Syncope in Primary Prevention Implantable Cardioverter Defibrillator Patients

Gustavo Goldenberg MD, Tamir Bental MD, Udi Kadmon MD, Ronit Zabarsky MD, Jairo Kusnick MD, Alon Barsheshet MD, Gregory Golovchiner MD and Boris Strasberg MD

Department of Cardiology, Rabin Medical Center (Beilinson Campus), Petah Tikva, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ABSTRACT: Background: Syncope is a common clinical condition spanning from benign to life-threatening diseases. There is sparse information on the outcomes of syncope patients who received an implantable cardiac defibrillator (ICD) for primary prevention of sudden cardiac death (SCD).

Objectives: To assess the outcomes and prognosis of patients who underwent implantable cardiac defibrillator (ICD) implantation for primary prevention of SCD and compare them to patients who presented with or without prior syncope.

Methods: We compared the medical records of 75 patients who underwent ICD implantation for primary prevention of SCD and history of syncope to those of a similar group of 80 patients without prior syncope. We assessed the episodes of ventricular tachycardia (VT), ventricular fibrillation (VF), shock, anti-tachycardia pacing (ATP) and mortality in each group during follow-up.

Results: Mean follow-up was 893 days (810–976, 95% CI) (no difference between groups). There was no significant difference in gender or age. Patients with prior syncope had a higher ejection fraction rate (35.5 ± 12.6 vs. 31.4 ± 8.67, P = 0.02), experienced more episodes of VT (21.3% vs. 3.8%, P = 0.001) and VF (8% vs. 0%, P = 0.01), and received more electric shocks (18.7% vs. 3.8%, P = 0.004) and ATP (17.3% vs. 6.2%, P = 0.031). There were no differences in inappropriate shocks (6.7% vs. 5%, P = 0.74), cardiovascular mortality (cumulative 5 year estimate 29.9% vs. 32.2%, P = 0.97) and any death (cumulative 5 year estimate 38.1% vs. 48.9%, P = 0.18).

Conclusions: Patients presenting with syncope before ICD implantation seemed to have more episodes of VT/VF and shock or ATP. No differences in mortality were observed.

KEY WORDS: syncope, sudden death, implantable cardiac defibrillator (ICD), ventricular fibrillation (VF), ventricular tachycardia (VT)

Syncope is a common and elusive diagnosis, accounting for approximately 3% of emergency room visits and 1% to 6% of hospital admissions [1,2]. Accordingly, its prognosis varies widely, with 1 year mortality rates ranging from 0% in the case of vasovagal events up to 30% in the presence of heart disease. Patients who are candidates for primary prevention of sudden cardiac death (SCD) with an implantable cardiac defibrillator (ICD) or cardiac resynchronization therapy device (CRT-D) frequently present with or have a history of previous syncope. The association between syncope and ventricular arrhythmias is not always clear and the cause of syncope may remain undiagnosed [3-9].

There is limited information regarding the outcome of patients implanted with an ICD or CRT-D for a primary prevention indication where syncope occurred prior to the implantation. The aim of this study was to assess the outcome and prognosis of patients implanted with an ICD or CRT-D for a primary prevention indication, comparing patients who had a syncopal history before the implantation to a similar group of patients without syncopal episodes.

PATIENTS AND METHODS

We conducted a retrospective evaluation of 155 consecutive patients who underwent ICD or CRT-D implantation at our institution for primary prevention of SCD during the period May 2009 to June 2012. We compared 75 patients with a history of prior syncope (up to 6 months before the implantation) to a non-matched control group of 80 patients without prior syncope. The mean follow-up after the ICD implantation was 893 days (range 810–976, 95% confidence interval).

We assessed the number of ventricular tachycardias (VT), ventricular fibrillations (VF), and shock and anti-tachycardia pacing (ATP) treatments, as well as cardiovascular and total deaths in each group during follow-up. Syncope was defined as a sudden loss of consciousness with inability to maintain postural tone, not related to anesthesia or seizure disorder, and spontaneous recovery reported by the patient or an observer. This excludes cardiac arrest, which requires resuscitation [3]. The ICDs were programmed in a similar way.

Statistical analyses were performed using IBM SPSS v.20 (IBM Corporation, USA). All tests were two-tailed, and P < 0.05 was considered significant. Baseline parameters and outcome measures in both groups were compared using the Students t-test for continuous variables and the Pearson chi-square test for categorical variables. Survival analysis was performed using the Kaplan-Meier procedure with log-rank testing for statistical significance. Cumulative survival was derived from life table analysis.
RESULTS

Patient’s baseline characteristics are presented in Table 1. Patients with prior syncope had a higher incidence of non-ischemic cardiomyopathy (CM): 40% (n=30) vs. 22.5% (n=18), P = 0.02; and a lower incidence of ischemic CM: 40% (n=30) vs. 67.7% (n=54), P = 0.001. 

Patients with prior syncope had a higher ejection fraction rate (35.5 ± 12.6 vs. 31.4 ± 8.76, P = 0.02), a higher rate of renal failure (14.7% vs. 2.5%, P = 0.008) and less atrial fibrillation than patients without syncope (14.7% vs. 33.8%, P = 0.008). 

