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Electrical Storm: Incidence, Prognosis and Therapy

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Abstract

The term "electrical storm" indicates a life-threatening clinical condition characterized by the recurrence of hemodynamically unstable ventricular tachycardia and/or ventricular fibrillation, in particular in patients with ICD implanted for primary or secondary prevention. Although there isn't a shared definition of electrical storm, nowadays the most accepted definition refers to three or more separate arrhythmia episodes leading to ICD therapies including antitachycardia pacing or shock occurring over a single 24 hours' time period. Clinical presentation can be dramatic and triggering mechanism are not clear at all yet, but electrical storm is associated with high mortality rates and low patients quality of life, both in the acute phase and in the long term. The first line therapy is based on antiarrhythmic drugs to suppress electrical storm, but in refractory patients, interventions such as catheter ablation or in some cases surgical cardiac sympathetic denervation might be helpful. Anyhow, earlier interventional management can lead to better outcomes than persisting with antiarrhythmic pharmacologic therapy and, when available, an early interventional approach should be preferred.

Introduction

Electrical storm is a state of cardiac electrical instability characterized by multiple episodes of ventricular arrhythmias within a relatively short period of time.[1] The clinical definition of electrical storm is varied, somewhat arbitrary, and is a source of ongoing debate.[2] Before cardioverter defibrillators (ICDs)reached a wide usage in clinical setting, the term 'electrical storm' was referred to the occurrence of two or more ventricular tachycardia (VT) or ventricular fibrillation (VF) in a 24 hour period.[3] At present, the most commonly accepted definition is 'three or more separate arrhythmia episodes leading to ICD therapies including antitachycardia pacing (ATP) or shock occurring over a s 24 hour period,[4-6] but there is a variety of other definitions.[7] This definition might be somewhat inadequate as it fails for those VT which are slower than the programmed detection rate of the ICD. Besides, ventricular tachyarrhythmias terminating with appropriate ICD therapy, are excluded from this definition, while those recurring shortly after (< 5 minutes) a successful therapy, are included by only some authors.[8,9]

Electrical storm can occur during the acute phase of a myocardial infarction (MI) or when the patient has a structural heart disease or an inherited arrhythmic syndrome. In addition, more and more patients are expected to undergo ICD implantation, as the prevalence of congestive heart failure rise continuously.[10]

Key Words:
Electrical Storm, Ventricular Tachycardia, Ventricular Fibrillation.

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Incidence and Basic Epidemiological Aspects

According to the commonly accepted definition of electrical storm, incidence is about 10% to 20% in patients who have an ICD for secondary prevention of sudden cardiac death.[8,11,12] The incidence is lower when ICDs are placed for primary prevention:[13] in the MADIT II study, 4% of patients developed electrical storm on an average of 20.6 months.[14]

Most of the arrhythmic episodes that occur during an electrical storm seems to be episodes of monomorphic VT (with an incidence of 86-97%), VF alone accounts for 1-21% of episodes, mixed VT7VF 3-14% and the incidence of polymorphic VT is lower (2-8%).[4,5,8,9,12,14-18] Patients with a prior history of VT are more likely to experience VT storm and a similar correlation is reported for patients with VF.[14,18] One of the earliest studies reported an average time of electrical storm onset of 4-5 months after ICD implantation.[15] More recent studies have reported a period of 2-3 years.[16,18] No adequate triggers have been identified yet, but some studies suggested that ischemia, infarction, severely compromised left ventricular function, chronic renal failure, hypo- or hyperkalemia and older age can be important risk factors for the onset of electrical storm.[4,9,12,14,15,17] A triggering mechanism is only identified in 10-25% of patients with electrical storm, while the majority of patients have no perceptible change in baseline cardiovascular health.[5,9,12,15] The role, as risk factor, of monomorphic VT without immediate hemodynamic failure, especially when successfully treated with ATP, is not certain at all. It is important to understand if some VT episodes do not represent a

Table 1: Definition, incidence and prognosis of electrical storm

Author	Definition	Incidence	Prognosis
Kowey[1]	≥ 2 hemo-dynamically relevant VT in 24 h	All patients	↓
Credner[15]	≥ 3 VT in 24 h	14/136 (10%)	Ø
Nademanee[11]	≥ 20 VT in 24 h or ≥ 4 in 1 h	All patients	↓ (1-year mortality 95% on AAD and 33% on β blocker)
Exner[8]	≥ 3 VT in 24 h	90/457 (20%)	↓ (RR 2.4)
Greene[4]	≥ 3 VT in 24 h	40/227 (18%)	Ø
Bansch[12]	≥ 3 VT in 24 h	30/106 (28%)	↓
Verma[18]	≥ 2 VT requiring shock in 24 h	208/2028 (10%)	↓
Wood[19]	≥ 3 VT in 24 h	50/521 (24%)	Not analyzed
Stuber[16]	≥ 3 VT in 2 weeks	51/214 (24%)	↓ (5 years mortality 33% vs 13%)
Hohnloser[5]	≥ 3 separate VT in 24 h	148/633 (23%)	Ø
Brigadeau[17]	≥ 2 separate VT in 24 h	123/307 (40%)	Ø
Gatzoulis[9]	≥ 3 VT in 24 h	32/169 (19%)	↓ (mortality 53% vs 14% during 33 ± 26 months)
Sesselberg[14]	≥ 3 VT in 24 h	169/719 (24%)	↓
Guerra[20]	≥ 3 VT in 24 h	857/5912 (14%)	↓ (RR 2.15)

