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# Syncope Predicts the Outcome of Cardiomyopathy Patients

## Analysis of the SCD-HeFT Study

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**Objectives** The outcome of congestive heart failure (CHF) patients with syncope is understood incompletely.

**Background** We analyzed data from patients enrolled in the SCD-HeFT (Sudden Cardiac Death Heart Failure Trial) to determine whether syncope predicted outcomes in patients with CHF.

**Methods** We compared outcomes (and associated clinical characteristics) in patients with and without syncope enrolled in SCD-HeFT.

**Results** In SCD-HeFT, 162 (6%) patients had syncope before randomization, 356 (14%) had syncope after randomization (similar incidence in each randomized arm), and 46 (2%) had syncope before and after randomization. A QRS duration ≥120 ms and absence of beta-blocker use predicted syncope during follow-up (hazard ratio [HR] 1.30 and 95% confidence interval [CI] 1.06 to 1.61, p = 0.014 and HR 1.25, 95% CI 1.01 to 1.56, p = 0.048, respectively). Syncope recurrence did not differ by randomization arm. However, in the implantable cardioverter-defibrillator (ICD) arm, syncope, before and after randomization, was associated with appropriate ICD discharges (HR 1.75, 95% CI 1.10 to 2.80, p = 0.019 and HR 2.91, 95% CI 1.89 to 4.47, p = 0.001, respectively). Post-randomization syncope predicted total and cardiovascular death (HR 1.41, 95% CI 1.13 to 1.76, p = 0.002 and HR 1.55, 95% CI 1.19 to 2.02, p = 0.001, respectively). The elevated relative risk of mortality for syncope versus nonsyncope patients did not vary significantly across treatment arms (ICD, HR 1.54, 95% CI 1.04 to 2.27; amiodarone, HR 1.33, 95% CI 0.91 to 1.93; and placebo, HR 1.39, 95% CI 0.96 to 2.02, test for difference p = 0.86).

**Conclusions** For CHF patients with ICDs, syncope was associated with appropriate ICD activations. Syncope was associated with increased mortality risk in SCD-HeFT regardless of treatment arm (placebo, amiodarone, or ICD). (SCD-HeFT Trial; NCT00000609) (J Am Coll Cardiol 2008;51:1277–82) © 2008 by the American College of Cardiology Foundation

Syncope is caused by conditions ranging from benign, self-limiting autonomic fluctuations to chronic, recurrent, and potentially fatal arrhythmic or cardiac mechanical causes (1). Syncope associated with cardiovascular disease may have a poor prognosis (1–3). Patients with syncope and inducible ventricular tachycardia at electrophysiology testing have a similar outcome to those patients with inducible ventricular tachycardia who have been resuscitated

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**Abbreviations and Acronyms**

**CI** = confidence interval
**ECG** = electrocardiogram
**HR** = hazard ratio
**ICD** = implantable cardioverter-defibrillator
**NYHA** = New York Heart Association

from cardiac arrest (4). Patients with syncope and inducible ventricular arrhythmias who undergo implantable cardioverter-defibrillator (ICD) implant use their ICDs (5–9).

The risk of death in heart failure patients with syncope is present even when the electrophysiology study is negative (10–12). Congestive heart failure appears to be an independent predictor of mortality in patients with syncope (13). Retrospective data suggest that patients with syncope and cardiomyopathy who undergo ICD implantation, whether or not they have a positive electrophysiology test, get appropriate ICD activations (9,14,15) and that this may reduce the risk of death (16–18), although the data on this are not definitive and the risk of death remains high (12,19). Therefore, ICDs have been recommended in heart failure patients with syncope (7,20). Data regarding syncope in patients with congestive heart failure are based largely on small single-site studies of highly select patients who often are not treated with standard medical therapy for heart failure.

The SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) offered an unusual opportunity to examine some of the outstanding questions about syncope in congestive heart failure.

