Biphasic Waveform External Defibrillation Thresholds for Spontaneous Ventricular Fibrillation Secondary to Acute Ischemia

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OBJECTIVES

The goal of this study was to determine if the defibrillation threshold (DFT) after spontaneous ventricular fibrillation (VF) secondary to acute ischemia differs from the DFT for electrically induced VF in the absence of ischemia in anesthetized, closed-chest dogs and pigs.

BACKGROUND

The efficacy of external defibrillators has been tested mainly in animals and humans using E-VF, yet external defibrillators are often used in patients to halt S-VF.

METHODS

Protocol 1: biphasic truncated exponential (BTE) waveform shocks were delivered through electrodes placed in an anterior-anterior (A-A) position (left and right lateral thorax) in nine dogs. After measuring the E-VF DFT, acute ischemia was induced with an angioplasty balloon in either the left anterior descending or left circumflex coronary artery, and the S-VF DFT was determined. Protocol 2: in a group of 12 pigs, the E-VF DFT and S-VF DFT were determined for electrodes in the A-A position and in the anterior-posterior position (A-P). Protocol 3: the S-VF DFT was determined in seven pigs. Then up to three shocks 1.5 × the E-VF DFT were delivered to S-VF. If defibrillation did not occur, a step-up protocol was used until defibrillation occurred.

RESULTS

Protocol 1: the DFT for E-VF was 65 ± 28 J (mean ± SD) compared with 226 ± 97 J for S-VF, p < 0.05. Protocol 2: the DFT was 152 ± 58 J for E-VF and 315 ± 123 J for S-VF for A-A electrodes. The DFT was 100 ± 43 J for E-VF and 206 ± 114 J for S-VF for A-P electrodes. Protocol 3: 11/37 shocks of strength 1.5 × E-VF DFT (182 ± 40 J) stopped the arrhythmia. The episodes of S-VF not halted by these shocks required energy levels of up to 400 J for defibrillation.

CONCLUSIONS

External defibrillation of S-VF induced by acute ischemia requires significantly more energy than VF induced by 60-Hz current in the absence of ischemia. A safety margin >1.5 × the DFT for electrically induced VF may be necessary in BTE external defibrillators to defibrillate S-VF.

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Sudden cardiac death is often caused by acute myocardial ischemia, with the majority of these deaths secondary to ventricular fibrillation (VF) (1). At least 80% of patients who experience sudden cardiac death have atherosclerotic coronary artery disease. In survivors of cardiac arrest, coronary heart disease with vessels exhibiting >75% cross-sectional stenosis are found in approximately 40% to 86% of patients, depending on the age and gender of the population studied (2). Although <50% of the patients resuscitated from VF show evidence of myocardial infarction by elevated cardiac enzymes and <25% have Q-wave myocardial infarction, autopsy studies have reported that a recent occlusive coronary thrombus was found in 15% to 64% of victims of sudden cardiac death with many hearts showing plaque fissuring, hemorrhage and thrombosis. Healed infarctions are present in >50% of hearts of sudden cardiac death victims at autopsy and in those of survivors of cardiac arrest.

Biphasic truncated exponential (BTE) waveforms, which have been shown to defibrillate at lower energies than monophasic waveforms for internal defibrillation (3,4), have recently been incorporated into external defibrillators (5,6). Most testing for these external defibrillators has been done in the electrophysiology laboratory in the nons ischemic heart in which VF is electrically induced and of short duration. Energy levels based on this testing may be inappropriate for defibrillating spontaneous, ischemic-induced VF in the prehospital setting.

The standard defibrillation protocol calls for an increase in energy levels after the first shock (200 J to 300 J to 360 J) (7). Other investigators have reported that multiple shocks at lower energy levels of 100 J to 200 J were successful in a majority of patients with VF (8,9). It is possible that multiple shocks delivered for spontaneous VF in the presence of acute ischemia at an energy somewhat greater than the defibrillation threshold (DFT) for electrically induced VF would be as effective as using escalating energy levels. Delivering multiple lower-energy shocks could decrease cardiac damage (10,11).

In this study, we tested the hypothesis that spontaneous VF secondary to acute ischemia requires significantly greater energy for successful external defibrillation with a BTE
waveform compared with the energy required to defibrillate VF induced by 60-Hz current in the nonischemic heart. We tested this hypothesis in two species, dogs (protocol 1) and pigs (protocol 2 and 3). We also tested the effect of two patch positions on defibrillation efficacy of a BTE waveform in halting electrically induced VF and spontaneous VF caused by acute ischemia. We hypothesized that the relation between the electric field and the ischemic bed would alter the relative efficacy of the two patch positions when comparing defibrillation of ischemic spontaneous VF to defibrillation of 60-Hz–induced VF. Finally, we sought to determine how effective multiple shocks at 1.5× the electrical VF DFT would be in stopping spontaneous VF secondary to acute ischemia.

