Transvenous Biventricular Defibrillation Halves Energy Requirements in Patients

Christian Butter, MD; Eckhard Meisel, MD; Juergen Tebbenjohanns, MD; Lothar Engelmann, MD; Eckart Fleck, MD; Bernd Schubert, MD; Stephen Hahn, PhD; Dietrich Pfeiffer, MD

**Background**—Defibrillation thresholds (DFT) with standard implantable cardioverter-defibrillator leads in the right ventricle (RV) may be determined by weak shock field intensity in the myocardium of the left ventricle (LV). Adding a shocking electrode in a coronary vein on the middle of the LV free wall, thereby establishing biventricular defibrillation, substantially reduced defibrillation requirements in animals. We investigated the feasibility of this approach in 24 patients receiving an implantable cardioverter-defibrillator using a prototype over-the-wire temporary LV defibrillation lead.

**Methods and Results**—The LV lead was inserted through the coronary sinus, using a guide catheter and guidewire, into a posterior or lateral coronary vein whose location was determined by retrograde venography. Paired DFT testing compared a standard system (RV to superior vena cava plus can emulator [SVC+Can], 60% tilt biphasic shock) to a system including the LV lead. The biventricular system was tested with a dual-shock waveform (20% tilt monophasic shock from LV→SVC+Can, then 60% tilt biphasic shock from RV→SVC+Can). Twenty patients completed DFT testing. Venography and LV lead insertion time was 46±40 minutes. The biventricular system reduced mean DFT by 45% (8.9±1.1 J versus 4.9±0.5 J, \( P<0.001 \)). Twelve patients (60%) had a standard system DFT \( \leq 8 \) J, and the biventricular system gave a lower DFT in all patients. There were no adverse events related to the use of the LV lead, which was removed after testing.

**Conclusions**—Internal defibrillation using a transvenously inserted LV lead is feasible, produces significantly lower DFTs, and seems safe under the conditions tested. Biventricular defibrillation may be a useful option for reducing DFTs or could be added to an LV pacing lead for heart failure. (*Circulation*. 2001;104:2533-2538.)

Key Words: defibrillation ■ patients ■ veins

A major focus of internal defibrillation research has been to reduce the defibrillation threshold (DFT). Numerous studies suggest that further DFT reduction with right ventricular (RV) implantable cardioverter-defibrillator (ICD) lead systems may be limited by their inability to raise the shock field strength in the posterolateral myocardium of the left ventricle (LV). Animal studies showed large energy reductions were achieved by using a small electrode sutured to the LV epicardium and sequential shock waveforms. Another study demonstrated DFT reductions >50% when using a transvenous LV lead inserted through the coronary sinus (CS). The success of recent clinical studies of transvenous LV pacing leads for the treatment of heart failure encouraged investigation of transvenous LV defibrillation.5,6 The purpose of this human study was to examine a transvenous approach for inserting a prototype, over-the-wire, temporary defibrillation lead into a vein on the LV. A new dual-shock defibrillation waveform (monophasic LV to superior vena cava plus can emulator [SVC+Can], then biphasic RV→SVC+Can) was tested in conjunction with the biventricular lead system. The study had 2 primary objectives: (1) to determine the LV lead’s effect on ventricular DFTs and (2) to assess the feasibility of placing the prototype LV lead in a specific region of the posterolateral LV.

**Methods**

**Patients**

Twenty-four consecutive patients undergoing implantation of a new ICD system for standard indications were enrolled at 4 investigational centers. Demographics for the patient population are shown in Table 1. Patients <18 years of age or those with known intolerance to x-ray contrast agents were excluded. The study was reviewed and approved by an institutional review committee, and all patients gave written informed consent. All procedures were performed in accordance with institutional guidelines.
**TABLE 1. Patient Demographics for the 20 Patients Completing All Required Testing**

