Syncope in Primary Prevention Implantable Cardioverter Defibrillator Implantation

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ABSTRACT: **Background:** Syncope prognosis varies widely: 1 year mortality may range from 0% in the case of vasovagal events up to 30% in the presence of heart disease.

Objectives: To assess the outcomes and prognosis of patients with implantable cardiac defibrillator (ICD) and indication of primary prevention and compare patients presenting with or without prior syncope.

Methods: We reviewed the charts of 75 patients who underwent ICD implantation with the indication of primary prevention and history of syncope and compared them to a control group of 80 patients without prior syncope. We assessed the number of episodes of ventricular tachycardia (VT), ventricular fibrillation (VF), shock, anti-tachycardia pacing (ATP), and death in each group during the follow-up.

Results: Mean follow-up was 893 days (810–976, 95% confidence interval) (no difference between groups). Patients with prior syncope had a higher ejection fraction (EF) (35.5 ± 12.6 vs. 31.4 ± 8.76, $P = 0.02$), more episodes of VT (21.3% vs. 3.8%, $P = 0.001$) and VF (8% vs. 0%, $P = 0.01$) and also 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%, $P = 0.74$), in 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% $P = 0.18$) during the follow-up.

Conclusions: Syncopal patients before ICD implantation seem to have more episodes of VT/VF and shock or ATP. No mortality differences were observed

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

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Syncope is a common and elusive diagnosis, accounting for approximately 3% of emergency room visits and 1%–6% of hospital admissions [1,2]. Accordingly, its prognosis varies widely, with 1 year mortality 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 remains undiagnosed [3-8]. There is limited information regarding the outcome of patients implanted with an ICD or CRT-D for a primary prevention indication in which 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 with a syncopal history prior to 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 between May 2009 and June 2012. We compared 75 patients with a history of prior syncope (up to 6 months prior to 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 episodes of ventricular tachycardia (VT), ventricular fibrillation (VF), shock therapy, anti-tachycardia pacing (ATP), and cardiovascular and total mortality 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 a seizure disorder, followed by 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 a life table analysis.

RESULTS

Patient's baseline characteristics are depicted in Table 1. Patients with prior syncope compared to those without prior syncope had a higher incidence of non-ischemic cardiomyopathy, 40% (n=30) vs. 22.5% (n=18), $P = 0.02$; and a lower incidence of ischemic cardiomyopathy, 40% (n=30) vs. 67.7% (n=54), $P = 0.001$. Patients with syncope had a higher ejection fraction (35.5 ± 12.6 vs. 31.4 ± 8.76, $P = 0.02$), more 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%, $P = 00.3$) and a lower incidence of beta-blocker intake (72% vs. 92%, $P = 0.01$). No difference in age (65.0 ± 13.4 vs. 68.9 ± 11.7, $P = 0.058$) or gender (77.3% vs. 86.3%, $P = 0.2$) was observed.

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 therapy (17.3% vs. 6.2%, $P = 0.031$). There were no differences in 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 2A and B].

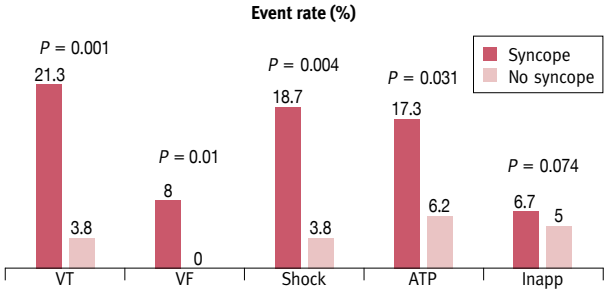
We re-analyzed our data in patients without hypertrophic cardiomyopathy: 61 patients had a prior syncope and 71 did not. Baseline characteristics are depicted in Table 2. In this analysis, patients with prior syncope had a higher incidence of non-ischemic cardiomyopathy, 41.2% (n=21) vs. 21.7% (n=15), $P = 0.01$; and a lower incidence of ischemic cardiomyopathy, 58.8% (n=30) vs. 78.3% (n=54), $P = 0.01$.

Table 1. Baseline characteristics of the study population

	Syncope (75 patients)	No syncope (80 patients)	*P* value
Age, years	65.0 ± 13.4	68.9 ± 11.7	0.058
Men, %	77.3	86.3	0.210
Hypertension, %	60	67.5	0.403
Diabetes mellitus, %	36	47.5	0.193
Dyslipidemia, %	61.3	68.8	0.4
Renal failure, %	14.7	2.5	0.008
AF, %	14.7	33.8	0.008
Ischemic CM, % (n)	40 (30)	67.7 (54)	0.001
Non-ischemic CM, % (n)	40 (30)	22.5 (18)	0.024
HCM, % (n)	18.7 (14)	7.5 (6)	0.054
EF, %	35.5 ± 12.6	31.4 ± 8.76	0.02
ACEI/ARB, %	66.7	78.8	0.105
BB, %	72	92	0.01
Spironolactone, %	26.7	41.3	0.06
Amiodarone, %	24	16.3	0.2
Class 1 AAD, %	9.3	1.3	0.03

AF = atrial fibrillation, CM = cardiomyopathy, HCM = hypertrophic cardiomyopathy, EF = ejection fraction, ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blockers, BB = beta-blockers, AAD = anti-arrhythmic drugs

Figure 1. Events in patients with and without previous syncope



VT = ventricular tachycardia, VF = ventricular fibrillation, ATP = anti-tachycardia pacing, Inapp = inappropriate shocks

