VENTRICULAR ARRHYTHMIAS: WHO SHOULD BE REFERRED TO AN ELECTROPHysiologist?

John M Morgan

VENTRICULAR arrhythmia management can present a difficult clinical challenge. A proportion of the presenting population will be at high risk of sudden cardiac death (SCD). Little or no protection against SCD is afforded by simple prescription of drug treatment. Antiarrhythmic drugs may be proarrhythmic and prescribed without secure understanding of drug effect. Though many ventricular arrhythmias are dangerous, the spectrum of risk ranges from the immediately life-threatening to very benign (for example, from ventricular fibrillation through to true right ventricular outflow tract tachycardia). Generating the range of ventricular arrhythmias are diverse disease processes and understanding of the relation between witnessed arrhythmia and underlying disease process is often incomplete. There is debate over whether right ventricular outflow tract tachycardia overlaps with right ventricular cardiomyopathy—the one being a “benign” arrhythmia whose disease process is not understood, the other being a disease process whose principal manifestation is “malignant” arrhythmia.

A parallel management challenge to ventricular arrhythmia control is the prevention of SCD in patients with no previous symptomatic ventricular arrhythmia but who are at high risk. SCD may have non-arrhythmia causes, but evidence strongly suggests that many or even most patients suffering or rescued from SCD have ventricular arrhythmia as the index event. Depending on the clinical scenario, the approach to the management of the phenomenon of SCD includes risk stratification, family screening, genetic analysis, and prophylactic therapeutic strategies in addition to the management of an SCD survivor (fig 1).

The electrophysiology specialist has the choice of sophisticated device therapies or interventional ablation techniques, and their combination, for the management of symptomatic ventricular arrhythmias and SCD risk. However, the optimal way to deliver ventricular arrhythmia and SCD management strategies to appropriate patient populations is debatable. There is a tension between the need to make treatments available to appropriate populations, by delegation of clinical services to general cardiologists who express subspecialty interest, and the need to ensure that patients are offered optimal clinical care, which often can only be provided by experts in the field.

Most patients with or at risk of ventricular arrhythmias will benefit from specialist electrophysiological assessment. Generally, SCD prophylaxis, management of SCD syndromes, and management of patients in whom symptomatic ventricular arrhythmias carry a significant burden of morbidity with or without SCD risk is best provided by shared care rather than in electrophysiological exclusivity. Table 1 lists those patients who do not require referral to an electrophysiologist, and those who do.

MANAGEMENT OF SUDDEN CARDIAC DEATH RISK

SCD risk may be generated by the presence of a primary disorder of cardiac electrical activity in the absence of any “structural” heart disease (considered here as SCD syndromes), or may be secondary to a cardiac disease process (most often myocardial in origin), which by its legacy of myocardial scarring and dysfunction creates the electrical substrate for sudden lethal arrhythmia, without premonitory symptoms. The evidence base shows that the most effective treatment for SCD prevention is to fit an implantable cardioverter-defibrillator (ICD), but the cost, morbidity, and mortality of this must be weighed against SCD risk in an otherwise (arrhythmia) asymptomatic population.

LEFT VENTRICULAR IMPAIRMENT AS A Marker FOR SCD RISK

The majority of patients at risk of unexpected SCD are those with left ventricular impairment as a consequence of coronary heart disease, a lesser proportion having ventricular impairment as part of another myopathic process. The SCD syndromes are discussed separately. The MADIT (multicenter defibrillator implantation trial) study first offered evidence that primary prophylactic ICD implantation may reduce SCD risk in a high risk population. The complexity of that study design reflected then current electrophysiological practices and focused on antiarrhythmic drug regimens as alternate solutions. Over the past decade there has been a move towards device based
therapy. Novel antiarrhythmic agents have been long in development, amiodarone continues to offer an unenviable side effect profile and uncertain efficacy, while the newest class III drugs have at best shown neutrality of effect in SCD risk populations. The MADIT 2 study recently concluded and demonstrated effective reduction in SCD risk when patients received ICD therapy predicated on left ventricular dysfunction alone.

If the trend to identification of SCD risk based on substrate identification rather than characterisation continues, given the increasing clinical simplicity of ICD implantation technique, it would seem desirable that the therapy diffuses to the recipient population through the general cardiological community. The increased ease of delivery of ICD therapy may enable device implantation to be performed in district general hospitals by cardiologists with training in implant techniques. However, the potential complexity of ICD therapy should not be underestimated. An understanding of the physical principles governing effective ICD therapy is important. Overlap indications for therapy with resynchronisation in devices may make system implantation and overall treatment delivery more complicated again. As many as one fifth of patients who are candidates for prophylactic ICD implantation may benefit from resynchronisation therapy also. Ultimately, well trained physicians and technicians, whose clinical skills are maintained and refined by large volume clinical practice, optimally deliver device therapy.

