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Optimal Strength and Number of Shocks at Upper Limit of Vulnerability Testing Required to Predict High Defibrillation Threshold Without Inducing Ventricular Fibrillation(心室細動を誘発することなく高除細動閾値患者を同定することを目的とした心室細動誘発閾値上限テストにおける最適なショックの強さと回数)

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Optimal Strength and Number of Shocks at Upper Limit of Vulnerability Testing Required to Predict High Defibrillation Threshold Without Inducing Ventricular Fibrillation

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Background: The upper limit of vulnerability (ULV) closely correlates with the defibrillation threshold (DFT). The aim of this study was to establish the optimal protocol for using the ULV test to predict high DFT (>20 J) without inducing ventricular fibrillation (VF).

Methods and Results: The 10-J and 15-J ULV test with 3 coupling intervals (-20, 0, and +20 ms to the peak of T-wave) and the DFT test were performed in 96 patients receiving implantable cardioverter defibrillator. ULV ≤10 J was confirmed in 47 (49%). ULV ≤15 J was confirmed in 70 (77%) of 91 patients (15-J ULV test could not be done in 5). The sensitivity and negative predictive value of both ULV >10 J and >15 J for predicting high DFT were 100%. The specificity and positive predictive value of ULV >15 J were higher than those for ULV >10 J (85% vs. 55%, 43% vs. 22%, respectively). The rate of VF inducibility for confirming ULV ≤15 J was lower than that for ULV ≤10 J (23% vs. 51%, P<0.0001). On analysis of single 15-J ULV test only at the peak of T-wave, VF was not induced in 79 of 91 patients, but 4 of these had high DFT.

Conclusions: The 15-J ULV test with 3 coupling intervals could correctly identify high-DFT patients and reduce the necessity for VF induction at defibrillator implantation. (Circ J 2013; 77: 2490–2496)

Key Words: Defibrillation; Defibrillation threshold; Implantable cardioverter defibrillator; Upper limit of vulnerability; Ventricular fibrillation
Methods

Patients
The subjects consisted of 96 patients (80 men, 16 women) undergoing implantation of an ICD/CRTD for the first time (n=75) or as a replacement (n=21) between March 2006 and November 2008. All patients underwent transthoracic echocardiography and routine laboratory testing, and all patients gave written informed consent before the device implantation.

Device Implantation
Patients were anesthetized with propofol or midazolam. Heart rhythm, O₂ saturation, and continuous systemic blood pressure were monitored throughout all procedures. Disposable adhesive defibrillator pads were applied to the patients and attached to the external defibrillator for rescue cardioversion. Various defibrillator models were implanted. The defibrillator system was inserted through a left pectoral incision in all patients except for 3 who had a history of device infection (n=1) and dialysis vascular access (n=2). The tip of the ventricular shock lead was placed at or near the right ventricular apex if the R wave was ≥5 mV and the pacing threshold was ≤1.5 mV at 0.5 ms. Before defibrillator replacement, previously implanted shock leads were confirmed to satisfy all the aforementioned criteria.

Determination of Vulnerable Period
During right ventricular pacing with a cycle length (CL) of 500 ms via the shock lead, the latest peak of the monophasic T-wave was determined on standard 12-lead electrocardiography (ECG) displayed at 100 mm/s, and the interval from the stimulus to the latest peak of the T-wave (St-T peak interval) was measured. A limb-lead ECG was substituted if a 12-lead ECG was unavailable. The vulnerable period was determined from -20 to +20 ms of the latest T peak, as described.19,22

Definition of Ventricular Fibrillation
Arrhythmias with CL <280 ms with polymorphic and irregular (A CL >40 ms) QRS complexes on surface ECG were classified as VF. Arrhythmias with monomorphic QRS complexes or CL >280 ms were defined as ventricular tachycardia and excluded from the VF count.23

