Predictors of First Discharge and Subsequent Survival in Patients With Automatic Implantable Cardioverter-Defibrillators

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Background. Two hundred eighteen patients were evaluated in a two-phase approach (time to first appropriate discharge, survival after discharge) to identify factors that may be related to maximal benefit derived from use of an automatic implantable cardioverter-defibrillator (AICD).

Methods and Results. One hundred ninety-seven patients survived implantation of AICD, with or without concomitant cardiac surgery. One hundred five patients had an AICD discharge associated with syncope, presyncope, documented sustained ventricular tachycardia or fibrillation, or sleep at 9.1±11.1 months after implantation. Patients survived 23.8±18.0 months after AICD discharge. Left ventricular dysfunction (p=0.008 for ejection fraction less than 25%) was associated with earlier AICD discharge and shortened survival after AICD discharge (p=0.008 for ejection fraction less than 25%; p=0.01 for New York Heart Association functional class III and IV). β-Blocker administration (p=0.006) and coronary bypass surgery (p=0.06) were associated with later AICD discharge. Coronary bypass surgery (p=0.035) but not β-blockers was associated with more prolonged survival after AICD discharge.

Conclusions. These data suggest that a relatively easy algorithm can be applied to predict which patient will benefit most from AICD implantation. (Circulation 1991;84:558–566)

Automatic implantable cardioverter-defibrillators (AICD) have become an important alternative to conventional treatment of patients with recurrent hypotensive ventricular tachyarrhythmias. Several groups, including our own, have demonstrated effective termination of sustained ventricular tachycardia or fibrillation by this device.1–9 AICD implantation thus far has been largely reserved for cardiac arrest survivors when antiarrhythmic medication is not efficacious. Prolongation of life by this device has not been proven by a prospective, randomized trial because withholding AICD therapy has not been possible because of ethical considerations. Whether survival has been improved by the AICD, therefore, has been the subject of discussion.10 Similarly, factors associated with improved survival or enhanced benefit in patients with the AICD remain unknown.

For a patient to benefit from an AICD, two conditions must be met. First, there must be an appropriate discharge of the device (e.g., because of a hemodynamically destabilizing rhythm such as sustained ventricular tachycardia or fibrillation); second, the patient must survive a reasonable period of time after AICD discharge. For example, no benefit is obtained if the patient dies at the time of first appropriate AICD discharge. Similarly, a patient who never has an AICD discharge may not benefit from the device. Conversely, a patient who survives for an extended period after an AICD discharge probably has enhanced survival attributable to this device.

This study identifies baseline variables associated with the first appropriate AICD discharge as well as those that are associated with extended survival after first discharge. It is anticipated that these findings will help select patients most likely to benefit from AICD placement.

Methods

Patient Population

Two hundred eighteen patients who had an AICD implanted as a single operation or as a planned
TABLE 1. Clinical Characteristics

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>218</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients discharged alive (n)</td>
<td>197</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>56.5±12.8</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>34.6±16.4</td>
</tr>
</tbody>
</table>

Heart disease
- Coronary artery disease (n) | 167 |
- Cardiomyopathy (n) | 33 |
- Other (n) | 18 |

Cardiac surgery
- AICD only (n) | 154 |
- AICD+bypass surgery (n) | 29 |
- AICD+aneurysmectomy+subendocardial resection (n) | 33 |
- AICD+other (n) | 2 |

Follow-up (mo) | 0–86.2 |

Patients with AICD discharge (n) | 105/197 (53.3%) |

Time to first firing (mo) | 9.1±11.1 |

Time from first firing to death (mo) | 23.8±18.0 |

Deaths in follow-up (n) | 82 |
- Arrhythmic | 24 |
- Infarction | 7 |
- Heart failure | 19 |
- Noncardiac | 11 |
- Operative | 21 |

Two-stage procedure at The Johns Hopkins Hospital or Sinai Hospital, Baltimore, Md., between February 1980 and June 1987 are included in this study. Their clinical characteristics are summarized in Table 1. Patients were followed up to 86.2 months after implantation. All patients met the following criteria for AICD placement: 1) They had survived an out-of-hospital cardiac arrest or had recurrent sustained ventricular tachycardia unrelated to an acute myocardial infarction or a reversible metabolic condition. 2) No effective or tolerated antiarrhythmic regimen could be identified using serial electrophysiological testing. 3) They were considered suitable surgical candidates.