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/female</td>
<td>17/3</td>
</tr>
<tr>
<td>Age, y (median)</td>
<td>64±6 (64)</td>
</tr>
<tr>
<td>Ejection fraction, % (median)</td>
<td>39±12 (36)</td>
</tr>
<tr>
<td>NYHA class, n</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Primary cardiac disease, n</td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>17</td>
</tr>
<tr>
<td>Nonischemic cardiomyopathy</td>
<td>2</td>
</tr>
<tr>
<td>Dilative cardiomyopathy</td>
<td>1</td>
</tr>
<tr>
<td>Primary arrhythmia, VF/VF</td>
<td>12/8</td>
</tr>
<tr>
<td>Drugs at implantation, n</td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>4</td>
</tr>
<tr>
<td>Sotalol</td>
<td>3</td>
</tr>
<tr>
<td>History of MI, n</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>12</td>
</tr>
<tr>
<td>Posterior</td>
<td>4</td>
</tr>
<tr>
<td>Surgical history, n</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>8</td>
</tr>
<tr>
<td>Angioplasty</td>
<td>8</td>
</tr>
<tr>
<td>Stent</td>
<td>7</td>
</tr>
</tbody>
</table>

Values are mean±SD (median) or number of patients.

**Lead Implantation**

Under local or general anesthesia, a standard RV defibrillation lead with 2 shocking coils and a pace/sense electrode (Guidant, Model 0145) was implanted using standard procedures. An ICD can emulator (Guidant, Model 6967) was inserted into a submuscular left pectoral pocket. Successful defibrillation with the standard lead system (RV→SVC+Can) at 15 J was demonstrated before proceeding to the investigational aspects of the procedure.

Retrograde venography was performed using a commercially available balloon occlusion catheter inserted into the CS (Arrow, model AI-07127, or equivalent). The balloon was temporarily inflated, and contrast agent was hand-injected to opacify as much of the LV venous system as possible. Right anterior oblique (30°), anteroposterior, and left anterior oblique (30°) views were recorded.

A modified guide catheter (Guidant, model ETC034) was inserted into the CS using the subclavian venous approach. A 0.014-inch guidewire was advanced through the guide catheter and steered deep into a vein on the posterior or lateral aspect of the LV free wall using the saved venograms for guidance. The prototype LV lead (Guidant, model ETT037) was advanced over the wire as deeply into the vein as possible. Right anterior oblique, anteroposterior, and left anterior oblique views of the final lead position were recorded. The LV lead, guidewire, guide catheter, and can emulator were removed after defibrillation testing.

The LV lead was constructed using a 1.22-mm diameter platinum-titanium wire coils and polytetrafluoroethylene insulation. The distal end had a flexible silicone tip to aid tracking over the wire and to minimize blunt trauma to the vein. The proximal end had a 6.1-mm feed-through style connector pin. A 5-cm section of the coil at the distal end remained exposed to serve as the shocking electrode (shadow surface area ~192 mm²).

**Defibrillation Testing**

Randomized, paired DFT testing was performed to compare the standard RV system (Figure 1a) to the biventricular system (Figure 1b). The standard system was tested with a 60% tilt biphasic waveform. Neither the LV lead nor the guidewire was in place during DFT testing of the standard system. The biventricular system was tested with a dual-shock waveform consisting of a 20% tilt monophasic shock from LV→SVC+Can, then a 60% tilt reverse-polarity biphasic shock from RV→SVC+Can. There was a 5-ms delay between the 2 shocks. All test shocks were delivered from a research defibrillation system (Guidant, model ETT034), with a 225-micro-Farad (μF) output capacitor that generated all shocks and shock phases in a manner consistent with a single capacitor discharge. (ie, the leading edge voltage of the second shock equaled the trailing edge voltage of the first shock).

DFTs were determined using a binary search protocol beginning at 6.5 J (Figure 2). Fibrillation was induced using a 50-Hz pulse train and continued for 10 s before delivery of the test shock. If the test shock failed, a rescue shock was delivered using an internal shock via the standard system or an external shock via cutaneous patches. A minimum of 5 minutes separated each fibrillation/defibrillation episode. Depending on test shock success or failure, subsequent defibrillation trials used higher or lower energies, as shown in Figure 2. The biventricular system was not tested at >10 J to minimize potential risks.

**Data Collection and Statistics**

The DFT, stored energy, peak voltage, peak current, and pulse width reported by the defibrillation system were recorded for each shock. Procedure times were also recorded. Venogram time included placement of the guide and/or occlusion catheter into the CS and collection of all the required x-ray views. LV lead insertion time included recannulization of the CS with a different guide catheter (if necessary), insertion of the guidewire, and LV lead manipulation time until the final LV lead position was achieved.

