Systematic Review of Defibrillation Threshold Testing at De Novo Implantation

Kevin Phan, BS(adv); Hakeem Ha, BMed; Peter Kabunga, MBchB, MRCP; Michael J. Kilborn, BMBCh, DPhil; Edward Toal, RN; Raymond W. Sy, MBBS, PhD

Background—Recent results from the largest multicenter randomized trial (Shockless IMPLant Evaluation [SIMPLE]) on defibrillation threshold (DFT) testing suggest that while shock testing seems safe, it does not reduce the risk of failed shocks or prolong survival. A contemporary systematic review of DFT versus no-DFT testing at the time of implantable cardioverter–defibrillator implantation was performed to evaluate the current evidence and to assess the impact of the SIMPLE study.

Methods and Results—Electronic searches were performed using 6 databases from their inception to March 2014. Relevant studies investigating implant DFT were identified. Data were extracted and analyzed according to predefined clinical end points. Predefined outcomes for interrogation were all-cause mortality, composite end point of implantable cardioverter–defibrillator efficacy (arrhythmic deaths and ineffective shocks), and composite safety end point (the sum of complications recorded at 30 days). Meta-analysis was performed including 13 studies and 9740 patients. No significant differences between DFT versus no-DFT cohorts were found in terms of all-cause mortality (risk ratio, 0.90; 95% confidence interval, 0.71–1.15; \( P = 0.41 \)), composite efficacy outcome (risk ratio, 1.24; 95% confidence interval, 0.65–3.37; \( P = 0.51 \)), and 30-day postimplant complications (risk ratio, 1.18; 95% confidence interval, 0.87–1.60; \( P = 0.29 \)). No significant difference was found in the trends observed when the results of the SIMPLE study were excluded or included.

Conclusions—This systematic review of contemporary data suggests a modest average effect of DFT, if any, in terms of mortality, shock efficacy, or safety. Therefore, DFT testing should no longer be compulsory during de novo implantation. However, DFT testing may still be clinically relevant in specific patient populations.

Key Words: cardiac arrhythmias □ electrophysiology □ implantable defibrillator □ systematic review □ ventricular fibrillation

The implantable cardioverter–defibrillator (ICD) is the standard of care for patients with potentially life-threatening ventricular arrhythmias or at high risk of sudden cardiac death. ICDs are efficacious for primary2–4 and secondary prevention5 of sudden cardiac death. To ensure functionality, sensitivity and electric integrity of the ICD generator and leads, defibrillation threshold (DFT) testing has been traditionally performed to prove the ability of the ICD to detect and abort lethal arrhythmias.6,7 Although strict DFT testing was considered mandatory in the past, the practice of routine DFT testing has come under close scrutiny in recent years.8–12 DFT has been the matter of intense debate, over the potential health risks involved and whether these risks are justified by the perceived benefits, if any, of DFT testing.

Contemporary surveys have demonstrated that the practice of DFT testing during implantation can vary widely from <25% to 99%.13 Recently, the results were published from the Shockless Implant Evaluation (SIMPLE) trial,14 to date the largest multicenter randomized controlled trial investigating the efficacy and safety of DFT at ICD implantation.

Their analysis of >2500 patients suggested that while DFT shock testing seemed to be safe, this practice does not reduce the likelihood of failed shocks or prolong survival. In light of these recent study results, a systematic review of DFT versus no-DFT testing at ICD implantation was performed to evaluate the current evidence. Furthermore, an analysis of the pooled data, with and without the SIMPLE randomized trial, was performed to determine whether this contemporary multicenter study is consistent with the previous evidence of DFT.

Methods

Literature Search Strategy

Electronic searches were performed using Ovid Medline, PubMed, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, ACP Journal Club, and Database of Abstracts of Review of Effectiveness from their date of inception to March...
WHAT IS KNOWN

- Recent studies suggest that defibrillation threshold testing at the time of initial implantation of an implantable cardioverter–defibrillator does not reduce the risk of failed shocks or prolong survival.

WHAT THE STUDY ADDS

- This contemporary systematic review confirmed that defibrillation threshold testing was not associated with measurable benefit in terms of mortality, shock efficacy, or safety.
- Defibrillation threshold testing should no longer be considered compulsory during de novo implantable cardioverter–defibrillator implantation.

