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REVIEW

Contemporary Management of Electrical Storm

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Cardiac electrical storm (ES) is characterised by three or more discrete episodes of ventricular arrhythmia within 24 hours, or incessant ventricular arrhythmia for more than 12 hours. ES is a distinct medical emergency that portends a significant increase in mortality risk and often presages progressive heart failure. ES is also associated with psychological morbidity from multiple implanted cardioverter defibrillator (ICD) shocks and exponential health resource utilisation. Up to 30% of ICD recipients may experience storm in follow-up, with the risk higher in patients with a secondary prevention ICD indication. Storm recurs in a high proportion of patients after an initial episode, and multiple storm clusters may occur in follow-up. The mechanism of storm remains elusive but is likely influenced by a complex interplay of inciting triggers (e.g., ischaemia, electrolyte disturbances), with autonomic perturbations acting on a vulnerable structural and electrophysiologic substrate. Triggers can be identified only in a minority of patients. An emergent treatment approach is warranted, if possible with emergent transfer to a high-volume centre for ventricular arrhythmia management with a multi-modality approach including ICD reprogramming, sympathetic blockade (sedation, intubation, ventilation, beta blockers), and anti-arrhythmic drugs, and adjunctive intervention techniques, such as catheter ablation and neuraxial modulation (e.g., thoracic epidural anaesthesia, stellate ganglion block). Outcomes of catheter ablation of ES are excellent with resolution of storm in over 90% of patients at 1 year with a low complication rate (~2%). ES may occur in the absence of structural heart disease in the context of channelopathies, Brugada syndrome, early repolarisation and premature ventricular contraction-induced ventricular fibrillation. There are unique treatment approaches to these conditions that must be recognised. This state-of-the-art review will summarise the incidence, mechanism, and multi-modality treatment of ES in the contemporary era.

Keywords Ventricular tachycardia • Electrical storm • Ventricular fibrillation • Catheter ablation • Neuraxial modulation

Abbreviations: AAD, anti-arrhythmic drugs; ATP, anti-tachycardia pacing; CRT, cardiac resynchronisation therapy; CSD, cardiac sympathetic denervation; DCM, dilated cardiomyopathy; ES, electrical storm; ICM, ischaemic cardiomyopathy; ICD, implanted cardioverter defibrillator; IV, amiodarone; LV, left ventricular; SG, stellate ganglion blockade; TEA, thoracic epidural anaesthesia; VF, ventricular fibrillation; VT, ventricular tachycardia

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Introduction

Electrical storm (ES) is a distinct medical emergency characterised by multiple episodes of sustained ventricular arrhythmia within a short time period, typically 24 hours. In the majority of cases, monomorphic ventricular tachycardia constitutes the primary arrhythmia, however, polymorphic ventricular tachycardia and ventricular fibrillation (VF) are also implicated. In patients without an implantable cardioverter defibrillator (ICD), it is generally accepted that three or more discrete episodes of ventricular arrhythmia within 24 hours, or incessant ventricular arrhythmia for more than 12 hours, constitutes ES [1,2]. In patients with an ICD, this condition is defined as the occurrence of three or more appropriate device therapies within a 24-hour period, separated from one another by at least 5 minutes [1–3]. ES predominantly afflicts patients with severe structural heart disease, however, this condition is also reported in those with channelopathies such as Brugada and Long QT Syndrome. Clinical factors associated with a higher incidence of ES include: lower left ventricular ejection fraction, implantation of a secondary prevention ICD, treatment with class I anti-arrhythmic agents, and monomorphic ventricular tachycardia (VT) as the underlying arrhythmia [4]. The development of ES is associated with increased risk of death, heart transplantation and hospitalisation for decompensated cardiac failure [5,6]. The management of ES requires complex multi-disciplinary care including ICD re-programming, haemodynamic support, the use of antiarrhythmic medications, identification and reversal of precipitating factors, and consideration of catheter ablation and neuraxial modulation. This state-of-the-art review will summarise the contemporary knowledge and treatment of ES.

Incidence Of ES

The overall reported incidence of ES is 10–30% in patients with a secondary prevention ICD, occurring at an average of 4–9 months after ICD implantation [3,7]. The incidence is 4–7% in patients with a primary prevention ICD, occurring ~18–24 months after ICD implant [8,9]. In a longitudinal study of patients with ischaemic cardiomyopathy (ICM) and dilated cardiomyopathy (DCM), storm occurred with similar incidence between the two groups (5.8% vs. 6.9%, respectively). This study showed that critically, storm recurrences were common, occurring in 65.4% of ICM and 50% of DCM patients [9].

