European Heart Journal Supplements (2024) **26** (Supplement 1), i44–i48
The Heart of the Matter
https://doi.org/10.1093/eurheartjsupp/suae016

The point on the treatment of arrhythmic storm

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KEYWORDS
Arrhythmic storm;
Implantable cardiac defibrillator;
Transcatheter ablation

Arrhythmic storm is a clinical emergency associated with high mortality, which requires multi-disciplinary management. Reprogramming of the implantable cardiac defibrillator (ICD) aimed at reducing shocks, adrenergic blockade using beta-blockers, sedation/anxiolysis, and blockade of the stellate ganglion represent the first simple and effective manoeuvres, but further suppression of arrhythmias with antiarrhythmics is often required. A low-risk patient (e.g. monomorphic ventricular tachycardia, functioning ICD, and haemodynamically stable) should be managed with a beta-blocker (possibly non-selective) plus amiodarone, in addition to sedation with a benzodiazepine or dexmedetomidine; in patients at greater risk (high burden and haemodynamic instability), autonomic modulation with blockade of the stellate ganglion and the addition of a second antiarrhythmic (lidocaine) should be considered. In patients refractory to these measures, with advanced heart failure, general anaesthesia with intubation and the establishment of a haemodynamic circulatory support should be considered. Ablation, performed early, appears to be superior in terms of mortality and reduction of future shocks compared with titration of antiarrhythmics.

Introduction

Arrhythmic storm [electrical storm (ES)] is a clinical emergency associated with a severe prognosis and complex clinical management. The most used definition is that of three or more separate episodes of ventricular arrhythmia, interrupted by therapeutic intervention, within 24 h, or the occurrence of incessant ventricular tachycardia (VT) lasting at least 12 h. In patients with an implantable cardiac defibrillator (ICD), the most commonly used definition is that of three or more appropriate interventions for anti-tachycardia pacing (ATP) or shock within 24 h, separated by at least 5 min.[1]

The incidence of ES varies between 4% of patients with ICDs in primary prevention[2] to 10–28% of patients in secondary prevention and is associated with an increase in both short- and long-term mortality risk of approximately 2.5 times compared with isolated VT episodes and 3.3 times compared with patients with non-sustained episodes.[3]

Pathophysiology

The development of ES requires the presence of an arrhythmic substrate, often a structural heart disease as a consequence of diffuse fibrosis (non-ischaemic cardiomyopathy) or one organized in discrete scars (ischaemic heart disease, arrhythmogenic dysplasia of the right ventricle, sarcoidosis, and myocardial infiltrative diseases) necessary for the occurrence of a macro-return, resulting in monomorphic VT,[1] a hereditary (long QT syndrome, Brugada syndrome, and catecholaminergic polymorphic VT) or acquired pathology of ion channels (drugs). These substrates then interact with a pro-arrhythmogenic trigger (ischaemia, haemodynamic instability, or electrolyte imbalance) and modulating

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factors such as autonomic imbalance, consisting of various combinations of sympathetic hyperactivity and reduction of vagal output (Coumel's triangle).

Less commonly, the mechanism is secondary to activity triggered by early after depolarizations (EADs), the mechanism of polymorphic VT, and torsades de pointes during congenital or acquired QT interval prolongation or from delayed after depolarizations from an increase in intracellular calcium during acute ischaemia and digitalis toxicity or in catecholaminergic polymorphic VT.[1]

Clinical presentation

Patients without an ICD and\or with left ventricular dysfunction and\or with short-cycle or incessant\ frequent ventricular arrhythmias may not tolerate the arrhythmia leading to syncope, haemodynamic deterioration, or sudden cardiac death. In the presence of preserved systolic function or for slow ventricular arrhythmias, the clinical presentation may be limited to heart palpitations or lipothymia. Patients with ICDs can go from being completely asymptomatic, with episodes of VT treated with ATP, to having recurrent shock with haemodynamic deterioration.

Electrical cardioversion represents the approach of choice both in cases of haemodynamically non-tolerated VT (IB recommendation) and tolerated if the risk related to sedation is considered low (IC recommendation).[1]

In all other cases, antiarrhythmic drugs (AADs) have a role both in the acute interruption of VT and in the prevention of relapses. With the exception of some peculiar forms, such as the use of beta-blockers in outflow tract VTs and verapamil in fascicular VTs (IC recommendation),[1] AADs used in the presence of structural heart disease belong to Class I (reducing excitability and slowing intra-myocardial conduction) or to Class III (with an increase in refractoriness).

It is critical to obtain a 12-lead electrocardiogram (ECG) of both the native rhythm and each of the patient's VT morphologies as identifying the exit is critical to planning the approach to use during the ablation.