Vulnerability and Defibrillation Testing
Vulnerability testing was started at 10J in the early enrolled 49 patients (Figure). The first 10J T-wave shock was delivered at the ST-T peak interval after 8 right ventricular pacing beats with
Table: Patient Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Outcome (n=96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63±14</td>
</tr>
<tr>
<td>M/F</td>
<td>80/16</td>
</tr>
<tr>
<td>Underlying heart disease</td>
<td></td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>39</td>
</tr>
<tr>
<td>Non-ischemic cardiomyopathy</td>
<td>41</td>
</tr>
<tr>
<td>No structural heart disease</td>
<td>16</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>43±18</td>
</tr>
<tr>
<td>CRTD</td>
<td>15</td>
</tr>
<tr>
<td>Indication for defibrillator</td>
<td></td>
</tr>
<tr>
<td>If VF or cardiac arrest</td>
<td>32</td>
</tr>
<tr>
<td>VT</td>
<td>48</td>
</tr>
<tr>
<td>Non-sustained VT</td>
<td>16</td>
</tr>
<tr>
<td>Anti-arrhythmic drugs</td>
<td>22</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>15</td>
</tr>
<tr>
<td>Sotalol</td>
<td>7</td>
</tr>
<tr>
<td>Class I</td>
<td>4</td>
</tr>
<tr>
<td>β-blockers</td>
<td>7</td>
</tr>
<tr>
<td>ACE or ARB</td>
<td>70</td>
</tr>
</tbody>
</table>

Data given as mean±SD or n. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CRTD, cardiac resynchronization therapy defibrillator; LVEF, left ventricular ejection fraction; VF, ventricular fibrillation; VT, ventricular tachycardia.

CL=500 ms. If VF was not induced, a subsequent 10-J shock was delivered at -20 ms and +20 ms to the St-T peak interval. If three 10-J shocks with different timing did not induce VF, we determined that the ULV was ≤10 J, and then subsequent shocks were decreased to 5 or 11, and delivered in the same sequence until VF was induced. If VF was not induced by a series of induction shocks, VF was induced by alternative methods such as a high frequency burst for defibrillation testing.

Vulnerability was tested at 1-min intervals between shocks. If VF was induced, defibrillation was tested. Five minutes after VF defibrillation, the energy of the next ULV test shock was increased to 15 J and delivered in the same manner. If VF was also induced at 15 J, it was determined that the ULV was >15 J. If VF was not induced by any 15-J-wave shocks, the ULV was determined as ≤15 J.

The aim of this study was to estimate the DFT without inducing VF. The first 10-J-T-wave shocks, however, induced VF in many patients (53%) using this protocol. Therefore, we changed the first induction shock to 15 J in the next 47 patients (Figure). The protocol for the 15-J shocks was the same as that described for the 10-J shocks.

During defibrillation testing for induced VF, we evaluated only whether DFT was ≤20 J or not. The first defibrillation shock was set at 20 J and the second was set at the maximum delivered energy of each device. If the first 20-J shock could not defibrillate (DFT >20 J), the first shock was increased by 5 J until VF was defibrillated in subsequent defibrillation tests. We defined DFT as the smallest shock strength that defibrillated twice.

In both vulnerability and defibrillation testing, shock energy was unified as delivered energy. Therefore, the programmed (charged) energy was adjusted to obtain the required delivered energy for the Guidant defibrillator (delivering energy for the Guidant defibrillator (delivering energy of 10, 15, and 20 J was equivalent to charged energy of 11, 17, and 23 J, respectively).

If a patient became hemodynamically unstable or fell into VF several times during these tests, vulnerability and defibrillation testing were stopped according to the decision of the operator.

Statistical Analysis
Baseline characteristics are given as mean±SD and were analyzed for statistical significance using paired t-test for continuous variables and Fisher’s exact test for categorical variables. P<0.05 was considered statistically significant.

Results
Table 1 lists the patient characteristics. Anti-arrhythmic drugs (amiodarone, n=15; sotalol, n=7; mexiletine, n=2; pimelolin, n=1; procainamide, n=1) were given to 26 patients and β-blockers were given to 70 (73%) at the time of the procedure.

Device Implantation
At the time of ICD implantation, the mean R wave amplitude on the ventricular sensing lead was 12.0±5.11 mV (range, 5.0-29.1 mV). The stimulation threshold was <1.5 V at 0.5 ms in all patients. Dual-chamber ICDs and CRTDs were implanted in 73 and 15 patients, respectively. No major perioperative complications developed that required additional procedures.

Vulnerable Period
The mean St-T peak interval was 351±35 ms. No visible T-wave alternans developed at right ventricular pacing at 500 ms CL.

Vulnerability and Defibrillation Testing
The ULV test was started at 10 J in the early enroled 49 patients (Figure). VF was induced at 10 J in 26 patients (53%; ULV >10 J) and not induced in 23 (47%; ULV ≤10 J). Among the 26 patients in whom VF was induced at 10 J ULV test, 21 of them underwent testing at 15 J. Among these 21 patients, the 15 J ULV test induced VF in 11 patients (ULV >15 J) and did not induce VF in 10 patients (10 J < ULV ≤15 J; Figure C). But the 15 J ULV test could not be done in 5 patients because of unstable hemodynamics (hypotension or bradycardia) after VF defibrillation. Interestingly, 2 of these 5 patients had high DFT (Figure B).