**SUDDEN CARDIAC DEATH SYNDROMES**

Genetically determined abnormalities of cardiac cell membrane ion transport result in disturbance of myocardial repolarisation or activation. This allows triggering of polymorphic ventricular tachycardia or ventricular fibrillation in the absence of structural damage to ventricular myocardium. Syncope or SCD may follow. The description of clinical signs and symptoms preceded the understanding of the relevant arrhythmia mechanisms and for the time being they continue to be classified by syndrome name rather than by mechanism.

**Long QT syndromes**

Long QT syndromes comprise a genetically and phenotypically heterogeneous series of abnormal repolarisation syndromes caused by altered potassium and sodium ion transport mechanisms. Multiple gene abnormalities with many polymorphisms of those genes have been identified, making simplistic genetic analysis in any individual difficult. However, it is already established that there is a correlation between specific gene defects and SCD risk. A consistent clinical feature in many sufferers is surface ECG QT interval prolongation, from which the syndrome derives its name. A characteristic type of

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Table 1

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<th>Do not refer:</th>
<th>Do refer:</th>
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<tr>
<td>Patients with mildly symptomatic or asymptomatic ventricular ectopic activity</td>
<td>Patients with highly symptomatic ventricular ectopic activity</td>
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<tr>
<td>Asymptomatic patients with “benign” ventricular tachycardia on or off antiarrhythmic drug treatment</td>
<td>Symptomatic patients with “benign” ventricular tachycardia or controlled only with unacceptable side effects from antiarrhythmic drugs</td>
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<tr>
<td>Patients who are candidates for prophylactic ICD implantation but without symptomatic arrhythmia</td>
<td>Patients who are candidates for prophylactic ICD implantation but with symptomatic arrhythmia</td>
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<td>Any patient with symptomatic ventricular tachycardia with or without prophylactic ICD indication</td>
<td>Any patient suspected of having a “sudden cardiac death syndrome”</td>
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<td>Any patient in whom arrhythmia mechanism is uncertain</td>
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ICD, implantable cardioverter-defibrillator.
polymorphic ventricular tachycardia (torsades de pointe) can be generated. There are associations between specific genetic mutations (if identifiable) and risk of SCD. For risk stratification, young age at symptomatic presentation, family history of SCD, and history of cardiac arrest are variably powerful markers of SCD risk but interpretation of ambulatory monitoring, exercise stress testing, and T wave alternans are unproven. There are no currently available electrical provocation tests to aid assessment. β Blockade, other antiarrhythmic drugs, atrial pacing, and ICD implantation may all be indicated.

**Brugada syndrome**

Patients with Brugada syndrome are predominantly male and in the third to fourth decades of life. Symptomatic presentation is with syncope or cardiac arrest in the absence of structural heart disease. In its most typical form the sufferer’s ECG shows a characteristic pattern comprising a right bundle branch-like ECG configuration with ST segment elevation in leads V1 to V3. Changes in autonomic tone or intravenous administration of sodium channel blocking drugs (ajmaline, flecainide, procainamide) can unmask ECG features. There is evidence that transmural differential in action potential characteristics, particularly in the right ventricular free wall epicardium, facilitates re-entry during phase 2 of the action potential, resulting in closely coupled cycles of ventricular activation which then precipitate ventricular fibrillation. Death occurs as a result of rapid polymorphic ventricular tachycardia, often initiated during rest or sleep rather than after symptomatic ventricular tachycardia. However, exhibition of these ECG changes may be variable both between and within individuals with time so that intermittent and concealed forms (in terms of ECG manifestation) make diagnosis difficult. There are insufficient data to base risk stratification on ECG analysis or family history. Screening of relatives of index cases should be performed, but there is no agreed approach to management of asymptomatic patients, the only therapy available being ICD implantation. Screening should consist of ECG recording with and without pharmacological challenge with a sodium channel blocker. Investigation of the role of programmed electrical stimulation has suggested that inducibility of ventricular fibrillation is a marker for SCD risk, but the data supporting this observation are insufficient to allow a definitive conclusion.

**Polymorphic cathecholaminergic ventricular tachycardia**

Polymorphic cathecholaminergic ventricular tachycardia (fig 2) is a rare condition characterised by a bidirectional pattern of polymorphic ventricular tachycardia. It seems likely that the arrhythmia mechanism is adrenergically mediated and related to intracellular calcium overload. There is no evidence that programmed extrastimulation or non-invasive assessments can guide risk stratification, and the roles of both β blocker treatment and ICD implantation must be decided upon individual assessments of history severity and family history of SCD.

