Electrical storm is an independent predictor of adverse long-term outcome in the era of implantable defibrillator therapy

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KEYWORDS
electrical storm; implantable defibrillators; antiarrhythmic therapy

Abstract
Aims Electrical storm (ES) is a life-threatening arrhythmia complication affecting patients treated with an implantable cardioverter defibrillator (ICD). Despite its increasing importance, existing data on prognosis and management of ICD patients affected by ES are limited and conflicting.

Methods We prospectively studied 169 consecutive patients receiving an ICD. Thirty-two patients presented with at least one episode of ES during the period of observation (33 ± 26 months). ES patients were older (64 ± 9 vs. 59 ± 13 years, \( P = 0.013 \)) with more advanced congestive heart failure (CHF) but a similar incidence of an underlying organic heart disease.

Results Long-term total and cardiac mortality were both increased among ES patients. Seventeen of the 32 ES patients died as opposed to 19 of the 137 ICD patients without ES (53 vs. 14%, \( P < 0.001 \)). In multivariate Cox regression analysis adjusted for the main confounders, history of ES was significantly and independently associated with total and cardiac mortality (risk ratio (RR) = 2.13, \( P = 0.031 \) and RR = 2.59, \( P = 0.019 \), respectively).

Conclusion ES is a relatively frequent complication affecting ICD patients treated for secondary prevention of sudden cardiac death (SCD). Although the acute management of this serious arrhythmia complication is usually successful, occurrence of ES is a strong independent predictor of poor outcome in ICD patients.
Introduction

Electrical storm (ES) has been increasingly recognized as an acute emergency arrhythmia complication not infrequently affecting high-risk patients treated with an automatic implantable defibrillator (ICD) for the prevention of sudden cardiac death (SCD) [1–7]. The occurrence of multiple electrical therapies delivered for termination of recurrent ventricular tachycardia (VT) or ventricular fibrillation (FV) episodes over a short period of time by the ICD, has been reported to occur in 10–20% of defibrillator patients depending on the duration of the observational study period [1–3]. Although the acute management of this arrhythmia emergency seems to be successful in the majority of the reported cases, the available data on the long-term outcome of affected patients are limited [1–3]. In the study by Villacastin et al. among 80 patients with a history of malignant ventricular arrhythmias treated with an ICD, the 16 patients with multiple consecutive ICD therapies tended to have greater risk of death over a follow up period of 21±19 months [1]. On the contrary, Credner et al. did not observe an increased mortality in the 14 ICD patients with ES when compared with those without this arrhythmia complication out of a total ICD population of 136 patients followed up for 13±7 months [2]. In the more recent and larger study by Exner et al., the 90 patients with ES of a total ICD population of 457 patients followed up for 31±13 months [3]. Furthermore, the clinical setting surrounding the ES event has not been adequately described. It has been recently suggested that ES heralds a worsening prognosis in the immediate period following its occurrence [3].

The present study provides prospectively collected data on the clinical and laboratory characteristics of patients presenting with ES. The main aim of this study was to examine whether occurrence of ES could serve as an independent predictor of adverse outcome in a population of consecutive, unselected, patients who had been implanted with an ICD in accordance with the current recommendations.

Methods

Patients

One hundred and sixty-nine consecutive patients receiving an ICD over the last 7 years were the study population. Most of the patients received the ICD for secondary prevention of SCD after one or more episodes of sustained ventricular tachyarrhythmias occurring in an outpatient setting or in the context of presumed tachyarrhythmic syncopal attacks. Before the implantation of the ICD, every effort was made to correct any ischaemic or mechanical cardiac dysfunction surgically followed by a baseline electrophysiological study in the drug-free state. When a sustained ventricular tachyarrhythmia was induced, a repeat follow-up study most commonly after an oral loading dose period of amiodarone was performed in the majority of the cases. Only when the malignant ventricular arrhythmia was reinduced on repeat programmed ventricular stimulation did the ICD implantation follow. This study complies with the Declaration of Helsinki, the local ethics committee has approved the research protocol and informed consent was obtained from all participants.