## Methods

**Major trial results and patient population.** The SCD-HeFT was a large, multicenter, randomized, controlled clinical trial of ischemic and nonischemic cardiomyopathy patients with New York Heart Association (NYHA) functional class II and III congestive heart failure who had left ventricular ejection fraction ≤35% who were treated with standard medical therapy for heart failure (including beta-adrenergic blocking drugs and vasodilators) and subsequently were randomized to receive amiodarone, a placebo pill, or a single-chamber, shock-only, ICD (programmed VVI-34) (21). The predetermined outcome of the trial was total mortality. The methodology and results are reported elsewhere (21).

All patients enrolled in SCD-HeFT were included in this analysis. For the purpose of this analysis, syncope was defined as a sudden loss of consciousness with loss of postural tone and with rapid complete recovery without need for cardioversion or defibrillation. Syncope was identified before enrollment and during the follow-up period ("post-randomization").

The clinician's judgment established the presumptive cause of syncope. No algorithm or guidance was given to manage or diagnose syncope. No standardized definitions were used for syncope diagnoses. Data were not collected systematically that could define temporal relationships between syncope and ICD shocks, heart failure exacerbations, electrocardiogram (ECG) changes, ventricular or supraventricular arrhythmias, heart block, or transient hypotension.

For a patient to be enrolled in SCD-HeFT, any episodes of syncope occurring before randomization needed to be considered by the investigator unrelated to any life-threatening ventricular arrhythmia (otherwise, the patient would have had an indication for an ICD and could not be included in the study). No registry was kept of patients excluded from SCD-HeFT for this reason. Preferably, any identified episodes of syncope were present in the distant past. Despite this, it was possible that pre-randomization syncope was misdiagnosed as a benign problem. Outcomes included "appropriate" ICD shocks (shocks for ventricular tachycardia or ventricular fibrillation as assessed by a blinded adjudicating committee) (22), cardiovascular mortality, sudden cardiac death, and all-cause mortality.

**Statistical analyses.** Predictors of post-randomization syncope were evaluated both univariably with single-predictor Cox proportional hazards survival models (referred to hereafter as "Cox model") and multivariably, in a single Cox model that included candidate predictors used in the main trial (i.e., functional class, ejection fraction, heart failure etiology, atrial fibrillation, nonsustained ventricular tachycardia, QRS duration, and standard cardiovascular medications). Ventricular pacing was not included because the amount of ventricular pacing was nearly absent (but was not quantitated) in the ICD arm (programmed at 34 beats/min). Recurrent syncope, defined as more than 1 syncope occurrence during follow-up, was compared among treatment arms with a logistic regression model adjusted for heart failure etiology (ischemic or nonischemic) and NYHA functional class.

Association of post-randomization syncope with mortality, cardiovascular death, and sudden death was evaluated with Cox models. Both unadjusted (syncope as the only predictor) and adjusted (including other mortality predictors) were used to ascertain how much of syncope's relationship with mortality risk was driven by other risk factors associated with mortality. Adjusted models included other baseline prognostic factors identified in SCD-HeFT (randomized treatment, age, gender, heart failure etiology, NYHA functional class, time since heart failure diagnosis, ejection fraction, 6-min walk distance, systolic blood pressure, diabetes, angiotensin-converting enzyme inhibitor use, digoxin use, presence of mitral regurgitation, renal insufficiency, substance abuse, baseline ECG intervals, and the Duke Activity Status Index). Other factors that appeared imbalanced between syncope and nonsyncope patients also were evaluated but were not retained in the final model if they were found to be unrelated to mortality risk. Because post-randomization syncope could occur at any time during follow-up, it was included in these models as a time-dependent covariate. In addition, an interaction test

**Table 1** Presumptive Causes for All Post-Randomization Syncopal Episodes (458 Episodes Among 356 Patients)

| Cause | n |
|---|---|
| Orthostatic hypotension | 65 |
| Ventricular tachycardia | 44 |
| Drug-induced hypotension | 38 |
| Vasomotor | 33 |
| Cardiac arrest* | 24 |
| Drug-induced arrhythmia | 2 |
| Seizures | 7 |
| Other | 159 |
| Unknown | 86 |

*Cardiac arrest defined as loss of consciousness necessitating cardiopulmonary resuscitation and/or transthoracic defibrillation. The other categories were classified based on clinical judgment of the local investigator.

was used in the all-cause mortality model to determine whether the relationship of post-randomization syncope to mortality risk differed across randomized treatment arms, and pre-randomization syncope was added to the model as a separate variable to determine its relationship to mortality risk. Among patients who received an ICD, the associations of pre- and post-randomization syncope to appropriate shock therapy were assessed using an unadjusted Cox model.