Unpaired descriptive data (patient demographics and procedure times) are reported as mean±SE. A paired Student’s t test was used to compare the defibrillation efficacy parameters of the standard system to the biventricular system. A minimum sample size of 18 patients was prospectively determined using α=0.05 and 80% power to detect a 2.5-J reduction in an expected standard system DFT of 8±3.5 J.

**Results**

Of the 24 patients enrolled, 20 completed all testing and were included in the paired DFT analysis. Reasons for dropout included pneumothorax during initial puncture of the subclavian vein (1 patient; no attempt to place the LV lead),...
inability to place the LV lead (2 patients), and a standard system DFT $>$ 20 J (1 patient; LV lead was placed but biventricular shocks were not successful at the maximum allowable energy of 10 J). There were no adverse events related to the insertion or shock testing of the LV lead.

Venogram and LV Lead Positioning Success
The mean time to obtain the venogram was 24 ± 26 minutes (range, 4 to 104 minutes; median, 15 minutes; mode, 10 minutes). The LV lead was successfully positioned in a posterior or lateral vein in 21 of the 23 patients attempted (91%). Mean LV lead insertion time for the 21 successful patients was 21 ± 22 minutes (range, 2 to 78 minutes; median, 10 minutes; mode, 7 minutes). Unsuccessful LV lead positioning was due to an unusually tortuous vein in one patient and to a severe entry angle from the great cardiac vein in the other patient. The procedure in these 2 patients was stopped after 32 and 44 minutes, respectively. Examples of

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Figure 2. Binary search DFT protocol. The standard RV system was tested at 15 J before the start of the study. The DFT protocol began at 6.5 J. The biventricular system was not tested with energies $>$ 10 J. F indicates failure; S, success.

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Figure 3. Venogram and final LV lead position for 2 patients. Upper panels (a through d) show left and right anterior oblique views of the venogram, and lower panels (e through h) show the corresponding view with the LV lead inserted. The 4 panels on the left (a, b, e, and f) show a patient with the LV lead in the left marginal vein. This patient had a prior bypass procedure and a posterior myocardial infarction. The middle vein, a small posterior vein, and the anterior vein were also visible. The standard system’s DFT was 15 J, and the biventricular system’s DFT was 8 J. The 4 panels on the right (c, d, g, and h) show a patient with the LV lead in a very posterior vein that originated at the posterolateral apex but drained into the CS near the ostium of the middle vein. The majority of the LV veins were small and originated near the base, probably due to a prior bypass and posterior myocardial infarction. The standard system’s DFT was 15 J, and the biventricular system’s DFT was 6.5 J.
venograms and final LV lead positions are shown in Figure 3. A composite rendering of the final lead position for the 20 patients that completed all testing is shown in Figure 4.

Defibrillation Data

Mean defibrillation parameter data are given in Table 2. Paired DFT data are illustrated in Figure 5. Results showed that the biventricular system reduced DFT by 45%, reduced stored energy by 44%, reduced peak voltage by 25%, and reduced peak current by 40%. All reductions were statistically significant at \( P < 0.001 \). Twelve patients had a standard system DFT between 8 and 15 J, and the biventricular system had a lower DFT in all 12.

Discussion

Major Findings

This clinical study showed that a very large reduction in mean DFT (45%) can be achieved using a lead transvenously inserted deep into a vein on the middle of the LV free wall. DFT reduction did not seem to depend on LV lead position (Figure 4) and, perhaps most importantly, the biventricular system reduced DFTs in all patients with higher standard system DFTs (between 8 and 15 J). Standard errors were also reduced by half, suggesting biventricular defibrillation narrows the distribution of possible DFTs.

This study also demonstrated the clinical feasibility of inserting a relatively simple prototype LV lead with a defibrillation electrode deep into a vein on the LV. A high LV lead insertion success rate (91%) was achieved, despite the fact that 75% of patients had a prior myocardial infarction and 35% had prior bypass surgery. The venogram was important in enabling identification of an acceptable vein (lateral or posterior) on the middle of the LV free wall. LV lead insertion times were generally acceptable, but longer times were needed in individual patients. These results were consistent with our prior report of retrograde venography and LV lead insertion.7

