

# Syncope in congestive heart failure

Rakesh Gopinathannair, Alexander Mazur and Brian Olshansky

Division of Cardiovascular Medicine, University of Iowa Hospitals and Clinics, Iowa City, IA, USA

## A common scenario

A 50-year-old male was found on the street confused. He had little recollection about the event but thought he might have passed out. Recently he has had progressive exertional dyspnea and fatigue but no other specific complaints. He was admitted to the hospital for further evaluation and treatment. Physical examination revealed blood pressure of 120/80 without orthostatic changes. Carotid massage was negative. The lungs were clear. Cardiac examination revealed an S3 gallop. There was no peripheral oedema. ECG showed normal sinus rhythm and a left bundle branch block. Chest x-ray showed an enlarged heart and vascular redistribution. The echocardiogram showed a left ventricular ejection fraction of 35%. Coronary angiography revealed normal coronary arteries. Electrophysiology study was negative for inducible ventricular arrhythmias. This review addresses issues regarding the assessment and management of patients such as this with systolic heart failure and syncope.

## Introduction

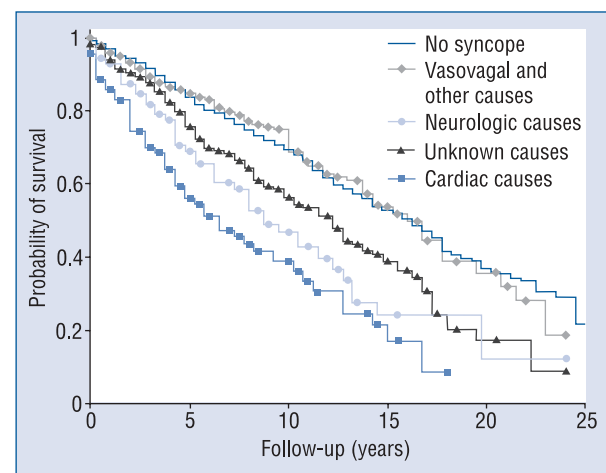
Syncope is a transient loss of consciousness and postural tone due to cerebral hypoperfusion followed by rapid and complete recovery. It is a common clinical problem that is responsible for approximately 1–6% of hospital admissions and 3% of emergency room visits annually in the United States [1]. Syncope is a nonspecific symptom with multiple causes ranging from benign to potentially life threatening. Syncope can be debilitating in nature. It may indicate a poor prognosis.

## Syncope and risk of death

The prognostic significance of syncope has been related primarily to its specific cause and to

the presence of structural cardiac disease [2, 3]. The presence of structural heart disease has been associated with increased mortality in patients with syncope [4–6]. The independent prognostic value of syncope in patients with structural heart disease has been questioned in a study by Kapoor and Hanusa [3], in which 470 patients with and without syncope had similar rates of overall and cardiac mortality over one-year follow-up. Underlying heart disease, not syncope, predicted mortality. Only 14.7% of syncope patients were thought to have a cardiac cause of syncope. Almost half of the patients were thought to have a non-cardiac cause for syncope.

The Framingham study [2] indicated that there is a relationship between the presumed cause for syncope and its prognosis (Fig. 1). Presumed car-



**Figure 1.** Overall survival of participants with syncope according to cause, and participants without syncope.  $P < 0.001$  for the comparison between participants with and those without syncope. The category “Vasovagal and other causes” includes vasovagal, orthostatic, medication-induced and other infrequent causes of syncope. Reproduced with permission from [2].

**Address for correspondence:** Brian Olshansky, MD, Professor of Medicine, University of Iowa Hospitals and Clinics, 200 Hawkins Drive, 4426a JCP, Iowa 52242, Iowa City, USA, tel: 319 356 2344, 319 331 0342, fax: 319 384 6247, e-mail: brian-olshansky@uiowa.edu

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diac syncope was an independent predictor of the risk of death (HR 2.01,  $p < 0.001$ ). Vasovagal syncope was associated with benign prognosis while syncope of unknown cause carried intermediate risk for all-cause mortality (HR 1.32,  $p < 0.01$ ). From these data, it remained unclear whether syncope was causally related to the risk of death or an unrelated marker of poor prognosis.

Syncope, as a prognostic indicator, may be disease dependant. Syncope indicates a particularly high risk of death in patients with specific genetic cardiac disorders such as arrhythmogenic cardiomyopathies, short and long QT syndromes and Brugada syndrome [7–10]. When present along with other non-invasive risk factors, recurrent syncope is generally accepted as an indicator of sudden death in patients with hypertrophic cardiomyopathy [11].

### Patients with heart failure

Syncope has been associated with adverse prognosis in patients with depressed left ventricular function and heart failure. In a retrospective analysis [12], 60 of 491 patients with NYHA class III–IV heart failure and mean left ventricular ejection fraction of 20% had syncope. The one-year rate of sudden death was 45% in patients with syncope regardless of cause versus 12% in patients without syncope ( $p < 0.00001$ ). In a multivariate analysis, reduced left ventricular ejection fraction was the only independent predictor of sudden death in syncope patients [13].