The ULV test was started at 15 J in the next 47 patients (Figure). VF was induced by 15 J ULV test in 10 J (21%; ULV >15 J) and not induced in 37 (79%; ULV ≤15 J). The ULV test at 10 J was done in 37 patients with ULV ≤15 J. VF was induced by 10 J ULV in 13 patients (35%; 10 J < ULV ≤15 J; Figure E) and VF was not induced in 24 patients (65%; ULV >15 J).

Among the 47 patients without VF induction on the 10 J ULV test, 39 patients underwent the 5 J-ULV test and VF was induced in 28 patients (5 J < ULV ≤10 J). The 1 J-ULV test was done in 19 patients (11 patients without VF induction by the 5 J-ULV test and 8 patients who did not undergo the 5 J-ULV test) and VF was induced in 17 patients (1 J < ULV ≤5 J in 10 patients and 1 J < ULV ≤10 J in 7 patients). In the remaining 2 patients, high frequency burst pacing was required for inducing VF.

ULV and High DFT
In all of the 96 patients, ULV ≤10 J was confirmed in 47 patients (49%; Figure A) and ULV >10 J was confirmed in 49 patients (51%; Figure B-E). In total, 11 patients (11%) had high DFT (>20 J) and ULV >10 J in all of these 11 patients. In 38 of 49 patients with ULV >10 J, however, DFT was <20 J (acceptable DFT). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of ULV >10 J for predicting high DFT were 100%, 55%, 22% and 100%, respectively (Table 2).

Because 15 J ULV test could not be done in 5 patients (Figure B), the decision as to whether ULV was ≤15 J or >15 J...
Table 2. Confirmation of ULV ≤10J and ≤15J, and DFT

<table>
<thead>
<tr>
<th>DFT ≤20 J (n)</th>
<th>DFT &gt;20 J (n)</th>
<th>Total (n)</th>
<th>SS (%)</th>
<th>SP (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ULV ≤10J</td>
<td>47</td>
<td>0</td>
<td>47</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ULV &gt;10J</td>
<td>38</td>
<td>11</td>
<td>49</td>
<td>100</td>
<td>55</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>85</td>
<td>11</td>
<td>96</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ULV ≤15J</td>
<td>70</td>
<td>0</td>
<td>70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ULV &gt;15J</td>
<td>12</td>
<td>9</td>
<td>21</td>
<td>100</td>
<td>85</td>
<td>43</td>
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<tr>
<td>Total</td>
<td>82</td>
<td>9</td>
<td>91</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Five patients could not undergo ULV testing at 15J. DFT; defibrillation threshold; NPV, negative predictive value; PPV, positive predictive value; SP, specificity; SS, sensitivity; ULV, upper limit of vulnerability.

Table 3. ULV Test at 10J and 15J; VF Inducibility and High DFT (>20J)

<table>
<thead>
<tr>
<th>DFT ≤20 J (n)</th>
<th>DFT &gt;20 J (n)</th>
<th>Total (n)</th>
<th>SS (%)</th>
<th>SP (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-J ULV test with 3CI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No VF</td>
<td>47</td>
<td>0</td>
<td>47</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VF</td>
<td>31</td>
<td>8</td>
<td>39</td>
<td>100</td>
<td>66</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>8</td>
<td>86</td>
<td></td>
<td></td>
<td></td>
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<td>15-J ULV test with 3CI</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No VF</td>
<td>47</td>
<td>0</td>
<td>47</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VF</td>
<td>12</td>
<td>9</td>
<td>21</td>
<td>100</td>
<td>80</td>
<td>42</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>9</td>
<td>68</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-J ULV test with 1CI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No VF</td>
<td>52</td>
<td>4</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VF</td>
<td>7</td>
<td>5</td>
<td>12</td>
<td>55</td>
<td>88</td>
<td>42</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>9</td>
<td>68</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI, coupling interval. Other abbreviations see in Tables 1, 2.

