Functional Cardiac Depression Caused by Defibrillator Shocks

Quantitation of the Safety Factor for Electrical Defibrillation*

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SUMMARY

The overdose shock strengths required to depress ventricular contraction were determined for damped sinusoidal current in 7 metabolically supported, isolated contracting canine hearts. Each heart was suspended in an isoresistive and isotonic solution through which the defibrillating shocks were delivered. Defibrillation thresholds were determined with standard damped sine wave shocks of 4.4–5.5 msec duration. Then overdose shocks were delivered and the depressant effect on systolic left ventricular pressure was measured for shocks of 3–12 times threshold current. The minimum (threshold) current and energy densities required to defibrillate were 59.5±4.6 mA/cm² (average) and 3.12±0.2 mJ/cm³. Increasing the shock strength above threshold produced a concomitant reduction of postshock left ventricular systolic pressure. The current and energy densities required to produce 50% depression (TD50) of left ventricular systolic pressure were 5.0 and 24.1 times the threshold current and energy densities respectively, indicating a wide safety margin using this criterion.

Additional Indexing Words:
Defibrillation safety Defibrillation toxicity Damped sine wave

In clinical medicine ventricular defibrillation is most frequently achieved with damped sinusoidal current countershock. The shock strength is selected on

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* Supported by Grant-in-Aid 53–003–801 from the American Heart Association, Indiana Affiliate, Inc.
** Supported by Grant HL 00587 from the National Heart, Lung, and Blood Institute.
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Received for publication March 22, 1983.
Manuscript revised July 29, 1983.
the basis of experience. Within reasonable limits, the probability of successful defibrillation can be improved by increasing shock strength\(^1\),\(^2\) to offset factors such as the degree of ischemia\(^3\) and the presence of drugs\(^4\),\(^5\) which can affect defibrillation success and ultimate survival. Ideally, one should select a shock strength that is likely to be above the defibrillation threshold, but not so strong that it will impair pumping capability or damage the heart. The shock strength selected should be based on the margin of safety between threshold and damaging electrical shocks. To date, studies on the effect of overdose defibrillator shock have focussed on myocardial enzyme release,\(^6\),\(^7\) structural damage,\(^8\)–\(^10\) and rhythm disturbances.\(^11\) The functional effects of defibrillator shocks on cultured myocardial cells have been studied;\(^12\) however, the applicability of these results to intact, working hearts is unknown. Koning,\(^13\) Rowe,\(^14\) and Kerber\(^15\) investigated various toxic effects of defibrillator shocks on intact hearts. However, the relationships of the damaging doses to the effective dose (defibrillation threshold) were not reported. In the present study we determined the margin of safety for damped sine wave defibrillator shocks in the isolated, working canine heart. The goal of this study was to define the overdose ratio (delivered shock strength / threshold shock strength) required to produce a specified degree of post-defibrillation myocardial depression.

**Methods**

The canine isolated heart model shown in Fig. 1 was developed to measure the functional changes in the left ventricle following defibrillator shocks. The isolated heart is not affected by the autonomic reflexes elicited by circulatory arrest in fibrillation.\(^16\) Thus, this model can demonstrate toxic effects due to defibrillator current overdose alone which may be masked in the intact animal preparation.

**Animal preparation:**

In each of 7 studies, 2 dogs (15 to 25 Kg) were anesthetized with sodium pentobarbital (30 mg/Kg, i.v.) and given 2 mg/Kg intravenous heparin to inhibit clot formation. The larger dog was used to provide circulatory support for the heart removed from the smaller (donor) dog. Catheterization of both femoral arteries and both femoral veins was performed in the support dog. Coronary blood flow from the support dog was accomplished within 7 min of ligation of the great vessels in the donor dog. To ensure adequate blood flow to the isolated heart, the two arterial catheters were joined by a “Y” tube connected to a 10 mm internal diameter catheter which was connected
to the aortic stump of the isolated heart. The venous effluent blood from the isolated heart was returned to the support dog via a large-bore catheter joined by a “Y” tube to the two femoral venous catheters.

Surgical isolation of the heart from the donor dog was accomplished by placing ligatures around all great vessels entering and leaving the heart. The aortic arch was then rapidly cannulated with the large arterial catheter from the support dog. The heart was then dissected from the thorax and suspended in an isotonic and isoosmotic solution at 37°C, as shown in Fig. 1, where it continued to beat regularly throughout the study.