Prior Studies

Numerous prior studies suggest RV lead systems provide relatively weak electric field strength to the LV.1,2 Although present ICD systems using RV leads provide excellent performance, DFTs might be substantially reduced if electric field strength to the LV could be increased. A variety of electrodes, such as subcutaneous patches and arrays,8,9 active pulse generator “cans,”10 and coils in the CS,11 have been studied clinically. These approaches typically produce moderate DFT reductions of 20% to 30% and, although many probably increase the electric field strength on the LV, they do not specifically place an electrode in the middle of the LV free wall. Kudenchuk et al11 reported that adding a CS lead to

### Table 2. Mean Defibrillation Data

<table>
<thead>
<tr>
<th>Configuration</th>
<th>DFT, J</th>
<th>Stored Energy, J</th>
<th>Peak Voltage, V</th>
<th>Peak Current, Amp</th>
<th>Shock Impedance, Ohms</th>
<th>Pulse Width, ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard RV system</td>
<td>8.9 ± 1.0</td>
<td>10.7 ± 1.3</td>
<td>297 ± 20</td>
<td>7.3 ± 0.2</td>
<td>43 ± 1</td>
<td>10.3 ± 0.3</td>
</tr>
<tr>
<td>Biventricular system</td>
<td>4.9 ± 0.5*</td>
<td>6.0 ± 0.6*</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>18.9 ± 0.3*</td>
</tr>
<tr>
<td>Dual shock 1 (LV)</td>
<td>2.1 ± 0.2</td>
<td>...</td>
<td>224 ± 12*</td>
<td>3.1 ± 0.2*</td>
<td>76 ± 3*</td>
<td>4.0 ± 0.1</td>
</tr>
<tr>
<td>Dual shock 2 (RV)</td>
<td>2.9 ± 0.3</td>
<td>...</td>
<td>174 ± 9*</td>
<td>4.4 ± 0.3*</td>
<td>43 ± 1</td>
<td>10.0 ± 0.2</td>
</tr>
</tbody>
</table>

Values are mean ± SE. Stored energy was calculated using \( \frac{1}{2} \cdot C \cdot (V_{peak})^2 \), where \( C \) indicates capacitance and \( V \), voltage. The total pulse width for dual shocks included the 5-ms intershock delay.

* \( P < 0.001 \) vs standard system.
an RV→Can system gave a nonsignificant DFT reduction of 12% and suggested that the added complexity of inserting a CS lead is not offset by its potential benefits. Thus, our data suggests placing a lead in the middle of the LV free wall rather than in a border region, such as the CS, may be important in achieving large DFT reductions.

Prior studies also showed sequential shock schemes can produce lower DFTs than single shock schemes, but none placed a lead transvenously on the middle of the LV free wall.12,13 Animal and clinical studies demonstrated substantial reductions in DFT using a small epicardial patch on the LV free wall and a sequential shock waveform, but this approach is no longer clinically acceptable due to the need for transthoracic patch insertion.3,11 Other sequential shock studies used small, temporary defibrillation catheters that bear little resemblance to modern ICD leads, and most studies used 2 monophasic shocks delivered with equal amplitudes.12 The present study bears closest resemblance to that of Exner et al,14 who reported a 44% reduction in DFT with sequential biphasic waveforms. However, their study required the addition of both a CS lead and a subcutaneous patch, did not include the subcutaneous patch (or an active can) as part of the control system, and used 2 biphasic waveforms of equal amplitude (thereby requiring an ICD with 2 sets of discharge capacitors). Because other studies have shown the addition of a subcutaneous patch or active can alone reduces DFTs by 25% to 30%,8,10 it is unclear how much the addition of a CS lead and sequential shocks might have contributed to the DFT reduction. Our study used a modern, clinically relevant, 3-electrode active can system as a control and showed an additional DFT reduction of 45% using the LV lead and dual-shock waveform.

Recently, the use of transvenously inserted LV pacing leads to treat patients with heart failure has been proven feasible.5,6 This suggested a similar approach for transvenous insertion of a LV defibrillation lead might also be feasible. An animal study using a transvenously inserted LV defibrillation lead showed 42% to 62% reductions in DFT were possible.4 Additional animal studies showed that dual shocks produced significantly more DFT reduction than a single shock and showed that the dual-shock approach required a posterolateral LV lead position.15