Hazard ratios, generated by Cox models, took the entire follow-up period into account. The reported 2.5-year Kaplan Meier rates (chosen because 75% of the cohort had that much follow-up) were intended to give an indication of the absolute rates of syncope, which hazard ratios do not provide.

## Results

**Syncope occurrence.** Syncope before or after randomization in SCD-HeFT occurred in 19% (472) of enrolled subjects during a median follow-up of 45.5 months. Presumptive causes for syncope are listed in Table 1.

Before randomization, 162 patients (6%) had syncope. After randomization, 356 patients (14%) had at least 1 episode of syncope. Forty-six of these patients (2%) had syncope before and after randomization. The median (25th, 75th percentiles) time between the episode of syncope and randomization into SCD-HeFT was 11 (4, 39) months. The median (25th, 75th percentile) time from randomization to the first episode of syncope was 15 (5, 28) months.

**Predictors of syncope post-randomization.** In univariable tests, NYHA functional class III, QRS duration ≥120 ms, and absence of beta-blocker use were predictors of post-randomization syncope (Table 2). Variables unrelated to syncope risk were randomization arm, heart failure etiology, left ventricular ejection fraction, atrial fibrillation or flutter, nonsustained ventricular tachycardia, and baseline angiotensin-converting enzyme inhibitor, warfarin, or statin use. In the multivariable model, the only significant predictors were QRS duration ≥120 ms (hazard ratio [HR] 1.30,

**Table 2** Univariate Predictors of Syncope Post-Randomization

| Baseline Characteristic | Category | n | 2.5-yr KM Syncope Rate, % | HR (95% CI) for Syncope Risk | p Value |
|---|---|---|---|---|---|
| Randomized arm | ICD | 829 | 21.7 | 1.10 (0.86–1.42) vs. placebo | 0.27 |
| | Amiodarone | 845 | 18.0 | 0.96 (0.74–1.24) vs. placebo | |
| | Placebo | 847 | 21.4 | | |
| Heart failure etiology | Ischemic | 1,310 | 20.3 | 1.05 (0.85–1.29) vs. nonischemic | 0.67 |
| | Nonischemic | 1,211 | 20.2 | | |
| NYHA functional class | II | 1,761 | 19.4 | 1.28 (1.03–1.60) vs. II | 0.029 |
| | III | 760 | 22.6 | | |
| Left ventricular ejection fraction | <25 | 1,227 | 20.3 | 1.02 (0.94–1.10) (continuous variable, for 5% increase) | 0.68 |
| | ≥25 | 1,294 | 20.2 | | |
| QRS duration (>120 ms) | >120 | 1,033 | 14.2 | 1.30 (1.06–1.61) | 0.012 |
| | <120 | 1,487 | 11.0 | | |
| Atrial fibrillation/atrial flutter | Yes | 390 | 23.5 | 0.96 (0.71–1.28) | 0.77 |
| | No | 2,131 | 19.7 | | |
| Nonsustained VT | Yes | 583 | 20.2 | 1.21 (0.96–1.54) | 0.11 |
| | No | 1,937 | 20.3 | | |
| Beta-blocker | Yes | 1,738 | 17.9 | 0.78 (0.63–0.97) | 0.026 |
| | No | 783 | 24.4 | | |
| ACE inhibitor | Yes | 2,133 | 20.9 | 1.10 (0.81–1.47) | 0.55 |
| | No | 388 | 16.6 | | |
| Warfarin | Yes | 857 | 23.2 | 1.01 (0.81–1.25) | 0.95 |
| | No | 1,664 | 18.7 | | |
| Statin | Yes | 965 | 19.0 | 0.91 (0.73–1.13) | 0.39 |
| | No | 1,566 | 20.9 | | |

ACE = angiotension-converting enzyme; CI = confidence interval; HR = hazard ratio; ICD = implantable cardioverter-defibrillator; KM = Kaplan-Meier; NYHA = New York Heart Association; VT = ventricular tachycardia.