A post hoc analysis of the Electrophysiologic Study Versus Electrocardiographic Monitoring (ESVEM) trial showed that patients with syncope, structural heart disease (mean left ventricular ejection fraction of 32%), frequent ventricular ectopy and inducible ventricular tachycardia at electrophysiology study have a similarly high risk of death as cardiac arrest survivors with similar degrees of left ventricular dysfunction, ventricular ectopy and electrophysiology test findings. The actuarial 4-year mortality rate in patients with syncope was 48% compared to 33% in cardiac arrest survivors [5].

Another line of evidence, suggesting a high risk of sudden arrhythmic death in heart failure patients with syncope, comes from studies using analysis of implantable cardioverter-defibrillator (ICD) data. In patients with syncope, structural heart disease and inducible sustained ventricular arrhythmias at electrophysiology testing, appropriate ICD therapies occur frequently and at rates comparable to patients with documented spontaneous ventricular arrhythmia [14–16]. Similarly, a high rate of appropriate ICD therapies has been observed in patients with syncope, idiopathic dilated cardiomyopathy and negative electrophysiology testing [6, 17–19].

A major limitation of the ICD-based analysis is the use of appropriate ICD therapies as a measure of outcome. Many ventricular tachycardia episodes terminate spontaneously without event. Therefore, ICD shocks may not be a reliable surrogate for sudden cardiac death [20, 21]. A recent post hoc analysis of Defibrillators in Non-Ischemic Cardiomyopathy Trial Evaluation (DEFINITE) trial, which evaluated primary prevention ICD strategy in patients with non-ischemic cardiomyopathy, found that the rate of appropriate ICD therapies in ICD patients was twice as high as risk of sudden death in patients without ICD [20]. These data strongly suggest that the use of appropriate ICD shocks overestimate the risk of sudden death and mortality benefit from ICD therapies in syncope patients.

None of the uncontrolled and retrospective studies were designed to address whether syncope was an independent prognostic indicator of poor outcome in heart failure patients. These issues were recently addressed in a retrospective analysis of the Sudden Cardiac Death Heart Failure Trial (SCD-HeFT) data [22].

The SCD-HeFT was a multicenter, randomized, controlled clinical trial that evaluated primary prevention strategy with ICD or amiodarone versus placebo in patients with ischemic or non-ischemic cardiomyopathy, NYHA functional class II–III heart failure and left ventricular ejection fraction  $\leq 35\%$  who were treated with standard heart failure medications. Syncope after randomization (14% of patients) was a predictor of total mortality (HR 1.41,  $p = 0.002$ ) and cardiovascular death (HR 1.55,  $p = 0.001$ ) but not sudden cardiac death (HR 1.41,  $p = 0.13$ ). These data indicate that heart failure patients with syncope may be at a greater risk of death than those without syncope (Table 1). However, all syncope patients had similarly poor outcomes regardless of treatment arm (ICD, amiodarone, placebo) suggesting a lack of mortality benefit from ICDs in these patients [22].

Further studies are warranted to establish the prognostic significance of syncope in heart failure patients, to elucidate the casual relationship between syncope and increased mortality, and to define the optimal therapeutic strategy.

### Evaluation of syncope in patients with heart failure

No universally applicable “cookbook” approach exists to evaluate syncope in heart failure patients. The cause for syncope can be difficult or even impossible to diagnose even after an extensive work-up. The history and the physical exam are the key

**Table 1.** Syncope after randomization predicts death. Reproduced with permission from [22].

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	0.002	0.001	0.13

CI — confidence interval; HR — hazard ratio; ICD — implantable cardioverter-defibrillator

to the diagnosis. A careful history and physical examination can identify a cause for syncope in up to 50% of cases. However, no symptom appears to be able to predict mortality or syncope recurrence [23].

The history should focus on establishing whether the event was truly syncope and if so, should identify clues that might point towards a specific etiology. Old records (and outside records) should be reviewed for clues. Further evaluation is guided by clinical findings derived from the patient's history and physical examination. The following clinical features may indicate a higher risk of a cardiac cause for syncope: the presence of heart disease, male gender, family history of syncope or sudden death, blurred vision, syncope during exertion or while supine, and a history of antecedent palpitations or chest pain [24].

The presence of heart disease does not necessarily indicate that syncope has a cardiac cause [24]. Nevertheless, sudden unexpected loss of consciousness without prodrome in a patient with heart failure is very worrisome and could indicate an arrhythmic cause or sudden hemodynamic collapse. If this is the case, the patient should be admitted to the hospital and evaluated while being monitored.

In patients with diagnosed or suspected heart failure, careful physical examination is crucial to determine the extent of the heart failure and how sick the patient is. Evaluation should consider orthostatic vital signs. The cardiac examination may reveal a murmur suggestive of aortic stenosis or hypertrophic cardiomyopathy, systemic or orthostatic hypotension, tachycardia or rhythm disturbances.

Diagnostic testing should be selective and guided by findings from the patient's history and physical examination. In cases of syncope, electrocardiogram (ECG) and echocardiogram are the next logical steps for patients suspected of having heart failure, after a history and physical examination are obtained. The ECG may indicate the underlying

cause with findings such as sinus bradycardia, heart block, intraventricular conduction abnormalities, abnormal QT intervals, myocardial infarction, Brugada pattern, Wolff-Parkinson-White pattern or right ventricular cardiomyopathy. An abnormal ECG, however, is a non-specific finding.