To achieve the maximum sensitivity of the search strategy, we combined the terms: defibrillator and threshold testing and implantation or generator change as either key words or MeSH terms. The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies.

Selection Criteria

Eligible studies for the systematic review included those in which patient cohorts underwent DFT testing or no-DFT testing during ICD implantation. Studies that did not include mortality or complications as end points were excluded. When institutions published duplicate studies with accumulating numbers of patients or increased lengths of follow-up, only the most complete reports were included for quantitative assessment at each time interval. Reference lists were also hand searched for further relevant studies. All publications were limited to those involving human subjects and in the English language, and any pediatric studies were excluded from this analysis.

Data Extraction and Statistical Analysis

All data were extracted from article texts, tables, and figures from the date of inception from each study. Two investigators independently reviewed each retrieved article (K.P. and H.H.). Discrepancies between the 2 reviewers were resolved by discussion and consensus. For the meta-analysis, clinical outcomes were assessed using risk ratio (RR) as a summary statistic. Predefined outcomes for interrogation were all-cause mortality, composite end point of ICD efficacy (arrhythmic deaths and ineffective shocks, as defined in the SIMPLE study14), and composite safety end point (the sum of complications recorded at 30 days). As mentioned, the meta-analysis was designed to evaluate the pooled data, with and without the SIMPLE study to further determine the impact of this contemporary study on the overall evidence of DFT. Both fixed- and random-effect models were tested and used to calculate the pooled odds ratio (OR) for the surgical literature. χ² tests were used to study heterogeneity between trials. F statistic was used to estimate the percentage of total variation across studies, owing to heterogeneity rather than chance, with values >50% considered as substantial heterogeneity. If there was substantial heterogeneity, the possible clinical and methodologic reasons for this were explored qualitatively. All P values were 2 sided. All statistical analysis was conducted with Review Manager version 5.2.1 (Cochrane Collaboration, Software Update, Oxford, United Kingdom).

Critical Appraisal

The quality of the evidence from each study was assessed using the Grading of Recommendations, Assessment, Development and
Evaluations (GRADE) approach.13 Data were extracted from texts, tables, and figures of selected studies.

**Results**

**Literature Search**

A total of 445 references were identified through 6 electronic database searches. After exclusion or duplicate or irrelevant references, 22 potential relevant articles were retrieved. After manual search of reference lists and applying the inclusion and exclusion criteria, 13 studies were selected for analysis (Figure 1). The study characteristics are summarized in Table 1. In these 13 studies, 9740 patient results were available for analysis to compare DFT testing at implantation (n=5080) versus no DFT testing (n=4660).

**Quality Assessment**

This meta-analysis included 13 studies,9,14,16–26 2 of which were registry studies,25,26 and 3 randomized studies.14,23,24 Four of the included studies were prospectively designed,14,21,23,24 whereas the other 9 studies were retrospective in design. There were 5 studies14,17,19,21,26 that included at least 100 patients in each arm, whereas 4 studies9,18,23,24 had <100 patients in both arms. Five studies9,14,24–26 reported mean 12 months of follow-up, 1 study with follow-up of 18 months,18 5 studies16,19,21–23 reported mean follow-up of ≥24 months, whereas 3 studies14,17,26 reported follow-up beyond 30 months.

The DFT testing protocol varied between the included studies. A full step-down protocol was described in 2 studies.17,18 The majority of studies measured DFT via successful shocks terminating VF at least 10J below the maximum output of the ICD device.9,14,16,19,20,22,24 Three studies did not specify a particular protocol,21,25,26 and stated that the DFT testing was according to the standard practice of the centers studied.

The majority of the studies were observational in nature, and thus the quality of evidence was limited. The quality of evidence according to the GRADE system (on a scale of + to ++++ confidence) is reported for each study in Table 1.