Baseline variables considered in this analysis are listed in Table 2. All except one patient had preoperative electrophysiological testing. Early in our experience, the laboratory protocol included stimulation with single and double extrastimuli as well as burst pacing at two right and one or two left ventricular sites. Later, a third extrastimulus was used in the right ventricular pacing protocol, and left ventricular stimulation was omitted. For an antiarrhythmic agent to be considered effective, it was well tolerated and prevented induction of hemodynamic destabilizing ventricular tachycardia. Patients in whom no antiarrhythmic agents were effective were referred for AICD implant.

After AICD implantation, “best” antiarrhythmic medication was continued in a majority of patients. Decreased frequency and complexity of ventricular arrhythmias on Holter recordings were used to guide this antiarrhythmic therapy.

Surgical techniques used to implant the AICD have been described previously.1,2,4,8 Most patients received an epicardial patch–superior vena cava spring electrode system with endocardial sensing leads. The earliest model of the automatic implantable defibrillator (33 patients) did not have a rate-sensing lead. More recently, a patch–patch configuration was used where possible. Most devices used were probability density function active. Concomitant surgery (coronary artery bypass, valve repair or replacement, aneurysmectomy, and subendocardial resection) was performed if clinically indicated.

Defibrillation thresholds were tested before the AICD generator was attached to electrodes. Alternating current was used to induce ventricular tachycardia and/or fibrillation, and decreasing amounts of

TABLE 2. Baseline Variables

<table>
<thead>
<tr>
<th>Clinical variables:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Type of heart disease</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
</tr>
<tr>
<td>Presenting arrhythmia (VT vs. VF)</td>
</tr>
<tr>
<td>CHF class</td>
</tr>
</tbody>
</table>

Electrophysiological variables:
- Baseline EP study findings
- Noninducible, inducible nonsustained VT and inducible sustained VT
- PredischARGE EP study findings
- Noninducible, inducible nonsustained VT, and inducible sustained VT
- PredischARGE Holter findings
- VT vs. no VT
- PVB/hr
- Defibrillation threshold (±20 vs. 20 J)

Angiographic variables:
- Ejection fraction
- Number and location of diseased coronary arteries
- Presence of left ventricular aneurysm

Surgical variables:
- Type of surgery
- AICD only or in combination with CABG, SER, valve replacement
- Type of generator
- AID vs. AICD-B vs. AICD-C (Ventak)
- Lead configuration (patch-patch vs. spring-patch)
- Discharge antiarrhythmic drugs:
  - Antiarrhythmics (1A, 1B, 1C)
  - Amiodarone
  - Digoxin
  - β-Blockers

VT/VI, ventricular tachycardia/fibrillation; CHF, New York Heart Association congestive heart failure; EP, electrophysiology; PVB, premature ventricular beat; AICD, automatic implantable cardioverter defibrillator; CABG, coronary artery bypass graft surgery; SER, subendocardial resection; AID, first-generation automatic implantable defibrillator.
energy were applied from an external cardioverter-defibrillator across leads so that the minimum energy required to defibrillate the heart was identified (defibrillation threshold). All patients underwent a defibrillation test at 20–23 J at the time of implantation. Because of changes in defibrillation threshold protocol over time, it was defined as high (more than 20 J) or low (20 J or less) for the purposes of analysis rather than treating it as a continuous variable. Successful recognition and termination of ventricular tachycardia or fibrillation were also confirmed with the implanted AICD generator unit.