In case of intermittent symptoms, correlating the event with a cardiac rhythm disturbance should be sought by means of monitoring. Ambulatory ECG monitoring, either continuous (24–48 h Holter) or patient-triggered event monitoring, are of low value if the episodes are rare. External loop monitoring is limited by the inability of many syncope patients to activate the device in a timely fashion. The diagnostic yield of external recording devices for arrhythmia detection has recently been improved by auto-triggering as well as by continuous ECG transmission to a central monitoring station (so-called mobile cardiac outpatient telemetry) [25, 26]. Implantable loop recorders are effective in patients with infrequent but worrisome symptoms [27, 28].

The role of other non-invasive tests in evaluating syncope in heart failure is unclear. Some preliminary data suggest that patients with idiopathic dilated cardiomyopathy and unexplained syncope commonly have a positive tilt test [29]. Nonetheless, some important issues concerning the use of the test in heart failure patients with syncope, such as optimal protocol, diagnostic value and long-term prognostic significance of positive results as well as optimal therapeutic strategy for patients with a positive test, remain to be determined. The utility of risk stratification methods such as microvolt T-wave alternans specifically for the evaluation of syncope in heart failure is uncertain.

The type and extent of heart disease needs to be characterized. The patient should be evaluated and treated appropriately for their underlying heart disease. For heart failure patients, an arrhythmic cause for syncope should always be seriously

considered. If left ventricular function is reduced, an ICD implant should be considered based on standard implant recommendations (independent of the presence of syncope).

If the patient does not meet the criteria for an ICD and appears to be at low risk of sudden death, long-term monitoring with an external or implantable device would be an appropriate next step. This may be a patient with heart failure symptoms and a relatively well-preserved left ventricular ejection fraction. For patients with moderately impaired ventricular systolic function, a bundle branch block, worsening heart failure symptoms, evidence for ventricular ectopy or recurrent nonsustained ventricular tachycardia on the monitor, electrophysiology testing should be considered. While the electrophysiology test may lack sensitivity and specificity, it is an important step in the evaluation process.

### The role of electrophysiology testing

Electrophysiology testing helps risk stratify syncope patients with heart failure, but this is disease dependant; overall, its diagnostic and predictive value is limited. The prognostic value is best for patients with ischemic heart disease [30]. Inducible ventricular or supraventricular tachyarrhythmias and some bradycardia [31] can provide a presumptive cause for syncope. With respect to the type of induced ventricular tachyarrhythmia, inducible monomorphic ventricular tachycardia is the most specific when compared to induction of nonsustained ventricular tachycardia, polymorphic ventricular tachycardia or ventricular fibrillation [32].

Patients with syncope, heart failure and impaired left ventricular function, regardless of the etiology of their heart disease, are at high risk for sudden death and total mortality whether they have inducible ventricular arrhythmias or not [33]. The test has a particularly low negative predictive value and is not useful for risk stratifying patients with non-ischemic cardiomyopathy [30]. The test has little or no value in patients with hypertrophic or arrhythmogenic right ventricular cardiomyopathies [11, 34].

Currently, electrophysiology testing is rarely performed in patients with depressed left ventricular systolic function and heart failure who would otherwise be candidates for primary prevention ICDs regardless of syncope. The test is generally reserved for patients with organic heart disease or conduction system abnormalities who do not meet criteria for ICD placement.

Electrophysiology testing can be helpful to evaluate conduction system abnormalities in syn-

cope patients with bundle branch block, prolonged PR interval, episodic AV block and sinus pauses, but the test lacks the sensitivity to detect most causes for bradycardia. A prolonged HV interval and/or procainamide induced infra-Hisian block has been associated with a high risk of subsequent AV block [35].

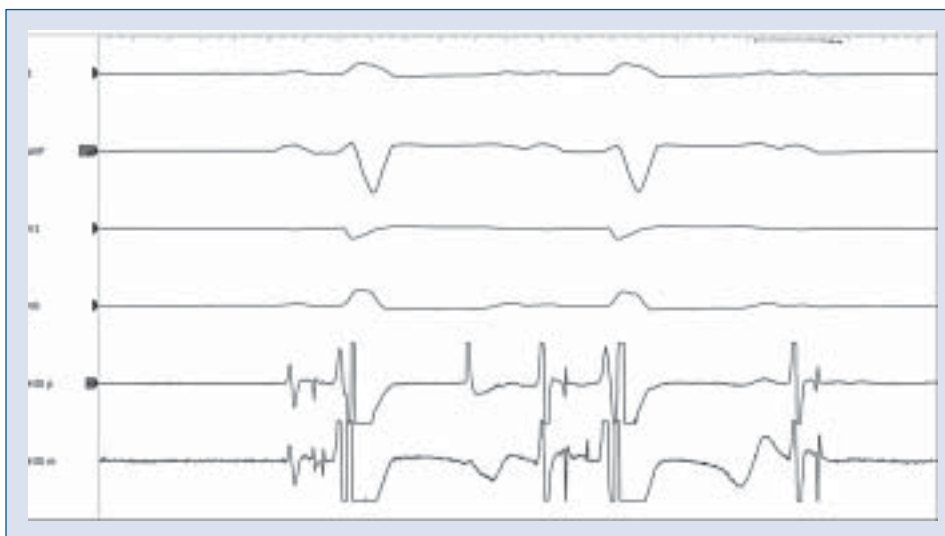
A quarter of patients with HV interval > 100 ms developed AV block over a follow up period of 30 months [36]. A prolonged HV interval (usually > 100 ms) suggests heart block as the etiology of syncope but does not necessarily imply causality. Some data indicate that electrophysiology testing is relatively insensitive for identifying clinically significant bradycardia [37, 38]. In a study by Brignole et al. [37], almost a third of patients with recurrent syncope, bundle branch block and a negative electrophysiology test had transient AV block documented by an implantable loop recorder.