**Table 1. Study Characteristics**

<table>
<thead>
<tr>
<th>First Author Year</th>
<th>Study Period</th>
<th>Country</th>
<th>Type of Study</th>
<th>N (DFT)</th>
<th>N (No-DFT)</th>
<th>Follow-Up (Mo)</th>
<th>DFT Protocol</th>
<th>GRADE Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russo et al16 2005</td>
<td>NR</td>
<td>United States</td>
<td>OS, R</td>
<td>1085</td>
<td>54</td>
<td>25±</td>
<td>At least 2 inductions of VF with successful first shocks terminating VF at least 10J below max output</td>
<td>++</td>
</tr>
<tr>
<td>Bianchi et al19 2009</td>
<td>2000–2004</td>
<td>Italy</td>
<td>OS, R</td>
<td>137</td>
<td>154</td>
<td>23</td>
<td>VF induced by T-wave shock. 2 Defibrillations at minimum 10J below maximum output applied</td>
<td>++</td>
</tr>
<tr>
<td>Calvi et al6 2010</td>
<td>1996–2008</td>
<td>Italy</td>
<td>OS, R</td>
<td>42</td>
<td>80</td>
<td>12</td>
<td>VF induced with T-wave shock. First defibrillation shock of 18–20J</td>
<td>+</td>
</tr>
<tr>
<td>Michowitz et al20 2011</td>
<td>2003–2007</td>
<td>USA</td>
<td>OS, R</td>
<td>204</td>
<td>52</td>
<td>32</td>
<td>Defibrillation safety margin testing, vulnerability safety margin testing, and combined testing</td>
<td>++</td>
</tr>
<tr>
<td>Brignole et al21 2012</td>
<td>2006–2009</td>
<td>Italy</td>
<td>OS, P</td>
<td>836</td>
<td>1284</td>
<td>24</td>
<td>According to standard practice of each center</td>
<td>+++</td>
</tr>
<tr>
<td>Codner et al22 2012</td>
<td>2004–2009</td>
<td>Israel</td>
<td>OS, R</td>
<td>80</td>
<td>133</td>
<td>24</td>
<td>DFT defined as shock able to successfully revert inducible VF with at least 10J below maximal output</td>
<td>++</td>
</tr>
<tr>
<td>Kovacevic-Kostic et al24 2013</td>
<td>2006–2010</td>
<td>Serbia</td>
<td>RCT, P</td>
<td>20</td>
<td>20</td>
<td>12</td>
<td>VF induced by T-wave shock. 2 defibrillations at minimum 10J below maximum output applied</td>
<td>++</td>
</tr>
<tr>
<td>Sadoul et al25 2013</td>
<td>NR</td>
<td>France</td>
<td>OS registry, R</td>
<td>810</td>
<td>94</td>
<td>12</td>
<td>Individual physician preference of each center</td>
<td>++</td>
</tr>
<tr>
<td>Aronson et al26 2014</td>
<td>2010–2013</td>
<td>Israel</td>
<td>OS registry, R</td>
<td>352</td>
<td>1214</td>
<td>12</td>
<td>Individual physician preference of each center</td>
<td>+++</td>
</tr>
<tr>
<td>Healey et al24 2015</td>
<td>2009–2011</td>
<td>18 Countries</td>
<td>RCT, P</td>
<td>1253</td>
<td>1247</td>
<td>37.2±12</td>
<td>DFT goal was to achieve one successful defibrillation at 17J or 2 at 21J</td>
<td>++++</td>
</tr>
</tbody>
</table>

DFT indicates defibrillator threshold testing; M, median; NR, not reported; OS, observational study; P, prospective; R, retrospective; and RCT, randomized controlled trial.
Studies rated +++ indicate that reviewers had a moderate level of confidence in the effect estimate, but there may be a possibility that it is substantially different.

**Baseline Characteristics**

Baseline characteristics are summarized in Table 2. The DFT cohort was younger than the no-DFT cohort (63.3 versus 64.9 years; \( P = 0.01 \)). Overall, 82.6% of the DFT cohort and 80.9% of the no-DFT cohort were male (\( P = 0.45 \)). The DFT cohort had a weighted mean LVEF that was significantly but marginally higher than the no-DFT group (28.0% versus 26.1%, \( P = 0.006 \)). There was no significant difference between patients undergoing DFT versus no-DFT in terms of the underlying condition, with ischemic cardiomyopathy (63.2% versus 62.4%, \( P = 0.91 \)) and dilated cardiomyopathy (29.7% versus 28.1%, \( P = 0.65 \)) accounting for the majority of patients. It was notable that hypertrophic cardiomyopathy, valvular disease, congenital heart disease, and channelopathies were under-represented in all component studies. Comorbid diseases such as diabetes mellitus (26.8% versus 32.4%, \( P = 0.31 \)) and atrial fibrillation (20.0% versus 25.1%, \( P = 0.11 \)) occurred with similar frequency between the 2 groups. In terms of baseline medications, use of digoxin (11.6% versus 16.3%, \( P < 0.0001 \)) and statins (41.8% versus 44.6%, \( P = 0.02 \)) was significantly lower in the DFT group compared with no-DFT. Four studies included cardiac resynchronization therapy devices,\(^{14,20,21,25}\) representing 24% of patients in the DFT group and 23% in the no-DFT group.