Table 4. Patient Characteristics vs. ULV Level

<table>
<thead>
<tr>
<th>Variables</th>
<th>ULV ≤10J (n=47)</th>
<th>ULV &gt;10J (n=49)</th>
<th>P-value</th>
<th>ULV ≤15J (n=70)</th>
<th>ULV &gt;15J (n=21)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63±14</td>
<td>62±14</td>
<td>0.93</td>
<td>62±15</td>
<td>64±11</td>
<td>0.50</td>
</tr>
<tr>
<td>M/F</td>
<td>39/8</td>
<td>41/8</td>
<td>&gt;0.99</td>
<td>58/12</td>
<td>18/3</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Underlying heart disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>23</td>
<td>16</td>
<td>0.14</td>
<td>29</td>
<td>8</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Non-ischemic cardiomyopathy</td>
<td>16</td>
<td>25</td>
<td>0.10</td>
<td>29</td>
<td>9</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>No structural heart disease</td>
<td>8</td>
<td>8</td>
<td>&gt;0.99</td>
<td>12</td>
<td>4</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>43±17</td>
<td>43±18</td>
<td>0.88</td>
<td>45±18</td>
<td>38±17</td>
<td>0.10</td>
</tr>
<tr>
<td>LVDD (mm)</td>
<td>57±9</td>
<td>55±14</td>
<td>0.38</td>
<td>55±10</td>
<td>57±16</td>
<td>0.51</td>
</tr>
<tr>
<td>LVDs (mm)</td>
<td>44±12</td>
<td>42±17</td>
<td>0.51</td>
<td>42±13</td>
<td>45±19</td>
<td>0.35</td>
</tr>
<tr>
<td>CRTD</td>
<td>4</td>
<td>11</td>
<td>0.09</td>
<td>8</td>
<td>5</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Anti-arrhythmic drugs</td>
<td>14</td>
<td>12</td>
<td>0.65</td>
<td>20</td>
<td>6</td>
<td>0.59</td>
</tr>
<tr>
<td>β-blockers</td>
<td>36</td>
<td>34</td>
<td>0.49</td>
<td>53</td>
<td>13</td>
<td>0.27</td>
</tr>
<tr>
<td>ACEI or ARB</td>
<td>37</td>
<td>33</td>
<td>0.25</td>
<td>51</td>
<td>14</td>
<td>0.17</td>
</tr>
<tr>
<td>St-T peak interval (ms)</td>
<td>349±34</td>
<td>353±35</td>
<td>0.58</td>
<td>348±33</td>
<td>353±37</td>
<td>0.55</td>
</tr>
<tr>
<td>DFT ≥20 J</td>
<td>0</td>
<td>11</td>
<td>0.0005</td>
<td>0</td>
<td>9</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data given as mean± SD or n. *Five patients could not undergo ULV testing at 15J. LVDD, left ventricular end-diastolic dimension; LVDs, LV end-systolic dimension; St-T, stimulus-T wave. Other abbreviations see in Tables 1, 2.

was made in 91 patients. ULV ≤15J was confirmed in 70 patients (77%; Figure A, C, E) and ULV >15J was confirmed in 21 patients (23%; Figure D). A high DFT was not found in patients with ULV ≤15J, whereas 9 of 21 patients with ULV >15J had a high DFT. The sensitivity, specificity, PPV and NPV of ULV >15J for predicting high DFT were 100%, 85%, 43% and 100%, respectively (Table 2).

The rate of VF inducibility to confirm ULV ≤15J was lower than that for ULV ≤10J (23% vs. 51%; P<0.0001).

10-J ULV vs. 15-J ULV Test
A total of 86 patients underwent 10-J ULV test and VF was induced in 39 patients (45%; Table 3). And 68 patients underwent 15-J ULV test and VF was induced in 21 patients (31%). The
sensitivity and NPV of VF inducibility for both the 10-J and 15-J ULV test for predicting high DFT were 100%. Importantly, the specificity and PPV of VF inducibility for the 15-J ULV test were higher than those for the 10-J ULV test (Table 3). Furthermore, the rate of VF inducibility for the 15-J ULV test was lower than that for the 10-J ULV test (31% vs. 45%, P=0.07).

Patient Characteristics and ULV
Patient characteristics did not differ significantly between ULV ≤10 J and >10 J, and ULV ≤15 J and >15 J. Patients with high DFT, however, were more often identified with ULV >10 J than ≤10 J (P=0.0005), and with ULV >15 J than ≤15 J (P<0.0001; Table 4).