Mechanism of ES

The pathophysiological mechanisms which underlie ventricular arrhythmia storm are not well characterised. It is likely that there is a complex interplay between enhanced sympathetic tone, calcium-related signalling abnormalities, dysregulation of protein phosphorylation and a susceptible arrythmogenic substrate [10]. The working theory is that three key factors culminate in storm: a vulnerable heart (i.e., presence of pre-existing heart disease that creates the necessary ''substrate''), an inciting trigger and a disruption in sympathetic nervous system activity (Figure 1) [11]. However, the evidence for this hypothesis is scant and the relative contribution of these factors to the development of ES has not been examined. Moreover, there is a suggestion that predilection for storm may have a genetic basis. Patients with channelopathies (e.g. long QT syndrome, Brugada syndrome, catecholaminergic polymorphic VT) may develop ES; mutations in genes implicated in channelopathies and arrhythmogenic cardiomyopathies have been

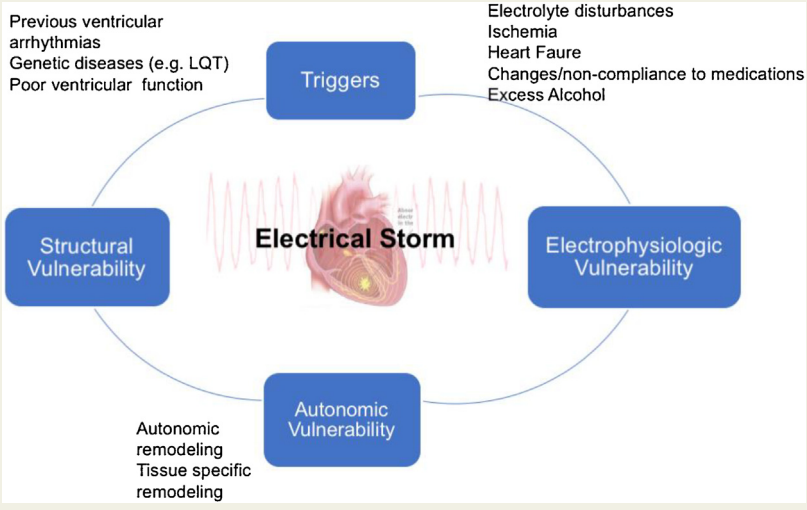

Figure 1 Putative pathophysiologic mechanism of electrical storm (ES).
A complex interplay between predisposing factors, triggers, structural, autonomic and electrophysiologic vulnerability likely interact in genesis of ES.

reported in ES patients with a prior history of myocardial infarction, and early repolarisation phenotypes noted in ES patients with ischaemic and non-ischaemic cardiomyopathies [12,13]. In patients with structural heart disease, those presenting with electrical storm have been shown to have differences in endocardial scar size and distribution compared to non-storm presentations, which may serve to explain their arrythmogenic susceptibility to this phenomenon [14]. Patients with ES are more likely to have advanced cardiac disease. One study found that ES patients, compared to those without ES, were older, were more frequently men, and had a lower ejection fraction, more advanced heart failure, and a higher prevalence of cardiovascular comorbidities compared with those without ES. They also had more inducible VTs, and required longer catheter ablation procedures to control VT, suggesting a more complex VA substrate [4].

Recurrent ventricular arrhythmia and ICD shocks have been identified as having the potential to mediate left ventricular (LV) dysfunction and myocardial injury, which may lead to activation of the sympathetic nervous system, in turn worsening cardiac failure [15]. Known reversible precipitants of electrical storm include acute myocardial ischaemia, electrolyte derangements (e.g. hypokalaemia), sepsis, decompensated cardiac failure, non-compliance to heart failure and/or anti-arrhythmic medications [7]. However, a specific trigger is identified in a minority of cases [16]. In the SHIELD (SHock Inhibition Evaluation with AzimiLiDe Investigators. trial, a storm trigger was only identified in 13% of the patients [16]. Impaired LV function and higher use of class Ia AADs were significant predictors of storm [17].

Implications of ES

The occurrence of electrical storm has been associated with a mortality rate of up to 14% in the first 48 hours from presentation [18,19]. The AVID (Antiarrhythmics Versus Implantable Defibrillators) study, which followed patients with secondary prevention ICDs, demonstrated a 5.6-fold increase in mortality in the first 12 weeks subsequent to the development of ES [18]. Similarly, in a subset analysis of the MADIT (Multicenter Automatic Defibrillator Implantation Trial) II trial, the occurrence of storm was associated with a 18-fold increase risk of death in the first 3 months after the event [8]. In fact, it has been demonstrated that, in general, an increased burden of ICD shocks is associated with increased morbidity and mortality [20]. Observational studies have consistently demonstrated that increased mortality of ES is due to rapidly deteriorating heart failure, with a small proportion of sudden cardiac death [3,16,21]. Implantable cardioverter device shocks do portend a two- to five-fold increase in mortality, predominantly due to heart failure [20]. Whether ES is a marker of advanced structural heart disease with likely inexorable progression to end-stage heart failure and increased mortality or whether ES is the inciting trigger than consequently leads to deterioration in cardiac function is unknown. Experimental studies have shown that multiple shocks lead to myocardial injury, acute inflammation and fibrosis [22,23]; recurrent VF can cause intracellular calcium overload that may contribute to progressive LV dysfunction [15,24,25].

