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Electrical storms in patients with an implantable cardioverter defibrillator: Primary vs. secondary prophylaxis

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ABSTRACT

Electrical storm (ES) defined as the occurrence of three or more distinct episodes of ventricular tachycardia (VT) or ventricular fibrillation (VF) in 24 hours, requiring the intervention of the ICD, are not rare events. Identification of the risk predictors of ES occurrence appear to be important, since these events are associated with increased morbidity and mortality. The aim of the study was to assess the prevalence, features, and predictors of ES in patients with ICD and in patients in whom ICD was implanted for primary prophylaxis vs. secondary prophylaxis. A retrospective analysis of 250 patients with ICD and mean age 62.76 ± 11.20 years, with a mean follow-up of 52.4 ± 33.2 months was made based on initial files at implantation and on subsequently results from the devices interrogation. The ICD was implanted for primary prevention of sudden cardiac death in 198 patients (79,2%) and for secondary prevention in 52 patients (20.8%). ES was present in 22 (8.8%) of patients, 17 (8.5%) patients with primary prophylaxis and in 5 (9.6%) patients with secondary prophylaxis. We found no clinical predictors of ES. In our study, the patients presenting ES had a slightly higher LVEF as compared with patients without ES: (35.5 ± 10.47% vs. 29.9 ± 11.63%, $p = 0.03$ for the whole study population and 34.7% vs. 28.31%, $p = 0.011$ for primary prophylaxis group). Lack of administration of spironolactone seems to be associated with a higher incidence of ES (18% vs.5.9%, $p = 0.003$ for the whole study group and 20% vs. 6%, $p = 0.004$ for primary prophylaxis group).

KEYWORDS

electrical storm; implantable cardiac defibrillator; ventricular tachycardia; ventricular fibrillation; sudden cardiac death; spironolactone

Introduction

Implantable cardiac defibrillators (ICDs) are lifesavers and have improved mortality rates in patients at risk of sudden cardiac death (SCD), both in primary and secondary prevention. However, they are unable to modify the myocardial substrate, which remains susceptible to life-threatening ventricular arrhythmias.

Electrical storm is defined as the occurrence of three or more distinct episodes of ventricular tachycardia (VT) or ventricular fibrillation (VF) in 24 hours, requiring the intervention of the ICD. [1]. The principal aim of this study is to assess the prevalence, features, and predictors of ES in patients with ICD in general and in patients treated for primary prophylaxis vs. secondary prophylaxis.

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Materials and methods

We assessed the prevalence, features, and predictors of ES in 250 patients with ICD implanted at ICCO Clinics between 01. 02.2009–30.02.2015. We made a retrospective analysis of the patient's files and of the recordings obtained from devices interrogations during ambulatory follow-up visits.

Implant indication was made according to European Society of Cardiology (ESC) guidelines. Resynchronization therapy (CRT-P) or resynchronization therapy with defibrillator support (CRT-D) was recommended for reducing the morbidity and mortality in patients with heart failure NYHA III or ambulatory NYHA IV which had a left ventricular ejection fraction (LVEF) $\leq$ 35% and QRS $\geq$ 120 msec and for reduction of morbidity and prevention of disease progression in patients with NYHA II class having (LVEF) $\leq$ 35% and QRS $\geq$ 120 msec. [2,3]

Implantable cardioverter–defibrillator devices were implanted for SCD prevention in patients with LVEF $\leq$ 35% after myocardial infarction and NYHA class II and III; non-ischaemic cardiomyopathy (NICMP) with LVEF $\leq$ 35% and NYHA class II and III, in patients with LVEF 30–40% after myocardial infarction and positive electrophysiological study and for secondary prophylaxis in patients already experienced an aborted cardiac death or severe sustained ventricular tachycardia.[1]

The type of device and the program settings were left at the discretion of the implanting physician. Detection in the VF zone required that 18 of the last 24 R–R intervals had a cycle length starting at 260–240 msec (214–230 beats/min). The fast ventricular tachycardia (FVT) detection zone was defined starting with a cycle length of 330 to 300 ms (181–200 beats/min). Ventricular tachycardia therapy consisted of antitachycardia pacing attempts followed by shock. The ventricular tachycardia zone (usually monitored) was defined starting with cycle lengths up to 400 to 350 msec (171–150 beats/min).