Optimal Number of Shocks at ULV Test
We delivered 3 shocks within the vulnerable period (~20, 0, +20 ms to the peak of T-wave wave). The effectiveness of the 15-J ULV test with single shock only at the peak of the T-wave was analyzed. VF was induced by single shock at 15 J in 12 of 68 patients, and a high DFT was found in 5 (42%) of these 12 patients. Among 56 patients without VF induction by the single 15 J ULV test, 4 patients (7.1%) had a high DFT. The sensitivity, specificity, PPV and NPV of VF inducibility by single 15 J shock for predicting a high DFT were 55%, 88%, 42% and 93%, respectively (Table 3). The sensitivity of single 15 J ULV test was considerably lower than that for the 15-J ULV test with 3 coupling intervals, and the NPV of single ULV test was <100%.

Defibrillation Testing and High DFT
The ICD immediately sensed VF in all patients during defibrillation testing, and the R wave was not under-sensed during VF even when sensitivity was sufficiently blunted. Induced VF could not be terminated by a first rescue 20-J shock in 11 patients (high DFT). System modification such as repositioning of the shock lead or changing of the direction of the shock wave was required in 4 of them to achieve an adequate DFT safety margin (DFT maximum device output energy ~10 J).

Prevalence of non-ischemic cardiomyopathy (P=0.05), lower left ventricular (LV) ejection fraction (P=0.05), larger LV end-diastolic and end-systolic dimension (P=0.05 and 0.07, respectively) were more common in patients with high DFT but the differences did not reach significance (Table 5).

Number of Induction Shocks and Procedure Duration
The mean number of induction T-wave shocks was 5.7±2.3; the total duration of the test was 14.2±2.4 min and the amount of time required to confirm effective defibrillation energy (twice) or acceptable ULV (≤10 or ≤15 J) was 6.2±4.7 min for all patients.

Complications
Neither major complications nor prolonged unstable hemodynamics requiring inotropic agents or mechanical support were encountered in this series.

Discussion
The major findings can be summarized as follows. The ULV test at 10 and 15 J is a reliable method to identify patients with an acceptable DFT (≤20 J). In patients with acceptable DFT, the rate of VF inducibility by 15-J ULV test was significantly lower than that for the 10-J ULV test. Single ULV test at the peak of T-wave sometimes underestimated the ULV. Baseline patient characteristics could not predict high DFT, but ULV could.

Based on these findings, the 15 J-ULV test with 3 coupling intervals (~20, 0, and +20 ms to the peak of T-wave) was thought to be a reliable method to identify high-DFT patients without inducing VF.

Previous Reports
To date, a close correlation between the ULV and DFT at the time of defibrillator implantation has been reported.12-14 These findings suggest that vulnerability testing can be safely and reliably substituted for conventional defibrillation testing. Regarding device implantation without induction of VF, the 15-J ULV test was more feasible compared with the 10-J ULV test. Hwang et al showed that the ULV was ≤20 J in 75% of 60 patients, and all of them had DFT ≤20 J.4 Swerdlow et al showed that inductionless implantation is feasible in >80% of patients based on vulnerability testing at 15 J.25

The ASSURE study compared vulnerability safety margin testing vs. defibrillation safety margin test with a single VF induction/defibrillation.15 14 J vulnerability testing with 3 coupling intervals was carried out in 420 patients. VF was not induced in 322 patients (76.7%) and defibrillation was achieved with 21-J shocks in 317 of them (98.4%). Among the 98 patients (23.3%) in whom VF was induced at 14-J vulnerability testing, 21 (21.4%) did not achieve sufficient defibrillation. The predictive value of VF inducibility for detecting high DFT in the present study was comparatively higher than that of ASSURE. The ICD device produced by Guidant was used in the ASSURE study. In the Guidant ICD system, the programmed energy of 14 J is converted into 12 J at shock delivery and the programmed energy of 21 J is converted into 18 J at shock delivery. Vulnerability test at "12 J" in the ASSURE study seems to be a reason for the relatively lower predictive value of VF inducibility for detecting high DFT.

Determination of Vulnerable Period and Underestimation of ULV
The vulnerable zone was defined as a combination of coupling intervals and the strength of the T-wave shock. It is shown as a 2-D, diamond-shaped space defined by the coupling interval on the abscissa and shock strength on the ordinate.26 Swerdlow et al investigated the timing of the peak of the human vulnerable zone using right ventricular pacing at a CL of 500 ms and showed that the peak of the human vulnerable zone is narrow and includes a median of only two 20-ms intervals.24 They re-

Table 5. Patient Characteristics vs. Presence of High DFT (>20 J)
ported that a 20-ms difference could cause underestimation of the ULV, and the most reliable method to define the ULV is to scan the vulnerable period of the T-wave shock within a window of 40 ms (in 20-ms steps) before and after the T-wave peak. We determined the vulnerable period as a window of 20 ms before and after the T-wave peak. Although this method might underestimate the ULV, none of the patients with either ULV ≤10J or ≤15J had a high DFT.

