Heart Failure and the Risk of Shocks in Patients With Implantable Cardioverter Defibrillators

Results From the Triggers Of Ventricular Arrhythmias (TOVA) Study

William Whang, MD, MS; Murray A. Mittleman, MD, DrPH; David Q. Rich, MPH; Paul J. Wang, MD; Jeremy N. Ruskin, MD; Geoffrey H. Tofler, MD; James E. Muller, MD; Christine M. Albert, MD, MPH; for the TOVA Investigators

Background—Left ventricular ejection fraction (LVEF) predicts device discharges in patients with implantable cardioverter-defibrillators (ICDs). The relationship between severity of congestive heart failure (CHF) and ICD discharges is less clear.

Methods and Results—We prospectively analyzed the association between CHF and risk of appropriate ICD discharges in the Triggers Of Ventricular Arrhythmias (TOVA) study, a cohort study of ICD patients conducted at 31 centers in the United States. Reported shocks were confirmed for sustained ventricular tachycardia (VT) or fibrillation (VF) by analysis of stored electrograms. Proportional hazards models included CHF categorized by New York Heart Association class. Baseline CHF was present among 502 (44%) of 1140 patients; 170 (34%) had class I, 230 (46%) had class II, 97 (19%) had class III, and only 5 (1%) had class IV symptoms. During median follow-up of 212 days, 92 patients experienced 1 or more appropriate ICD discharges. Class III CHF was associated in a statistically significantly manner with ICD discharge for VT/VF (hazard ratio 2.40, 95% CI 1.16 to 4.98), even with adjustment for LVEF. The combination of LVEF <0.20 and class III symptoms resulted in a particularly high risk of shocks for VT/VF (hazard ratio 3.90, 95% CI 1.28 to 11.92).

Conclusions—Class III CHF, an easily accessible clinical measure, is an independent risk factor, along with LVEF, for ventricular arrhythmias that require shock therapy among ICD patients. Whether patients with class III CHF benefit to a greater degree from ICDs and whether aggressive treatment of CHF in ICD patients may prevent ventricular arrhythmias remains to be determined. (Circulation. 2004;109:1386-1391.)

Key Words: heart failure • tachyarrhythmias • defibrillation • cardioversion

The benefits of implantable cardioverter-defibrillators (ICDs) have been established in the primary and secondary prevention of ventricular arrhythmias and sudden cardiac death (SCD). Patients with congestive heart failure (CHF) are at particularly high risk of death from ventricular arrhythmias, and ~50% of deaths among patients with CHF are sudden. Higher New York Heart Association (NYHA) functional class has been associated with higher absolute rates of SCD due to a higher overall mortality rate, but the percentage of deaths that are sudden decreases as NYHA class increases. Among patients with ICDs, multiple studies have found that ICD discharges or arrhythmic deaths are more frequent in patients with reduced left ventricular ejection fraction (LVEF), but relatively few have documented a relationship with CHF symptoms. The Triggers Of Ventricular Arrhythmia (TOVA) study presented a unique opportunity to assess prospectively whether CHF severity is associated with the risk of appropriate ICD discharges for ventricular tachycardia (VT) or ventricular fibrillation (VF), after adjustment for LVEF.

Methods

Study Design

The TOVA study is a multicenter prospective cohort study of ICD patients conducted at 31 centers in the United States designed to identify triggers of VT/VF among susceptible patients. To be included in the study, patients had to meet the 1998 American College of Cardiology/American Heart Association guidelines for ICD implantation (Class I to IIb indications), which include the following: (1) cardiac arrest; (2) spontaneous sustained VT; (3) primary or recurrent syncope with inducible VT refractory to drug
therapy; (4) nonsustained VT with coronary disease, prior myocardial infarction, left ventricular dysfunction, and inducible sustained VT or VF; or (5) familial or inherited condition with high risk of life-threatening arrhythmia, such as long-QT syndrome or hypertrophic cardiomyopathy.