The 2006 ACC/AHA/ESC guidelines recommend electrophysiologic testing for evaluation of syncope in the following situations: Class I: electrophysiology testing is recommended in patients with syncope of unknown cause with impaired left ventricular function or structural heart disease (level of evidence: B). Class IIa: electrophysiology testing can be useful in patients with syncope when bradyarrhythmias or tachyarrhythmias are suspected and in whom non-invasive diagnostic studies are not conclusive (level of evidence: B).

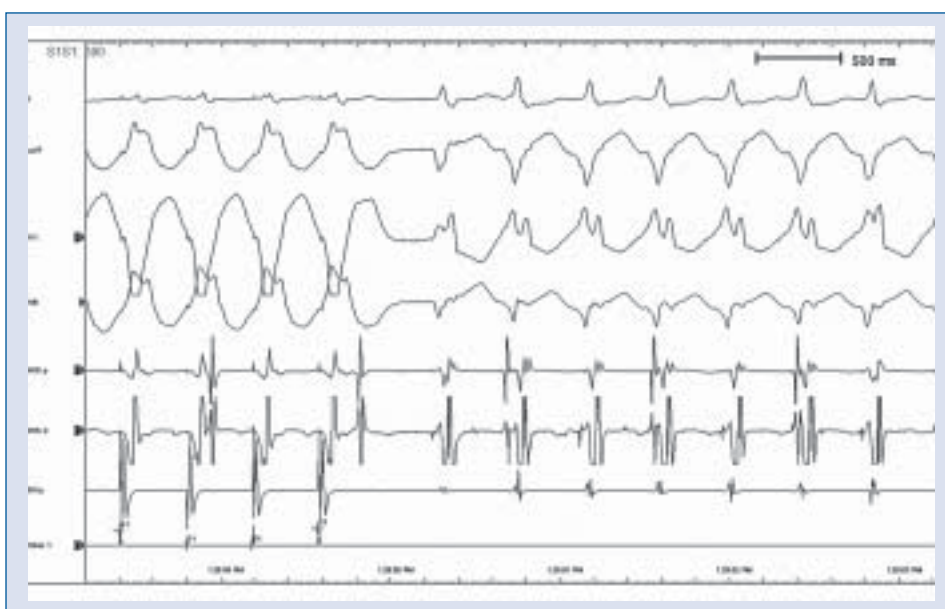
Let us consider a 55-year-old male patient who has ischemic dilated cardiomyopathy but has recurrent syncope. Electrocardiogram shows left bundle-branch block, and echocardiogram shows a left ventricular ejection fraction of 40%. In further evaluation of this patient it may be worth performing an electrophysiology study since he would not meet the criteria for a primary prevention ICD in any event and may not benefit from one. He should, however, be treated with proper medical therapy including a beta-blocker and an angiotensin converting enzyme inhibitor. In this case, an electrophysiology study is performed and shows an HV interval of 180 ms (Fig. 2) and inducible sustained monomorphic ventricular tachycardia (Fig. 3). In this case, the patient would be a candidate for an ICD. However, it remains unclear whether his syncope has been due to bradycardia or tachycardia or some other cause including hemodynamic collapse.

### The role of ICDs

ICDs can play an important role in reducing the risk of total mortality in patients with heart failure.



**Figure 2.** Electrophysiology study demonstrating markedly abnormal His-Purkinje conduction. Shown are recordings from surface leads I, aVF V1, V6 and intracardiac recordings from the proximal, mid and distal His bundle electrodes.



**Figure 3.** Electrophysiology study demonstrating inducible monomorphic ventricular tachycardia following programmed ventricular stimulation. Shown are recordings from surface leads I, aVF V1 and V6.

This role is independent of the presence or absence of syncope. Any clinical decision made regarding the use of an ICD in a heart failure patient must first include consideration of the risk of mortality to the patient, and an ICD should be considered whether or not syncope is present. However, data showing that syncope increases the risk of arrhythmic and/or total mortality is less clear.

Prior retrospective data show that patients with syncope and cardiomyopathy who undergo ICD implan-

tation get appropriate ICD activations, irrespective of whether or not they have a positive electrophysiology test [16, 18, 39]. ICDs appear to improve survival when used in patients with cardiomyopathy and syncope [33, 40]. However, the data are from small, single-site, retrospective studies and are not definitive.