VT = ventricular tachyarrhythmia; AAD = antiarrhythmic drugs; RR = relative risk; ↓ = reduced prognosis; Ø = no influence on prognosis.

higher risk and if there is a threshold of arrhythmia or therapy frequency that may cause adverse outcome.[7]

Prognosis

Most studies suggest that electrical storm is an independent adverse prognostic factor, associated whit higher mortality in both secondary and primary prevention.[6,7,17,18] The mortality rate is also increased after storm episodes in patients with non-ischemic cardiomyopathy.[12,21,22] Electrical storm is also associated with an increased rate of hospitalization and might have a negative impact on patients' quality of life.[8,9,19,23] Despite the certainty of these data, is still not clear whether electrical storm contributes to higher mortality directly or is a consequence of advanced heart disease or systemic illness.[24]

In patients implanted with ICD for primary prevention, electrical storm has been associated with higher mortality. In MADIT II study, patients with electrical storm had a significantly higher risk of death: the hazard ratio for death in the first 3 months, after the electrical storm, was 17.8, compared with patients with no VT/VF. The hazard ratio decreased to 3.5 after these first 3 months.[14]

In the AVID trial for secondary prevention, electrical storm was a significant independent risk factor for subsequent death (RR 2.4, p = 0.003). In this trial, 38% of patients with electrical storm died during follow-up, compared to 15% of those without electrical storm. The risk of death was higher within the first 3 months and then decreased8. Gatzoulis et al. studied 32 patients with ICD for secondary prevention whom presented electrical storm: 53% of patients died during 3 years of follow-up, compared with 14% of ICD patients who did not experience electrical storm (p < 0.001).[9] This data suggest that electrical storm is a strong independent predictor of poor outcome in ICD patients.

A recent meta-analysis of 5912 patients (857 with electrical storm) compiled from 13 studies, found that electrical storm is a strong mortality risk factor and it is associated with an increased combined risk of death (RR 3.15; 95% IC 2.22-4.48), heart transplantation and hospitalization for acute heart failure (RR 3.39; 95% IC 2.31-4.97). Besides, ICD for secondary prevention, monomorphic VT as triggering arrhythmia, lower ejection fraction and class I anti-arrhythmic drug therapies are all associated with electrical storm and could be used to define specific populations with higher risk to develop electrical storm.[20]

It is not clear yet if the ventricular tachyarrhythmias or repeated ICD shocks themselves contribute to cardiac mortality or are secondary to a degenerating cardiac status. Only few evidence are reported by some studies about this issue and additional studies are needed for more clarity. A potential mechanism is suggested by the experimental observation that recurrent VF results in increases intracellular calcium concentrations which might contribute to deterioration of left ventricular systolic function.[25,26] Repeated shocks, moreover, can cause myocardial injury leading to acute inflammation and fibrosis.[27-29] Lastly, myocardial injury or stunning from recurrent defibrillations may activate the neurohormonal cascade responsible for worsening heart failure and cardiovascular mortality.[11,30,31]

Electrical storm also increases the rate of hospitalization and adversely affects the quality of life of ICD patients, in addition to undermine the perception of security provided by the device. A sub-analysis of the SHIELD trial showed that electrical storm increases by about 3 times arrhythmia-related hospitalization (p < 0.0001) compared with patients with isolated VT/VF. A recent review pointed out how ICD therapies, especially frequent and repeated shocks, have significant psychological effects on both patients and their families.[32] Besides, results from AVID trial suggested that both sporadic shocks and adverse symptoms were associated with reduced physical and mental well-being.[8]

Management of The Electrical Storm: Pharmacologic Therapy

Electrical storm is a clinical emergency. The physical and emotional distress that patients experience in case of electrical storm and frequently recurrent shocks may increase the sympathetic tone and facilitate further arrhythmias.[9] In this patients sedation may help prevent psychological distress.[11,33] The psychological effects of shocks, also related to pain, should be consider both early and subsequent to electrical storm, and a psychological approach to the patient should be considered, if necessary.[32]

Antiarrhythmic drugs may stabilize ventricular rhythm in many electrical storm patients.

