indicates that delaying defibrillation for an initial period of CPR may be beneficial in cases of prolonged cardiac arrest, such a protocol was not examined in this study. This study also combined the effects of defibrillation waveform, energy protocol, and nontherapeutic time delays, a grouping that reflects practical implementations in commercially available AEDs. Differences in nontherapeutic delays are partly attributable to the differences in energy protocol, with higher energies requiring inherently longer charge times, but are also affected by other design factors, such as duration of arrhythmia analysis and capacitor charging strategy. Thus, it cannot be directly determined from these results whether escalation with a higher-energy waveform or associated delays are primarily responsible for the observed differences.

Conclusions
In conclusion, the present study demonstrated that when a conventional 3-shock defibrillation protocol was used, design variations among commercially available AEDs had a significant impact on the initial success of resuscitation, postresuscitation myocardial dysfunction, and 72-hour survival after prolonged VF. Adoption of a 1-shock protocol, however, improved survival and minimized AED-based outcome differences. These results may provide a scientific basis for changing the current clinical practice.

Sources of Funding
This work was supported in part by a grant-in-aid from the American Heart Association and by a grant-in-aid from Philips Medical Systems, Seattle, Wash.

Disclosures
Mr Snyder is a former employee of Philips Medical Systems, a division of Philips Electronics North America Corp, and a shareholder of its parent, Royal Philips Electronics of the Netherlands. The other authors report no conflicts.

References
Survival after sudden cardiac arrest depends on proper execution of the chain of survival: early activation of emergency medical services, early cardiopulmonary resuscitation (CPR) (precordial compression and ventilation), early defibrillation, and early advanced care. Recent clinical studies, however, have suggested that the effectiveness of CPR is often compromised by frequent interruptions encountered during resuscitation attempts. Some interruptions are avoidable and can be minimized by education and training, but others are imposed by the equipment and protocols in use. In particular, CPR must be interrupted to provide defibrillation, and wide variations in the interval imposed by different automated external defibrillators (AEDs) have been reported. This study examined a new 1-shock defibrillation protocol designed to minimize interruptions of CPR. Success of resuscitation was compared with a conventional 3-shock defibrillation protocol subject to the range of treatment variation imposed by currently available AEDs. We have demonstrated that when a conventional 3-shock defibrillation protocol was used, AED design variations had a significant impact on the initial success of resuscitation, postresuscitation myocardial dysfunction, and 72-hour survival after prolonged ventricular fibrillation. Adoption of a 1-shock protocol, however, improved survival and minimized AED-based outcome differences. These results may provide a scientific basis for changing the current clinical practice.
One-Shock Versus Three-Shock Defibrillation Protocol Significantly Improves Outcome in a Porcine Model of Prolonged Ventricular Fibrillation Cardiac Arrest

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*Circulation*. 2006;113:2683-2689; originally published online June 5, 2006; doi: 10.1161/CIRCULATIONAHA.105.592121

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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