All except nine patients had preoperative coronary angiography. Significant coronary obstruction was defined as greater than 70% obstruction in a major vessel and greater than 50% obstruction in the main left coronary artery. A left ventricular aneurysm was defined as a dyskinetic area of the cardiac silhouette identified during ventricular systole. Left ventricular ejection fraction (EF) was determined by the area-length method. Classifications for congestive heart failure by the New York Heart Association (NYHA) criteria were based on clinical history and physical findings before implantation of the AICD device.

In a subset of patients, Holter monitor recordings and electrophysiology studies were performed on discharge antiarrhythmic medications (Holter: 140 of 197 patients, 71%; electrophysiology study: 137 of 197 patients, 70%).

Follow-up

Follow-up in this study began at the time of AICD surgery. All perioperative deaths (within 30 days of surgery) were included. After hospital discharge, all patients were routinely seen at 1–3-month intervals. AICD discharges were confirmed by transcutaneous telemetry/magnet testing.

Because underlying cardiac rhythm at time of AICD discharge was almost never recorded, criteria for appropriate AICD discharge were developed.6,7,9 All AICD discharges accompanied by hypotensive symptoms (severe presyncope or syncope) or recorded sustained ventricular tachycardia were judged appropriate and considered secondary to ventricular tachycardia or ventricular fibrillation. AICD discharges occurring during sleep were also considered appropriate. All patients who experienced an AICD discharge had follow-up Holter monitoring and exercise electrocardiography. To remain in the appropriate AICD discharge group, there was no Holter evidence of an atrial arrhythmia (atrial fibrillation or paroxysmal atrial tachycardia), and exercise testing determined that sinus tachycardia exceeding AICD rate threshold was not achieved. AICD discharges were considered inappropriate if there were no hypotensive symptoms, follow-up Holter recording showed an atrial arrhythmia, or minimum rate threshold was achieved on exercise electrocardiography.

Variables Studied and Statistical Methods

Demographic, clinical, electrophysiological, angiographic, and surgical variables were included in this analysis. These are listed in Table 2. Within each subgroup, various representations of the variables in question were attempted. Continuous variables were examined as both linear and nonlinear variables. Nonlinear forms of the variables used both polynomial regression and transformation techniques. Univariate analyses were used to determine the form of the variable to be used. In addition, several two-variable interaction terms were tested when appropriate. Final equations were developed by recognizing clinical considerations and then deriving the best fit statistically. Final predictive equations were arrived by consensus of the best fit of clinical and statistical findings.

Data are reported as distributions and mean±SD values. Actuarial survival curves are plotted using the Kaplan-Meier method. For categorical variables, statistical analysis of differences between survival curves was done by Peto and Breslow methods. The significance between continuous variables was evaluated by Cox hazards analysis. Variables were considered significant at p≤0.05. Variables were subsequently included in multivariate analysis if their univariate significance was p≤0.10. The multivariate Cox hazards analysis was used to simultaneously evaluate these variables. Student’s t tests and χ² tests were used to compare discrete variables where appropriate. The primary analysis was divided into two sections, each with two parts. First, considering the first AICD discharge as the dependent variable, each separate baseline variable was evaluated for its ability to demonstrate significant association with time to first AICD discharge in a univariate actuarial curve analysis. Variables demonstrating sufficient association (p≤0.10) were then included in a multivariate stepwise Cox hazards analysis from which an optimum set of variables was derived.

Second, for those patients with an appropriate AICD discharge, using the time of AICD discharge as time zero, a second analysis examining death as the dependent variable was initiated. Again, univariate and multivariate survival methodology was used, with the univariate result determining which baseline variables were included in multivariate testing.

Our multivariate analysis takes into consideration any differences that may be confounding. Thus, even if differences were present among groups in EF, NYHA functional class, or other variables listed and evaluated, the multivariate analysis takes these into consideration. Any significant factors noted in the multivariate analysis on the time to first AICD discharge or on survival after said discharge is that over and above the differences in other variables noted.