Defibrillator implantation

The majority of the ICDs used were combined antitachycardia pacemaker defibrillators with intracardiac electrogram storage capabilities available for subsequent analysis of treated episodes. Dual-chamber systems were used in the presence of sinus rhythm after early 1999. The majority of the devices were implanted in the left upper thorax under local anaesthesia in the Electrophysiology laboratory. A defibrillation threshold of at least 10 J below the maximum device output was considered adequate. Antitachycardia pacing, cardioversion and defibrillation therapies were programmed according to the characters of the presenting arrhythmia.

Long-term follow-up

Patients were seen in the outpatient pacemaker clinic one month after implantation and thereafter every three months. A complete physical examination, 12-lead electrocardiography and telemetry device interrogation was routinely performed. Laboratory examination was required at least every six months. Any VT or VF events treated by the device were recorded. Inappropriate therapies delivered for supraventricular tachyarrhythmias or any other reason were also recorded. According to the clinical picture, the number of appropriate electrical therapies delivered and the laboratory investigations, a decision was made for adjusting the medical regimen during each visit. In case of death, an effort to ascertain the conditions surrounding the fatal event was made by contacting relatives or physicians in the hospital where the
patient was treated. Death was considered to be an SCD when it occurred within 1 h after the onset of cardiac symptoms in the absence of rapidly deteriorating unresponsive heart failure and whenever there was no high likelihood of other acute cardiovascular catastrophe such as massive pulmonary embolism or aortic rupture.

Hospitalization for electrical storm

ES was defined as the occurrence of three or more episodes of ventricular tachyarrhythmias terminated by either the device or an external defibrillator in a period less than 24 h. Multiple device activation from supraventricular tachyarrhythmias or other factors not related to ventricular tachyarrhythmia events as judged by the clinical picture and analysis of stored electrograms were excluded. In the majority of the cases either synchronized cardioversion and/or defibrillation therapies were delivered at least four times within this period requiring early assessment and hospitalization for control. Most of the admitted patients were treated in the Cardiac Care Unit under continuous haemodynamic and electrocardiographic monitoring. Any metabolic or electrolytic disturbance was identified and corrected. Intravenous amiodarone in loading doses (6 mg/kg per hour followed by maintenance dose of 0.5–1.0 mg/min) was started together with β-blocker therapy orally. Intravenous lignocaine infusion (1 mg/kg bolus followed by 1–4 mg/min) was also given in those cases with repeat device activation immediately before or after admission. In case the tachyarrhythmia was not controlled within the first 24 h by the above regimen, sedation, with the occasional addition of intravenous flecainide, was added. After controlling the arrhythmia, the regimen was switched to oral antiarrhythmics, mostly β-blockers with amiodarone. In severely resistant cases, mexiletine was added. The patient was discharged home only when at least 2 days of quiescence elapsed after the final electrical therapy had been delivered. In those cases where the tachyarrhythmia was not controlled by pharmacological treatment, being incessant but haemodynamically relatively well tolerated with the device being programmed to defibrillatory shocks only, the patient was brought to the Electrophysiology Laboratory for intracardiac mapping and ablation of the arrhythmia focus.

Statistics

Values are expressed as mean ± SD. Chi-square test and Student’s t-test, where appropriate, were employed to compare baseline characteristics of the groups of interest. Stepwise logistic regression analysis was employed in order to detect possible significant associations between a dichotomous dependent variable (total and cardiac mortality) and a number of independent ones. In order to assess the effect of the studied variables on the associations of interest we included all univariate predictors in the Cox proportional hazard models we used. Contrary to other variables, age was modelled as a continuous variable. All tests of statistical significance were two-tailed and were considered to be significant at a 0.05 level of statistical significance. Statistical analyses were performed with SPSS statistical software (version 8.0, SPSS, Chicago, IL, USA).

Results

There were 169 consecutive patients with an ICD who were studied. One hundred and thirty-seven patients had no ES during the long-term period of observation while in the other 32 patients (18.9% of the study population) at least one hospitalization for ES occurred. In four patients with three to six episodes of ventricular tachycardia interrupted by the ICD within a period of 24 h, no hospitalization was required. Patients with ES were older and had more advanced congestive heart failure (CHF) than those without (Table 1). ES was not observed during follow-up amongst the 18 patients in whom the ICD was implanted for the primary prevention of sudden cardiac death (Table 2). Details of the clinical characteristics and management of the patients with ES are presented in Table 3.