95% confidence interval [CI] 1.06 to 1.61, p = 0.014) and the absence of beta-blockers (HR 1.25, 95% CI 1.01 to 1.56, p = 0.048).

Patients with syncope before randomization had median (25th, 75th percentile) systolic blood pressure at baseline of 118 (108, 130) mm Hg compared with patients without syncope before randomization, who had a systolic blood pressure of 118 (105, 131) mm Hg (p = 0.90). When this was added to the mortality model, blood pressure had no impact on the estimates for either pre- or post-randomization syncope.

**Syncope recurrence.** Seventy-one patients had more than 1 episode of syncope (3% of all enrolled patients). Twenty-three patients in the ICD arm, 25 patients in the placebo arm, and 23 patients in the amiodarone arm had syncope recur. There were no differences in recurrence rates between arms (p = 0.95).

**Association of syncope with appropriate ICD shocks.** In SCD-HeFT, 811 patients received an ICD. Of these patients, 6% (52) had syncope before randomization and 20 (38%) of those with syncope before randomization had an appropriate shock. In contrast, 19% (157) with no syncope had an appropriate shock. Syncope before randomization was associated with a greater likelihood of an appropriate ICD shock (HR 1.75, 95% CI 1.10 to 2.80, p = 0.019).

In the ICD arm, 16% (128) had syncope after randomization and 52 of those (41%) with syncope had an appropriate shock, although the syncope occurred before the shock in only 27 patients (21% of the total and 52% of those having an appropriate shock). Of these 27 patients, 18 had syncope and a shock in the same month. In the remaining 9, the shock was 6 to 41 months after syncope. In contrast, of those who had no syncope after randomization, 125 (12%) had an appropriate shock. Syncope after randomization was associated with increased risk of an appropriate ICD shock (HR 2.91, 95% CI 1.89 to 4.47, p = 0.001) (23,24).

**Syncope and mortality.** Syncope occurring before randomization was not associated with death (HR 0.98, 95% CI 0.73 to 1.33; p = 0.91). However, syncope occurring after randomization was associated with increased risk (Table 3). Patients with syncope, compared with those without syncope, had a higher risk of all-cause mortality (HR 1.41, 95% CI 1.13 to 1.76, p = 0.002) and a greater risk of cardiovascular death (HR 1.55, 95% CI 1.19 to 2.02, p = 0.001). Risk of sudden cardiac death was not significantly greater (HR 1.41, 95% CI 0.90 to 2.21, p = 0.13). Unadjusted HRs for post-randomization syncope were 1.61, 1.80, and 1.54 for death, cardiovascular death, and sudden cardiac death, respectively. These are only slightly greater than the adjusted HRs, indicating that the relationship between syncope and mortality risk was largely independent of other correlated factors.

Importantly, syncope's association with mortality risk was independent of randomization arm (interaction p = 0.86). Syncope HRs were similar for patients randomized to amiodarone (HR 1.33, 95% CI 0.91 to 1.93), to placebo (HR 1.39, 95% CI 0.96 to 2.02), and to ICD (HR 1.54, 95% CI 1.04 to 2.27). A mechanistic relationship between syncope and mortality was not established.

## Discussion

Syncope was common in the SCD-HeFT population, a population well-treated with standard medical therapy for heart failure. Post-randomization syncope was associated with increased risk of all-cause mortality, cardiovascular mortality, and sudden cardiac death (despite randomization to an ICD). Those patients randomized to an ICD, who had syncope, were more likely to receive appropriate ICD shocks than those without syncope; yet, a single-chamber, shock-only ICD with backup ventricular pacing did not protect patients against syncope and did not protect against the risk of death.

Syncope has been associated with adverse outcomes in patients with structural heart disease, especially when cardiomyopathy and congestive heart failure are present (1,25–27) and even in some patients without heart failure (28). This is true whether or not ventricular arrhythmias are inducible at electrophysiology testing (1,5,8,17,25–27,29).

The results of our analyses provide several important and novel observations. First, syncope after randomization in SCD-HeFT was a risk factor for mortality, and those subjects randomized to an ICD had similar outcomes compared with those randomized to amiodarone or placebo. Second, syncope in heart failure patients is a risk factor for appropriate ICD discharge.