METHODS

Animal preparation. All animals were managed in accordance with the guideline established in the “Position of the American Heart Association on Research Animal Use” adopted by the American Heart Association on November 11, 1984 (12). The University of Alabama at Birmingham Institutional Animal Care and Use Committee approved the experimental protocols.

We used two different closed-chest animal models (dog and pig). Nine mongrel dogs of either gender weighing 30 kg to 37 kg were studied in the first group of experiments. Mixed-breed pigs of either gender weighing 26 kg to 30 kg to 37 kg were studied in the second group of experiments. Nine mongrel dogs of either gender weighing 43 kg were studied in the second (n = 12) and third (n = 7) groups of experiments.

Anesthesia was induced in dogs with intravenous thioental sodium (30 mg/kg) and in pigs with intramuscular zolazepam-tiletamine (4.4 mg/kg) and xylazine (2.2 mg/kg). All animals were intubated, and anesthesia was maintained by inhalation of isoflurane (1.0% to 2.5%) administered in a 50:50 mixture of oxygen:nitrous oxide. Skeletal muscle paralysis was induced with intravenous succinylcholine (2 mg/kg) and repeated as needed to minimize contraction during defibrillation testing. Animals were given intravenous lactated Ringer’s solution and mechanically ventilated throughout the experiment. Core body temperature, arterial blood gas values and electrolyte levels were checked every 30 min and maintained within the normal range throughout the experiment (13). Intravenous heparin (5,000 IU) was administered just before angioplasty balloon occlusion of a coronary artery and repeated every hour (500 IU).

Animals were placed in dorsal recumbency, and 115 cm² adhesive external defibrillator patches (Quick-Combo, Physio-Control Corp., Redmond, Washington) were applied to the shaved cutaneous surfaces of the left and right lateral thorax in a standard anterior-anterior (A-A) position. The left patch was centered over the point of maximal impulse on the left chest wall. The right patch was placed in a parasternal position with the superior edge of the patch at the second thoracic interspace. The left chest patch was anode for the monophasic waveform and the first phase of the biphasic waveform. In the second protocol, patch position was alternated between A-A and anterior-posterior (A-P) positions in each animal. The A-A patch position was the same as in protocol 1. For the A-P patch position, the anterior patch was placed over the sternum with the superior edge of the patch at the second thoracic interspace. The posterior patch was placed overlying the spine directly posterior to the anterior patch. The anterior patch was anode for the first phase of the biphasic waveform. Both external jugular veins and the right carotid artery were surgically isolated and cannulated with vascular sheaths. A catheter was advanced into the apex of the right ventricle for 60-Hz induction of VF and for recording a local electrogram. Systemic arterial pressure, right ventricular electrogram and three surface electrocardiogram (ECG) traces (leads II, aVF and the defibrillator patch electrogram) were monitored throughout the study. Shock parameters including delivered energy and impedance for each shock were recorded.

At the end of the study, the anesthetized animal was euthanized with an injection of potassium chloride solution.

Protocol 1: defibrillation of electrically induced VF and ischemically induced spontaneous VF in dogs. The purpose of this protocol was to compare the external biphasic waveform DFT for electrical VF and spontaneous VF in a closed-chest model of ischemia and reperfusion. The electrical VF monophasic waveform DFT was also measured as a control.

Ventricular fibrillation was induced with 60-Hz alternating current applied to the nonischemic heart via the right ventricular electrode and confirmed by observing a rapid decay of arterial blood pressure and disorganized appearance of the surface ECG. The DFTs for electrical VF were determined for monophasic and BTE waveforms delivered by an external defibrillator (Lifepak 6s-modified; Physio-Control Corp., Redmond, Washington). The monophasic waveform was a critically damped sinusoidal waveform (14). The phase 1 duration of the BTE waveform was the optimal phase 1 duration as defined by Walcott et al. (15) using a model time constant of 5 ms. Phase 2 duration was two-thirds the duration of phase 1. The phase 1 duration was 6.6 ms for 40 ohms and 8.8 ms for 80 ohms. A step-up protocol was used for each VF episode to determine the DFT after 10 s of electrical VF (16). The mean starting energy to defibrillate electrically induced VF was 43 J for the monophasic and 38 J for the BTE waveform. If the first
shock failed, shocks of increasing strength in 0.1 log energy steps were given 8 s to 15 s apart until VF was halted. Successful defibrillation had to occur within four shocks. If defibrillation required >4 shocks, the animal was rescued with a 360 J shock, and the step-up protocol for that waveform was repeated during another VF episode beginning at a higher initial energy with a minimum of 4 min between VF episodes. The DFT was defined as the lowest energy shock that successfully defibrillated the animal. The DFTs were performed twice for each waveform. The waveform used was alternated between episodes.