Two prior clinical research studies, performed in part by our group and by other collaborators, tested different LV defibrillation lead designs with a variety of waveforms and shock schemes, but consistent DFT reduction was not achieved.16,17 In the first study,16 a 0.018-inch guidewire was modified to serve as the LV shocking electrode. Results showed the wire could be inserted deep into a randomized LV target vein, but the wire proved to be a poor defibrillating electrode, with a shock impedance >120 Ω. Large DFT reductions were observed in selected patients, which provided incentive to continue studying this approach. In the second study,17 a 3-cm, over-the-wire LV lead was used. Testing was performed with either single biphasic shocks from RV→LV→SVC+Can or a different dual-shock scheme of biphasic shock from RV→SVC+Can, then another biphasic shock from RV→SVC+Can. Results did not show a statistically significant reduction in DFT, but subanalysis indicated consistent DFT reduction occurred with the dual-shock scheme when the LV lead was placed in a posterolateral area of the LV free wall.

Present Study
The present study was specifically designed to target the middle of the LV free wall with a new, optimized, dual-shock waveform. The optimized dual-shock waveform (choice of capacitance, tilts, vectors, intershock delays, etc) was guided by numerous animal studies.18–22 Collectively, these animal studies suggested effective dual-shock waveforms for biventricular defibrillation required a balance of current and energy between the RV and LV electrodes. Results showed this new dual-shock waveform delivered 50% more current to the LV than the prior clinical studies and had an LV:RV energy ratio of ~40% to 60% (Table 2). Thus, optimization of the dual-shock waveform seemed to play an important role in DFT reduction, and further studies aimed specifically at optimizing the waveform for humans may lead to even larger DFT reductions.

The dual-shock waveform was designed for easy implementation in an ICD by using a single 225-µF output capacitor that is smaller than the two 250-µF capacitors typically used in ICDs. The 225-µF capacitor would also deliver a smaller amount of energy, but this should be acceptable due to the much lower energy requirement of the biventricular defibrillation system. Generating the dual-shock waveform also requires the addition of some switching circuitry, but its volume would be almost negligible compared with the smaller capacitor volume. Thus, ICD volume could be reduced.

As a final comment, although reduction of mean DFTs was the main objective of this study, treatment of high DFT patients (>15 J) may be an important use for biventricular defibrillation. One patient with a very high standard system DFT (25 J) did not convert at 10 J with the biventricular system, but the lack of data in high DFT patients should not be considered a major detriment to the overall results. Every patient with a DFT between 8 and 15 J had a lower DFT with the biventricular system, demonstrating that consistent DFT reduction can be achieved. There is no reason to believe this would not also be true for higher DFT patients if they could be enrolled and tested at energies >10 J. The 10 J limit on biventricular shock strength was artificially imposed because the safety of LV shocks had not been fully investigated. Animal studies including histopathology of the LV myocardium, coronary arteries, and veins might be prudent before attempting to test higher energies in patients with higher DFTs. However, the large DFT reductions observed in this study, along with the lack of any adverse events related to LV shock delivery, should encourage further investigations in the field of biventricular defibrillation.

Limitations
The LV defibrillation lead used in this study was a prototype, and the implantation tools proved to be less than optimal. Improvements to the lead and delivery system should reduce procedure times and increase insertion success rates. An asymmetric DFT protocol was used as a practical means to limit the number of ventricular fibrillation inductions. This
may have slightly biased the mean DFTs but, because of the paired nature of DFT testing, it should not have a significant effect on the large DFT reduction observed with the LV lead. Finally, although no adverse events due to the delivery of LV shocks were observed, no specific testing was done to determine the impact of LV shocks on the vein or adjacent arteries. Additional studies are needed to determine the specific impact of LV shocks and the long-term consequences of a defibrillation lead permanently implanted in a LV vein.

Clinical Implications
An LV defibrillation lead may be useful for many reasons. A defibrillation-only LV lead could be used to reduce DFTs as an alternative to a subcutaneous patch, subcutaneous array, or larger, higher-energy output device. An LV shock electrode could be also be added to LV pace/sense leads being designed to treat patients with heart failure. Such patients would already be receiving an LV lead and could also receive the benefits of lower DFTs with the same lead. Furthermore, future studies may demonstrate the value of LV pacing for the broader population of ICD patients and, thus, many more patients could receive LV leads that include defibrillation therapy. Finally, an LV defibrillation lead would reduce the maximum energy requirement, so device size could be reduced and longevity increased, positively impacting the entire ICD population.

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