In a study by Knight et al. [17], 14 syncope patients with non-ischemic dilated cardiomyopathy and a negative electrophysiology study were compared with 19 cardiac arrest survivors. All the patients

had ICDs implanted. Appropriate ICD shocks occurred in about the same number over a mean follow-up of about 24 to 45 months for both groups, indicating that patients with cardiac arrest and those with syncope have a similar risk for ventricular arrhythmias that may lead to sudden death. On the other hand, one of the observations was that the mortality was high in both groups (28% and 32%, respectively, over the follow-up period) despite an ICD. Several issues arise from this very small study: It remained uncertain whether syncope had anything to do with the need for ICDs. It is also unclear if ICDs improve mortality.

Sanchez et al. [33] conducted a blinded matched case-control analysis of 51 patients with unexplained syncope, cardiomyopathy and a negative electrophysiology study. Comparing patients who received ICDs to those who simply received medical therapy for their condition, there were a high number of patients with death or cardiac arrest, and this number was much greater in those who did not have an ICD suggesting that patients with ICDs will do better even if electrophysiology testing is negative when cardiomyopathy is present. In this study, appropriate ICD shocks occurred in 26% of the patients at two years and the conclusion was that ICDs improve the outcome of patients with unexplained syncope, ischemic or nonischemic cardiomyopathy and a negative electrophysiology study. These data extended the information provided above even for patients with ischemic cardiomyopathy.

Russo et al. [18] evaluated 46 consecutive patients with non-ischemic dilated cardiomyopathy and mean left ventricular ejection fraction of 25%, who presented with syncope and had ICDs implanted. All patients were on proper medical therapy and 43 of the 46 patients underwent electrophysiology testing. Only 21% of the patients had inducible sustained monomorphic ventricular tachycardia. When observed over a period of  $17 \pm 15$  months, 33% of the patients had appropriate ICD discharges, indicating a high-risk group where electrophysiology testing may not be of great value. The results also support the idea that ICDs are better than conventional medical therapy for patients with non-ischemic dilated cardiomyopathy and poor left ventricular function who present with syncope.

Results from a prospective registry and a sub-study of the Antiarrhythmics Versus Implantable Defibrillators (AVID) Study [14], which evaluated the impact of ICD therapy in patients with unexplained syncope, structural heart disease and inducible ventricular tachycardia/ventricular fibrillation with symptoms, indicated that when an ICD was

used as the treatment, survival for patients presenting with syncope was similar to patients who presented with ventricular tachycardia, and was better than for ventricular tachycardia patients treated with an antiarrhythmic drug. Mortality events in the sub-study were marginally predicted by ejection fraction ( $p = 0.06$ ) but not by the type of ventricular arrhythmia induced in the electrophysiologic study. A significant predictor of increased mortality in the registry was age ( $p = 0.003$ ), and of reduced mortality was treatment with ICD ( $p = 0.006$ ). The authors concluded that ICD should be considered as primary therapy in patients with unexplained syncope, structural heart disease and inducible ventricular tachycardia/ventricular fibrillation at electrophysiologic study.

Based on the above-mentioned data, the most recent ACC/AHA/ESC guidelines indicate that heart failure patients with syncope should be considered for an ICD [41]. The ACC/AHA/NASPE 2002 guidelines [42] include this class-I indication for an ICD: syncope of undetermined origin with clinically relevant, hemodynamically significant, sustained ventricular tachycardia or ventricular fibrillation induced at electrophysiology study when drug therapy is ineffective, not tolerated or not preferred (level of evidence: B). Despite these guidelines, electrophysiology study may not be a good predictor of outcome and may not indicate who is or is not at risk of a life threatening arrhythmia. No data support use of any specific drug therapy to reduce the risk of arrhythmias in syncope patients. A class-II indication for an ICD includes syncope in patients with advanced structural heart disease in which thorough invasive and non-invasive investigation has failed to define the cause for syncope (level of evidence: C). The 2006 ACC/AHA/ESC 2006 guidelines [41] have the following class-IIa indication for an ICD: patients with unexplained syncope, significant left ventricular dysfunction and non-ischemic dilated cardiomyopathy, who are receiving chronic optimal medical therapy even without electrophysiology testing (level of evidence: C). Again, there are no randomized controlled clinical trials that have carefully evaluated ICD use in patients with structural heart disease and syncope.

Data from SCD-HeFT have shed new light regarding the use of ICDs in such patients [22]. When comparing patients receiving amiodarone or placebo to ICD, while syncope was associated with a greater risk for all-cause and cardiovascular death, the ICD group had the same, if not greater, risk for death than the amiodarone or placebo group. Syncope predicted appropriate ICD shocks (hazard ratio 2.91,

**Table 2.** Presumptive causes for all post-randomization syncopal episodes (458 episodes among 356 patients). Reproduced with permission from [22].

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.

$p = 0.001$ ). Despite the fact that the ICD population with syncope received more ICD shocks than the patient group that did not have syncope, they did not benefit in the sense that they still had a risk of death as great as or even greater than the amiodarone and placebo arm of the study. The patients with ICDs had backup bradycardia pacing at 34 beats per minute. This makes the lack of benefit in the ICD group even more intriguing as asystole did not appear to be the mechanism responsible for syncope or death. Recurrent syncope occurred at the same rate, independent of the treatment arm. This highlights the fact that heart failure patients are sick and may develop hemodynamic problems that could explain syncope.