**Table 3** Syncope After Randomization Predicts Death

| | By Treatment Arm | | |
|---|---|---|---|
| Syncope | Amiodarone | Placebo | ICD |
| HR (95% CI) | 1.33 (0.91–1.93) | 1.39 (0.96–2.02) | 1.54 (1.04–2.27) |

| | By Cause of Death | | |
|---|---|---|---|
| Syncope | All-Cause Mortality | Cardiovascular Mortality | Sudden Death |
| HR (95% CI) | 1.41 (1.13–1.76) | 1.55 (1.19–2.02) | 1.41 (0.90–2.21) |
| p value | 0.002 | 0.001 | 0.13 |

Abbreviations as in Table 2.

In SCD-HeFT, excess mortality for syncope patients compared with the nonsyncope patients was not ameliorated by a single-chamber, shock-only ICD. Syncope, a marker for mortality in this population, may be due to hemodynamic collapse and may represent evidence for a poorer substrate that was not determined by other means. Although the mechanism for syncope was uncertain, it remains an important predictor and the excess risk is not altered by amiodarone or ICD intervention.

Several reports implicate a greater risk for arrhythmic episodes in patients with heart failure, cardiomyopathy, and syncope. Sudden death due to a life-threatening arrhythmia is suspected to be the reason that syncope patients who have structural heart disease and congestive heart failure die. The tacit assumption is that arrhythmias responsible for syncope may contribute to the increased mortality of these syncope patients. Several small, single-center, nonrandomized, retrospective analyses supporting this thesis have had substantial influence on therapies and have affected guideline development (12,30,31), despite the fact that these reports are very small, not comparative, and not randomized.

The benefits of ICD therapy and of a standard medical regimen for heart failure in the syncope patient remain uncertain. One recent nonrandomized retrospective report evaluated 51 patients with unexplained syncope, cardiomyopathy, and a negative electrophysiology test. Those who underwent an ICD implant had a lower probability of death or cardiac arrest compared with those who did not (17). It is likely that syncope and death are due to hemodynamic collapse rather than an arrhythmia in many heart failure patients (10).

The mechanisms responsible for and the relationships between syncope and death in heart failure patients are generally obscure. Syncope may be an indicator of an unstable, end-stage, cardiomyopathic process in this patient population and, therefore, predicts a poor prognosis. Death in patients with syncope may be due to sudden hemodynamic collapse rather than an arrhythmia. In SCD-HeFT, patients received what were considered optimal doses of angiotensin-converting enzyme inhibitors, beta-adrenergic blockers, spironolactone, and other standard medications for congestive heart failure. The doses were titrated, as tolerated, for the patients, generally by heart failure physicians. Abrupt, unexpected hypotension due to, or in lieu of, medical therapy is still possible.

Perhaps, syncope was not due to malignant ventricular arrhythmias for many SCD-HeFT patients. Rather, a malignant ventricular arrhythmia, like syncope, may be another marker for a more advanced cardiovascular condition and just associated with syncope. Patients in the SCD-HeFT with syncope had a greater risk of appropriate ICD shocks, yet ICDs (with back-up bradycardia pacing) did not protect these patients from dying.

It is even possible that a malignant ventricular arrhythmia was exacerbated by the ICD (32) or that ICD shocks facilitated death. On the other hand, even for patients without an ICD, the mortality was high. Perhaps ICD shocks are a marker for a poor prognosis (24).

The SCD-HeFT syncope data represent the largest collection of patients with syncope, cardiomyopathy, and heart failure treated with or without an ICD. The SCD-HeFT offered the opportunity to assess the incidence of syncope and subsequent outcomes based on randomization to amiodarone, to a placebo, or to an ICD. The high incidence of syncope in this population likely testifies to the fact that heart failure patients, such as those enrolled in SCD-HeFT, can be at immanent risk of hemodynamic collapse. No specific therapy has been shown to improve outcomes in these syncope patients. In fact, ICD shocks may indicate a poor prognosis as they correlate with poorer heart function (unpublished data, Poole JE, 2008).