Limitations

A limitation of our study is that electrocardiographic documentations of cardiac rhythm at the time of AICD discharge was not available for all patients. As noted previously, strict criteria for appropriate AICD discharge used by other investigators and by us6,7,10 make it unlikely that we have
TABLE 3. Predictors of Appropriate Automatic Implantable Cardioverter-Defibrillator Firing After Hospital Discharge

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF&lt;25% and CHF= class III</td>
<td>p=0.001</td>
<td>p=0.003</td>
</tr>
<tr>
<td>No β-blocker therapy</td>
<td>p=0.006</td>
<td>p=0.021</td>
</tr>
<tr>
<td>Coronary artery bypass grafting not done</td>
<td>p=0.064</td>
<td>p=0.053</td>
</tr>
<tr>
<td>EF&lt;25%</td>
<td>p=0.008</td>
<td>NS</td>
</tr>
<tr>
<td>CHF class III or IV</td>
<td>p=0.081</td>
<td>NS</td>
</tr>
<tr>
<td>Digoxin</td>
<td>p=0.052</td>
<td>NS</td>
</tr>
<tr>
<td>Automatic implantable cardioverter-defibrillator only</td>
<td>p=0.065</td>
<td>NS</td>
</tr>
</tbody>
</table>

EF, ejection fraction; CHF, congestive heart failure (New York Heart Association class).

seriously overestimated the frequency of true AICD discharges. Although some supraventricular arrhythmias can mimic ventricular tachycardia in their rate and as causes of hypotensive symptoms, one could argue that if the AICD reversed any rhythm (supraventricular or ventricular) causing severe presyncope or syncope, it would be functioning appropriately. Conversely, our experience as well as that of others suggests that nonhypotensive ventricular tachycardia leading to an asymptomatic discharge is also prevalent, and, as such, it is possible that we have underestimated rather than overestimated the frequency of appropriate AICD discharges secondary to sustained ventricular tachycardia. That our data regarding the time course and factors predicting AICD discharge (bypass surgery, left ventricular function) are similar to those reported previously for recurrent arrhythmic events in survivors of out-of-hospital cardiac arrest suggests that our definitions are, for the most part, valid and accurate.

A second limitation is that the overall operative mortality was somewhat high. This is attributable to a higher mortality in patients undergoing AICD and concomitant surgery, but it nonetheless may have influenced the analysis of benefit.

Results

Predictors of First Appropriate AICD Discharge

One hundred ninety-seven of the 218 patients survived to 1 month after AICD implant (with or without concomitant surgery). One hundred thirty-three of 139 patients who had the AICD implanted as the sole procedure and who were not NYHA class IV heart failure patients survived the procedure. Of these 197 patients, 105 (53.3%) had an appropriate AICD discharge at 9.1±11.1 months of follow-up, that is, a discharge accompanied or immediately preceded by presyncope, syncope, witnessed cardiac arrest, or electrocardiographic documentation of a sustained ventricular tachyarrhythmia.

Shown in Table 3 are the variables that were significant univariate predictors of first appropriate AICD firing after discharge from the hospital. The seven variables, including one interaction term (EF less than 25%; NYHA class III or IV), were statistically significant between p<0.001 and p<0.10. These were then tested with a stepwise multivariate Cox model. Only three variables remained significant multivariate predictors of first appropriate AICD discharge. These are also presented in Table 3. The combination of severe congestive heart failure (NYHA class III or IV) and low EF (less than 25%) before AICD surgery, no coronary artery bypass surgery, and no β-blocker treatment after hospital discharge were significant positive predictors of first appropriate AICD discharge when applied in a Cox hazards model.

A family of derived survival curves is presented in Figure 1. The proportion of patients without AICD discharge (ordinate) as a function of time (abscissa) are plotted. Evidence or symptoms of myocardial dysfunction (EF, less than 25%; NYHA class III or IV) were associated with an increased likelihood of AICD discharge. This result is consistent with the notion that AICD discharge is determined, in part, by left ventricular function (the interaction of heart failure class and EF). In addition, the presence of anti-ischemic interventions (coronary artery bypass surgery and/or β-blocker administration) was associated with later AICD discharge.