After an initial episode of storm, recurrent storm may occur in 50–81% of patients over the subsequent year. Multiple ICD shocks also lead to substantial psychological morbidity with a markedly impaired quality of life [26]. Implantable cardioverter device shocks have a long-lasting adverse effect on physical activity as well as objective and subjective patient-reported outcomes of quality of life and shock anxiety [27]. As a consequence of the medical and psychological morbidity, storm often results in exponential health care utilisation from prolonged hospital stay and repeated clinic visits [11,28].

Electrocardiographic Morphology

Electrical storm can be classified on the basis of gross electrocardiographic morphology. Monomorphic ventricular tachycardia accounts for the vast majority of storm cases, caused by re-entry within heterogeneous ventricular scar in the context of ischaemic and non-ischaemic cardiomyopathy. In contrast to monomorphic ventricular tachycardia storm related to an identifiable electrophysiological substrate, polymorphic ventricular tachycardia and ventricular fibrillation storm are most often related to acute myocardial ischaemia, ion channelopathies or idiopathic VF, in patients with structurally normal hearts. Twelve-lead electrocardiograph (ECG) documentation of the triggering premature ventricular contraction is critical in pre-procedural planning to allow targeting of the triggering beat with ablation.

Treatment of ES

Overview

The treatment of electrical storm, regardless of underlying aetiology and electrophysiological substrate, requires a multimodal approach. Several therapeutic modalities have been proposed for the treatment of electrical storm including device reprogramming, pharmacotherapy, sedation, neuraxial modulation and radiofrequency catheter ablation. Radiofrequency catheter ablation is emerging as the standard-of-care in patients with electrical storm refractory to optimal medical management. There is very limited randomised controlled data to guide therapy in storm, and most evidence comes from observational studies and expert consensus. A key paradigm is that of providing emergent care to patients with ES, with immediate referral and transfer to a high volume tertiary care facility for ES management. Two European centres have reported an inter-hospital collaborative network that facilitates emergent transfer of storm patients to a tertiary hospital to allow ablation within 8 hours (generally within 24 hours) of storm presentation. This approach gives all co-operating hospitals an opportunity to admit patients with storm for 24 hours a day, 7 days a week with a pre-specified ''best practice pathway'' and a staged treatment protocol allowing emergent ablation to be performed. Within this framework, 50% of

patients were ablated within 24 hours of storm presentation in an Italian centre [29]. Outcomes were favourable in that there was no acute procedural mortality, long-term (~2 year) freedom from recurrent storm was achieved in ~94% of patients and freedom from VT in 66–79% of patients [29,30]. No randomised trial data for early versus delayed ablation for storm exists, however it is feasible that early ablation in the appropriately selected cohort yields favourable outcomes [31,32].

Emergency Treatment

The primary goal of emergent therapy in both low and high-risk patient groups is the suppression of sustained ventricular arrhythmia and the prevention of further ICD shocks. Determination and treatment of reversible precipitants, where present, is essential. Early risk stratification of patients with electrical storm is necessary to ensuring care is provided in an appropriate clinical environment. High risk features include haemodynamic instability, in addition to, a left ventricular ejection fraction of less than 30%, moderate-to-severe renal impairment and severe chronic obstructive pulmonary disease [33]. Those patients who are identified as high risk should be transferred to the intensive care unit where mechanical ventilation and circulatory support can be provided as needed.

Implantable Cardioverter Defibrillator Interrogation and Reprogramming

Implantable cardioverter device interrogation is essential in all patients presenting with recurrent ICD shocks. Saved events should be reviewed to assess underlying rhythm and whether appropriate therapies have been delivered for the termination of ventricular arrhythmia. Inappropriate shocks secondary to over-sensing, atrial arrhythmias and lead fracture must be excluded. If present, a magnet should be placed over the device until shocks can be permanently disabled with a programmer. Aggressive ICD programming, including lower VF detection rates, reduced detection time periods and lack of anti-tachycardia (ATP) during capacitator charge, has been associated with the development of ventricular arrhythmia storm [34]. Furthermore, repeated ICD shocks have been associated with increased morbidity and mortality [35]. In this context, the aim of reprogramming should be to reduce the burden of ICD shocks, favouring ATP interventions for cessation of ventricular arrhythmias. This can be achieved by increasing detection duration and heart rate detection threshold. Importantly, increases in both detection duration and heart rate detection threshold have been shown to reduce ICD-shocks without increasing the incidence of syncope, and decreased mortality [35–37]. Moreover, ATP can effectively terminate most slow VTs with a low risk of acceleration [38,39].