Myocardial ischemia was initiated by inflating an angioplasty balloon in a coronary artery. Most animals underwent two episodes of balloon-induced ischemia, one with the balloon in the left anterior descending (LAD) coronary artery just beyond the first diagonal branch and one with the balloon in the left circumflex (LCX) coronary artery approximately 2 cm beyond the origin of the left main coronary artery. At least 30 min of recovery was allowed between each ischemic episode. The initial artery occlusion was randomized for each animal. Angiography was performed to ensure optimal balloon positioning and to confirm the absence of antegrade flow. The balloon occlusion of the artery continued for 20 min (17). With the development of VF, external defibrillation was attempted using the BTE waveform with a step-up protocol beginning at 50 J and increasing by 50-J steps. The angioplasty balloon was left inflated during attempted defibrillation. Defibrillation was considered successful if the animal remained in a perfusing rhythm (systolic arterial blood pressure >60 mm Hg) for longer than 30 s. If VF did not occur during the 20 min of acute ischemia, the balloon was released to allow reperfusion to occur. If reperfusion caused a spontaneous arrhythmia, defibrillation was attempted in the same way.

The DFTs for electrical VF were repeated in the final four dogs of the protocol 30 min after determining the last DFT for spontaneous VF. The electrical DFTs were performed in the same fashion as described above.

Protocol 2: defibrillation of electrically induced VF and ischemically induced spontaneous VF in pigs. The purpose of this protocol was to answer two questions. Is the DFT for spontaneous VF also significantly higher than the DFT for 60-Hz–induced VF before ischemia. If VF continued after the three shocks at this energy level, the energy delivered was increased by 50-J steps until defibrillation occurred. If VF did not occur during the 20 min of acute ischemia, the balloon was released to allow reperfusion to occur.

Because we were unable to defibrillate two pigs during ischemia, the DFT for electrical VF was repeated in only five of the seven pigs at the end of the study.

Statistical analyses. Results are expressed as the mean ± SD. Two-way analysis of variance was used to compare means. Post-hoc comparisons were made using the Student-Newman-Keuls test. Linear regression analysis was used to determine the effect of multiple ischemic episodes on the DFT and the effect of ischemia time on the DFT. Results were considered significant if p < 0.05.

RESULTS

Protocol 1: defibrillation of electrically induced VF and ischemically induced spontaneous VF in dogs. The heart rate was 146 ± 16 beats/min, and the arterial blood pressure was 128/85 ± 31/19 mm Hg for the animals throughout the study.

Similar to other studies (5,6), the DFT for the monophasic waveform was significantly higher than the DFT for the BTE waveform (Table 1). A mean of 46% more energy was required to defibrillate with the monophasic than with the BTE waveform.

There were 19 episodes of VF after angioplasty balloon-
induced ischemia in the nine dogs studied. Four episodes occurred during balloon occlusion of the coronary artery. The DFT for these episodes was 300 ± 95 J. Fifteen episodes occurred with reperfusion after 20 min of balloon occlusion. The DFT for these episodes was 210 ± 95 J (p = NS). Spontaneous VF during reperfusion occurred almost immediately after the balloon was deflated. Two to 14 shocks (7 ± 2 shocks) were required to convert the 19 episodes of spontaneous VF to an organized, perfusing rhythm. The energy necessary to defibrillate spontaneous VF with the BTE waveform was over 3× greater than the energy necessary to defibrillate electrically induced VF.

The DFT for electrical VF at the end of the study in the final four dogs studied for the monophasic waveform was 87 ± 31 J and 62 ± 17 J for the BTE waveform. These values were not significantly different from the DFTs for these waveforms at the beginning of the study.

**Protocol 2: defibrillation of electrically induced VF and ischemically induced spontaneous VF in pigs.** The heart rate was 111 ± 32 beats/min, and the arterial blood pressure was 111/77 ± 18/16 mm Hg for the animals throughout the study.

Twice as much energy was required to defibrillate spontaneous VF compared with electrical VF (p < 0.05). The DFT for the A-A patch position was significantly higher than the DFT for the A-P patch position for both electrically induced VF and spontaneous VF (Table 2). There was a trend towards a positive interaction between patch position and method of VF induction, though this trend did not reach significance (p = 0.17).