The relative risk and probability of being free from an AICD discharge at 3 months, 6 months, and 1, 2, and 3 years for patients with various combinations of these factors are presented in Table 4. The relative risk of having an AICD discharge varies from 0.27 in patients with better left ventricular function (EF > 25% or NYHA class I or II), who underwent bypass surgery and were discharged on β-blockers, to 1.99 in patients with poor left ventricular function (EF < 25% and NYHA class III or IV), who did not have concomitant bypass surgery and were not taking.
Table 4. Probability of No Automatic Implantable Cardioverter-Defibrillator Discharge

<table>
<thead>
<tr>
<th>EF&lt;25% and CHF=class III</th>
<th>β-Blocker</th>
<th>CABG</th>
<th>Relative risk</th>
<th>3 Mo</th>
<th>6 Mo</th>
<th>12 Mo</th>
<th>24 Mo</th>
<th>36 Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>0.27</td>
<td>0.95</td>
<td>0.89</td>
<td>0.84</td>
<td>0.78</td>
<td>0.75</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>0.52</td>
<td>0.90</td>
<td>0.81</td>
<td>0.73</td>
<td>0.63</td>
<td>0.58</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>0.53</td>
<td>0.90</td>
<td>0.81</td>
<td>0.72</td>
<td>0.62</td>
<td>0.57</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>No</td>
<td>1.00</td>
<td>0.82</td>
<td>0.67</td>
<td>0.54</td>
<td>0.41</td>
<td>0.35</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>0.55</td>
<td>0.90</td>
<td>0.80</td>
<td>0.71</td>
<td>0.61</td>
<td>0.57</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>1.03</td>
<td>0.82</td>
<td>0.66</td>
<td>0.53</td>
<td>0.40</td>
<td>0.34</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>1.06</td>
<td>0.81</td>
<td>0.65</td>
<td>0.52</td>
<td>0.39</td>
<td>0.33</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>1.99</td>
<td>0.68</td>
<td>0.45</td>
<td>0.29</td>
<td>0.17</td>
<td>0.13</td>
</tr>
</tbody>
</table>

EF, ejection fraction; CHF, New York Heart Association congestive heart failure class; CABG, coronary artery bypass graft.

β-blockers. There was a similar range noted for the probability of not having an AICD discharge in the subgroups at each of these times. For example, the 3-year probability varies from 0.75 to 0.13. Thus, the likelihood of having an appropriate AICD discharge early after implantation appears to be a function of severity of left ventricular dysfunction (anatomically as EF and physiologically as NYHA functional class) and anti-ischemic interventions.

It should be noted that several other baseline variables that might be considered important were not significant predictors of AICD discharge. Presenting arrhythmias (ventricular tachycardia versus ventricular fibrillation, baseline and predischarge electrophysiological findings), predischarge Holter findings, number of coronary arteries narrowed, and discharge antiarrhythmic drug status at hospital discharge did not correlate with presence or time to first AICD discharge.

Predictors of Time From First AICD Discharge to Death

To derive benefit from the AICD, there must not only be an appropriate discharge of the AICD device but also prolonged survival after this AICD discharge. One hundred five of the 197 patients who survived AICD implant procedure had an appropriate AICD discharge. Mean survival after AICD discharge was 23.8±18.0 months.

Variables that were significant predictors of survival after AICD discharge are listed in Table 5.

Table 5. Predictors of Survival After Automatic Implantable Cardioverter-Defibrillator Discharge

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction</td>
<td>0.022</td>
<td>NS</td>
</tr>
<tr>
<td>New York Heart Association functional class</td>
<td>0.001</td>
<td>0.002</td>
</tr>
<tr>
<td>Automatic implantable cardioverter-defibrillator only</td>
<td>0.003</td>
<td>0.027</td>
</tr>
<tr>
<td>First-generation automatic implantable defibrillator</td>
<td>0.019</td>
<td>0.026</td>
</tr>
<tr>
<td>Coronary artery bypass graft</td>
<td>0.035</td>
<td>*</td>
</tr>
</tbody>
</table>

*All patients in coronary artery bypass graft group survived following automatic implantable cardioverter-defibrillator discharge.