Patients with prior syncope had a higher incidence of class 1 anti-arrhythmic drug intake (9.3% vs. 1.3%, P = 0.03) and a lower incidence of beta-blocker intake (72% vs. 92%, P = 0.01).

There were no differences in age (65.0 ± 13.4 vs. 68.9 ± 11.7, P = 0.058) or gender (77.3% vs. 86.3%, P = 0.2).

Patients with syncope had more episodes of VT (21.3% vs. 3.8%, P = 0.001) and VF (8% vs. 0%, P = 0.01) and received more electric shocks (18.7% vs. 3.8%, P = 0.004) and ATP treatments (17.3% vs. 6.2%, P = 0.031). There were no differences with regard to inappropriate shocks (6.7% vs. 5%, P = 0.74) [Figure 1]. There were no differences in cardiovascular mortality (cumulative 5 year estimate 29.9% vs. 32.2%, P = 0.97) and total mortality (cumulative 5 year estimate 38.1% vs. 48.9%, P = 0.18) during the follow-up [Figure 2].

Re-analysis of our data excluding patients with hypertrophic cardiomyopathy (HCM) revealed 61 patients with a prior syn-
Syncope in patients with left ventricular dysfunction may indicate an arrhythmic event and, therefore, a worse prognosis. Nevertheless, the cause of syncope is usually difficult to establish and raises the possibility that in any particular patient device implantation may represent a primary or secondary prevention indication.

According to current guidelines, ICD is indicated in syncopal patients who developed sustained VT or VF on electrophysiology study (EPS) (class I indication), in patients with non-ischemic CM and significant left ventricular dysfunction (class IIa indication), or in patients with advanced structural heart disease and negative syncopal evaluation (class IIb indication) [10-15].

There are an increasing number of patients with a clear-cut indication for primary ICD implantation who present with or developed syncope prior to the implantation. In these cases ICD is implanted without extensive invasive diagnostic tests such as EPS.

Only the Canadian Implantable Defibrillator Study (CIDS) [14], a secondary prevention trial, included patients with unmonitored syncope and subsequent documentation of either spontaneous VT (> 10 seconds) or sustained (> 30 seconds) monomorphic VT induced by EPS. In this subgroup of patients no differences were observed between patients treated with amiodarone and those who received an ICD.

In our study population patients implanted with an ICD for a primary prevention of SCD indication and a history of syncope had a significant higher incidence of VT, VF, appropriate shock therapy and ATP therapy compared to similar patients without previous syncope, suggesting that syncope in this population is usually related to ventricular arrhythmia or is a marker for future development of ventricular arrhythmia. Interestingly, despite a higher incidence of episodes of VT/VF and shocks or ATP no differences in mortality were observed.

The limitations of our study include the retrospective evaluation of patient outcomes, small sample size, and the non-matched population.

In conclusion, our study suggests that in patients who fulfill the indications for ICD implantation for primary prevention of SCD, the presence of syncope indicates an increased risk of future development of ventricular arrhythmia.

**Correspondence**

Dr. B. Strasberg  
Dept. of Cardiology, Rabin Medical Center (Beilinson Campus), Petah Tikva 49100, Israel  
Phone: (972-3) 937-7108  
Fax: (972-3) 921-3221  
email: strasbergb@clalit.org.il

**References**


---

**Capsule**

**The microRNA miR-148a functions as a critical regulator of B cell tolerance and autoimmunity**

Autoreactive B cells have critical roles in a large diversity of autoimmune diseases, but the molecular pathways that control these cells remain poorly understood. Gonzalez-Martin et al. performed an in vivo functional screen of a lymphocyte-expressed microRNA library and identified miR-148a as a potent regulator of B cell tolerance. Elevated miR-148a expression impaired B cell tolerance by promoting the survival of immature B cells after engagement of the B cell antigen receptor by suppressing the expression of the autoimmune suppressor Gadd45a, the tumor suppressor PTEN and the pro-apoptotic protein Bim. Furthermore, increased expression of miR-148a, which occurs frequently in patients with lupus and lupus-prone mice, facilitated the development of lethal autoimmune disease in a mouse model of lupus. These studies demonstrate a function for miR-148a as a regulator of B cell tolerance and autoimmunity. *Nature Immunol* 2016; 17: 433

**Capsule**

**Potassium loss stresses out kidney cells**

African-Americans are five times more likely than Caucasians to develop advanced kidney disease. Two sequence variants in a gene called *APOL1* confer most of this elevated risk. Scientists think that the prevalence of these sequence variants in people of African descent probably arose because they cause excessive loss of potassium from the cells. This in turn activates stress-activated enzymes called kinases, which ultimately leads to kidney cell death. *Proc Natl Acad Sci USA* 2016; 113: 830

---

“*We must be willing to let go of the life we have planned, so as to have the life that is waiting for us*”

E.M. Forster (1879-1970), English novelist, short story writer and essayist. He is known best for his ironic and well-plotted novels examining class difference and hypocrisy in early 20th-century British society. *A Room with a View* and *A Passage to India* brought him his greatest success. He was nominated for the Nobel Prize in Literature in 13 different years.