Of the 25 VF episodes, 14 (56%) occurred during occlusion and 11 (44%) occurred with reperfusion after 20 min of balloon occlusion. There was no significant difference between the DFTs for spontaneous VF that occurred while the balloon was inflated (lateral patch position: 315 ± 125 J, A-P patch position: 206 ± 115 J) and spontaneous VF that occurred after reperfusion (lateral patch position: 260 ± 130 J, A-P patch position: 173 ± 126 J), regardless of the patch position.

Up to four ischemic VF episodes were induced in each animal. There was no significant change in DFT as a function of ischemic episode.

**Protocol 3: defibrillation of ischemically induced spontaneous VF in pigs with multiple shocks of the same energy.** The heart rate was 119 ± 35 beats/min and the arterial blood pressure was 108/76 ± 16/15 mm Hg for the animals throughout the study.

### Table 2. Defibrillation Thresholds: Protocol 2

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<tr>
<th>Electrically Induced VF†</th>
<th>Spontaneous VF†</th>
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<tr>
<td>Patch A-A* 152 ± 58 J</td>
<td>315 ± 123 J</td>
</tr>
<tr>
<td>Patch A-P* 102 ± 42 J</td>
<td>206 ± 114 J</td>
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* p < 0.05 external patch in A-A compared with A-P position; †p < 0.05 comparing biphasic truncated exponential energy for spontaneous and electrical VF in each patch position.

A-A = anterior-anterior; A-P = anterior-posterior; VF = ventricular fibrillation.

The DFT for electrical VF using the BTE waveform with the external patches in the standard A-A position was 119 ± 35 J.

Fifty-eight shocks were delivered to treat 18 episodes of spontaneous VF that occurred during balloon occlusion. The shock level that was 50% above the DFT for electrical VF was 182 ± 40 J. The average strength of successful shocks was 233 ± 95 J. A total of 30% of the shocks (11/37) delivered at 50% above the DFT for electrical VF successfully stopped spontaneous VF (Fig. 1). Eight of the 11 successes occurred with the first shock, while the other three occurred with the second shock at the same energy. Six of 12 shocks (50%) delivered at 2 to 2.5× the electrical DFT successfully converted the arrhythmia. Two of nine shocks (22.2%) delivered at >2.5× the electrical DFT successfully converted the arrhythmia. Two pigs could not be defibrillated after the development of spontaneous VF even after multiple shocks of approximately 400 J (data not included in any of the above analyses). Five of seven pigs required a shock energy >50% above the DFT for electrically induced VF for successful defibrillation at some point during the ischemic event.

In addition to the 18 episodes of spontaneous VF that occurred during occlusion, nine episodes of VF occurred with reperfusion after 20 min of balloon occlusion of the LAD or LCX. All episodes of reperfusion VF were reversed at the initial shock energy of 1.5× the DFT for electrical VF. Seven of the nine episodes of reperfusion VF were reversed with a single shock; one episode required two shocks and one episode required three shocks.

After defibrillation, examination of the ECG showed that during three episodes the rhythm was organized before VF recurred. In these three episodes, the VF recurrence
time was 9.8 ± 10 s. After shock delivery for the rest of the episodes, the rhythm was VF as soon as the ECG was interpretable, usually 3 to 5 s.

After occlusion and reperfusion of the coronary arteries, the DFT for electrical VF using the BTE waveform could be determined a second time in five pigs. The DFT was 121 ± 55 J, not significantly different than the DFT at the beginning of the study.

We combined the data from protocols 2 and 3 to determine the distribution of energy levels that successfully defibrillated spontaneous VF induced by acute ischemia or reperfusion (Fig. 2). The histogram of successful defibrillation shock strengths shows that approximately 78% of arrhythmias are defibrillated at a shock strength slightly higher than the electrical DFT, while about 22% of arrhythmias required much higher shock strengths to stop the arrhythmia. There was no relation between the time at which the arrhythmia started during occlusion and the amount of energy that was necessary to stop the arrhythmia.

**DISCUSSION**

The main finding of this study is that defibrillation of spontaneous VF caused by acute ischemia requires significantly more energy than defibrillation of VF caused by the application of 60-Hz current in the absence of ischemia. This finding holds true for two different species and for ischemic arrhythmias as well as reperfusion arrhythmias and so may be more robustly generalized to humans. Further, five of seven pigs in protocol 3 could not be defibrillated with three shocks at 50% stronger than the electrical DFT strength. These results suggest that clinical studies that involve defibrillating spontaneous arrhythmias in either a prehospital or intensive care unit setting are necessary to determine optimal defibrillation energy levels for defibrillators using BTE waveforms and should include shock strengths to 360 J.