Univariate predictors of survival after AICD discharge include good ejection fraction, absence of significant congestive heart failure, any concomitant surgery at AICD placement (coronary bypass surgery, aneurysmectomy, or endocardial resection), coronary bypass graft surgery at AICD placement, and implantation of second- or third-generation AICD generators (all p<0.05).

Results of multivariate analysis of variables that remained significant predictors of survival after AICD discharge are shown in Table 5. No patient with concomitant coronary artery bypass graft surgery died in follow-up after an appropriate AICD discharge. Thus, concomitant coronary bypass surgery was the strongest predictor of survival in these patients. Because there were no deaths in this subgroup, no other factor could be analyzed in the presence of concomitant bypass surgery. When patients with bypass surgery were excluded from analysis, three other factors were significant predictors of survival: advanced congestive heart failure class, first-generation AICD generator, and AICD implant as the only surgical procedure (all p<0.05). These data are presented in Figure 2.

The relative risks and probabilities of survival after first AICD discharge are presented in Table 6. The relative risk of dying ranged from 2.21 (NYHA class I, concomitant surgery, and newer AICD generator) to 284.98 (NYHA class IV, no concomitant surgery, and first-generation AICD generator). Analysis in this manner results in a wide range of probabilities for survival. For example, the probabilities of survival noted ranged from 0.99 to 0.28 at 1 year and from 0.97 to 0.00 at 5 years. With the newer AICD generator, more than 80% of patients survive longer than 1 year after discharge of the device, even in the presence of NYHA class III congestive heart failure. If these class III patients had concomitant surgery, there was a 78% expected survival at 3 years and a 69% expected survival at 5 years. Thus, even patients with moderate to severe symptoms of congestive heart failure secondary to left ventricular dysfunction benefit from the AICD (i.e., they have a significant increment in survival after the first appropriate AICD discharge).
In contrast, AICD implantation does not appear to be a good alternative for patients with class IV heart failure. Although ventricular tachyarrhythmias are a frequent cause of death in this subgroup, our data suggest that survival in this subgroup is not appreciably extended by AICD implantation. There were 12 patients with class IV heart failure in our series. Five patients had intraoperative or perioperative death. Of the seven surviving patients, two were alive at follow-up and have not had an AICD discharge. Three patients had appropriate AICD discharge; two of these three died suddenly (at 57 and 239 days) after AICD discharge. Thus, of the 12 patients, only three were alive at follow-up, and the mean survival of the group was only 13.1±19.8 months. More important, the increment of survival for the group of 12 in its entirety was only 0.92±2.3 months (zero was used for patients without AICD discharge). Thus, in this subset of patients, operative mortality appears unacceptably high, and survival may be limited. Whether an AICD can be used to obtain enhanced short-term survival as a bridge to transplantation was not tested in this study and awaits a larger, controlled prospective study (immediate transplantation versus AICD and later transplantation in class IV patients).

### Discussion

The AICD has been proposed as an alternative to conventional medical therapy for patients at high risk of arrhythmic death; it reliably terminates ventricular tachyarrhythmias and very likely also reduces mortality from a sustained ventricular tachyarrhythmic event. 

It is our premise that two factors must occur for a patient to benefit from AICD placement: The AICD must discharge and successfully convert an episode of ventricular tachycardia or fibrillation, and the patient must survive for a meaningful period of time after this appropriate AICD discharge. Neither the patient who has never had an episode of ventricular tachycardia or ventricular fibrillation that requires AICD use nor the patient who dies soon after an inappropriate AICD discharge can be considered to have appreciably benefited from AICD placement. This study is the first to identify baseline variables that are associated with appropriate discharge of an AICD and with enhanced survival after AICD discharge. This two-phase approach, therefore, provides guidelines to help decide when to implant an AICD.

### Role of Left Ventricular Function

Left ventricular function is an important factor that influences both time to first AICD discharge and subsequent survival. Both time to first AICD discharge and survival after this AICD discharge correlated with EF and congestive heart failure class (see Figure 3). Severe left ventricular dysfunction (EF, less than 25%; p=0.008) and severe congestive heart failure were associated with increased probability of AICD discharge and reduced survival. CHF class, New York Heart Association congestive heart failure class. For all probabilities presented, the use of second- or third-generation automatic implantable cardioverter-defibrillators were considered.