**Assessment of Association With Mortality**

All-cause mortality was reported in all 13 included studies. There was no significant difference in all-cause mortality between DFT versus no-DFT cohorts, excluding the SIMPLE study (13.4% versus 11.2%; RR, 0.89; 95% confidence interval [CI], 0.65–1.20; \( F = 0.44 \)) when the results from the SIMPLE randomized trial were included, similar trends were obtained (14.2% versus 12.9%; RR, 0.90; 95% CI, 0.71–1.15; \( F = 0.41 \)). Significant heterogeneity was detected across the studies for this outcome.

**Assessment of Safety**

The composite end point of arrhythmic deaths and ineffective shocks was used as a surrogate of ICD efficacy. This composite outcome could be derived from 4 previously published studies excluding the SIMPLE study\(^{9,17,18,23}\) with no significant difference between DFT and no-DFT groups (5.0% versus 7.2%; \( P = 0.31 \)). When all the data were considered together, the same trends were maintained (7.6% versus 6.3%; RR, 1.24; 95% CI, 0.65–2.37; \( F = 0.51 \), Figure 3).

**Table 2. Baseline Characteristics of Included Studies in the Meta-Analysis**

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>DFT</th>
<th>No-DFT</th>
<th>n</th>
<th>N</th>
<th>RR or WMD (95% CI)</th>
<th>Heterogeneity</th>
<th>Z for Overall Effect</th>
<th>P for Overall Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>63.3</td>
<td>64.9</td>
<td>8639</td>
<td>12</td>
<td>−1.40 (−2.49 to −0.32)</td>
<td>0.002</td>
<td>63</td>
<td>2.53</td>
</tr>
<tr>
<td>Male, %</td>
<td>82.6</td>
<td>80.9</td>
<td>8609</td>
<td>12</td>
<td>1.02 (0.97 to 1.06)</td>
<td>0.002</td>
<td>63</td>
<td>0.75</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>28.0</td>
<td>26.1</td>
<td>7035</td>
<td>11</td>
<td>2.02 (0.58 to 3.45)</td>
<td>&lt;0.000001</td>
<td>87</td>
<td>2.76</td>
</tr>
<tr>
<td>CAD, %</td>
<td>66.0</td>
<td>70.1</td>
<td>4186</td>
<td>3</td>
<td>0.98 (0.93 to 1.02)</td>
<td>0.09</td>
<td>0</td>
<td>1.06</td>
</tr>
<tr>
<td>Ischemic CM, %</td>
<td>63.2</td>
<td>62.4</td>
<td>3690</td>
<td>6</td>
<td>1.00 (0.99 to 1.01)</td>
<td>0.68</td>
<td>0</td>
<td>0.11</td>
</tr>
<tr>
<td>Dilated CM, %</td>
<td>29.7</td>
<td>28.1</td>
<td>7630</td>
<td>7</td>
<td>1.08 (0.77 to 1.53)</td>
<td>&lt;0.000001</td>
<td>93</td>
<td>0.46</td>
</tr>
<tr>
<td>AF, %</td>
<td>20.0</td>
<td>25.1</td>
<td>7243</td>
<td>5</td>
<td>0.86 (0.72 to 1.03)</td>
<td>0.03</td>
<td>62</td>
<td>1.60</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>26.8</td>
<td>32.4</td>
<td>4257</td>
<td>6</td>
<td>0.91 (0.77 to 1.09)</td>
<td>0.12</td>
<td>42</td>
<td>1.01</td>
</tr>
<tr>
<td>Primary prevention, %</td>
<td>70.1</td>
<td>73.8</td>
<td>7261</td>
<td>9</td>
<td>0.94 (0.86 to 1.03)</td>
<td>&lt;0.000001</td>
<td>94</td>
<td>1.30</td>
</tr>
<tr>
<td>ACE inhibitors, %</td>
<td>71.8</td>
<td>73.4</td>
<td>5419</td>
<td>8</td>
<td>0.99 (0.95 to 1.03)</td>
<td>0.12</td>
<td>39</td>
<td>0.62</td>
</tr>
<tr>
<td>β-blockers, %</td>
<td>71.7</td>
<td>73.7</td>
<td>5896</td>
<td>10</td>
<td>1.01 (0.94 to 1.09)</td>
<td>&lt;0.000001</td>
<td>83</td>
<td>0.35</td>
</tr>
<tr>
<td>Amiodarone, %</td>
<td>23.7</td>
<td>21.8</td>
<td>8474</td>
<td>10</td>
<td>0.99 (0.81 to 1.22)</td>
<td>&lt;0.000001</td>
<td>83</td>
<td>0.05</td>
</tr>
<tr>
<td>Statins, %</td>
<td>41.8</td>
<td>44.6</td>
<td>2829</td>
<td>5</td>
<td>0.90 (0.82 to 0.98)</td>
<td>0.64</td>
<td>0</td>
<td>2.42</td>
</tr>
<tr>
<td>Digoxin, %</td>
<td>11.6</td>
<td>16.3</td>
<td>2272</td>
<td>3</td>
<td>0.65 (0.53 to 0.79)</td>
<td>0.52</td>
<td>0</td>
<td>4.21</td>
</tr>
<tr>
<td>Diuretics, %</td>
<td>70.6</td>
<td>75.3</td>
<td>4363</td>
<td>5</td>
<td>0.98 (0.84 to 1.13)</td>
<td>&lt;0.000001</td>
<td>90</td>
<td>0.33</td>
</tr>
</tbody>
</table>