Enrollment began in June 2000, and patients were identified at the time of implantation or through the ICD clinics in participating institutions. At entry into the study, extensive information was collected on baseline clinical characteristics through medical record review. CHF severity was categorized according to NYHA class (I through IV) at the baseline interview. Using a structured data abstraction form, the clinical site study staff reviewed the patient’s medical record for a history of CHF and used a standardized questionnaire to obtain data on CHF symptoms. The study staff categorized the patient’s NYHA class with reference to NYHA scales that were included with the questionnaire.

Patients were then monitored for ICD discharges by the study and clinical staff at participating institutions. Patients were asked to call the staff within 72 hours of an ICD discharge. Because one of the primary aims of the TOVA study is to identify lifestyle and psychological triggers of ICD discharge, study participants were interviewed after an ICD discharge about lifestyle and psychological symptoms. The study staff categorized the patient’s NYHA class with reference to NYHA scales that were included with the questionnaire.

Patients were then monitored for ICD discharges by the study and clinical staff at participating institutions. Patients were asked to call the staff within 72 hours of an ICD discharge. Because one of the primary aims of the TOVA study is to identify lifestyle and psychological triggers of ICD discharge, study participants were interviewed after an ICD discharge about lifestyle and psychological exposures that occurred before ICD discharge. Reported device discharges were then confirmed by an electrophysiologist (PJW/CMA) by analysis of stored electrograms at the central core laboratory for instances of sustained VT or VF. Only shocks for VT or VF are included in the present analysis.

### Statistical Analysis

Means or proportions for baseline clinical variables and ICD programming settings were calculated for patients with and without CHF. $\chi^2$ tests were used to compare categorical variables, and Student’s $t$ tests or linear regression was used to compare continuous variables. Cumulative event proportions were calculated by the Kaplan-Meier method, and outcome differences of patients with CHF versus those without were assessed with the log-rank test. Cox proportional hazards models were used to evaluate associations between CHF class at enrollment and the risk of ICD discharges for a confirmed episode of VT/VF both before and after adjustment for other variables, including LVEF. Because there were only 5 patients with class IV CHF, we were unable to analyze these patients separately in Cox proportional hazard models. All of the covariates included in the multivariable model varied significantly between patients with and without CHF or resulted in a change of $>10\%$ in the coefficient for CHF in a model that already included age and gender, and none were thought to be causal intermediates. We also estimated separate hazard ratios in a multivariable proportional hazards model of ICD discharges for each combination of CHF class (no CHF, I/II, or III) and LVEF ($<0.35$, $0.20$ to $0.34$, or $<0.20$) by including 8 separate binary variables. All probability values are 2-tailed, and all CIs were computed at the 95% level (SAS version 8.2, SAS).

### Results

Among 1140 patients enrolled in TOVA, baseline CHF was present in 502 patients (44%) and absent in 615 (54%; Table 1); data on CHF were missing for 23 patients (2%). CHF patients were older and more frequently male. Hypertension, diabetes, history of atrial fibrillation or atrial flutter, coronary artery disease, and prior coronary artery bypass surgery were more common among CHF patients. As expected, LVEF was lower among CHF patients, and CHF patients were more frequently prescribed spironolactone, other diuretics, digoxin, and ACE inhibitors or angiotensin II receptor blockers. In addition to standard therapy for CHF, 29 patients with CHF (5.8%) had a biventricular ICD implanted. With respect to antiarhythmic agents, amiodarone use was more frequent among CHF patients, but $\beta$-blocker use was not. CHF patients were more likely to have had prior ICD discharges, and cardiac arrest was less often the indication for the ICD.

Among the 502 CHF patients, 170 (34%) had NYHA class I, 230 (46%) had class II, 97 (19%) had class III, and only 5 (1%) had class IV symptoms. There was a statistically significant but weak correlation between CHF class and LVEF (Spearman correlation 0.18, $P<0.01$). Twenty-one percent of patients with LVEF $<0.20$ had class I symptoms, and 14% of patients with LVEF $>0.34$ had class III or IV symptoms.