If a patient experiences recurrent shocks due to otherwise haemodynamically well tolerated VT, it may be appropriate to temporarily disable device therapies whilst as an inpatient and initiate anti-arrhythmic drugs or command ATP to terminate VT, until a definitive plan for anti-arrhythmic drugs, device reprogramming or catheter ablation is made. A further decision can then be made to reprogram the VF/VT zone to a longer cycle length to avoid further shocks, and/or increasing the detection time for the clinical tachycardia before delivery of shocks.

Cardiac re-synchronisation therapy can trigger ES, if the LV lead induces premature ventricular contractions or results in activation of scar border zones and facilitate slow conduction that creates re-entry. Worsening heart failure or recurrent VA after CRT implantation is a clue—temporary discontinuation of LV pacing may abolish ES—until arrangements are made for either catheter ablation and/or anti-arrhythmic drugs (AADs) and/or LV lead repositioning. Epicardial catheter ablation may be highly efficacious in this population where LV lead position was within an area of epicardial scar [40].

Identification and Correction of Triggers

Electrolyte disturbances (e.g. hypokalaemia, hypomagnesaemia) are rapidly identified and corrected. Acute ischaemia is an uncommon cause of sustained monomorphic VT, but can trigger rapid polymorphic VT. Exclusion of ischaemia may be necessary in patients with ICM with rapid monomorphic VTs. Aggressive treatment of volume overload and optimisation of heart failure treatments is critical in cardiomyopathic patients.

Sedation and Mechanical Ventilation

Sympathetic overactivity is fundamentally implicated in the genesis of ES [41]. Blunting of the sympathetic drive may be achievable with sedation. In patients at high risk and intractable VA despite AADs, emergent intubation, sedation and mechanical ventilation should be considered. Furthermore, sedation allows for patient comfort and serves to minimise the psychological distress associated with this condition. In terms of specific sedatives, benzodiazepines and short-acting analgesics should be considered first-line owing to their ability to provide sedation and analgesia without associated negative inotropy [42]. Case reports have also demonstrated the efficacy of propofol in terminating storm where pharmacological therapy has failed. However, this agent must be used with caution given its negative inotropic effects and associated potential to precipitate cardiac failure [43].

In cases of ventricular arrhythmia storm with associated haemodynamic instability, invasive haemodynamic support including intra-aortic balloon pump, left ventricular assist device and extracorporeal membrane oxygenation therapy may be indicated [29]. These therapies allow for improved coronary perfusion and foster improved outcomes by way of preventing multiple organ failure [44,45].

Anti-Arrhythmic Pharmacotherapy: Overview

Anti-arrhythmic pharmacotherapy has, historically, constituted the mainstay of treatment for ventricular storm. A meta-analysis by Santangeli, has demonstrated a 1.5-fold

decrease in recurrence of storm in those treated with anti-arrhythmic drugs, but no overall effect on mortality [46]. Selection of a specific pharmacologic agent requires consideration of underlying storm aetiology, severity of comorbid cardiac failure and potential drug toxicities. Drug pro-arrhythmia may be seen in ~7% of patients, especially in those with severely impaired ventricular function [47].

Beta Blockers

Increased sympathetic tone is integral to the development and maintenance of ventricular arrhythmias [48]. In VT storm, a vicious cycle may ensue where ICD shocks may precipitate increased sympathetic tone, resulting in further VAs and shocks, and so forth. Consequently, suppression of sympathetic tone with beta blockers constitutes first line pharmacologic therapy in the treatment of electrical storm. In the MADIT II trial, use of beta blockers for the treatment of ventricular arrhythmias was associated with a 52% risk reduction for recurrent ventricular arrhythmia [49]. Sympathetic blockade has been found to be superior to AADs in the treatment of ES. In one of the few randomised controlled trials (RCTs) of management of ES, Nandamanee et al. randomised 49 patients with ES post myocardial infarction to sympathetic blockade (n = 27; 6 left stellate ganglionic blockade, 7 esmolol, and 14 propranolol) or AADs (n = 22; lignocaine IV, then IV procainamide or bretylium). Sympathetic blockade was associated with a lower 1-week mortality than AADs (22% vs. 82%, respectively); ES survivors had a better survival with sympathetic blockade (67% vs. 5%, respectively) [50].

There are specific benefits to the use of non-selective ß-blockers in ES. A significant proportion of patients presenting with storm have chronic heart failure, which is known to be associated with downregulation of, specifically, ß1 receptors. Consequently, non-selective agents, such as propranolol are preferred. Short-acting agents, such as esmolol, may be a more appropriate choice in those with associated haemodynamic compromise. A recent trial randomised 60 ICD with ES to receive, within 24 hours of ES presentation, either propranolol or metoprolol intravenously combined with IV amiodarone for 48 hours [51]. Propanolol was associated with a higher proportion of patients free of recurrent VA (90% vs. 53%, respectively), shorter time to arrhythmia termination and hospital length of stay [51].