ACE indicates angiotensin-converting enzyme; AF, atrial fibrillation; CAD, coronary artery disease; CI, confidence interval; CM, cardiomyopathy; DFT, defibrillation threshold; LVEF, left ventricular ejection fraction; n, number of patients; N, number of studies; RR, relative risk; and WMD, weighted mean difference.
not result in an excess of complications (6.5% versus 5.6%; P=0.33). When the evidence was considered collectively, there was also no significant difference in safety outcomes (4.5% versus 2.5%; RR, 1.18; 95% CI, 0.87–1.60; P=0.29).

**Discussion**

Advances in ICD technology and reliability have led to questions about whether DFT testing at the time of implantation is required. Although DFT testing was traditionally the gold standard for ensuring electric integrity of the ICD, this practice remains controversial given the paucity of prospective, randomized evidence. The present systematic review was performed to evaluate the role of DFT shock testing at ICD implantation, especially in light of the recently published SIMPLE study. The present review found that DFT testing, while safe, does not improve outcomes in terms of mortality or ICD efficacy. The review also confirmed that the results of the SIMPLE trial were consistent with previous studies, and it supports the notion that DFT testing should no longer be considered mandatory during de novo implantation.

Many physicians have argued against routine DFT testing on the basis of a perceived lack of benefit, the lack of correlation between induced and spontaneous ventricular arrhythmia and the potential for complications, including anesthesia-related risks and systemic embolism in patients with atrial fibrillation and severe left ventricular dysfunction. Induction of VF has also been associated with increased risk of heart failure, hypoxic brain injury, and electromechanical dissociation (stunning) phenomenon. In contrast, proponents of shock testing have emphasized the role of DFT in assessing system integrity, reliable sensing, and appropriate detection. When high-DFTs are identified, system revisions can be performed to optimize ICD performance, such as repositioning of leads, use of an azygos vein coil, subcutaneous array, removal of the superior vena cava coil from the circuit, or optimizing biphasic waveforms and changing shock vector. However, it is important to note that apparent success of DFT testing after system revision does not guarantee clinical benefit and may increase procedural risks.