Data regarding baseline device settings were collected in the first half of the study and were available for 697 patients. Of these, 359 patients (52%) had at least 2 zones programmed for differential treatment of faster and slower VTs. Table 2 compares the programming settings among patients with CHF to those of patients without CHF. There was a statistically significant relationship between NYHA class and rate cutoffs, such that each increase in CHF class was associated

---

**TABLE 1. Baseline Characteristics Among Patients With and Without CHF**

<table>
<thead>
<tr>
<th></th>
<th>CHF (n=502)</th>
<th>No CHF (n=615)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>65.7 ± 11.0</td>
<td>62.6 ± 13.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Female, %</td>
<td>17.5</td>
<td>23.6</td>
<td>0.02</td>
</tr>
<tr>
<td>White, %</td>
<td>87.0</td>
<td>87.8</td>
<td>0.76</td>
</tr>
<tr>
<td>≥High school education, %</td>
<td>79.1</td>
<td>82.1</td>
<td>0.23</td>
</tr>
<tr>
<td>Indication for device implantation, %</td>
<td>25.5</td>
<td>32.3</td>
<td>0.07</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>30.6</td>
<td>30.5</td>
<td>0.01</td>
</tr>
<tr>
<td>Sustained VT</td>
<td>24.7</td>
<td>19.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Syncope with inducible VT</td>
<td>11.9</td>
<td>12.5</td>
<td>0.63</td>
</tr>
<tr>
<td>Prophylaxis</td>
<td>5.7</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1.6</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>59.8</td>
<td>49.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>28.7</td>
<td>15.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>History of atrial fibrillation/atrial flutter, %</td>
<td>40.0</td>
<td>22.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Past/current smoking, %</td>
<td>74.5</td>
<td>70.8</td>
<td>0.20</td>
</tr>
<tr>
<td>Body mass index &gt;30, %</td>
<td>31.4</td>
<td>29.9</td>
<td>0.63</td>
</tr>
<tr>
<td>Coronary artery disease, %</td>
<td>82.1</td>
<td>67.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Previous CABG surgery, %</td>
<td>46.4</td>
<td>32.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>0.20</td>
<td>2.0 to 0.34</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>≥0.35</td>
<td>29.5</td>
<td>67.4</td>
<td></td>
</tr>
<tr>
<td>Prior ICD discharge, %</td>
<td>21.1</td>
<td>15.9</td>
<td>0.09</td>
</tr>
<tr>
<td>Monomorphic VT by EPS, %</td>
<td>32.5</td>
<td>33.0</td>
<td>0.90</td>
</tr>
<tr>
<td>Amiodarone, %</td>
<td>32.3</td>
<td>14.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Digoxin, %</td>
<td>49.6</td>
<td>22.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diuretics, %</td>
<td>68.9</td>
<td>29.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Spironolactone, %</td>
<td>18.7</td>
<td>5.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ACE inhibitors/ARBs, %</td>
<td>47.6</td>
<td>32.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>$\beta$-Blocker, %</td>
<td>62.9</td>
<td>63.1</td>
<td>0.99</td>
</tr>
</tbody>
</table>

EPS indicates electrophysiology study, ARB, angiotensin II receptor blocker.
with a rate cutoff that was 1.3 bpm lower for VF (95% CI -2.4 to -0.1) and 2.6 bpm lower for VT (95% CI -4.4 to -0.7). However, rate cutoffs did not differ between patients who received appropriate ICD shocks and those who did not (P=0.47 and P=0.61 for VT and VF rate cutoff, respectively). With respect to antitachycardia pacing (ATP), neither the proportion of patients with ATP nor the rate settings for VT detection among patients with ATP programmed differed according to CHF class.

During a median follow-up time of 212 days (interquartile range 180 to 370 days), 92 patients experienced 1 or more appropriate ICD discharges and 33 patients died before the occurrence of an ICD discharge. The actuarial risk of ICD discharge for VT or VF at 1 year was 12.1% among patients with CHF and 6.5% among those without (Figure 1; P=0.01, log-rank test).