In preliminary studies, the coronary blood flow through the isolated heart was measured using an electromagnetic flowmeter (Carolina Med. Elec., King, NC) in the large venous catheter returning blood to the support dog. The flow rate ranged between 0.8 and 1.2 ml/min/Gm, which is within normal limits for canine coronary blood flow.17)

Resistivity matching:
To obtain the most uniform distribution of current through the isolated heart, the resistivity of the solution in the bath was matched to that of the heart. This was accomplished by measuring the 50-kHz impedance of the fluid between two rod electrodes spaced 12 cm apart in the bath and successively raising and lowering the heart between the electrodes in the solution. Two isotonic solutions were used to achieve the resistivity match. One solution was 5% glucose, which has a high resistivity (ca. 200,000 ohm-cm) and the other was 0.9% saline, which has a low resistivity (ca. 55 ohm-cm). Beginning with the 5% glucose solution, 0.9% NaCl was added until there was no change in impedance when the heart placed between the electrodes. At this point, the resistivity and the osmolar concentration of the fluid were equal to those of the heart. The resulting resistivity value was typically about 250 ohm-cm.

Measurement of cardiac function:
Cardiac function was evaluated by measuring the left ventricular pressure using a catheter inserted through the left atrial appendage as shown in Fig. 1. The end of the catheter was connected to an isolated pressure transducer (Statham p 231ID). Left ventricular end-diastolic pressure was adjusted so that left ventricular systolic pressure was always below aortic diastolic pressure. Thus, the aortic valve did not open and the left ventricle contracted isovolumically. This adjustment was accomplished easily by adding or withdrawing blood from the left ventricle via the pressure-recording catheter. In this way the isovolumic left ventricular pressure was continuously recorded
during the course of the study. Although the adjustment was required infrequently, pressure checks were made often during the study.

**Measurement of delivered shock strength:**

Two parallel-plate electrodes (each 21 cm²) were placed 15 cm apart at the ends of the shock bath and the isolated heart was suspended in the fluid between them. The electrodes were connected to an experimental defibrillator which delivered a damped sine wave. Delivered voltage and current were recorded on a storage oscilloscope (Model 5103N, Tektronix Inc., Portland, OR). Since Bourland et al showed that the efficacy of different waveform can be evaluated on the basis of their average currents, the average currents for threshold defibrillation and overdose shock were determined. The average current and delivered energy were calculated from the solution of the differential equation describing the damped sine wave discharge.

Although current and energy values will be reported here as measurements of shock strength, others can be derived from these two. The delivered charge can be calculated by multiplying the average current by the duration of the pulse (typically 5 msec). The average voltage can be calculated by
multiplying the average current by the resistance of the shock bath (approximately 15 ohms). The peak voltage and current values of the damped sine wave shocks can be calculated by multiplying the corresponding average values by 1.7, which is the crest factor. The current density was calculated by dividing the average current by the cross-sectional area of the bath. Energy density was calculated by dividing the delivered energy by the volume of the bath. Peak or average voltage gradients can be calculated by dividing the appropriate value by the distance between the electrodes in the bath (15 cm).

**Experimental protocol:**
In each isolated heart, ventricular fibrillation was induced using a 60-Hz, 2-ms, 10-volt stimulus applied to the ventricular epicardium with a handheld bipolar electrode. Then defibrillation threshold was established by successively increasing the delivered current until defibrillation was attained. The sequence was then repeated using a shock strength slightly lower, or higher, depending on the result of the first trial. Defibrillation threshold was established when there was a difference of no more than 10% between a successful shock strength and an unsuccessful shock strength.

**Measurement of cardiac depression:**
Overdose shocks, ranging from 3 to 12 times threshold current, were
delivered to the isolated heart and 2–3 repetitions of each shock strength were delivered. The amount of myocardial depression following the test shocks was quantitated as the percentage by which the left ventricular systolic pressure for the first postshock beat decreased from the preshock value (Fig. 1, inset). Preliminary studies have shown that the percentage cardiac depression was independent of pre-load and related only to the shock intensity. In addition, preliminary studies had shown that left ventricular systolic pressure and left ventricular dP/dt behaved identically in response to overdose shocks. A plot of the percent depression versus overdose ratio (delivered current or energy divided by threshold current or energy) permitted determination of the overdose ratio required to produce a 50% depression (Fig. 3). The current and energy overdoses required to produce 50% depression were interpolated from the linear plots of probit percent depression versus log overdose ratio. The overdose shocks were delivered in randomized order and 2–5 min were allowed for recovery of a stable sinus rhythm before another trial was made, since transient arrhythmias often occurred approximately 10 sec after the shock.