### Table 6. Probability of Survival After Automatic Implantable Cardioverter-Defibrillator Discharge

<table>
<thead>
<tr>
<th>CHF class</th>
<th>Automatic implantable cardioverter-defibrillator only</th>
<th>Relative risk</th>
<th>1 Yr</th>
<th>2 Yr</th>
<th>3 Yr</th>
<th>5 Yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No</td>
<td>1.00</td>
<td>0.99</td>
<td>0.98</td>
<td>0.98</td>
<td>0.97</td>
</tr>
<tr>
<td>0</td>
<td>Yes</td>
<td>4.52</td>
<td>0.98</td>
<td>0.93</td>
<td>0.90</td>
<td>0.86</td>
</tr>
<tr>
<td>1</td>
<td>No</td>
<td>2.21</td>
<td>0.99</td>
<td>0.97</td>
<td>0.95</td>
<td>0.93</td>
</tr>
<tr>
<td>1</td>
<td>Yes</td>
<td>9.99</td>
<td>0.96</td>
<td>0.86</td>
<td>0.80</td>
<td>0.71</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
<td>4.88</td>
<td>0.98</td>
<td>0.93</td>
<td>0.90</td>
<td>0.85</td>
</tr>
<tr>
<td>2</td>
<td>Yes</td>
<td>22.08</td>
<td>0.91</td>
<td>0.71</td>
<td>0.61</td>
<td>0.47</td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>10.79</td>
<td>0.95</td>
<td>0.85</td>
<td>0.78</td>
<td>0.69</td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>48.78</td>
<td>0.80</td>
<td>0.47</td>
<td>0.33</td>
<td>0.19</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>23.84</td>
<td>0.90</td>
<td>0.69</td>
<td>0.58</td>
<td>0.45</td>
</tr>
<tr>
<td>4</td>
<td>Yes</td>
<td>107.78</td>
<td>0.62</td>
<td>0.19</td>
<td>0.09</td>
<td>0.03</td>
</tr>
</tbody>
</table>
failure (NYHA class III or IV, \( p=0.08 \)) were associated with a higher probability of early AICD discharge. The simultaneous presence of both low EF and advanced congestive heart failure class together was a better predictor of early AICD discharge than either variable alone. These data are consistent with findings of Swerdlow and coworkers,\(^\text{12}\) who documented a similar relation between left ventricular dysfunction and subsequent arrhythmic events in patients surviving an initial sustained ventricular tachyarrhythmia.

A similar correlation between these two variables and survival after AICD discharge was also present (see Figure 4). Lower EF (\( p=0.06 \)) and congestive heart failure class III or IV (\( p=0.01 \)) were associated with shorter survival after AICD discharge. Survival after AICD discharge correlated better with heart failure class than with EF or the interaction of these two variables. In addition, for the case of EF but not heart failure class the differences in the survival curves were primarily due to differences noted subsequent to year 2, when fewer patients remained in the analysis.

Even though patients with severe left ventricular dysfunction have a shortened survival after first AICD discharge compared with patients with better cardiac function, patients with very poor left ventricular function still appear to benefit from an AICD implant. For example, in patients with an ejection fraction of less than 25\%, the expected median survival after first appropriate AICD discharge determined by Kaplan-Meier analysis is 29.7±5.6 months (mean±SEM). Thus, our data suggest that outcome after AICD implant is different from that after other device implantation. For example, improved survival has not been demonstrated after prophylactic permanent pacemaker implantation in all patients with high-degree atrioventricular block.\(^\text{13}\)

**Role of Anti-ischemic Interventions**

In this retrospective multivariate analysis, interventions that improved coronary blood flow (bypass surgery) or reduced myocardial ischemia (\( \beta \)-blocker therapy) were associated with a favorable outcome. Both bypass surgery (\( p=0.06 \)) and \( \beta \)-blocker use (\( p=0.006 \)) were associated with a delay to first AICD discharge (see Figure 5). Bypass surgery (\( p=0.035 \)) but not \( \beta \)-blocker therapy was also associated with improved survival after an AICD discharge (see Figure 6). These data are consistent with those of Wilber and coworkers,\(^\text{11}\) in which coronary bypass surgery after surviving a cardiac arrest was associated with improved survival.