Before the SIMPLE study, there were only 2 small underpowered randomized studies addressing the issue of DFT testing. Kovacevic-Kostic et al randomized 40 patients to DFT versus no-DFT and showed that both groups had a shock efficacy of 100% >12 months of follow-up. Similarly, the Resynchronization for Ambulatory Heart Failure Trial (RAFT Trial) substudy randomized 145 patients to DFT versus no-DFT, and it demonstrated that perioperative complications, failed shocks, and arrhythmic deaths were uncommon and comparable between DFT
no-DFT groups. Larger nonrandomized observational studies such as SAFE-ICD Study,\(^{21}\) which enrolled 2120 patients from 41 Italian centers, have also reported extremely low and comparable event rates in terms of intraoperative complications and failed ICD therapy between DFT and no-DFT cohorts. Dissemination of results from such studies

![Table 3. Summary of Complications](#)

<table>
<thead>
<tr>
<th>Study</th>
<th>30-D Deaths, %</th>
<th>Stroke, %</th>
<th>Systemic Embolism, %</th>
<th>Myocardial Infarction, %</th>
<th>Heart Failure, %</th>
<th>Nonelective Intubation/Aspiration</th>
<th>Arterial Line Complication</th>
<th>Unplanned ICU Admission</th>
<th>Pneumothorax</th>
<th>Pericarditis/Tamponade</th>
<th>Device Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russo et al(^{26})</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Pires et al(^{17})</td>
<td>0.8</td>
<td>0.5</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hall et al(^{18})</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Bianchi et al(^{19})</td>
<td>0</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Calvi et al(^{20})</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Michowitz et al(^{21})</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Brignole et al(^{22})</td>
<td>0.2</td>
<td>0.2</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Codner et al(^{23})</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Healey et al(^{24})</td>
<td>0</td>
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<tr>
<td>Kovacevic-Kostic et al(^{25})</td>
<td>0</td>
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</tr>
<tr>
<td>Sadoul et al(^{26})</td>
<td>0.9</td>
<td>0.1</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Arson et al(^{27})</td>
<td>NR</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Healey et al(^{28})</td>
<td>0.4</td>
<td>0.6</td>
<td>0.2</td>
<td>0.2</td>
<td>0.1</td>
<td>0.3</td>
<td>2.3</td>
<td>1.6</td>
<td>0.6</td>
<td>0.1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

DFT indicates defibrillation threshold testing; ICU, intensive care unit; and NR, not reported.
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precipitated or at least legitimized a shift in practice away from routine DFT testing in many centers. However, many physicians remained reluctant to abandon DFT testing on the basis of the existing data alone.

To address this debate, the SIMPLE trial randomized 2500 patients in >80 centers undergoing ICD implantation to DFT versus no-DFT. The results of the SIMPLE study were consistent with the meta-analysis of previously published literature, in terms of mortality, ICD efficacy, and safety. Moreover, the results of the pooled meta-analysis, reinforced by the addition of data from the SIMPLE study, suggest that routine DFT testing at device implantation has no significant impact on all-cause mortality in a combined total of 9740 patients and 19 950 patient-years of follow-up. Although one may argue that the current studies are not adequately powered or have insufficient follow-up to detect small differences in outcomes, the data support the notion that DFT testing only has a modest effect, if any, on outcomes in the contemporary ICD era, and further studies are unlikely to alter the analysis in support of routine DFT testing in the general ICD population.

Nevertheless, it is also reassuring that the systematic review confirmed that DFT testing is largely safe. Although the SIMPLE study suggested a trend toward an increased rate of specific complications possibly related to the induction of ventricular fibrillation (such as nonelective intubation and chest compression), mortality specifically related to DFT testing is rare, and the composite safety outcome in the meta-analysis was not significantly increased in patients undergoing DFT testing.

Moreover, one must remain cautious about abandoning DFT testing at ICD implantation in all patients. It is important to note that certain patient populations were under-represented in the meta-analysis. These include hypertrophic cardiomyopathy, channelopathies, congenital heart disease, and right-sided device implants. Patients with these conditions are known to have elevated or unpredictable DFTs and may be at risk for increased defibrillation energy requirements. Therefore, DFT testing may still be warranted for these patients. The majority of patients underwent ICD implants for primary prevention, and it is possible that DFT may be more important in the setting of secondary prevention. Unfortunately, a subgroup analysis (primary versus secondary prevention) was not feasible based on the available data. Moreover, the present data should not be applied to DFT testing at the time of generator replacement because there is the additional variable of ageing lead components, which may be susceptible to clinically silent lead malfunction, undetected with routine electric testing or fluoroscopy, and only identified with high-voltage shock testing. Finally, DFT testing remains mandatory in subcutaneous ICDs.

