Left ventricular geometry immediately following defibrillation: shock-induced relaxation

AMY L. DE JONGH,1 VIJAYA RAMANATHAN,1 BRENT K. HOFFMEISTER,2 AND ROBERT A. MALKIN1
1Joint Graduate Program in Biomedical Engineering, The University of Memphis and University of Tennessee Health Sciences Center, Memphis 38152; and
2Department of Physics, Rhodes College, Memphis, Tennessee 38112

Submitted 6 February 2002; accepted in final form 29 October 2002

De Jongh, Amy L., Vijaya Ramanathan, Brent K. Hoffmeister, and Robert A. Malkin. Left ventricular geometry immediately following defibrillation: shock-induced relaxation. Am J Physiol Heart Circ Physiol 284: H815–H819, 2003. First published October 31, 2002; 10.1152/ajpheart.00093.2002.—A previous two-dimensional (2D) ultrasound study suggested that there is relaxation of the myocardium after defibrillation. The 2D study could not measure activity occurring within the first 33 ms after the shock, a period that may be critical for discriminating between shock- and excitation-induced relaxation. The objective of our study was to determine the left ventricular (LV) geometry during the first 33 ms after defibrillation. Biphasic defibrillation shocks were delivered 5–50 s after the induction of ventricular fibrillation in each of the seven dogs. One-dimensional, short-axis ultrasound images of the LV cavity were acquired at a rate of 250 samples/s. The LV cavity diameter was computed from 32 ms before to 32 ms after the shock. Preshock and postshock percent changes in cross-sectional area of the LV were analyzed as a function of time with the use of regression analysis. The normalized mean pre- and post-LV diameter were analyzed as a function of time with the use of regression analysis. The pre-LV cavity diameter was significantly different (P < 0.005). Our results confirm that the bulk of the myocardium is relaxing immediately after defibrillation.

A study by Malkin et al. (11) measured left ventricular (LV) geometry in canines after defibrillation by using two-dimensional (2D) ultrasound imaging. Their study was the first to measure the mechanical activity in the myocardium after a defibrillation shock. The 2D study showed that the cross-sectional area of the LV cavity rapidly increased within ~200 ms after defibrillation, suggesting that there is relaxation of the myocardium after defibrillation. Using the principles of excitation-contraction coupling of cardiac tissue (1, 6, 8, 9, 12, 15), we hypothesize that this observed relaxation is a result of direct deexcitation of the bulk of the myocardium. One limitation of the previous study (11) is that the first 33 ms after the shock may not have been captured due to their sampling rate of 30 Hz. The first 33 ms may be critical for discriminating between shock- and excitation-induced relaxation.

METHODS

Animal preparation. The experimental protocol for this study is the same as reported in Malkin et al. (11) and is only...
briefly described here. Seven mongrel dogs were anesthetized with pentobarbital sodium (30–35 mg/kg iv initially) and then maintained with doses of 3 mg·kg⁻¹·h⁻¹. Skeletal muscle paralysis was maintained with the use of succinylcholine (0.3 mg/kg initially and maintenance doses at 0.3 mg/kg every 20 min as indicated) to prevent excessive motion artifact. The ECG (lead II), blood pressure (femoral artery), and rectal temperature were continuously monitored. A hot water blanket was used whenever necessary to maintain body temperature.

Twenty ventricular fibrillation episodes were induced in each animal. Truncated exponential biphasic defibrillation shocks (model HVS-02, Ventritex; Sunnyvale, CA) were delivered 5–50 s after ventricular fibrillation induction. The biphasic shock waveform consisted of 6-msec duration phases, where the leading edge voltage of the second phase was set to the trailing edge voltage of the first phase. The first 10 shocks determined the voltage level that would successfully defibrillate 50% of the time (DF50) using a 10-step Bayesian up-down protocol (3). The latter 10 shocks were administered at the DF50 and were the only ones analyzed in this study. If the primary shock failed to defibrillate, backup shocks were administered but not analyzed.

Ultrasound measurements were made with a Hewlett-Packard Sonos 1000 ultrasonic imaging machine and M-mode data were recorded on a VHS tape recorder at a sampling rate of 250 Hz before the defibrillation pulse, during the defibrillation pulse, and for several seconds after the pulse. The ultrasonic transducer was placed on the left thorax so that the 2D image showed well-defined endocardial walls with the M-mode line in the center of the LV cavity.

**Ultrasound image analysis.** The duration chosen for image analysis was 32 ms before each shock and 32 ms after the shock. The anterior and posterior endocardial walls were outlined by hand with the use of Image software (Scion; Frederick, MD). The pixel locations of the endocardial walls were exported and converted to centimeters by using the depth setting recorded on the ultrasound image. The depth setting of the ultrasound was either 8 or 10 cm.