Appropriate ICD therapy was defined as anti-tachycardia pacing (ATP) or discharge therapy (shock) for VT or VF. Only appropriate shocks were included for analysis in the study.

Follow-up. Each patient was followed-up one month after the implant and every three months thereafter. The programmed parameters were every time analyzed and changed if needed. At each interrogation we also evaluated the number and type of arrhythmia – related events (sustained/non-sustained VT, number of ATP delivered, number and appropriateness of shocks). If the patient was missing from follow-up visit, we made calls to find out the patient status (hospitalized or death). The mean follow-up was 52.4 $\pm$ 33.2 months.

Statistical Analysis. All data are reported as mean $\pm$ SD. Univariate analysis was performed using the Student t test for continuous variables and the chi square test for categorical variables. A univariate Cox proportional hazards model was used to evaluate the significance of baseline variables. $P < 0.05$ was considered significant. Analyses were performed using SPSS 15 (SPSS Inc.; Chicago, Ill) statistical software.

Results

The study group consisted of 250 patients. Most of them were men (220 p, 88,8%). The mean age of patients was 62.76 $\pm$ 11.20 years (24–84). Eighty seven patients (34.8%) had hypertension, 155 (62%) had dyslipidemia, 59 (23.6%) had diabetes mellitus and 40 patients (16%) were smokers. The mean left ventricle ejection fraction (LVEF) was 30.4% $\pm$ 11.62% (10%—65%). Fifty five per cent of patients (119) were in NYHA class III or IV.

Table 1. Baseline demographics and clinical characteristics of patients implanted for primary prophylaxis vs. secondary prophylaxis.

Characteristics	Patients with ICD for primary prophylaxis	Patients with ICD for secondary prophylaxis	p
Mean age (years)	62.54 ± 11.37	63.57 ± 10.57	NS
Male	87.8%	92.3%	NS
Ischaemic dilated cardiomyopathy (%)	37.2%	11.5%	P = 0.0004
Non-ischemic dilated cardiomyopathy (%)	54.59%	53.8%	NS
Other ethiology (%)	8.1%	34.6%	P < 0.0001
LVEF (%)	28.88 ± 10.01	36.19 ± 15.12	P < 0.0001
QRS duration (msec)	117.95 ± 32.82	110.27 ± 35.49	NS
Revascularization (%)	81%	78%	NS
Atrial fibrillation	27.2%	29.3%	NS
Serum creatinine mg/dl	1.17 ± 0.51	1.39 ± 0.87	P = 0.03

The ICD was implanted for primary prevention of sudden cardiac death (PPSCD) in 198 patients (79,2%) and for secondary prevention of sudden cardiac death (SPSCD) in 52 patients (20.8%). According to the type of the device, 142 pts (56.8%) received a single chamber defibrillator, 20 pts (8%) received a dual chamber defibrillator and 88 pts (35.2%) received resynchronization therapy with defibrillation support.

All patients were treated according to guidelines. Most of the patients - 240 (96%) received a beta-blocker, 180 patients (72%) were prescribed an angiotensine conversion enzyme inhibitor or angiotensin receptor inhibitor and spironolactone was administered in 184 patients (73.6%). Only 18 patients (7.2%) were treated with digoxin and 129 patients (51.6%) received a loop diuretic.

Atrial fibrillation was present in 77 patients (30.8%) and 29 patients (1.16%) have experienced at least one syncope before the device implantation.