One comment should be made concerning the role of coronary bypass surgery and use of \( \beta \)-blocker therapy. This is a retrospective analysis of outcome and use of coronary bypass surgery and \( \beta \)-blocker therapy were not used in a prospective, randomized fashion. In this
multivariate analysis, we did control for a multitude of potentially confounding variables (see Table 2) and thus it is unlikely that the favorable outcome of patients who underwent bypass surgery or received β-blocker therapy was merely because they were better surgical candidates with better ventricular function. As noted in “Methods,” because of the type of multivariate analysis used, the differences noted for bypass surgery patients and patients taking β-blockers are over and above any differences in other variables analyzed. Hence, these factors remain significant despite the fact that the mean EF differed among those taking (EF, 45.9±20.0%) and not taking (EF, 33.1±14.8%) β-blockers. No differences, however, were present in mean EF or heart failure class in the group undergoing versus those not undergoing bypass surgery (EF, 40.5±15.1% versus 34.6±16.5%, respectively; p=NS).

Other Variables

Several factors did not influence time of first appropriate AICD discharge or subsequent survival after the first AICD discharge. Baseline or electrophysiological testing before AICD discharge, ambulatory electrocardiographic findings, extent of coronary artery disease, and discharge antiarrhythmic drug status did not predict first AICD discharge or survival after AICD discharge. These results differ from those of other investigators who have shown enhanced survival with conversion from positive to negative for induction of sustained ventricular tachycardia during electrophysiological testing or with a reduction of ambient ectopy on ambulatory monitors.14-16 One possible explanation for this difference is that our patient population differs from those reported previously. Patients thought to be treated successfully (by electrophysiological testing or ambulatory monitoring) were not candidates for AICD implantation, and, as such, our patients represent the subset of cardiac arrest survivors most refractory to medical therapies.

Time to first appropriate AICD discharge and survival after AICD discharge were independent of underlying cardiac disease. Patients with cardiomyopathy derived benefit from the device similar to that of patients with coronary artery disease. This differs from other reports in which response to antiarrhythmic drug therapy appears to be more effective in patients with coronary artery disease compared with those with dilated cardiomyopathy.14-17

Although data of others10 suggest that survival among patients with appropriate AICD discharges is less than that among patients without shocks, no such differences were noted in our study (mean survival of patients with versus without shocks, 32.8±19.5 months versus 28.0±19.9 months, respectively; p=NS). Thirty-seven of the 82 deaths reported in our series occurred after the first appropriate AICD discharge, whereas 45 occurred before an AICD discharge.

This study has direct clinical utility because it is the first study to examine which patient will most likely benefit from implantation of the AICD device. In addition, operative mortality associated with AICD placement has been included and was debited from benefit in this study. The probabilities for AICD discharge and survival after AICD discharge allow relatively simple evaluation of prospective patients for AICD implantation and hence provide data that may help define which patients will benefit most from AICD implantation and which patients might be better served by cardiac transplantation and/or ablative maneuvers.

A limitation of the study is that benefit from AICD was not directly compared in a randomized prospective way with that derived from other therapies. Although such a study would be of interest, it was not feasible or ethical in this population of patients, most of whom were referred as treatment failures from other tertiary institutions.

This study is also of importance to help guide therapy during the expected times of limited or fixed resources and cost containment, as the AICD is apparently effective but expensive therapy. Our data suggest that it may be possible to determine which patient will benefit most from an AICD and, perhaps more important, which patient will derive little or no benefit. Thus, the data from this study, if confirmed by others, may help to define subsets of patients who can be triaged not only to best medical therapy but also to the most cost-effective approach.

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