M-mode echocardiography has limitations that resulted in the rejection of some data. The problems included motion artifact (diaphragmatic, sternal, or operator motion), poor contrast of the endocardial walls, and, rarely, failure to record the M-mode image during defibrillation. We rejected images based on motion artifact when the M-mode analysis line, visible in simultaneous 2D images, moved completely outside the LV cavity. Single data points were rejected due to electrical interference when the shock saturated the ECG, obscuring one sample.

The LV diameter was computed as the distance between the anterior and posterior endocardial walls for each sample time. The time of shock was taken as the time of ECG saturation, defined as the sample when the ECG reached at least twice its normal amplitude (negative or positive).

**Statistical analysis.** Before analysis began for each episode, data points were normalized to the LV diameter of the sample immediately preceding the shock. The preshock and postshock points were regressed separately to determine the pre- and postshock slopes of the LV diameter. A sign test was used to test for random occurrence of an increase in the LV diameter after a defibrillation shock for both successful and unsuccessful shocks. A single valued t-test was performed to compare the random variable (the LV diameter slope) to a constant to test the hypothesis that the slopes were >0. A sequential t-test using Dunnett’s correction was used to compare the average LV diameter at \( t = 0, 4, \ldots, 32 \) ms to the preshock diameter \( (t = -4 \) ms) for successful and unsuccessful defibrillation shocks were recorded and 51 episodes were analyzed. Entire episodes were rejected because of poor contrast between the blood pool and the anterior and posterior endocardial walls (4 of 70), because of translation of the heart and shifting of the M-mode line outside the ventricular cavity (10 of 70), or because no images were captured (5 of 70). Of the 19 rejected episodes, 10 were from one animal; therefore that animal was completely removed from the study. Single samples were rejected due to ECG saturation at \( t = 0 \) and/or \( t = 4 \) ms in 23 episodes and motion artifact at \( t \approx 20 \) ms in 10 episodes.

Figure 1 shows a sample ultrasound image. In this case, the defibrillation shock occurred at a large positive deflection of the ECG. Before the shock, the LV cavity diameter was constant. Immediately after the shock, the cavity increased dramatically. This is best seen in the normalized diameter versus time graph (Fig. 2). Table 1 gives the mean LV diameter slopes for each animal. The overall mean pre- and postshock slopes are 0.2 ± 2.2% and 3.3 ± 7.9% of the preshock diameter per 10 ms, respectively. The postshock slopes were significantly >0 \( (P < 0.005) \). Additionally, the difference between post- and preshock slope showed a positive value for both successful and unsuccessful shocks \( (P < 0.01) \). When sequentially comparing the LV diameter at each postshock time instance to the preshock value \( (t = -4 \) ms), the average LV diameters for both successful and unsuccessful episodes (Fig. 2) did not change significantly until \( t = 32 \) ms \( (P < 0.05) \).
DISCUSSION

Malkin et al. (11) showed that relaxation of the bulk of the myocardium occurs within 200 ms after a defibrillation shock. The authors suggested that the relaxation was a result of direct deexcitation by the shock. However, they could not measure the changes in LV geometry within 33 ms after the shock with their technique. It is possible that the observed relaxation followed direct excitation immediately after the shock. If the relaxation followed direct excitation, we should then observe contraction in at least the first 30 ms after the shock. On the other hand, if the relaxation was a result of direct deexcitation, then we should observe relaxation immediately after the shock.

Indeed, our study suggests that the bulk of the myocardium relaxes ~4% per 10 ms immediately after defibrillation shocks. By using the principles of excitation-contraction coupling, we hypothesize that this observed relaxation is a result of direct deexcitation of the bulk of the myocardium. Recent in vitro studies (5) have suggested that deexcitation is a key mechanism for defibrillation, but they are limited to epicardial measurements. A distinct advantage of the ultrasonic technique used here is that it provides noninvasive in

![Fig. 2. The time course of preshock (●) and postshock (■) LV diameter for the single defibrillation episode (see Fig. 1). The shock occurs at t = 0. Data points were normalized to the LV diameter immediately preceding the shock (t = −4 ms). Pre- and postshock data were separately fit with linear regression. The pre- and postshock slopes of the linear fits (solid traces) are −1.19 and 11.8% of the preshock diameter per 10 ms, respectively. The average LV diameters for all defibrillation episodes in all animals for both successful (+) and unsuccessful (×) episodes (dashed traces) did not change significantly until t = 32 ms (P < 0.05). Note that the postshock LV diameter is increasing with respect to time in the single episode shown as well as the averages over all episodes, suggesting relaxation of the bulk of the myocardium.](image)