Reversible causes must be promptly excluded, which should be treated aggressively, but present only in approximately 10% of patients: acute heart failure, sepsis, pharmacological toxicity, QTc prolongation, thyrotoxicosis, or electrolyte imbalance (in particular hypokalaemia and hypo-magnesaemia) and acute myocardial ischaemia, however, generally associated with polymorphic VT.[1]

In the initial evaluation and management, the immediate definition of the haemodynamic status is therefore mandatory. Patients with a dilated left ventricle, mitral insufficiency, and increased filling pressures may benefit from an arterial vasodilator (sodium nitroprusside), in the presence of preserved right ventricular function, or a venodilator (nitroglycerin) if the right ventricle is dysfunctional; in the latter case, tolerance to the beta-blocker is unlikely, and therefore, the need for inotropic therapy (dobutamine and levosimendan) is likely. Patients in cardiogenic shock despite these measures are candidates for haemodynamic circulatory support (HCS).

Implantable cardiac defibrillator reprogramming

In the event of an ICD shock, the device must be promptly interrogated to verify the possible presence of inappropriate interventions for atrial fibrillation with high ventricular response, other supraventricular arrhythmias, over-sensing phenomena, and noise on the lead due to fracture or loss of insulation (*Figure 1*).

In the case of inappropriate interventions, recurrent but short and self-limiting VT or a haemodynamically stable patient in whom there is the possibility of performing

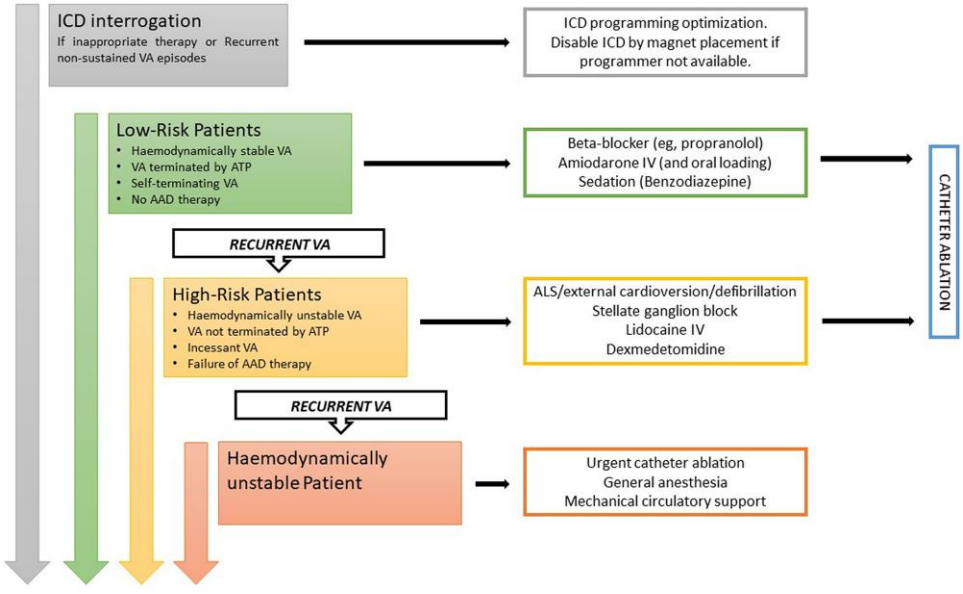

Figure 1 Individualized steps after interrogation of ICD. ICD, cardiac defibrillator.

manual ATP, deactivation of anti-tachycardia therapies by application of an external magnet or reprogramming is recommended (Class I).[1]

Programming aimed at reducing unnecessary shocks has an impact on mortality and reduces sympathetic hyper-activation, for which the guidelines recommend[1]:

- a long detection interval (6–12 s or 30 intervals);
- a detection of tachycardia at a threshold of ≥188 b.p.m. in primary prevention patients;
- to programme algorithms to discriminate supraventricular tachycardias for frequencies up to 230 b.p.m.;
- the activation of the discrimination algorithm in a 'conditional shock' zone < 250 b.p.m. for subcutaneous ICDs; and
- the systematic use of ATP before delivering the shock.

Anti-tachycardia pacing windows < 185 b.p.m. are generally scheduled in secondary prevention patients. To reduce the possibility of unnecessary shocks, it is advisable to programme a greater number of ATPs with 8–10 pulses, favouring bursts (fixed pacing cycle) over ramps (decremental cycle).