Amiodarone

Amiodarone is commonly used in the treatment of ES. It exerts a predominant Class III effect by way of potassium channel blockade and resultant prolongation of the refractory period in cardiac myocytes. It also exhibits Class I (sodium channel inhibition), Class II (L-type calcium channel blockade) and Class IV (sympathetic blockade) effects, most notably when administered intravenously. Amiodarone has been demonstrated to successfully terminate ventricular arrhythmias in approximately 40% of patients when used in isolation, and is useful in preventing long-term recurrence [52,53]. Amiodarone plus β-blockers significantly reduces the risk of recurrent ICD-shocks compared with β-blockers alone and sotalol alone [53]. In ES, amiodarone may reduce storm recurrences four-fold over 2 years follow-up [54]. Unfortunately, the long-term use of amiodarone is often limited by its associated toxicities, including liver dysfunction, hypo- and hyperthyroidism, pulmonary fibrosis and, most notably, pro-arrhythmic effects. Furthermore, chronic amiodarone therapy has been associated with increased defibrillation thresholds [55]. A recent meta-analysis has suggested amiodarone may be associated with increased mortality [46].

Sotalol

In its racaemic form, sotalol has potent, non-selective ß-blocking activity in addition to Class III activity. In a placebo-controlled randomised multicentre trial, sotalol, compared to placebo reduced the risk of any shock or death by 48% among ICD patients [56]. In the OPTIC (Optimal Pharmacological Therapy in Cardioverter Defibrillator Patients) trial, sotalol showed a trend to reduction in shocks, when compared to other ß-blockers [53].

Class I Anti-Arrhythmic Drugs

Class Ib AADs (mexiletine, lignocaine) are commonly used in the treatment of ventricular arrhythmia storm, with uncertain success. The effects of Class I agents are mediated by fast sodium channel inhibition in a use-dependent manner. Consequently, lignocaine can be useful in the context of storm precipitated by ischaemia, as in this setting binding is enhanced [57]. Although Class III agents are preferred in the context of cardiac failure, agents including lignocaine and mexiletine may be useful in selected patients. Mexiletine may reduce VA burden albeit with a trend toward increased mortality and is generally used as an adjunct to amiodarone in an effort to reduce ICD shocks when breakthrough events occur on amiodarone [58]. Mexiletine side effects are dose dependent and affect the central nervous system (tremor, hallucinations, seizures) and are rapidly reversible with dose reduction or drug cessation.

Procainamide, a class IC anti-arrhythmic, which also mediates its mechanism of action through blockage of fast sodium channels, has some evidence for use in the treatment of haemodynamically tolerated ventricular tachycardia. In the PROCAMIO study, procainamide was demonstrated to be more efficacious and safer than amiodarone in this particular clinical setting [59]. Procainamide is also more efficacious than lignocaine in the termination of VT [60]. However, evidence for prevention of recurrent arrhythmia is limited and procainamide's use is further limited by a lack of widespread availability.

Caution is advised with the use of class I drugs. They can worsen cardiac function due to their negatively inotropic effects, leading to more heart failure, and more arrhythmic episodes [61].

Radiofrequency Catheter Ablation

Use of catheter ablation as an adjunct to pharmacotherapy in the treatment of ventricular arrhythmia has demonstrated superiority compared to pharmacotherapy alone [46,62]. Specifically, analysis of the VANISH (Ventricular Tachycardia Ablation versus Escalated Antiarrhythmic Drug Therapy in Ischemic Heart Disease) trial demonstrated that, in patients with ICM and an ICD with ongoing episodes of ventricular tachycardia despite appropriate pharmacotherapy, there was a significantly lower rate of death, electrical storm and appropriate ICD shocks in those who underwent radiofrequency catheter ablation as opposed to escalation of medical therapy [62]. In that study, a trend towards a 34% relative risk reduction of ES recurrences was observed in patients treated by catheter ablation compared to escalation of AADs [62]. In this context, ablation should be considered in all patients with electrical storm unresponsive to medical therapy. Increasingly, early employment of this treatment modality has been shown to improve patient outcome.

In a recent meta-analysis of 471 patients with ES who received invasive treatment (catheter ablation, trans-coronary ethanol ablation, surgical ablation), acute elimination of all inducible VAs was achieved in 72% of patients. Clinical arrhythmia suppression was achieved in 92% of patients with a complication rate of 2% and peri-procedural death in <1%. At median follow-up of 1.2 years, 94% of the patients were free from ES and 72% were free from any VT. Overall mortality was 17% at 1.2-years follow-up with most of the deaths related to progressive heart failure (62%) [63]. Similarly, in a large series of patients undergoing ablation for ES, acute non-inducibility of any VA was achieved in 73%, and ES-free survival achievable in 93% at 60 months' follow-up. The procedure was similarly effective in ICM and DCM. Persistent inducibility of any VT at the end of the procedure was the only independent predictor of VT recurrence [64], as was confirmed by a multicentre series [4].