**Study limitations.** The causes of syncope in this analysis of SCD-HeFT were presumptive and not determined definitively. The diagnosis was not determined by an algorithmic approach. The evaluation of syncope was not uniform or mandated. The SCD-HeFT was not designed specifically to address issues related to syncope or its mechanism.

This paper does not address all issues regarding syncope in heart failure such as why syncope is associated with a particularly bad prognosis. Further studies may be needed, but this report is the first to show that patients with syncope, cardiomyopathy, and heart failure die at the same rate whether they receive an ICD or not.

## Conclusions

Syncope is common in a well-treated heart failure population. After randomization, syncope in SCD-HeFT patients was associated with an increased mortality risk. In the ICD arm, syncope predicted appropriate ICD shocks, but ICDs did not protect against and may have predicted death.

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### REFERENCES

1. Soteriades ES, Evans JC, Larson MG, et al. Incidence and prognosis of syncope. N Engl J Med 2002;347:878–85.
2. Kapoor WN, Hanusa BH. Is syncope a risk factor for poor outcomes? Comparison of patients with and without syncope. Am J Med 1996;100:646–55.
3. Racco F, Sconocchini C, Alesi C, Zappelli L, Pratillo G. Long-term follow-up after syncope. A group of 183 patients observed for 5 years. Minerva Cardioangiol 2000;48:69–78.
4. Olshansky B, Hahn EA, Hartz VL, Prater SP, Mason JW. Clinical significance of syncope in the electrophysiologic study versus electrocardiographic monitoring (ESVEM) trial. The ESVEM Investigators. Am Heart J 1999;137:878–86.
5. Steinberg JS, Beckman K, Greene HL, et al. Follow-up of patients with unexplained syncope and inducible ventricular tachyarrhythmias: analysis of the AVID registry and an AVID substudy. Antiarrhythmics Versus Implantable Defibrillators. J Cardiovasc Electrophysiol 2001; 12:996–1001.
6. Militianu A, Salacata A, Seibert K, et al. Implantable cardioverter defibrillator utilization among device recipients presenting exclusively