### Etiology of syncope in patients with cardiomyopathy

The presumed causes for syncope in the SCD-HeFT trial [22] were orthostatic hypotension, ventricular tachycardia and other causes, but in two-thirds of the population, the etiology for syncope was either unknown or due to a variety of potentially explainable but ultimately unverifiable causes (Table 2). In fact, it is even possible that patients with heart failure could have an extreme form of neurocardiogenic syncope. Recent tilt table test data support the fact that heart failure patients may be at increased risk of neurocardiogenic syncope [29].

The SCD-HeFT data should be viewed in light of the prospective study by Alboni et al. [24], in which many patients with suspected or diagnosed heart disease thought to cause syncope ultimately

were found not to have a cardiac cause for syncope. About half of them had neurally mediated or neurocardiogenic syncope despite the fact that they had an underlying cardiac diagnosis [24].

There are many reasons why a patient with heart failure, even with an ICD, can pass out. These patients may have spontaneous ventricular tachycardia treated by the ICD and can have syncope prior to ICD discharge. They may have untreated undetected ventricular tachycardia that are below the rate cutoff, and this may even be provoked by the ICD. There may be a ventricular tachyarrhythmia or a bradyarrhythmia that was missed due to lead or device malfunction or programming error. On the other hand, it is possible that another arrhythmia, such as atrial fibrillation below the ICD rate cutoff or even ventricular ectopy that is frequent enough, may cause hemodynamic compromise resulting in syncope. It could also be that syncope in this population represents a substantially poorer substrate that could lead to hemodynamic collapse that could not be detected or corrected by the ICD [22]. Alternatively, syncope may be due to another cause unrelated to an arrhythmia whatsoever. Thus, identifying the cause of syncope in a heart failure patient, even with a sophisticated monitoring device like the ICD, can be very challenging at times.

Consider a 43-year-old female with recurrent syncope, dilated cardiomyopathy, a left ventricular ejection fraction of 32%, left bundle-branch block and NYHA class-II heart failure. She has recurrent syncope despite an ICD implantation. No electrophysiology study was performed before the ICD implant. An electrophysiology study was ultimately performed due to recurrent syncope after the ICD implant. It showed inducible supraventricular tachycardia below the ICD rate cutoff. The tachycardia caused hypotension and resulted in syncope in the electrophysiology lab. Ablation of the supraventricular tachycardia stopped recurrent syncope. Contrary to guidelines [41], electrophysiology studies can be of value in the diagnosis of the etiology of syncope even if implantation of an ICD is planned.

With prophylactic ICD use, the tendency is to become relatively lax regarding complete patient evaluation for syncope. It is possible that the patient has an easily correctable cause for syncope, and that should be understood and should be independent of simply implanting an ICD. A full evaluation is still required and must include a complete history and physical examination. Other testing appropriate for the patient should be considered. Patients with heart failure and syncope do not necessarily benefit from or require an ICD, at least not

immediately. Standard evaluation rules in this regard still apply and it might be that an ICD is not adequate therapy or perhaps that it is overkill for these patients.

One should also be aware that there are many overlapping syndromes that can be present in a heart failure patient, resulting in syncope. Consider an 85-year-old male who is brought to the emergency room after a falling episode. It was not clear whether he passed out or tripped on a rug. On clinical assessment, he is found to have orthostatic hypotension and has been taking nifedipine for hypertension. Even if he has a left ventricular ejection fraction of 30%, left bundle-branch block, evidence for heart failure, and inducible ventricular tachycardia on electrophysiology testing, there are several concerns about simply implanting an ICD in this elderly man. It is also possible that proper treatment by changing medications might prevent the syncope and then a proper decision could be made about prophylactic use of an ICD in this patient who may otherwise be relatively free from ventricular arrhythmias that could cause syncope.

Consider an elderly demented man who has frequent episodes of syncope. He has been seen by several internists and cardiologists for left ventricular dysfunction. Monitoring is negative but the episodes continue. It is of note that he takes phenobarbital, haloperidol, diazepam and acetaminophen with codeine, and does not remember how much he takes. Simply by stopping these medications he stopped passing out. Therefore, ICDs are not always the answer to the problem of syncope in the heart failure patient.

### Driving restrictions

A major concern about patients with heart failure and syncope is restriction of driving. These patients should be strictly prevented from commercial driving, whether or not they have an ICD, until the etiology can be identified and completely treated. This restriction may be lifted later when the cause for syncope is known for certain and the problem can be corrected.

A standard recommendation [43] in the heart failure population with regard to non-commercial driving is a six-month restriction from driving after the ICD is implanted, when syncope is present. However, patients receiving ICDs for primary prevention who have no symptoms such as syncope can drive within 1 week after device implantation. These recommendations are supported by results from the AVID trial that found that people who drove against medical advice after resuscitated

ventricular tachycardia/ventricular fibrillation had a frequency of automobile accidents that was much less than the general driving population of the United States (3.4% per year *vs.* 7.1% per year). However, these were patients who did not have syncope [44].