In patients with cardiac resynchronization therapy, epicardial left ventricular stimulation can favour the triggering of re-entry arrhythmias if the stimulation bipole is located in the border zone of a scar; for this suspicion, left ventricular stimulation should be deactivated or another two-pole programmed. Ventricular arrhythmias for R on T from EAD on prolonged QTc, triggered by ventricular extrasystoles with short-long-short sequence or by very slow VT, can be suppressed by overdrive with an increase in the pacing frequency (e.g. 70–90 b.p.m.).

Analgesia sedation

The hyper-activation of the sympathetic nervous system, caused by anxiety and pain from external shocks, the ICD, or any resuscitation makeovers, contributes to the maintenance of the ES; for this reason, light-moderate sedation is recommended in all patients (IC recommendation).[1] For this purpose, benzodiazepines (e.g. midazolam) or short-acting opioids (e.g. remifentanil) can be used to reduce adrenergic hyper-activation and ensure analgesia without negative inotropism. Dexmedetomidine is associated with a reduction in sympathetic outflow with potential reduction in arrhythmia burden without respiratory depression. In patients with severe\refractory ES, endotracheal intubation under general anaesthesia with propofol may be considered (IIaC indication), may be associated with a risk of haemodynamic instability due to negative inotropism, but has demonstrated complete suppression of VT\VF within minutes or hours in 80% of patients.[4]

Autonomic modulation in the acute settings

Percutaneous blockade of the stellate ganglion and thoracic epidural anaesthesia are two techniques that can be performed at the patient's bedside, with the aim of reducing the sympathetic output directed to the heart. Current guidelines timidly reserve a role for it only in patients with ES refractory to pharmacological therapy in whom transcatheter ablation is ineffective or not feasible (IIbC indication).[1] However, the blockade of the stellate ganglion (responsible for cardiac and ocular sympathetic innervation), with a strong physiopathological rationale, simple and quick to implement, has been shown to provide 83% freedom from VT at 1 h.[5] It can be done through two main techniques. The anterior anatomical approach is carried out by injecting local anaesthetic (150–200 mg of 2% lidocaine combined with 50 mg of ropivacaine or bupivacaine) into the left paratracheal area at the level of the Chassaignac tubercle. The area of interest is 2 cm above the sternum, generally at the level of the cricoid cartilage, and 2 cm lateral to the midline; the needle is advanced perpendicularly from the skin to the bone, taking care to move the vascular nervous bundle of the neck laterally with the fingers. A bilateral block offers no additional benefits. The manoeuvre has also proven to be safe in patients on anticoagulant therapy and those on extracorporeal membrane oxygenation (ECMO). There is no correlation between the transient development of Horner's syndrome and the antiarrhythmic efficacy of the block.

Thoracic epidural anaesthesia consists of the percutaneous injection of a bolus of 1 mL of 0.25% bupivacaine followed by an infusion at 2 mL/h (titratable) into the epidural chest space. Being performed in lateral decubitus, the manoeuvre is often not suitable in emergency conditions and/or in the presence of devices to support the circulation and is contraindicated in case of anticoagulant or double anti-aggregant therapy due to the risk of epidural haematoma.

Beta-blockers

Since the sympathetic nervous system is central to the development and maintenance of SE, it goes without saying that beta-blockers play a primary role. Sympathetic modulation therapy (esmolol or propranolol or left stellate ganglion blockade) has been shown to be superior in reducing mortality (5% vs 67%) compared with antiarrhythmic therapy (lidocaine and procainamide),[6] as have non-selective beta-blockers (propranolol) have demonstrated a reduction in the incidence of ventricular arrhythmias of 2.67 times compared with B1 selective (metoprolol) in co-administration with amiodarone,[7] and, therefore, this association is recommended in Class IB.[1] The rationale derives from the fact that in heart failure, there is a down-regulation of beta1 receptors in favour of beta2.

Acute antiarrhythmic drug treatment

Procainamide

A sodium channel blocker, procainamide, also has potassium-blocking effects (with potential PQ, QRS, and QT prolongation). Administered IV (10 mg/kg/20 min), it has the greater capacity to interrupt (67% vs 38% at 40 min) haemodynamically tolerated monomorphic VTs in patients with known or suspected structural heart disease compared with amiodarone[8] (5 mg/kg/20 min), with a lower incidence of hypotension and greater

efficacy even compared with lidocaine (76% vs 35%), IIaB recommendation.[1] Since it has a negative inotropic effect, it is contraindicated in patients with advanced heart failure, myocardial infarction, and severe renal failure. In chronic therapy, it can cause a lupus-like syndrome.