**Primary ventricular fibrillation**

Survivors of cardiac arrest caused by documented ventricular fibrillation may be found to have no underlying structural heart disease or any of the identifiable primary electrical disorders discussed above. In some the ECG is consistently normal, while in others there may be non-specific abnormalities of repolarisation. It is likely that such patients have a forme fruste of the above conditions, but management must be on an individualised basis taking into account clinical and family history.

**Summary of genetically determined sudden cardiac death syndrome**

Understanding of these conditions is insufficient for algorithm guided management but it is evolving rapidly. Electrophysiologists are likely to be best placed to coordinate a multidisciplinary approach to optimal management of this vulnerable patient group, offer interventions when appropriate in the light of the evolving evidence base, screen relatives, and contribute to national and international databasing and research.

**CONTROL OF SYMPTOMATIC ARRHYTHMIA AND MANAGEMENT OF SUDDEN CARDIAC DEATH RISK**

Any cardiac disease which has interposition of fibrotic tissue and derangement or destruction of the specialised cardiac conduction system, as part of its effect on disorganisation of ventricular myocardium, has the potential to create the substrate for arrhythmogenesis. While life threatening arrhythmias may occur without premonition, many patients will present with palpitation and haemodynamic compromise and/or syncope. Such circumstances require the use of device or ablation therapies to control symptomatic occurrence as well as protect against SCD risk.

ICD therapy is established as standard of care for secondary prevention of SCD and symptomatic management in patients presenting with ventricular tachycardia or fibrillation. It is debatable whether all such patients need to be assessed by an
expert electrophysiologist. Shared care with an expert in the field may ensure exposure to ablation therapies and optimal device programming. The weight of patient responsibility may fall more towards the electrophysiologist if cardiac arrhythmia becomes the principal cause of morbidity.

Myocardial scarring secondary to coronary artery disease

The risk of ventricular arrhythmia both near and distant to myocardial infarction is well established. Myocardial re-entry is allowed by the complex interaction of viable myocardium with scarred myocardium in and around infarct territories. These patients represent the majority of patients presenting with ventricular arrhythmias. Antiarrhythmic drug treatment may have a role in suppressing arrhythmia occurrence and thereby reduce the morbidity of such arrhythmias, but the data to support protection from SCD are increasingly weak. Most such patients will therefore receive device therapy. However, while ICD therapy may be effective in reducing SCD risk, patients may have an unacceptable morbidity related to either frequency of antitachycardia pacing or delivery of defibrillating shock therapy. In this circumstance adjunctive ablation treatment may reduce this burden. Because such arrhythmias are frequently haemodynamically poorly tolerated, use of novel mapping techniques for rapid data acquisition and characterisation of the arrhythmia circuit may be highly advantageous.

Slow ventricular tachycardia

A subset of patients with “ischaemic heart disease ventricular tachycardia” present with slow rate, haemodynamically well tolerated arrhythmia, which is refractory to drug treatment. Such arrhythmias are often poorly handled by ICD antitachycardia pacing regimens which may fail to terminate the arrhythmia, confuse the arrhythmia with sinus tachycardia, deliver shock therapy to the conscious and uncompromised patient, or successfully terminate the arrhythmia only to see its almost immediate re-initiation. However, the stability of the arrhythmia mechanism and the patients’ haemodynamics lend themselves to catheter ablation using conventional techniques (fig 3A,B). The end point of the therapy need only be cessation of the target arrhythmia and not an attempt to abolish all inducible arrhythmia circuits. Target ablation may be a highly successful symptomatic strategy although ICD therapy will remain indicated to deal with SCD risk and non-targeted arrhythmias.

Idiopathic dilated cardiomyopathy

Ventricular arrhythmias are a major cause of mortality in this condition and standard electrophysiological techniques are less predictive of SCD risk than in ischaemia related left ventricular dysfunction. Patient prognosis is most closely linked to severity of left ventricular impairment. However, progressive heart failure and SCD are competing causes of death. Therefore, the role of ICD implantation in preventing SCD is uncertain as heart failure death may supervene, with ICD implantation impacting little on patient prognosis. Sudden death is reported as a reliable predictor of SCD. Non-sustained ventricular tachycardia is also a sensitive but non-specific marker for SCD risk. Other non-invasive tests have no clear role. Programmed extrastimulation has a low negative predictive accuracy. Catheter ablation is also less effective for arrhythmia control even with modern mapping techniques, in part because of the rapidly evolving nature of the underlying substrate. ICD implantation is often indicated for symptomatic control and prognostic benefit, although adjunctive ablation may be required to reduce the frequency of device therapy. As resynchronisation pacing efficacy becomes established there will be an overlap in indications for device therapy. There is a need for a multidisciplinary approach to the management of the condition.