Four of the 32 patients with ES presented with concurrent evidence of acute haemodynamic instability in the form of either cardiogenic shock in the patient with an extensive anterior wall myocardial infarction associated with high degree atrioventricular block or acute pulmonary oedema in three other patients with coronary artery disease (n=2) and dilated cardiomyopathy (n=1). Electrolytic abnormality in the form of hypokalaemia (K: 3.1 mEq/L) was observed in only one patient presenting with numerous tachyarrhythmic events interrupted by the ICD in the presence of acute pulmonary oedema. Thus 28 of the 32 patients with ES presented with serious electrical instability in the absence of any detectable haemodynamic, metabolic, or electrolytic abnormality. Based on interrogation data accumulated prior to the discharge from the hospital, the mean number of antitachycardia pacing (ATP)
metoprolol therapy was also initiated upon arrival managed with the addition of lignocaine. Oral...12.2, P<0.001) and a history of ES (RR=2.13, 95% CI 1.07–4.24, P=0.031) were significantly and independently associated with total mortality. Similarly, ES and an advanced NYHA class were the only variables, significantly and independently associated with cardiac mortality (ES: RR=2.59, 95% CI 1.16–5.78, P=0.019, NYHA class: RR=10.04, 95% CI 4.19–24.04, P<0.001). These multivariate survival function analyses for total and cardiac mortality are graphically presented in Figs. 2 and 3, respectively.
### Table 3  Clinical and laboratory characteristics of patients presenting with ES (n = 32)

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**Pts = Patients, LVEF = left ventricular ejection fraction, Implant = implantation, ATP = antitachycardia pacing, VT = sustained ventricular tachycardia, VF = ventricular fibrillation, S/P TOF = history of operated tetralogy of Fallot, VHD = valvular heart disease, Amio = amiodarone, Xylo = xylocaine, Flec = flecainide, BB = B-blocker, Mexil = mexiletine; A = alive, D = dead, ICD = automatic implantable defibrillator, CABG = coronary artery bypass grafting. In column 9 the available pacing mode is given which also shows the single- or dual-chamber characteristics of the ICD.**
The ever increasing number of ICD implantations among high risk cardiac patients has prolonged life, resulting in an increasing number of patients-years after one or more episodes of life threatening sustained ventricular tachyarrhythmia [4–7]. It is likely that the underlying arrhythmia substrate deteriorates over time in these patients despite the protection afforded by the ICD. ES appears to be a manifestation of such deterioration. Although this dramatic arrhythmia complication was known to cardiologists years before the introduction of implantable defibrillator therapy, it has been recently recognized as an arrhythmic complication affecting high-risk patients receiving an ICD [1–3,8–10]. In our prospectively collected database of 169 consecutive patients with a history of malignant ventricular tachyarrhythmias treated with an ICD, occurrence of ES during the three years of follow-up was rather common, affecting 18.9% of the study population. Two of the three previously reported series of patients treated with an ICD for the secondary prevention of sudden cardiac death by Villacastin et al. and Exner et al. gave a similar incidence of ES occurring over 2 to 3 years of follow-up [1,3]. A lower incidence (10%) was observed among 136 ICD recipients followed up over a shorter period of time in the third study by Credner et al. [2]. Thus, it is likely that the longer the observational study period, the higher the number of ICD patients will be affected by this severe arrhythmic complication.