Patients with syncope and heart failure will probably need to be restricted, at least for a short time, from driving and other potentially dangerous activities.

### Back to our original patient

— What are the chances that this patient's syncope event is cardiac in origin?

Available data indicates that this patient has up to a 40% chance that his syncope may be cardiac in origin. However, this may be difficult to prove.

— How predictive is this syncopal episode with respect to this patient's risk of death?

Syncope in this patient predicts a higher risk of all-cause and cardiovascular mortality and may increase his risk of sudden death.

— Would this patient benefit from implantation of an ICD? If so, should this be done immediately or after proper medical therapy?

The question as to whether this patient needs an ICD is a difficult one to answer. The data remain controversial with no uniform consensus. A thorough evaluation and aggressive heart failure therapy is warranted, but whether this will reduce recurrent syncope and reduce the risk of sudden death is unclear. This patient should be treated medically, as is appropriate for heart failure, and undergo ICD implantation based on current guidelines and studies showing benefit of ICD therapy in patients with severely reduced left ventricular function that persists despite optimal medical therapy. There is no evidence that a more aggressive approach should be taken for the newly diagnosed heart failure patient with syncope. It is likely that such a patient with syncope and recently diagnosed heart failure with severely impaired left ventricular ejection fraction would undergo ICD implantation before hospital discharge. However, an alternative approach involving the placement of an implantable loop recorder is not unreasonable based on available data.

### Conclusions

Syncope is a common problem in patients with heart failure. Syncope is a predictor of death in patients with heart failure, but the underlying mecha-



nisms responsible for this increased risk remain unresolved [22].

The key to proper management of the heart failure patient with syncope involves careful clinical assessment of the symptoms and appropriate treatment for heart failure. Ultimately, the goals of treatment are to prevent sudden death and total mortality and to reduce the risk of recurrent syncope.

ICDs may reduce the risk of arrhythmic death in heart failure patients with syncope but may not necessarily improve survival since syncope may be due to another mechanism that is not completely understood.

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### References

- Kapoor WN. Workup and management of patients with syncope. *Med Clin North Am*, 1995; 79: 1153–1170.
- Soteriades ES, Evans JC, Larson MG et al. Incidence and prognosis of syncope. *N Engl J Med*, 2002; 347: 878–885.
- Kapoor WN, Hanusa BH. Is syncope a risk factor for poor outcomes? Comparison of patients with and without syncope. *Am J Med*, 1996; 100: 646–655.
- Martin TP, Hanusa BH, Kapoor WN. Risk stratification of patients with syncope. *Ann Emerg Med*, 1997; 29: 459–466.
- 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: 878–886.
- Grimm W, Hoffmann JJ, Muller HH, Maisch B. Implantable defibrillator event rates in patients with idiopathic dilated cardiomyopathy, nonsustained ventricular tachycardia on holter and a left ventricular ejection fraction below 30%. *J Am Coll Cardiol*, 2002; 39: 780–787.
- Turrini P, Corrado D, Basso C, Nava A, Thiene G. Noninvasive risk stratification in arrhythmogenic right ventricular cardiomyopathy. *Ann Electrocardiol*, 2003; 8: 161–169.
- Brugada R, Hong K, Cordeiro JM, Dumaine R. Short QT syndrome. *CMAJ*, 2005; 173: 1349–1354.
- Vohra J. The long QT syndrome. *Heart Lung Circ*, 2007; 16 (Suppl. 3): S5–S12.
- Antzelevitch C. Brugada syndrome. *Pacing Clin Electrophysiol*, 2006; 29: 1130–1159.
- Behr ER, Elliott P, McKenna WJ. Role of invasive EP testing in the evaluation and management of hypertrophic cardiomyopathy. *Card Electrophysiol Rev*, 2002; 6: 482–486.
- 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: 110–116.
- Middlekauff HR, Stevenson WG, Saxon LA. Prognosis after syncope: Impact of left ventricular function. *Am Heart J*, 1993; 125: 121–127.
- 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.
- 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: 2023–2030.
- Link MS, Costeas XF, Griffith JL, Colburn CD, Estes NA 3<sup>rd</sup>, 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: 370–375.
- 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: 1964–1970.
- 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: 1444–1446.
- Phang RS, Kang D, Tighiouart H, Estes NA 3<sup>rd</sup>, Link MS. High risk of ventricular arrhythmias in patients with nonischemic dilated cardiomyopathy presenting with syncope. *Am J Cardiol*, 2006; 97: 416–420.
- Ellenbogen KA, Levine JH, Berger RD et al. Are implantable cardioverter defibrillator shocks a surrogate for sudden cardiac death in patients with nonischemic cardiomyopathy? *Circulation*, 2006; 113: 776–782.
- Wathen MS, DeGroot PJ, Sweeney MO et al. Prospective randomized multicenter trial of empirical antitachycardia pacing versus shocks for spontaneous rapid ventricular tachycardia in patients with implantable cardioverter-defibrillators: Pacing fast ventricular tachycardia reduces shock therapies (PainFREE rx II) trial results. *Circulation*, 2004; 110: 2591–2596.
- Olshansky B, Poole JE, Johnson G et al. Syncope predicts the outcome of cardiomyopathy patients: Analysis of the SCD-HeFT study. *J Am Coll Cardiol*, 2008; 51: 1277–1282.
- Oh JH, Hanusa BH, Kapoor WN. Do symptoms predict cardiac arrhythmias and mortality in patients with syncope? *Arch Intern Med*, 1999; 159: 375–380.
- Alboni P, Brignole M, Menozzi C et al. Diagnostic value of history in patients with syncope with or without heart disease. *J Am Coll Cardiol*, 2001; 37: 1921–1928.
- Reiffel JA, Schwarzberg R, Murry M. Comparison of autotriggered memory loop recorders versus standard loop recorders versus 24-hour Holter monitors for arrhythmia detection. *Am J Cardiol*, 2005; 95: 1055–1059.
- Rothman SA, Laughlin JC, Seltzer J et al. The diagnosis of cardiac arrhythmias: A prospective multi-center randomized study comparing mobile cardiac outpatient telemetry versus standard loop event monitoring. *J Cardiovasc Electrophysiol*, 2007; 18: 241–247.
- Brignole M, Sutton R, Menozzi C et al. Early application of an implantable loop recorder allows effective specific therapy in patients with recurrent suspected neurally mediated syncope. *Eur Heart J*, 2006; 27: 1085–1092.
- Krahn AD, Klein GJ, Yee R, Manda V. The high cost of syncope: Cost implications of a new insertable loop recorder in the investigation of recurrent syncope. *Am Heart J*, 1999; 137: 870–877.
- Livanis EG, Kostopoulou A, Theodorakis GN et al. Neurocardiogenic mechanisms of unexplained syncope in idiopathic dilated cardiomyopathy. *Am J Cardiol*, 2007; 99: 558–562.