Table 1. Pre- and postshock LV diameter slope

<table>
<thead>
<tr>
<th></th>
<th>Animal</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Mean Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preshock</td>
<td>Success</td>
<td>0.54±0.27</td>
<td>0.00±0.00</td>
<td>−0.39±0.74</td>
<td>0.58±0.62</td>
<td>0.60±0.84</td>
<td>0.41±1.84</td>
<td>0.19±1.16</td>
</tr>
<tr>
<td></td>
<td>Failure</td>
<td>−0.19±0.43</td>
<td>−0.75±1.05</td>
<td>3.62±6.27</td>
<td>0.89±1.44</td>
<td>−0.18±1.69</td>
<td>0.23±2.93</td>
<td></td>
</tr>
<tr>
<td>Postshock</td>
<td>Success</td>
<td>11.18±15.24</td>
<td>3.14±6.53</td>
<td>2.75±1.88</td>
<td>4.48±1.94</td>
<td>−1.48±0.57</td>
<td>4.06±7.44</td>
<td>3.98±7.09</td>
</tr>
<tr>
<td></td>
<td>Failure</td>
<td>4.25±19.78</td>
<td>−0.36±1.77</td>
<td>4.40±7.41</td>
<td>0.53±2.80</td>
<td>1.35±7.28</td>
<td>1.76±9.39</td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>Success</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Failure</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>8</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD. LV, left ventricular. Diameter slope is measured as a percentage of preshock per 10 ms. Although seven animals were tested, all ultrasound data from one animal were rejected.
vivo measurements that reflect the global activity of the myocardium.

There is direct evidence that forced repolarization by an electric stimulus causes relaxation (7, 10) and deactivates Ca\(^{2+}\) transients (7). Ferrier et al. (7) measured cell shortening in guinea pig ventricular cells after forced repolarization and discovered that the cells immediately relaxed and intracellular Ca\(^{2+}\) concentration immediately decreased after the repolarizing stimulus. Knisley et al. (10) has shown that the contraction strength significantly decreased immediately after a strong anodal or cathodal shock was delivered early in the plateau phase of the action potential in frog ventricular muscle. Zaugg et al. (17) showed that successful defibrillation shocks lead to sudden reduction in intracellular calcium overload, which also supports the results of the present study.

Thus the observed changes in LV geometry are very likely a direct result of deexcitation in the bulk of the LV myocardium. The 2D ultrasound study (11) previously described has shown that the defibrillation shock doubles the LV cavity area in <200 ms, and by 33 ms shows a significant increase in the area. Our study verifies that the LV is indeed only relaxing in the first 32 ms after defibrillation. We conclude that the relaxation observed by Malkin et al. (11) is shock induced and not a result of excitation-induced contraction, followed by relaxation.

**Limitations.** Although M-mode echocardiography has high time resolution, a wide range of factors such as electrical interference, motion artifacts, and other technical problems affect the quality of the 1D ultrasound image. The manual tracing of the endocardial walls may not be reproducible by either single or multiple operators when the contrast of the image is poor and may introduce operator bias. The M-mode might not always remain in the center of the LV cavity after a defibrillation shock. A lateral translation of the of the M-mode line relative to the heart would lead to an underestimation of the LV diameter because all chords are less than the diameter. Rotation of the M-mode line relative to the heart could produce an overestimation of LV diameter; however, this would also distort the approximately circular geometry of the LV in the 2D image in a way that was not observed in any episode. Thus increases after defibrillation might actually be even larger than we claim. Linear regression analysis was used to determine the LV diameter slope after defibrillation. This analysis was chosen to determine only if the LV diameter was increasing. A nonlinear fit to the data may be more accurate and show even more significant increases. Our data are not from the first shock given to the animal; therefore, prior shocks may have induced edema that may have influenced our results.

In conclusion, the objective of this study was to determine whether the LV diameter increased within 32 ms after defibrillation shocks. The results show that the LV diameter is increased and suggest that the LV relaxes immediately after defibrillation. The observed relaxation is shock induced and not excitation induced. No contraction was observed. Thus the relaxation is likely a direct result of deexcitation in the bulk of the myocardium. A distinct advantage of the ultrasonic technique used here is that it provides noninvasive in vivo measurements that reflect the global activity of the myocardium.

This study was supported in part by an American Heart Association Established Investigator Award (to R. A. Malkin).

**REFERENCES**