Clinical profile of ES patient

ES was observed in our ICD patients regardless of the type of the underlying organic heart disease.
Indeed, ES has been described among patients with various forms of cardiomyopathy as well as those without detectable organic heart disease [1–3,9–11]. However, we did not observe ES among our 18 patients in whom the ICD was implanted for the primary prevention of SCD [6,7]. Our ES patients were older with a somewhat lower LVEF and more advanced clinical stage of CHF when compared with the remaining ICD recipients without ES. Although our data suggest ES is more likely to occur in ICD patients with more advanced CHF, 3 of our 32 ES patients had a well-maintained LVEF and were in NYHA class I. In contrast to the previously reported data where ES occurred within the first year after ICD implantation, in our database the time of first ES occurrence after ICD implantation was significantly longer [2,3]. This difference may be due to different patient populations. It is interesting that the majority of our patients with ES presented with no obvious haemodynamic, electrolytic, ischaemic or metabolic derangement during the arrhythmia storm. It is possible that undetectable, transient aberrations in the electrophysiological substrate of affected patients may occur despite adequate monitoring, leading to recurrent episodes of sustained ventricular tachyarrhythmias. Whether such changes can be identified, and possibly aborted, by more intense monitoring of high-risk patients, is still unknown.

Short- and long-term management and outcome

The arrhythmia was suppressed by a combination of intravenous lignocaine and amiodarone, in most cases with the addition of oral β-blocker therapy [12–18]. We chose the intravenous combination of a type I agent with loading doses of amiodarone aiming to promote rapidity of action [15,16]. Given that ES has not been uniformly defined, this term has been used to describe an extensive range of clinical situations and tachyarrhythmia events. However, whether prognosis is largely affected by the exact number of tachyarrhythmic events is still uncertain [10]. The majority of our ES patients were discharged on a combination of amiodarone and β-blocker therapy with the addition of mexiteline in a few [15–18]. The long-term total mortality was increased in ES patients, mainly due to non-sudden cardiac mortality. Similar observations have been described among ES defibrillator patients in two of the three previously published series with an extended period of follow-up [1,3]. However, we did not observe an increased mortality in the 3 months following the ES [3]. It is interesting that besides the advanced CHF, ES carried an independent prognostic ability for both total and cardiac mortality. Thus, the presence of either significant left ventricular dysfunction with advanced CHF or of a worsening electrophysiological substrate was predictive of increased non-sudden cardiac mortality months after the ICD implantation. It remains unknown whether additional therapeutic adjustments may be required to improve prognosis in these extremely high-risk cardiac patients.

Implications of the present study

ES appears to be an independent marker for increased non-sudden cardiac mortality months after its occurrence as the present and the studies by Villacastin and Exner have previously suggested [1,3].

Whether recurrent shocks delivered by the ICD lead to a significant worsening of the already impaired ventricular function remains controversial [19–21]. Multiple shocks are associated with transient mild elevations of cardiac troponin levels indicative of minor myocardial injury [22,23] but significant depression of right or left ventricular function has not been described. Furthermore, an immediate worsening of CHF was not observed among our ES patients after the acute event. However, pathological studies have confirmed the presence of acute cellular injury in heart specimens of patients receiving multiple recent shocks [24,25]. Recent advances in pharmaceutical treatment of heart failure should be appropriately employed in ES patients to prevent deterioration of ventricular function and CHF [17,18,26–28]. Furthermore, we should consider surgical options for improving ventricular function including cardiac transplantation and biventricular pacing in appropriate candidates [29–32]. The possibility of favourably modifying the underlying arrhythmia substrate with non-pharmacological therapies should also be considered, especially when recurrent ES events occur despite extensive antiarrhythmic drug therapy [33,34].

The present study demonstrates that the prediction of ES among ICD patients with a history of malignant ventricular arrhythmias based on routine clinical and laboratory assessment is difficult. Whether more sophisticated assessment employing signal-averaging ECG techniques, autonomic nervous system measurements and repolarization abnormalities might identify those ICD patients prone to develop ES is unknown [35–39].
Conclusions

ES is expected to occur in almost one of five patients treated with an ICD for the secondary prevention of SCD when the period of observation exceeds 3 years. This arrhythmia emergency is unlikely to occur in ICD patients receiving the device for primary prevention of SCD. In most cases, ES is not associated with other detectable acute haemodynamic, ischaemic or metabolic derangements. However, ES is most likely to occur in older ICD patients with advanced left ventricular dysfunction and CHF. Although the acute drug therapy of this life-threatening arrhythmia is usually successful, long-term outcome is limited by an increased cardiac mortality.

References