30. Brilakis ES, Shen WK, Hammill SC et al. Role of programmed ventricular stimulation and implantable cardioverter defibrillators in patients with idiopathic dilated cardiomyopathy and syncope. *Pacing Clin Electrophysiol*, 2001; 24: 1623–1630.
31. Fujimura O, Yee R, Klein GJ, Sharma AD, Boahene KA. The diagnostic sensitivity of electrophysiologic testing in patients with syncope caused by transient bradycardia. *N Engl J Med*, 1989; 321: 1703–1707.
32. Brugada P, Green M, Abdollah H, Wellens HJ. Significance of ventricular arrhythmias initiated by programmed ventricular stimulation: The importance of the type of ventricular arrhythmia induced and the number of premature stimuli required. *Circulation*, 1984; 69: 87–92.
33. 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: 367–373.
34. Corrado D, Leoni L, Link MS et al. Implantable cardioverter-defibrillator therapy for prevention of sudden death in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia. *Circulation*, 2003; 108: 3084–3091.
35. Englund A, Bergfeldt L, Rosenqvist M. Pharmacological stress testing of the His-Purkinje system in patients with bifascicular block. *Pacing Clin Electrophysiol*, 1998; 21: 1979–1987.
36. Scheinman MM, Peters RW, Suave MJ et al. Value of the H-Q interval in patients with bundle branch block and the role of prophylactic permanent pacing. *Am J Cardiol*, 1982; 50: 1316–1322.
37. Brignole M, Menozzi C, Moya A et al. Mechanism of syncope in patients with bundle branch block and negative electrophysiological test. *Circulation*, 2001; 104: 2045–2050.
38. Menozzi C, Brignole M, Garcia-Civera R et al. Mechanism of syncope in patients with heart disease and negative electrophysiologic test. *Circulation*, 2002; 105: 2741–2745.
39. Link MS, Kim KM, Homoud MK, Estes NA 3<sup>rd</sup>, Wang PJ. Long-term outcome of patients with syncope associated with coronary artery disease and a nondiagnostic electrophysiologic evaluation. *Am J Cardiol*, 1999; 83: 1334–1337.
40. 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: 981–985.
41. Zipes DP, Camm AJ, Borggrefe M et al. European Heart Rhythm Association, Heart Rhythm Society, ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: A report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (writing committee to develop guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death). *J Am Coll Cardiol*, 2006; 48: e247–e346.
42. Gregoratos G, Abrams J, Epstein AE et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: Summary article: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE committee to update the 1998 pacemaker guidelines). *Circulation*, 2002; 106: 2145–2161.
43. Epstein AE, Baessler CA, Curtis AB et al. Addendum to “personal and public safety issues related to arrhythmias that may affect consciousness: Implications for regulation and physician recommendations. A medical/scientific statement from the American Heart Association and the North American Society of Pacing and Electrophysiology”. Public safety issues in patients with implantable defibrillators. A scientific statement from the American Heart Association and the Heart Rhythm Society. *Heart Rhythm*, 2007; 4: 386–393.
44. Akiyama T, Powell JL, Mitchell LB, Ehlert FA, Baessler C. Antiarrhythmics versus implantable defibrillators investigators. Resumption of driving after life-threatening ventricular tachyarrhythmia. *N Engl J Med*, 2001; 345: 391–397.