**Defibrillation of spontaneous VF.** Only one previous study has determined a DFT for spontaneous arrhythmias induced by acute ischemia (18). In that study, up to 6× more energy was required for internal defibrillation of spontaneous VF (whether after occlusion or reperfusion) than for electrically induced VF in the nonischemic heart. Our results extend these previous results in two ways. First, the electrodes were on the chest wall rather than on the heart itself. Second, a BTE waveform was used as the shocking waveform. Moving the electrodes away from the heart creates a more uniform shock potential gradient field (19,20). If the reason that more energy is required to defibrillate spontaneous arrhythmias is that the high gradient region interacts with the acutely ischemic region to reinuce VF, then moving the electrodes away from the heart should nullify this effect and the threshold should move closer to the DFT of electrically induced VF. Biphasic waveforms have been shown to cause less conduction block and delay than monophasic waveforms (21), which could also result in more similar DFTs for spontaneous and electrically induced VF.

**Why is spontaneous VF so difficult to defibrillate?** The reason that spontaneous VF is so difficult to defibrillate in both dogs and pigs is still not clear. Mapping studies of defibrillation of electrically induced VF have shown that a shock must do two things to successfully defibrillate the heart (22). First, it must stop most or all of the fibrillation wavefronts on the heart. Second, a shock must not restart fibrillation. In contrast to defibrillating electrically induced VF, there is a third factor involved in the defibrillation of ischemically induced spontaneous VF, namely the original initiator of the arrhythmia. We hypothesize that the reason spontaneous VF is so much harder to defibrillate than electrically induced VF is that the shock must not only stop most or all VF wavefronts without restarting VF, but it must also stop the original initiator of the arrhythmia. Mapping studies of the initiation of ischemically induced spontaneous VF have shown that both focal and re-entrant mechanisms are responsible (23,24). Our histogram data (Fig. 2) suggest that there are two populations of arrhythmias being defibrillated: one at a relatively low energy level and one at a much higher energy level. We hypothesize that these two groups are differentiated by the mechanism of initiation of the arrhythmia. Arrhythmias that are initiated by re-entrant mechanisms are similar to electrical VF and, therefore, are relatively easy to defibrillate, while arrhythmias initiated by focal mechanisms are much harder to defibrillate. Mapping studies are required to test these hypotheses.

Alternatively, it is possible that locally ischemic tissue may increase defibrillation energy requirements by making it harder for the shock to halt VF activation fronts within the ischemic region. Occlusion or embolization of a coronary artery has been reported to increase defibrillation current and energy thresholds during the 30 min to 60 min after the
onset of myocardial ischemia in dogs (25,26). Other reports did not find increases in DFTs after coronary artery occlusion (27,28) or found a lower threshold (29). In the study by Ouyang et al. (18), the DFT was significantly higher for electrically induced VF with locally ischemic tissue compared with electrically induced VF without locally ischemic tissue. But the measured threshold was significantly lower for electrically induced VF with locally ischemic tissue compared with spontaneous VF induced by local ischemia (18). Therefore, local ischemia may account for some of the increase in the DFT for spontaneous VF but probably does not account for all of the increase, especially in some of the cases with very high DFTs.

Effect of patch position on defibrillation efficacy. We hypothesized that there might be a change in defibrillation efficacy with a change in patch position. There was a trend towards a positive interaction between patch position and method of VF induction. It may be possible to optimize the placement of defibrillation electrodes for a given patient depending on what region of the heart was locally ischemic before the development of VF, though more data are necessary to validate this idea.

Study limitations. This study was performed in animals after a short period of VF. Yet a majority of patients treated in the prehospital setting receive shock therapy more than 5 min after they collapse (9). Future studies combining spontaneous arrhythmias caused by acute ischemia and prolonged VF are needed to define how the DFT changes during these arrhythmias over time.

All DFTs were measured using a multiple shock step-up method for each episode of VF. This method was necessary because it is not possible to obtain enough similar episodes of spontaneous arrhythmia to use a one-test shock/episode threshold method. A similar method has been used for internal defibrillation and did not yield different DFTs for the two methods (16).

This study was designed to determine if the DFT for electrically spontaneous VF secondary to acute ischemia was different from the DFT for electrically induced VF but was not meant to determine the reasons why the threshold might be different. Electrical or optical mapping may be helpful in determining why the thresholds are different.

Clinical implications. The results of these studies suggest that the DFT is significantly higher for spontaneous arrhythmias caused by acute ischemia than for electrically induced VF. Higher energy levels may allow biphasic defibrillators to defibrillate more patients and to defibrillate some patients sooner. Both of these outcomes may achieve higher survival rates.

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