Performance of catheter ablation in patients with ventricular storm is challenging and is associated with increased risk of peri-procedural morbidity and mortality compared with those not presenting in storm [64]. Furthermore, failure of catheter ablation in this patient group portends a high mortality. Santangeli and colleagues have developed the PAINESD (Patients Risk Profile and Mortality) score to aide in the identification of patients with ventricular tachycardia presenting for ablation, at high risk who may benefit from primary mechanical haemodynamic support [65].

Neuraxial Modulation

As previously discussed, increased sympathetic tone is a key factor in the initiation and potentiation of electrical storm. Consequently, modulation of various elements within the cardiac neural axis can be used to treat ventricular arrhythmia (VA), especially ES [41,48,66–68]. A detailed review of the techniques, mechanism of action, efficacy and side effects is expertly reviewed elsewhere [68,69]. There is evidence to support the use of cardiac sympathetic denervation in the treatment of ventricular arrhythmias secondary to long QT syndrome and catecholaminergic polymorphic ventricular tachycardia [70,71]. More recently, this technique has been employed in the treatment of electrical storm in patients with structural heart disease [67]. Neuraxial modulation is possible via: (i) thoracic epidural anaesthesia (TEA); (ii) stellate ganglion (SG) blockade; (iii) surgical cardiac sympathetic denervation (CSD); and, (iv) renal sympathetic denervation (RSD) [66,69].

Thoracic epidural anaesthesia involves percutaneous administration of local anaesthetic into the thoracic epidural space: injection of 1 mL of 0.25% bupivacaine followed by an infusion at 2 mL/h, which can be up-titrated according to the arrhythmic response. TEA is a short-lived treatment and best utilised as a bridge until more definitive neuraxial blockade or other interventional techniques are performed. It can also be a bailout if ES recurs despite catheter ablation; indeed, Bourke et al. showed that TEA achieved 80% reduction in VA burden in 75% of patients who had failed ablation and were experiencing ES [68].

Stellate ganglion blockade involves percutaneous injection of local anaesthetic into the left or both stellate ganglia, reducing sympathetic outflow to the heart via blockade of afferent and efferent neurons. Again, it is a temporising measure until definitive blockade or other interventional techniques can be established, and/or as a bail out for ES refractory to catheter ablation. One study showed a 93% reduction in VA acutely, followed by a 90% reduction in VA burden in 56% of patients >3 years of follow-up when LSG was used in conjunction with surgical cardiac sympathetic denervation (CSD) [72].

A permanent form of neuraxial blockade affecting both the afferent and efferent innervation of the heart can be achieved by CSD. Cardiac sympathetic denervation surgically removes the lower half of the left or bilateral stellate ganglia and the T2–T4 thoracic ganglia [66]. In one study, CSD markedly diminished the burden of ICD shocks in patients with refractory VT or ES from 19.6 ± 19 pre-procedure to 2.3 ± 2.9 post-procedure with 90% of patients experiencing a reduction in ICD shocks. Bilateral CSD is more beneficial than left CSD, with survival free of ICD shock in 30% in the left CSD and 48% in the bilateral CSD group [48].

Renal sympathetic denervation (RSD) involves catheter ablation of the neural plexus in and around the renal artery adventitia. It reduces central sympathetic efflux to the heart by virtue of reduction of whole body norepinephrine spillover and inhibition of the renin-aldosterone system [69]. A number of small studies have shown benefits in treatment of ES. Ukena et al. showed that RSD in 13 patients resulted in a reduction in VA episodes, from a median of 20 to 28.5 episodes before RSD to 0 episodes at 3 to 6 months' post RSD, with 85% of patients reportedly free from VA at 3 months [73]. Other approaches to neuraxial blockade in the experimental setting include vagal nerve stimulation [74], kilohertz frequency alternating current [75], charge-

balanced DC blockade of the stellate ganglia [76] and transtracheal blockade of the cardiac plexus [77].

Alternative Treatments

In the context of ES refractory to the treatment methods described, a number of alternative methods have been proposed. These are expertly reviewed elsewhere [69]. Sequential, simultaneous and bipolar ablation are variations of radiofrequency ablation methods designed to expand lesion size in order to target deep intramural VTs [69]. Half normal saline, instead of normal saline which is the usual irrigant for radiofrequency ablation, may also be used to make larger lesions for intramural substrates. Needle ablation is a new technique of plunging a small 27-gauge electrode up to 1 cm into the myocardium for intramural ablation. Surgical cryoablation has proved effective in in case series in those with non-ischaemic cardiomyopathy with ventricular tachycardia refractory to standard therapy [69,78]. Trans-coronary ethanol ablation has also been reported as an alternative therapy in refractory ventricular tachycardia in structural heart disease [69]. Transvenous ethanol ablation may be useful in intramural VTs, especially from the LV summit, but is best performed in expert hands with significant experience with the technique [79].