β-Blockers

Patients with electrical storm undergo an increase of the sympa-

Table 2: Time to first occurrence and arrhythmias causing electrical storm

Author	Time after ICD implantation	Arrhythmias
Credner[15]	133 ± 135 days	64% mVT, 21% VF, 14% mVT+FV (patients)
Exner[8]	9.2 ± 11.5 months	86% mVT, 14% VF or VT+VF (initial episodes)
Greene[4]	599 ± 710 days	97% mVT, 3% pVT+VF (episodes)
Bansch[12]	NA	87% mVT, 8% pVT/VF, 4% different mVT (electrical storms)
Verma[18]	814 ± 620 days	52% mVT, 48% VF (patients)
Stuber[16]	629 ± 646 days	93% mVT, 7% pVT (electrical storms)
Hohnloser[5]	Median 7 months	91% mVT, 8% mVT+VF, 1% VF (electrical storms)
Brigadeau[17]	Median 1417 days	90% mVT, 8% VF, 2% pVT (electrical storms)

mVT = monomorphic ventricular tachycardia; pVT = polymorphic ventricular tachycardia; VF = ventricular fibrillation

thetic tone and this can provoke further recurrent ventricular arrhythmias. The use of β-blockers, in particular those which antagonize both β1 and β2 receptors, has been shown to increase the fibrillation threshold and decrease the incidence of sudden death.[11] In the MADIT II study, patients with ischemic cardiomyopathy who received high doses of β-blockers (metoprolol, atenolol or carvedilol) had a 52% relative risk reduction for recurrent VT/VF requiring ICD therapies compared with those who did not take any β-blocker.[13] Adding β-blockers intravenously in electrical storm patients already on oral β-blocker therapy may help to suppress electrical storm episode.[34]

Amiodarone

Amiodarone has been widely used for the treatment of electrical storm.[35] In acute, rapid intravenous administration amiodarone blocks fast sodium channels, inhibits norepinephrine release and blocks L-type calcium channels, but does not prolong ventricular refractoriness. Conversely, prolonged ventricular refractory periods have been seen in patients in oral amiodarone therapy.[36] Amiodarone is also effective as adjunctive therapy to prevent recurrent ICD shocks.[37] The OPTIC study compared β-blocker, sotalol and β-blocker plus amiodarone in the prevention of ICD shocks. At 1-year follow-up, patients treated with sotalol or amiodarone plus β-blocker had a 56% risk reduction compared with patients treated with β-blocker alone.[38] As for β-blockers, intravenous amiodarone may be an effective drug even in patients already in chronic oral amiodarone therapy.[39]

Azimilide and Dofetilide

They belong to a class III antiarrhythmic. In the SHIELD study, azimilide (which blocks the calcium channels and prolongs the refractory period) reduced significantly the recurrence of shocks and symptomatic arrhythmias treated by ATP.[40] In a prospective study, conversely, azimilide did not significantly reduce the number of patients with electrical storm.[5]

Dofetilide selectively blocks the rapid component of the delayed rectifier potassium current and it is principally used for the treatment of atrial fibrillation. Only one small study reported efficacy and safety of dofetilide in the treatment of VT/VF after amiodarone intolerance or failure.[41]

Both azimilide and dofetilide were associated with a high incidence of Torsade de Pointes.[5,7]

In summary, the decision to prescribe an antiarrhythmic drug to an electrical storm patient should be individualized, taking into account not only the efficacy but also the increased risk of drug-related proarrhythmia and side effects. Antiarrhythmic drugs, in effect, reduce the number of ICD shocks, but they are associated with a relatively high incidence of side effects.[42] This, combined with the sometimes-limited efficacy of antiarrhythmic drugs, has prompted the need for the development of non-pharmacologic treatment strategies.

Management of the Electrical Storm: Catheter Ablation

As the majority of electrical storms consist of monomorphic ventricular tachycardia episodes characterized by a basic re-entry mechanism, catheter ablation is an important solution to stop electrical storm onset. With increasing experience and the rapid growth of ablation technologies, VT catheter ablation can be performed safely and with low complication rate.[43] A meta-analysis of 471 patients with electrical storm, compiled from 39 publications (case report and cohort studies), found a high initial success rates for ablation of all ventricular arrhythmias (72%), a low procedural mortality rate (0.6%) and a recurrence rate of 6%. In this review, the recurrence rate was significantly higher after ablation for electrical storm due to monomorphic VT compared with VF or polymorphic VT with underlying cardiomyopathy (OR 3.8; 95% CI 1.7-8.6).[44]