There were some differences between clinical characteristics and therapy in patients receiving ICD for primary versus secondary therapy. Thus, patients with ICD for primary prophylaxis had lower LVEF and had in higher percentage ischemic dilated cardiomyopathy as compared with patients with ICD for secondary prophylaxis. In turn, ICD was implanted in higher percentage for other etiologies like Brugada syndrome, hypertrophic cardiomyopathy in patients treated for secondary prophylaxis and these patients had more renal dysfunction – see table 1.

With respect of concomitant medication, there were no differences in administration of beta-blockers, angiotensine-converting enzyme inhibitors or angiotensin receptor inhibitors

Table 2. Baseline demographics and clinical characteristics of the study group with and without electrical storm.

Characteristics	Patients with ES	Patients without ES	p
Mean age (years)	63.13 ± 9.73	62.72 ± 11.35	NS
Male	90%	88.5%	NS
Ischaemic dilated cardiomyopathy (%)	36.6%	31.4%	NS
Non-ischemic dilated cardiomyopathy (%)	45.4%	55.3%	NS
Other ethiology (%)	18%	13.3%	NS
LVEF (%)	35.5 ± 10.47	29.9 ± 11.63	0.03
QRS duration (msec)	124.44	115.53	NS
Revascularization (%)	81%	78%	NS
Atrial fibrillation	27.2%	29.3%	NS
Serum creatinine mg/dl	1.04 ± 0.25	1.24 ± 0.63	NS

Table 3. Concomitant therapy in patients with ICD for primary prophylaxis of sudden cardiac death.

Medication	Patients with ES	Patients without ES	p
Beta-blocker	94.1%	98.3%	NS
ACEI	70.5%	76%	NS
Spironolactone	52.9%	82.2%	P = 0.004
Loop diuretic	60%	76%	NS
Cordarone	23.5%	17.6%	NS

and loop diuretics. Amiodarone however, was more frequently prescribed in patients receiving ICD for secondary therapy (65.38% vs. 18.1%, $p < 0.0001$) and more patients with ICD for primary prophylaxis were prescribed spironolactone (79.6% vs 59.6%, $p = 0.0028$).

Electrical storm was present in 22 (8.8%) of patients, 17 (8.5%) patients with ICD for primary prophylaxis and in 5 (9.6%) patients with ICD for secondary prophylaxis. When we have compared the two sub-groups (patients with and without ES), the only significant difference consisted in LVEF values, with higher LVEF values in patients which presented ES as compared with patients without ES ($35.5 \pm 10.47\%$ vs. $29.9 \pm 11.63\%$, $p = 0.03$). Table 2.

With respect of patients presenting ES, the only significant difference between those treated for PPSCD and those treated for SPSCD, consisted in larger end-systolic left ventricle diameter (ESLVD) and end-diastolic left ventricle diameter (EDLVD) in patients with primary profilaxys. (ESLVD 51.7 mm vs. 42.8 mm, $p = 0.033$ and EDLVD 65.11 mm vs. 56.6 mm, $p = 0.05$).

We have also analyzed comparatively, the characteristics of patients with ICD for PPSCD with and without ES. The sub-groups did no differ in terms of demographic, clinical characteristics and associated pathology, but the patients which presented ES have had a slightly higher LVEF than patients with no ES (34.7% vs. 28.31%, $p = 0.011$).

The analysis of the concomitant therapy revealed an interesting issue. For patients with PPSCD, the proportion of patients with ES treated with spironolactone was significantly lower as compared with patients with ES without spironolactone treatment (6% vs. 20%, $p = 0.004$). Table 3.

The same observation resulted after the whole study group analysis: a lower proportion of patients with ES among the ones treated with spironolactone than among the patients who did not receive spironolactone (5.9% vs. 18%, $p = 0.003$). However, the administration of loop diuretics was also more frequent in patients with ES than in patients without ES (19.2% vs.7.75%, $p = 0.02$). Table 4.