In multivariable proportional hazards models that included LVEF and adjusted for multiple clinical variables (Table 3), class III CHF was associated in a statistically significantly manner with appropriate ICD discharges, with a hazard ratio of 2.40 (95% CI 1.16 to 4.98, P=0.02; Table 3). LVEF <0.20 was also independently associated with an elevated risk of ICD shocks (hazard ratio 2.06, 95% CI 1.04 to 4.06). There was a significant linear relationship between LVEF and risk of shocks for VT/VF (P for trend 0.03). In contrast, there was not a significant linear relationship between NYHA class and ICD shocks (P for trend 0.12); instead, there appeared to be a threshold effect, with an elevation in risk only with severe CHF (class III).

To illustrate the separate effects of CHF class and LVEF on the risk of shocks, we constructed a multivariable proportional hazards model with separate binary variables for each combination of CHF class and LVEF. The hazard ratios from this analysis illustrated that worsened LVEF and functional class had multiplicative effects on the risk of shock (Figure 2). In particular, the combination of class III symptoms and LVEF <0.20 conferred a hazard ratio of 3.90 (95% CI 1.28 to 11.92) compared with the combination of no CHF symptoms and LVEF ≥0.35. The actuarial risk of shock for VT or VF by 12 months of follow-up among patients with both class III CHF and LVEF ≥0.20 was high (33.4%), although the number of patients at risk was small in this group (n=23). By contrast, the risk of appropriate shock with LVEF ≥0.20 and class I/II CHF was 9.2%.

To test whether device settings confounded the relationship between CHF and appropriate shocks, we performed a sensitivity analysis using our original multivariable models. Inclusion of rate-detection settings for VT and VF and presence of ATP programming, with indicator variables for missing data, resulted in a slightly higher hazard ratio for class III CHF (2.70, 95% CI 1.29 to 5.65). In addition, when we confined the analysis to the patients for whom data on rate settings were available (n=613), there was a higher hazard ratio for class III CHF (2.71, 95% CI 1.20 to 6.12).

**Discussion**

In this prospective cohort of ICD patients, class III CHF and severely reduced LVEF independently predicted appropriate shocks for VT/VF. Many, but not all, prior studies in ICD patients have shown that reduced LVEF is associated with device discharges or arrhythmic death. Rela-
The reference group consists of patients with LVEF ≥0.35 and no CHF.

Table 3. Multivariable Proportional Hazards Model of Time to ICD Discharge

<table>
<thead>
<tr>
<th>Hazard Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I CHF</td>
<td>0.99 (0.53–1.88)</td>
</tr>
<tr>
<td>Class II CHF</td>
<td>1.01 (0.53–1.91)</td>
</tr>
<tr>
<td>Class III CHF</td>
<td>2.40 (1.16–4.98)</td>
</tr>
<tr>
<td>LVEF 0.20 to 0.34</td>
<td>1.52 (0.90–2.59)</td>
</tr>
<tr>
<td>LVEF &lt;0.20</td>
<td>2.06 (1.04–4.06)</td>
</tr>
</tbody>
</table>

*The models include functional class and LVEF simultaneously and are adjusted for age, gender, smoking, hypertension, diabetes, history of atrial fibrillation/atrial flutter, coronary artery disease, history of CABG, history of prior discharges, indication for ICD placement, results of baseline electrophysiological testing, presence of biventricular pacer, and use of amiodarone, digoxin, diuretics, spironolactone, and ACE inhibitors/angiotensin II receptor blockers. The reference group consists of patients with LVEF ≥0.35 and no CHF.

The present study adds to this prior literature on the relationship between functional status, LVEF, and ICD shocks for VT/VF. To the best of our knowledge, the present study is the largest and also the first to prospectively address this issue. Unlike prior studies, the present sample of patients was from multiple centers and thus may be more representative of a general sample of ICD patients. In the present study, both severe CHF symptoms and severely reduced LVEF were significant independent predictors of similar magnitude for the occurrence of ICD shocks for documented VT/VF. Patients with the combination of these 2 were at particularly high risk for shocks. The statistical independence of LVEF and CHF class in proportional hazards models implies that these risks have a multiplicative relationship. Therefore, the effect of severe CHF symptoms on the overall risk of ICD discharges is accentuated in the setting of severely reduced LVEF and vice versa.