Amiodarone

Despite an intermediate efficacy in terminating haemodynamically tolerated monomorphic VT,[8] amiodarone, a potassium channel blocker (Class III) and therefore associated with QT prolongation, is generally preferred as a first-line AAD, as it can be administered in patients with structural heart disease (IIbB recommendation).[1] IV administration, it also confers Class I, II, and IV antiarrhythmic activity, with efficacy in interrupting arrhythmia and induced arterial hypotension proportional to the infusion rate. After acute use, it can be continued chronically as oral therapy to prevent relapses but requires accumulation of the active metabolite (600–1200 mg/24 h for 8–10 days). Long-term use is burdened by adverse effects limiting its use, such as corneal deposits, photosensitization, increased transaminases, pulmonary fibrosis, and dysthyroidism.

Lidocaine

IB sodium channel blocker is generally used as second-line therapy in case of ineffectiveness of amiodarone alone. Particularly effective in ischaemic myocardium, the dose must be reduced due to slow metabolism in conditions of hepatic hypo-perfusion such as cardiogenic shock. It has the lowest rate of hypotension upon IV administration (bolus of 50–200 mg, followed by 2–4 mg/min) and a modest negative inotropic effect.[8] Often, in the event of a favourable response, we move on to subsequent oral therapy with mexiletine, a drug with similar electrophysiological properties, effective in leading to a reduction in the burden of VT in 64% of the patients, compared with an incidence of gastrointestinal adverse events in 33% of patients.[9] Neither lidocaine nor mexiletine is associated with ECG changes.

Transcatheter ablation

In patients with monomorphic VT, catheter ablation has been shown to be superior in preventing arrhythmic relapses compared with titration of antiarrhythmic therapy[10-12] and therefore has an IB recommendation in patients with incessant VT or ES from monomorphic VT refractory to AAD therapy.[1]

In the VANISH trial (Ventricular Tachycardia Ablation vs Escalated Antiarrhythmic Drug Therapy in Ischemic Heart Disease), patients with ES presented similar benefits between ablation and titration of AAD therapy,[11] while the multi-centre study by the International VT Ablation Center Collaborative Group[10] highlighted that, although patients with ES generally present clinical characteristics of more advanced disease, with longer and more complex procedures and with a greater need for haemodynamic support, ablation achieves the non-inducibility of clinical VT in 87% of cases, with a complication rate of approximately 7%.

However, ablation is superior to medical therapy in terms of recurrent ICD shocks[11] and, if performed early, is associated with a better prognosis than standard treatment with AAD.[12]

In high-risk patients, to reduce the risk of intra-procedural haemodynamic deterioration, it is recommended to avoid general anaesthesia and, if possible, implement a substrate ablation strategy, with delineation of the edge of the scar and potentially critical channels, rather than a definition of the critical isthmus based on activation mapping.

To this end, the PAINESD score[13] (pulmonary disease, 5 points; age >60 years, 3 points; ischaemic aetiology, 6 points; New York Heart Association Class 3, 6 points; ejection fraction < 25%, 3 points; the presentation as ES, 5 points; and diabetes, 3 points) is useful for establishing the need for peri-procedural HCS: a score of ≥15 defines a high risk of instability, with evidence of significantly greater mortality in the case of rescue HCS implantation rather than its preventative use. The use of ECMO during ablation of unstable recurrent VTs is associated with haemodynamic stabilization in 68% of cases, with an overall survival of 88% at a mean follow-up of 21 months.[14]

Stereotactic radiotherapy

The use of stereotactic radiotherapy [stereotactic arrhythmia radioablation (STAR)] has the rationale of overcoming one of the limitations of conventional ablation, namely the accessibility to cardiac regions such as deep intramural or sub-epicardial sites, through the administration of single high-dose radiotherapy fraction over a small volume. The series currently published are small in size, with a success in reducing the burden of VT by 75%, which drops to 69% in the case of location in the interventricular septum.[15] At the moment, the STAR plays a role as a bailout for patients with monomorphic ventricular arrhythmias, refractory, and/or not eligible for ablation therapy.

Devices for circulatory mechanical assistance

The aortic counterpulsator (Intra Aortic Balloon Pump) is the most used device in low flow states due to its availability and rapidity of effectiveness, with low incidence of complications. Percutaneous HCS devices (Tandem Heart and Impella) offer a greater flow rate increase (from 2.5 to 5 L/min), limited to left ventricular support only, but interfere with electromagnetic mapping systems and preclude some modalities of transcatheter ablative approach.

Veno-arterial (VA) ECMO offers advantages in terms of biventricular support. The peripheral positioning also allows multiple accesses to the left ventricle and endo-epicardial mapping without vascular limitations or electromagnetic interference. The mortality of patients with ECMO-VA placed for cardiogenic shock following refractory ES is approximately 50%, allowing a bridge to ablation, cardiac transplant or left ventricular assist implant.

Funding

None declared.

Conflict of interest: none declared.

Data availability

No new data were generated or analysed in support of this research.

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