Table 3: Efficacy of catheter ablation for electrical storm treatment

Author	Population (n)	Results
Nayyar[44]	471	Success rate 72%
Reddy[45]	128	↓ ICD shocks of 22% ↓ VT of 21%
Kuck[46]	110	Survival free from VT/VF 47% with ablation vs 29% in control group
Deneke[34]	32	Success rate 94%
Carbucicchio[48]	95	Success rate 72%

VT = ventricular tachycardia; VF = ventricular fibrillation

There are two randomized trials that compared ICD implant and early prophylactic ablation after ICD implantation for secondary prevention in patients with a history of myocardial infarction (MI). Both showed that catheter ablation significantly decreased ICD therapies. In the first study, Reddy et al. (2007) enrolled 128 patients with VT not treated with antiarrhythmic drugs. Over a mean follow-up of 22.5 months, prophylactic substrate-based catheter ablation reduced ICD shocks from 31% to 9% (p = 0.003) and VT from 33% to 12% (p = 0.007).[45] In the second study, 110 patients with prior MI have been randomized to either catheter ablation or no additionally treatment. 35% of patients were treated with amiodarone at baseline and 25-30% were treated with amiodarone at 1 year. After catheter ablation, the number of appropriate ICD therapy events per patient and per year was significantly lower than in the control group, with a median of 0.2 versus 3.0 (p = 0.013).[46] Recent reports about ablation for electrical storm have shown not only a reduction in recurrent electrical storm, but also a survival benefit. A first study (2001) with 19 electrical storm patients who underwent catheter ablation, showed a procedure success rate of 79% and there were no deaths over a 26-week follow-up.[47] A prospective study (2008) enrolled 95 drug refractory electrical storm patients who had frequent ICD shocks. After one to three ablations, 89% of patients did not have any inducible clinical VT by programmed electrical stimulation. At a median follow-up of 22 months, 92% of patients was free of electrical storm and 66% was free of VT recurrence.[48] Recently, Deneke et al. studied 32 electrical storm patients, 27 undergoing catheter ablation within 24 h after admission and 5 underwent acute ablation within 8 h. The acute success rate was 94% and electrical storm recurrence or death was observed in 6% (acute ablation group) and 9% (control group) during a 15-months follow-up.[49]

Despite the lack of high-quality evidence supporting the benefit of intervention, if pharmacologic management fails and a catheter ablation facility with adequate expertise is available, the patient should be rapidly referred. Currently, the relative merits of early ablative therapy in comparison to early pharmacologic therapy are still unknown. A recent study compared the outcomes of catheter ablation between patients who were referred for ablation early and those who were only referred after drug therapy failure. Results shown that catheter ablation has a potential to reduce patient mortality and improve patients' quality of life.[50] Early intervention is also supported by other studies, which report a high mortality rate while awaiting catheter ablation for electrical storm.[49,51]

Most studies reported in the literature included patients with ischemic heart disease, but it is not clear if the outcomes would be sim-

ilar for patients with non-ischemic disease. Furthermore, there are no randomized controlled trial to date, highlighting the benefits of catheter ablation in comparison to the pharmacologic management of electrical storm. Likewise, it is not known the optimal timing of catheter ablation or whether ablation has a long term mortality benefit.

Management of the Electrical Storm: Surgical Treatment

There are limited data about the surgical management of electrical storm. Thoracic epidural anaesthesia (TEA) and the left cardiac sympathetic denervation (LCSD) can be used for their antiarrhythmic effects.[52,53] Bourke et al. studied 14 patients with frequent VT episodes: 12 patients had electrical storms and 8 had prior catheter ablation. Both TEA (9 patients) and LCSD (8 patients) were associated with a subsequent decrease in arrhythmia burden.[54] If LCSD is ineffective, adjunctive right sympathetic denervation can be carry out. Ajijola et al. reported a study result of bilateral cardiac sympathetic denervation in 6 electrical storm patients: after surgery complete response was observed in 4 patients, partial response at the therapy or no response in 2 patients.[55] Another recent study showed that bilateral cardiac sympathetic denervation is more beneficial than left CSD, with a ICD shocks-free survival of 48% (versus 30% of left cardiac sympathetic denervation) at mean follow-up of 1 year and a significant reduction in ICD shocks in 90% of patients ($p < 0.001$).[56]

Discussion

Electrical storm is an emergent life-threatening clinical condition. Even though there is not just one definition of electrical storm, it is known that this phenomenon is associated with adverse effects on patients' survival and quality of life. Although there is still a lack of clarity about triggering mechanism and role of electrical storm in accelerating mortality, it is mandatory to intervene aggressively when electrical storm occurs. Treatment of this clinical event often includes several simultaneous drug therapies (β blockers and amiodarone) and a subsequent step to nonpharmacologic therapies in drug-refractory patients, such as catheter ablation. Further researches should clarify timing and specific role of both drug therapy and catheter ablation to improve clinical care.

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