The fact that functional class provided significant prognostic information in addition to LVEF indicates that the degree of compensation for systolic dysfunction may independently affect ventricular arrhythmogenesis. Functional class has been shown to correlate poorly with LVEF in patients with CHF. There was only a weak statistically significant relationship between CHF class and LVEF in the present sample, and a nonnegligible proportion of patients with severely reduced LVEF had relatively preserved functional status.

There are several potential clinical implications of these data. First, ICD patients with worsening CHF symptoms may warrant more aggressive therapy for the prevention of arrhythmic events. Second, because patients with class III CHF were more likely to have an ICD shock for VT/VF, one might speculate that this category of patients might derive a greater benefit from defibrillator therapy. Although supportive of this hypothesis, the present data are by no means conclusive. ICD shocks for VT/VF cannot be equated with a mortality benefit from the ICD, because not all episodes of VT/VF that result in ICD discharge would have resulted in SCD. In addition, competing risks such as deaths due to pump failure may limit the benefit of the ICD, especially among patients with more severe CHF. This is particularly so for class IV CHF, which was not included in the present analysis and which is considered a contraindication to ICD therapy when cardiac transplantation is not planned.

At this point, the only data that directly address mortality reduction are from subgroup analyses in ICD trials. An analysis of the Canadian Implantable Defibrillator Study found that the presence of 2 or more of 3 factors (age ≥70 years, LVEF ≤0.35, and class III/IV CHF) predicted most likely to benefit from ICD therapy. However, an analysis of the Antiarrhythmics Versus Implantable Defibrillators trial based on these same 3 characteristics found that LVEF ≤0.35 alone predicted all the deaths preventable by ICDs. In the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II), the relative risk reduction with ICD therapy compared with conventional medical therapy did not differ when patients were stratified by class II or greater CHF. However, in the present study, we found that the elevation in risk for recurrent VT/VF was confined to those with class III CHF. Even if the relative risk reduction is similar, the absolute risk reduction may well be greater in patients with severely depressed functional status owing to higher absolute rates of arrhythmic death. The recent completion of the Comparison of Medical Therapy, Pacing, and Defibrillation in Chronic Heart Failure (COMPANION) trial and the pending completion of the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) will help to clarify the benefits of ICD therapy among patients with reduced LVEF and CHF.
Limitations of the present study include the fact that ascertainment of functional status was not based on physiological assessment, such as the 6-minute walk test. However, NYHA class as assessed in TOVA is a relatively easy measure to obtain in the clinical setting, and although measurement error would be expected to bias our results toward the null, we detected a statistically significant effect of NYHA class. In addition, we did not include ATP therapies for VT in our end point. Although incorporation of appropriate ATP would provide a greater number of end points and therefore increase the power of the present study, VT episodes terminated with ATP might include a greater proportion of clinically insignificant arrhythmias that may have self-terminated.

Another potential limitation of the present analysis is the lack of standardized device programming. We chose to defer to physician judgment at the various centers to allow a wide range of patients to be enrolled in the study. Although rate-detection settings tended to be lower in CHF patients, the lack of differences in rate-detection settings between patients who did and did not receive shocks, as well as the insensitivity of our models to the inclusion of device settings, argues against programming differences accounting for the results of the present study.

Finally, the single baseline measure of CHF class does not allow us to assess whether improvement in functional class subsequently lowers the risk of ICD shocks for VT/VF. At this time, with median follow-up of less than 1 year, we do not have enough events or patients with a significant change in functional status to analyze this important question. This issue may be particularly relevant in the current era of cardiac resynchronization therapy, which in up to 70% of cases results in an improvement in functional class and therefore might mitigate the risk of ventricular arrhythmias. With longer follow-up, this and other prospective studies will be able to address whether interventions to improve functional status lower the risk of ventricular arrhythmias over time.