**Results**

Functional depression of the heart was proportional to the overdose shock strength. Fig. 2 illustrates a typical response to an overdose current ratio of 9 which resulted in approximately 88% depression. Fig. 3 illustrates the percent myocardial depression produced by current and energy overdose ratios.
An overdose ratio of 1.0 represents a shock of threshold current and energy. The threshold average current density (SEM) was $59.5 \pm 4.6 \text{ mA/cm}^2$ and the threshold energy density was $3.12 \pm 0.2 \text{ mJ/cm}^3$. The average current density required to depress the ventricles by 50% was $299 \pm 34 \text{ mA/cm}^2$, or 5.0 times the threshold required for defibrillation. The energy density required to produce 50% depression was $71 \pm 6.8 \text{ mJ/cm}^3$ or 24 times that required for defibrillation. Although threshold and overdose current are expressed in average value units, the overdose ratio applies equally well to the peak current ratio. With the damped sine wave, the peak current is 1.7 times the average current.

**DISCUSSION**

Suprathreshold strength shocks produce functional depression of the ventricles. In these working, metabolically supported hearts, virtually no myocardial depression resulted from threshold intensity defibrillator shocks. The ratio between threshold and the shock causing 50% depression (TD50) was 5.0 in terms of current and 24 in terms of energy. We believe that 50% depression of cardiac function by a shock would significantly impair the chances for recovery from ventricular fibrillation in vivo. The significance of postshock cardiac depression in recovery from ventricular fibrillation arises from the fact that coronary flow in the intact subject depends on cardiac output and the presence of sufficient diastolic aortic pressure. In this study, coronary blood flow was maintained by the support dog during ventricular fibrillation, and therefore the rate of recovery following the initial depression may be dependent on that flow, although, as may be expected, left ventricular pressure required more time (maximum time $\approx 15$ sec) to return to preshock control values following higher intensity shocks and greater degrees of cardiac depression than after lower intensity shocks. Yet, if during clinical fibrillation the heart is depressed by a defibrillating shock, adequate coronary flow will not be present to reverse the effects of myocardial hypoxia resulting from fibrillation and the victim may die. For this reason, we believe that functional depression of the heart by defibrillator shock overdose may be an even more important threat than is the minor shock-induced histologic damage reported earlier.20)

The technique reported herein allows comparison of the safety factors for different waveforms in the same heart and such studies are needed to determine if the less frequently used waveforms (rectangular and high-tilt trapezoidal) have lower or higher margins of safety. With presently available (400 J) damped sine wave defibrillators, the maximum dose delivered to adults is well below 5 times threshold current or 24 times threshold energy. With
the 50% depression criterion used in this paper, today's damped sine wave defibrillators using thoracic electrodes are probably quite safe for defibrillation of normal healthy adult hearts. However, in patients any amount of cardiac depression may be unacceptable and caution should be exercised in selecting the shock strength. In addition, safety factors may be different with the local or global ischemia encountered clinically, depending upon whether the effective and deleterious shock doses change in a parallel or divergent fashion.

The isolated heart preparation used in this study exhibits several advantages over other experimental models used to study defibrillator shock efficacy and safety.

- Defibrillation threshold can be easily and accurately established so that the relationship between effective and toxic doses can be seen.
- Isolation of the heart eliminates the influences of autonomic reflexes on the heart. Such reflexes are triggered by cessation of blood flow to the brain in the intact animal.16
- Constant coronary blood flow to the heart tissue eliminates the confounding toxic effects of ischemia on myocardial cells. Thus, the effects of defibrillator shocks on the myocardium alone can be studied.
- Current density through the heart and the solution surrounding it is very nearly uniform. This ensures that all myocardial cells are exposed to approximately the same current and energy levels.
- Physical isolation of the heart will permit studies of temperature and drug effects on the heart. In addition, substances released from the heart following defibrillator shocks (e.g. enzymes and/or electrolytes) are easily collected via the venous effluent line to the support animal.
- Since the toxic response measured, cardiac depression, is non-cumulative and reproducible, several waveforms and shock intensities can be studied in each isolated heart preparation. This is an advantage over other intact heart preparations in which each delivered shock may produce permanent damage and affect the response of the heart to subsequent defibrillator shocks.

By using this isolated heart preparation, the effects of defibrillator waveform and duration can be elucidated. In conclusion, using the isolated heart preparation described herein, a threshold shock produces insignificant depression, while suprathreshold current produces myocardial depression in proportion to the overdose. A substantial overdose is required to produce a functional depression of 50% in the normal perfused heart.
REFERENCES