Limitations

The present systematic review was constrained by several limitations. First, there were only 3 published randomized controlled trials, and the remainder of studies were nonrandomized in design, with significant variability in the qualitative grading of the studies (Table 1). The nonrandomized studies were likely associated with selection bias, which may explain the
significant heterogeneity observed in baseline characteristics, such as ejection fraction, atrial fibrillation, β-blocker, amiodarone, and diuretic use, as well as the observed heterogeneity in pooled results in terms of all-cause mortality, that may limit the applicability of the findings. We also observed non-standardized DFT protocols and variability between centers in terms of monitoring of arrhythmic and complication end points, as well as nonblinded outcome assessment in some of the component studies. For example, the higher frequency of reported complications in the SIMPLE study compared with the other studies was related to more stringent and comprehensive reporting of events in that study (Table 3). Moreover, efficacy and safety outcomes were not universally reported in the component studies, resulting in wider CIs for the average estimate of effect for these outcomes. Publication bias was also assessed using funnel plots and Egger and Begg methods, but no significant publication bias was detected (Table I and Figure I in the Data Supplement).

Conclusions

This meta-analysis of contemporary data demonstrates no significant benefit for DFT testing in terms of mortality, ICD efficacy or 30-day postimplant complications. Therefore, DFT testing should no longer be routinely performed during de novo implantation. However, DFT testing may still be clinically relevant in specific patient populations.

Disclosures

None.

References

ICD Testing at Implant: Systematic Review


Systematic Review of Defibrillation Threshold Testing at De Novo Implantation
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**SUPPLEMENTAL MATERIAL**

**Supplementary Table 1. Fixed-effects vs random-effects models**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Fixed-effects model (RR, 95% CI)</th>
<th>Heterogeneity</th>
<th>Random-effects model (RR, 95% CI, P-value)</th>
<th>Heterogeneity</th>
<th>Egger’s test for publication bias</th>
<th>Begg’s test for publication bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality of prior studies</td>
<td>0.93 (0.81-1.07), P=0.33</td>
<td>$I^2=71%$, P=0.0003</td>
<td>0.89 (0.65-1.20), P=0.44</td>
<td>$I^2=71%$, P=0.0003</td>
<td>P=0.771</td>
<td>P=0.858</td>
</tr>
<tr>
<td>Mortality of prior studies + SIMPLE</td>
<td>0.94 (0.84-1.05), P=0.28</td>
<td>$I^2=68%$, P=0.0006</td>
<td>0.90 (0.71-1.15), P=0.41</td>
<td>$I^2=68%$, P=0.0006</td>
<td>P=0.737</td>
<td>P=0.756</td>
</tr>
<tr>
<td>Composite arrhythmic death and ineffective shock: prior studies</td>
<td>1.44 (0.73-2.84), P=0.29</td>
<td>$I^2=47%$, P=0.90</td>
<td>1.09 (0.29-4.04), P=0.90</td>
<td>$I^2=47%$, P=0.90</td>
<td>P=0.348</td>
<td>P=1.00</td>
</tr>
<tr>
<td>Composite arrhythmic death and ineffective shock: prior studies + SIMPLE</td>
<td>1.19 (0.92-1.53), P=0.18</td>
<td>$I^2=36%$, P=0.51</td>
<td>1.24 (0.65-2.37), P=0.51</td>
<td>$I^2=36%$, P=0.51</td>
<td>P=0.898</td>
<td>P=1.00</td>
</tr>
<tr>
<td>Composite primary safety outcome: prior studies</td>
<td>1.68 (0.48-5.93), P=0.42</td>
<td>$I^2=32%$, P=0.23</td>
<td>1.64 (0.26-10.47), P=0.60</td>
<td>$I^2=32%$, P=0.23</td>
<td>NA*</td>
<td>NA*</td>
</tr>
<tr>
<td>Composite primary safety outcome: prior studies + SIMPLE</td>
<td>1.20 (0.88-1.62), P=0.25</td>
<td>$I^2=0%$, P=0.49</td>
<td>1.18 (0.87-1.60), P=0.29</td>
<td>$I^2=0%$, P=0.49</td>
<td>P=0.649</td>
<td>P=1.00</td>
</tr>
</tbody>
</table>

*Not enough events to perform Egger’s and Begg’s tests for publication bias*
Supplementary Figure 1. Publication bias assessed via funnel plot asymmetry

(A) Mortality

(B) Composite outcome: arrhythmic deaths and ineffective shocks
(C) Composite safety outcome