Special Considerations for Patients Without Structural Heart Disease

A few conditions resulting in ES in the absence of structural heart disease are notable. Recurrent VF in patients with Brugada syndrome can be managed acutely with an infusion of intravenous (IV) isoprenaline, followed by oral quinidine (or cilostazol, if refractory to quinidine) [80]. Catheter ablation of the pericardial right ventricular outflow tract targeting areas of low voltage scar and/or areas of slow conduction present at baseline (or provocable by intravenous ajmaline) is shown to be highly efficacious for ES in Brugada syndrome (Figure 2A,B) [81]. Malignant early repolarisation characterised by J point elevation and recurrent VF, may also be temporised with IV isoprenaline, and subsequent catheter ablation [82]. Premature ventricular contractions can trigger recurrent VF in the absence of structural heart disease, but can also occur in the early phase post myocardial infarction from damaged Purkinje fibres [83], and in DCM patients [84]. When occurring in the absence of structural disease, the site of triggering PVCs are usually distinct, including Purkinje system (right ventricular moderator band, anterior or posterior fascicle in the LV), LV outflow tracts, tricuspid annulus, and the papillary muscles (RV or LV; Figure 2C,D) [85–87].

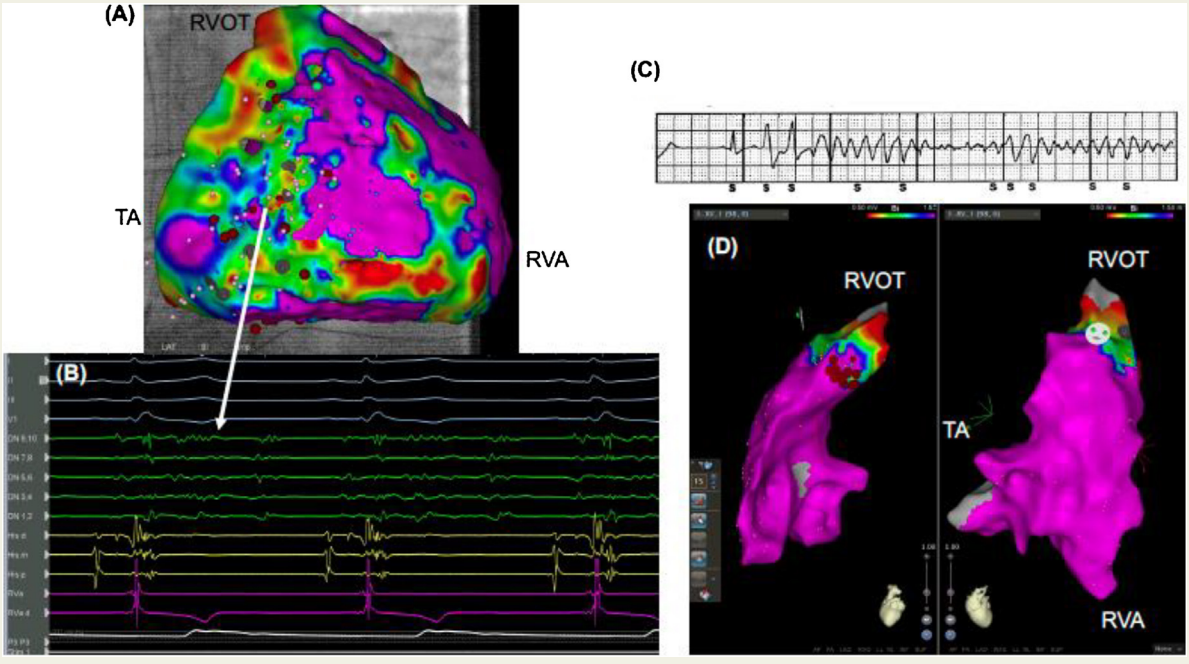

Figure 2 Examples of ventricular fibrillation in Brugada syndrome and PVC-induced VF storm treated with catheter ablation.
(A) Epicardial voltage map (0.5 mV-1.0 mV) with scar portrayed as yellow/red/green/blue (<0.5 mV) and normal voltage as purple (>1.0 mV) in a patient with VF storm with a history of Brugada syndrome. (B) Long duration fractionated electrograms were found on the epicardial surface (arrow) during mapping that were targeted for ablation. This resulted in non-inducibility of VF and long-term freedom from recurrent VF and normalisation of the Brugada pattern on ECG; (B) PVC-induced VF storm in a woman with structurally normal heart. The PVCs were ablated in the RV outflow tract.
Abbreviations: RVA, right ventricular apex; RVOT, right ventricular outflow tract; TA, tricuspid annulus; PVC, premature ventricular contractions; ECG, electrocardiograph; VF, ventricular fibrillation; RV, right ventricular