with syncope or near-syncope. J Cardiovasc Electrophysiol 1997; 8:1087–97.
7. Menon V, Steinberg JS, Akiyama T, Beckman K, Carillo L, Kutalek S. Implantable cardioverter defibrillator discharge rates in patients with unexplained syncope, structural heart disease, and inducible ventricular tachycardia at electrophysiologic study. Clin Cardiol 2000; 23:195–200.
8. Andrews NP, Fogel RI, Pelargonio G, Evans JJ, Prystowsky EN. Implantable defibrillator event rates in patients with unexplained syncope and inducible sustained ventricular tachyarrhythmias: a comparison with patients known to have sustained ventricular tachycardia. J Am Coll Cardiol 1999;34:2023–30.
9. Link MS, Costeas XF, Griffith JL, Colburn CD, Estes NA 3rd, Wang PJ. High incidence of appropriate implantable cardioverter-defibrillator therapy in patients with syncope of unknown etiology and inducible ventricular arrhythmias. J Am Coll Cardiol 1997;29:370–5.
10. Middlekauff HR, Stevenson WG, Stevenson LW, Saxon LA. Syncope in advanced heart failure: high risk of sudden death regardless of origin of syncope. J Am Coll Cardiol 1993;21:110–6.
11. Fruhwald FM, Eber B, Schumacher M, Zweiker R, Watzinger N, Klein WW. Syncope in dilated cardiomyopathy is a predictor of sudden cardiac death. Cardiology 1996;87:177–80.
12. Knight BP, Goyal R, Pelosi F, et al. Outcome of patients with nonischemic dilated cardiomyopathy and unexplained syncope treated with an implantable defibrillator. J Am Coll Cardiol 1999;33:1964–70.
13. Martin TP, Hanusa BH, Kapoor WN. Risk stratification of patients with syncope. Ann Emerg Med 1997;29:459–66.
14. Russo AM, Verdino R, Schorr C, et al. Occurrence of implantable defibrillator events in patients with syncope and nonischemic dilated cardiomyopathy. Am J Cardiol 2001;88:1444–6.
15. Link MS, Kim KM, Homoud MK, Estes NA 3rd, Wang PJ. Long-term outcome of patients with syncope associated with coronary artery disease and a nondiagnostic electrophysiologic evaluation. Am J Cardiol 1999;83:1334–7.
16. Fonarow GC, Feliciano Z, Boyle NG, et al. Improved survival in patients with nonischemic advanced heart failure and syncope treated with an implantable cardioverter-defibrillator. Am J Cardiol 2000;85: 981–5.
17. Sanchez JM, Katsiyiannis WT, Gage BF, et al. Implantable cardioverter-defibrillator therapy improves long-term survival in patients with unexplained syncope, cardiomyopathy, and a negative electrophysiologic study. Heart Rhythm 2005;2:367–73.
18. Nazarian S, Maisel WH, Miles JS, Tsang S, Stevenson LW, Stevenson WG. Impact of implantable cardioverter defibrillators on survival and recurrent hospitalization in advanced heart failure. Am Heart J 2005;150:955–60.
19. LeLorier P, Krahn AD, Klein GJ, Yee R, Skanes AC. Comparison of patients with syncope with left ventricular dysfunction and negative electrophysiologic testing to cardiac arrest survivors and patients with syncope and preserved left ventricular function and impact of an implantable defibrillator. Am J Cardiol 2002;90:77–9.
20. Cappato R, Negroni S, Bentivegna S, et al. Role of implantable cardioverter defibrillators in dilated cardiomyopathy. J Cardiovasc Electrophysiol 2002;13:S106–9.
21. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005;352:225–37.
22. Packer DL, Bernstein R, Wood F, et al. Impact of amiodarone versus implantable cardioverter defibrillator therapy on the mode of death in congestive heart failure patients in the SCD-HeFT trial (abstr). Heart Rhythm 2005;2 Suppl 1:S38–9.
23. Poole JE, Johnson G, Callans DJ, et al. Analysis of implantable defibrillator shock electrograms in the Sudden Cardiac Death-Heart Failure Trial (abstr). Heart Rhythm 2004;1:S178.
24. Poole JE, Johnson GW, Hellkamp AS, et al. Mortality after appropriate and inappropriate shocks in SCD-HeFT (abstr). Heart Rhythm 2006;13 Suppl 1:S40.
25. Shen WK, Decker WW, Smars PA, et al. Syncope Evaluation in the Emergency Department Study (SEEDS): a multidisciplinary approach to syncope management. Circulation 2004;110:3636–45.
26. Middlekauff HR, Stevenson WG, Saxon LA. Prognosis after syncope: impact of left ventricular function. Am Heart J 1993;125:121–7.
27. Kapoor WN, Karpf M, Wieand S, Peterson JR, Levey GS. A prospective evaluation and follow-up of patients with syncope. N Engl J Med 1983;309:197–204.
28. Goldschlager N, Epstein AE, Grubb BP, et al. Etiologic considerations in the patient with syncope and an apparently normal heart. Arch Intern Med 2003;163:151–62.
29. Olshansky B, Mazuz M, Martins JB. Significance of inducible tachycardia in patients with syncope of unknown origin: a long-term follow-up. J Am Coll Cardiol 1985;5:216–23.
30. Pires LA, May LM, Ravi S, Parry JT, Lal VR, Nino CL. Comparison of event rates and survival in patients with unexplained syncope without documented ventricular tachyarrhythmias versus patients with documented sustained ventricular tachyarrhythmias both treated with implantable cardioverter-defibrillators. Am J Cardiol 2000;85:725–8.
31. Strickberger SA, Benson DW, Biaggioni I, et al. AHA/ACCF scientific statement on the evaluation of syncope: from the American Heart Association Councils on Clinical Cardiology, Cardiovascular Nursing, Cardiovascular Disease in the Young, and Stroke, and the Quality of Care and Outcomes Research Interdisciplinary Working Group; and the American College of Cardiology Foundation: in collaboration with the Heart Rhythm Society: endorsed by the American Autonomic Society. J Am Coll Cardiol 2006;47:473–84.
32. Olatidoye AG, Verroneau J, Kluger J. Mechanisms of syncope in implantable cardioverter-defibrillator recipients who receive device therapies. Am J Cardiol 1998;82:1372–6.