Figure 2. Kaplan-Meier curve: **[A]** cardiovascular death and **[B]** total mortality during follow-up

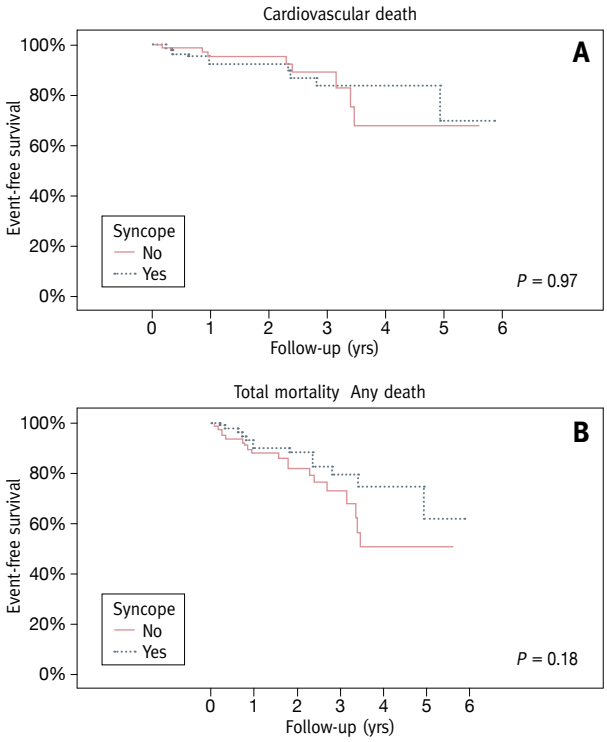


Table 2. Baseline characteristics of patients without hypertrophic cardiomyopathy

	Syncope (61 patients)	No syncope (74 patients)	*P* value
Age, yrs	67.0 ± 11.3	69.9 ± 12.6	0.06
Men, %	78.7	86.5	0.1
Hypertension, %	73	65.6	0.2
Diabetes mellitus, %	39.3	48.6	0.18
Dyslipidemia, %	65.6	71.6	0.2
Renal failure %	14.8	2.7	0.01
AF %	11.5	35.1	0.001
Ischemic CM, % (n)	58.8 (30)	78.3 (54)	0.01
Non-ischemic CM, % (n)	41.2 (21)	21.7 (15)	0.01
EF, %	32 ± 13.8	29.4 ± 6.3	0.09
ACEI/ARB, %	77	83.8	0.7
BB, %	77	93.2	0.07
Spironolactone, %	32.8	44.6	0.11
Amiodarone, %	27.9	16.2	0.07
Class 1 AAD, %	8.2	0	0.017

AF = atrial fibrillation, CM = cardiomyopathy, HCM = hypertrophic cardiomyopathy, EF = ejection fraction, ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blockers, BB = beta-blockers, AAD = anti-arrhythmic drugs

There were no differences in ejection fraction (32 ± 13.8 vs. 29.4 ± 6.3, $P = 0.09$), but patients with prior syncope had more renal failure (14.8% vs. 2.7%, $P = 0.01$) and less atrial fibrillation than patients without syncope (11.5% vs. 35.1%, $P = 0.001$). Patients with prior syncope had a higher incidence of class 1 anti-arrhythmic drug intake (8.2% vs. 0%, $P = 0.017$). No difference in age (67.0 ± 11.3 vs. 69.9 ± 12.6, $P = 0.06$) or gender (78.7% vs. 86.5%, $P = 0.1$) was observed.

Patients with syncope had more episodes of VT (23% vs. 4.1%, $P = 0.004$) and VF (7.2% vs. 0%, $P = 0.04$) and received more electric shocks (19.7% vs. 4.1%, $P = 0.008$). There were no differences in inappropriate shocks (6.5% vs. 5.5%, $P = 0.5$) or ATP therapy (19.7% vs. 6.8%, $P = 0.142$). No differences in cardiovascular mortality (cumulative 5 year estimate, $P = 0.22$) and total mortality (cumulative 5 year estimate, $P = 0.9$) were found during the follow-up

DISCUSSION

Traditionally the implantation of ICD and CRT-D for prevention of SCD is divided into primary and secondary indications and there are clear guidelines for these indications [9]. 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, suggesting that in any particular patient device implantation represents a primary or secondary prevention indication.

According to present guidelines ICD is indicated in syncopal patients who develop sustained VT or VF on electrophysiologic study (EPS) (class I indication), in patients with non-ischemic cardiomyopathy and significant left ventricular dysfunction (class IIa indication), or in patients with advanced structural heart disease and negative workup (class IIb indication) [9-14].

There are an increasing number of patients who have 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 an EPS.

Only the Canadian Implantable Defibrillator Study (CIDS) [13], a secondary prevention trial, included patients with unmonitored syncope with 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 significantly higher incidence of VT, VF, appropriate shocks and ATP therapy compared to similar patients without previous syncope, suggesting that syncope in this population is usually related to ventricular arrhythmias or is a surrogate for future development of ventricular arrhythmias. 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. The small sample and the different baseline features of the patients may have affected the results of the study. Finally, the non-matched population without prior syncope could have influenced the heterogenic nature of the sample and, consequently, the outcome of the evaluation.

In conclusion, our study suggests that in patients who fulfill the indications of ICD implantation for primary prevention of SCD the presence of syncope indicates a higher risk of future development of ventricular arrhythmias and these patients should be scheduled as soon as possible for ICD or CRT-D implantation.

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