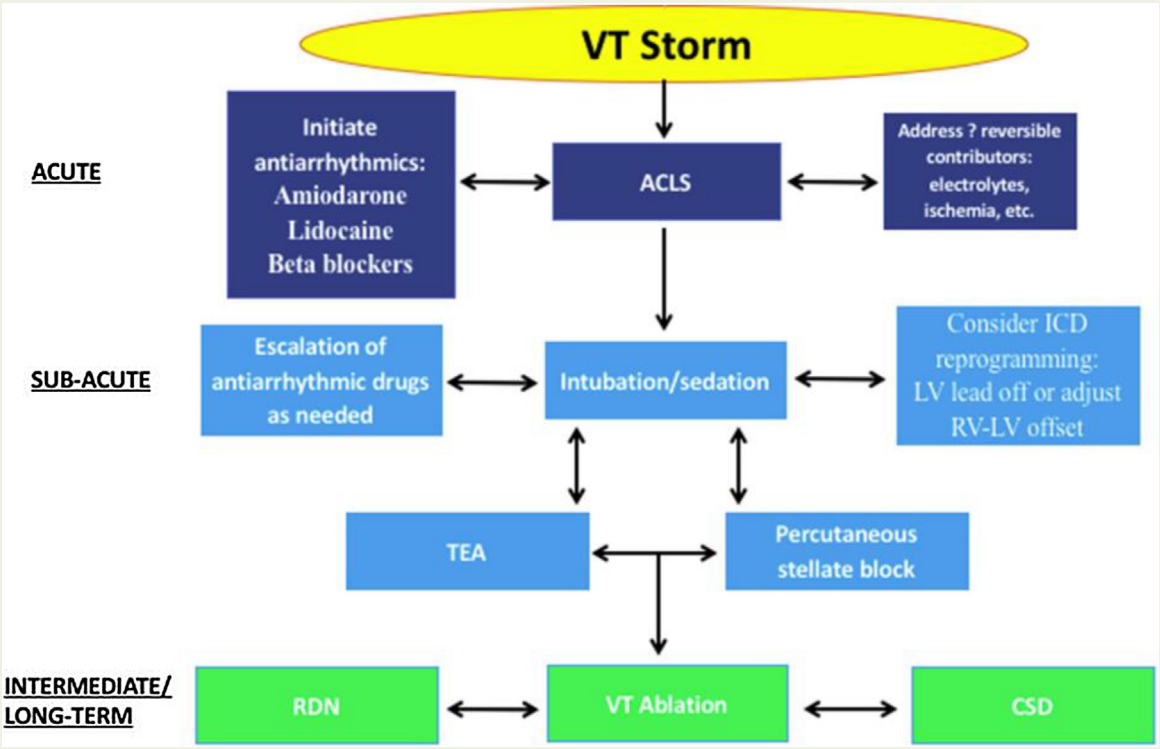

Figure 3 Flowchart showing interventions followed for the treatment of ES in the immediate, sub-acute and long term management. Reproduced from Bradfield et al, [66] with permissions.
Abbreviations: ACLS, advanced cardiac life support; CSD, cardiac sympathetic denervation; ICD, implanted cardioverter defibrillator; LV, left ventricular; RDN, renal sympathetic denervation; RV, right ventricular; TEA, transcoronary ethanol ablation; ES, electrical storm

Response to catheter ablation is excellent with a marked reduction or even elimination of recurrent VF, despite VF storm as the initial presentation [88], but new triggers do form in ~30% of patients in long term follow-up [89]. In catecholaminergic polymorphic VT characterised by bidirectional/polymorphic VT, beta blockers are the treatment of choice, but flecainide can be a useful addition.

Conclusions

Electrical storm is a distinct arrhythmic emergency which portends significant morbidity and mortality. In the context of increasing use of ICDs in primary and secondary prevention of sudden cardiac death, the occurrence of this clinical phenomenon is likely to increase. Treatment requires a multidisciplinary approach involving exclusion and treatment of triggers, optimal ICD and/or CRT programming (including turning off a pro-arrhythmic LV lead), anti-arrhythmic drug therapy, sedation, intubation/ventilation, haemodynamic support and consideration of catheter ablation and neuraxial blockade via interventional techniques (Figure 3). Whilst drug therapy has historically served as first line therapy, radiofrequency catheter ablation is emerging as the standard of care in patients with structural heart disease presenting with electrical storm.

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