In summary, we found that class III CHF is an important predictor, along with LVEF, of appropriate device discharges in this prospective cohort of ICD patients. Whether or not aggressive treatment of CHF in patients with ICDs may prevent ventricular arrhythmias and ICD shocks remains to be determined. Functional class as an adjunct to LVEF and other clinical factors may help identify patients at risk for ventricular arrhythmias and perhaps, although not proven in these data, SCD. Given the limited financial resources that can be allocated to health care, we must continue to refine the indications for the ICD and to allocate this life-saving technology to those patients who will benefit to the greatest extent. Further efforts to identify those patients who are most likely to benefit from ICDs using data from studies such as TOVA may help to develop more accurate screening criteria, and randomized, controlled mortality trials evaluating the effect of ICD therapy in patients based on these criteria will inform treatment and policy decisions regarding device therapy.

Appendix

TOVA Investigators were the following: Lawrence Rosenthal, MD (University of Massachusetts Memorial Medical Center Hospital, Worcester, Mass); Rachel Lampert, MD, Yale University School of Medicine (New Haven, Conn); Jeremy Ruskin, MD, Massachusetts General Hospital (Boston, Mass); Hugh Calkins, MD (Johns Hopkins Hospital, Baltimore, Md); Robert Peters, MD (University of Maryland Medical Center and Baltimore VA Medical Center, Baltimore, Md); Jamie Beth Conti, MD (University of Florida Health Science Center, Gainesville, Fla); Mina Chung, MD, Cleveland Clinic (Cleveland, Ohio); Leonard Chen, MD (Deborah Heart and Lung Center, Browns Mills, NJ); Douglas Packer, MD (Mayo Clinic, Rochester, Minn; Pratap Reddy, MD (Louisiana State University Health Sciences Center–Shreveport); Mark Josephson, MD (Beth Israel Deaconess Medical Center, Boston, Mass); Mark Estes, MD (Tufts–New England Medical Center, Boston, Mass); Jonathan Steinberg, MD (St. Luke’s–Roosevelt Hospital Center, New York, NY); Otto Costantini, MD (Case Western Reserve University/ MetroHealth Medical Center, Cleveland, Ohio); Karen Beckman, MD (University of Oklahoma Health Sciences Center, Oklahoma City); James Martin, MD (University of Iowa Health Care, Iowa City); Mark Woods, MD (Medical College of Virginia/Virginia Commonwealth University Health System, Richmond, Va); Dorothea A. Otis, MD (Mt. Sinai Medical Center, New York, NY); Ram Jadonath, MD (North Shore University Hospital, Manhasset, NY); Howard Frumin, MD (William Beaumont Hospital, Royal Oak, Mich); Nicholas Stamato, MD (Cardiology Associates, Wilson Memorial Regional Medical Center, Johnson City, NY); Igor Singer, MD (University of Louisville Health Sciences Center, Louisville, Ky); Edward Platia, MD (MedStar Research Institute, Washington Hospital Center, Washington, DC); Noel Boyle, MD, PhD (University of California, Los Angeles Medical Center, Los Angeles); R.K. Thakur, MD (Sparrow Hospital and Ingham Regional Medical Center, Lansing, Mich); Harry Kopelman, MD (St Joseph’s Hospital of Atlanta, Ga); Malcolm Bersohn, MD, PhD (West Los Angeles VA Medical Center, Los Angeles, Calif); Mark Roelke, MD (Diagnostic and Clinical Cardiology, Saint Barnabas Medical Center, Livingston, NJ); Robert Myerburg, MD (University of Miami, Jackson Memorial Hospital, Miami, Fla); Bruce Lerman, MD (New York Presbyterian Hospital, New York, NY); and Bruce Stumbler, MD (University Hospitals of Cleveland, Cleveland, Ohio).

Acknowledgments

This study was supported by funding from the National Heart, Lung, and Blood Institute (5R01-HL041016), Guidant Foundation, and Guidant Cardiac Rhythm Management. We are indebted to the patients who participated in the TOVA for their outstanding commitment and cooperation, and to Jennifer Merlan, Jane Sherwood, and all the study staff and investigators at the clinical sites.

References


Heart Failure and the Risk of Shocks in Patients With Implantable Cardioverter Defibrillators: Results From the Triggers Of Ventricular Arrhythmias (TOVA) Study
for the TOVA Investigators

Circulation. 2004;109:1386-1391; originally published online March 1, 2004;
doi: 10.1161/01.CIR.0000120703.99433.1E
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/109/11/1386

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/