Discussion

The incidence of electrical storm varies depending upon the populations that are studied. The condition occurs in approximately 10% to 20% of ICD recipients. [4, 5]

Table 4. Concomitant therapy in patients with ICD for primary and secondary prophylaxis of sudden cardiac death.

Medication	Patients with ES	Patients without ES	p
Beta-blocker	98.6%	90.9%	NS
ACEI	68.18%	74.32%	NS
Spironolactone	50%	77.9%	P = 0.003
Loop diuretic	58%	73.9%	NS
Cordarone	27.2%	28.25%	NS

According to literature, the incidence of electrical storm is lower when ICDs are placed for primary versus secondary prevention. [6]

Some studies tried already to identify some predictors of ES. Among of them: SCD secondary prophylaxis (device implantation for VT, VF), severely compromised left ventricular function, chronic heart failure, chronic renal failure, wide QRS (>120 msec), absence of beta-blocker therapy, use of digoxin, absence of revascularization therapy after index arrhythmia, coronary artery disease and VT as initial arrhythmia have the highest probability of experiencing electrical storm.[5,7,8,9,10]. The studies have had however, different criteria for defining ES and no predictor was constantly confirmed in all studies.

In general, a LVEF < 30% was described as a predictor of ES in patients with ICD. In our study however, patients experiencing ES have had slightly better LV function as compared with patients without ES with a mean LVEF exceeding 30%. This was also true when we have separately analyzed the subgroup of patients with ICD for PPSCD. Our result is in concordance with another important study based upon one of the largest series of ES patients studied, in which LV function in storm patients was slightly but significantly better than that of patients with isolated VT/VF episodes or patients without any ICD interventions.[11]

This aspect may be in relation with a well known phenomenon of a higher incidence of SCD in patients with lower NYHA class. Mortality rates increase the higher the New York Heart Association (NYHA) class, but the proportion of patients dying suddenly (arrhythmic death rather than from progressive pump failure) is highest among those with less severe heart failure (NYHA class II or III). [12]

Apart from these factors, the common triggers for ES are ischemia, electrolyte disturbances, heart failure decompensation but most of them remained unidentified. [13]

Concomitant medication may also play a role in the occurrence of ES. It is well known that antiarrhythmic medication can reduce the frequency of ICD shocks. In the multicenter Optimal Pharmacological Therapy in Cardioverter-Defibrillator Patients trial, amiodarone plus a beta-blocker had most effectively reduced the number of shocks. [14]

In our study group however, despite a very high percent of patients treated with beta blocker, the percent of patients receiving amiodarone was quite low (<30% of patients). The occurrence of ES was not thus influenced by the amiodarone administration.

We found instead a lower incidence of ES in patients in whom spironolactone was prescribed, both in the analysis of the whole group, as well as in the analysis of PPSCD group.

The effect of spironolactone in mortality reduction was demonstrated in HF patients with mild symptoms (EMPHASIS-HF), or severe symptoms (RALES), and in patients with HF after MI (Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study, or EPHESUS) [15, 16, 17]

With respect of patients with ICD, the results of SPIRIT Trial have been recently published. This trial was designed to test the hypothesis that spironolactone reduces the incidence of VT/VF in patients with ICDs who are at risk for recurrent VT/VF. In this study however, spironolactone failed to demonstrate significant protection against arrhythmic events while, as compared with placebo, its administration was associated with a similar risk of VT/VF. [18]. The present research limitations arise from the fact that the findings are derived from a single-centre retrospective study with a relative small sample size. The incidence of ES, although concordant with the previous data reported, was also quite low.

Conclusions

Electrical storm events are not rare in a real-world patient population with ICDs. The incidence of ES in our study was 8.8%. Apparently, there are no clinical predictors of ES.

In our study, the patients presenting ES have had a slightly higher LVEF as compared with patients without ES. Lack of administration of spironolactone seems to be associated with a higher incidence of ES.

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