A single T-wave shock underestimates the actual ULV in the present study. In the TULIP study vulnerability test was done at a single coupling interval on the T-wave of the ECG lead II. Although this simplified method reduced the number of required induction shocks and the procedure time, the accuracy of measuring ULV might be reduced.

A T-wave shock was delivered after ventricular pacing at a CL of 400 ms in the TULIP study. Most of the ULV studies used a basic CL of 500 ms. Pacing CL might affect the width of the vulnerable period. Furthermore, a shortened pacing CL might cause beat-to-beat instability of repolarization such as T-wave alternans.

Inducibility of VF During Vulnerability Testing
All the patients in whom VF was not induced by ULV test at both 10J and 15J had an acceptable DFT (≤20J). And in all the patients with high DFT, VF was induced by both 10J and 15J ULV test. The 10J and 15J ULV test, however, induced VF in 31 and in 12 patients with acceptable DFT, respectively. The higher delivered energy at ULV test might lower VF inducibility in patients without a high DFT, but it might involve a risk of missing a high DFT. Further detailed prospective study to identify the ideal energy at ULV test is required.

Avoidance of VF induction at defibrillator implantation is required in patients with severe heart failure. Unfortunately in these patients, VF is likely to be induced even by the vulnerability test. Patients with more advanced heart failure were more likely to have high DFT in the ASSURE study. In contrast, the parameters of cardiac function such as LV ejection fraction and LV dimensions did not predict high DFT in the present study, but ULV could predict high DFT. Although several studies have attempted to identify the predictive factors associated with high DFT, it has been difficult to identify high-DFT patients without vulnerability or defibrillation testing.

Study Limitations
The present study had some limitations. Shock energy other than 10 or 15J might be optimal in vulnerability testing. Some patients might have a lower limit of vulnerability >10J or >15J. This likelihood, however, seems to be vanishingly small because none of the patients without VF induced on 10J ULV testing had high DFT.

Without inducing VF, R-wave sensing during induced VF cannot be ensured. But in patients with sinus rhythm R-wave sensing amplitude >0.5 mV, R-wave sensing during VF was thought to be almost always reliable, and critical delay in detecting VF was not observed in previous reports.

Determination of the vulnerable period using 12-lead ECG is essential for the ULV test. This process requires extra time and adequate experience. Recently, the usefulness of automated vulnerability test for predicting high DFT has been reported. The vulnerable period that was automatically calculated by their software was well correlated with the ST-T peak interval. The 18J vulnerability test at 4 coupling intervals could correctly detect high-DFT patients with 19% of VF inducibility. The automated ULV test may be able to increase the utility of the ULV test in clinical practice.

Multiple induction shocks might increase DFT. More than 10 multiple induction shocks were sometimes required in the present study. If these induction shocks increased the DFT, DFT might be overestimated, but we did not identify a significant dissociation between ULV and DFT.

Clinical Implications
At the time of defibrillator implantation, the 15-J ULV test with 3 coupling intervals (-20, 0, and +20 ms to the peak of T-wave) was thought to be a reliable method to detect high DFT. The vulnerable period should be determined by -20, 0, and +20 ms to the ST-T peak interval using multi-lead ECG during pacing at a CL of 500 ms. If any of the 3 T-wave shocks cannot induce VF, no further induction is required and implantation without VF induction can be completed.

Although the ULV test can decrease the necessity for VF induction, VF tends to be induced by the ULV test in patients with depressed LV function, in whom VF induction is hoped to be avoided. Accordingly, we have considered the indication of the ULV test as follows. For the secondary prevention of sudden cardiac death, ULV test should be done. And, if VF is induced, defibrillation safety margin should be ensured, and system revision should be done if needed. For primary prevention, the ULV test might be avoided in patients with severely depressed LV function. Importantly, the necessity of ULV test should be decided on a patient-by-patient basis.

Conclusion
The ULV test at 10 and 15J with 3 coupling intervals (-20, 0, and +20 ms to the peak of T-wave) is a reliable method to identify patients with an acceptable DFT (≤20J). Baseline patient characteristics did not predict high-DFT patients, but ULV could detect high-DFT patients. For the purpose of defibrillator implantation without inducing VF, the 15-J ULV test was more feasible than the 10-J test.

Disclosures
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References