Idiopathic dilated cardiomyopathy/ischaemic heart disease and bundle branch re-entry tachycardia

Many patients’ first presentation with this arrhythmia is syncope or cardiac arrest. More common in dilated cardiomyopathy, it may occur in patients with left ventricular impairment caused by coronary disease. It employs the specialised conduction system as a limb in its re-entry circuit so that targeting and ablation of the right bundle branch may be a “curative” technique.
Hypertrophic cardiomyopathy
At its most threatening, hypertrophic cardiomyopathy may cause unexpected death in asymptomatic young individuals. However, in the majority of patients with the condition the prognosis is relatively benign. The role of the electrophysiologist is to define and manage those patients who are at high risk of SCD but who constitute a small proportion of the total hypertrophic cardiomyopathy population. The literature does allow conclusions to be drawn with respect to risk stratification. Previous cardiac arrest, syncope, a family history of sudden death, extreme left ventricular hypertrophy, a hypotensive blood pressure response to exercise stress testing, and documentation of non-sustained ventricular tachycardia are identified risk factors. In the presence of these observations programmed extrastimulation study does not further refine clinical decisions and in their absence is too non-specific to guide management alone. Assessments of ischaemia, signal averaged ECG, heart rate variability, and T wave alternans are unproven or ineffective as additional risk assessments. Improved genetic understanding will further refine prophylactic device indications.

Right ventricular cardiomyopathy
Fibro-fatty infiltration of right ventricular myocardium characterises this condition. Involvement of the septum or left ventricle is uncommon. It may be under-diagnosed at postmortem studies because of the subtleties of histopathological change, both macroscopically and microscopically. Patients most commonly present either with syncope or cardiac arrest, and the condition may be a major cause of sudden death in young (pre-coronary disease) age groups. Most patients will present with ECG abnormalities in the right precordial leads (T wave inversion, increased QRS duration) reflecting right ventricular disease. Necessary investigations include cardiac catheterisation, cross sectional imaging, and the range of non-invasive and invasive electrophysiological assessments. Antiarrhythmic drug treatment, catheter ablation, and ICD implantation all have evidence bases for control of symptoms, but prevention of SCD is probably only achieved by ICD implantation. Right ventricular disarticulation is an effective technique in selected patients and with skilled operators. There is an underlying genetic predisposition to the condition so that screening of family members is recommended. However, the role of prophylactic ICD implantation in asymptomatic individuals is undefined.

SYMPTOM CONTROL OF “BENIGN” VENTRICULAR ARRHYTHMIAS

Ventricular ectopic activity
Ventricular ectopy may occur because of myocardial disease causing electrical instability, when it is a marker for that disease rather than a primary electrical disorder, or as part of a specific arrhythmia substrate such as right ventricular outflow tract ventricular tachycardia. Attention should focus on optimum management of underlying heart disease, which may improve patient prognosis and reduce symptom burden. Long term antiarrhythmic drug use should be discouraged. If symptoms are greatly debilitating, catheter ablation, especially using novel mapping techniques, may allow targeting of an arrhythmogenic focus but this approach is rarely employed.

“Benign” ventricular tachycardia
There are a group of conditions which give rise to sustained ventricular tachycardia but, in the absence of any accompanying structural heart disease, are not life threatening. All are amenable to probable curative therapy with catheter ablation.

Right ventricular outflow tract tachycardia
The term right ventricular outflow tract tachycardia is purposefully descriptive. Occasionally the arrhythmia source is in the left ventricular outflow and ECG features do not always allow discrimination. Arrhythmia control may be achieved with drugs, principally β blockers, if ablation is refused. There is at least a presentational overlap between arrhythmogenic right ventricular dysplasia, which should be considered as a possible diagnosis if catheter ablation of the target arrhythmia is unsuccessful, the arrhythmia is recurrent, or there is imaging evidence of right ventricular abnormality. Inducibility of the arrhythmia is variable. Sophisticated mapping tools may aid catheter ablation.

Idiopathic left ventricular tachycardia
Idiopathic left ventricular tachycardia is also of unknown aetiology but is considered to be a focal triggered arrhythmia and commonly emanates from the interventricular septum. It too is optimally managed by catheter ablation in symptomatic individuals (fig 4).

Fascicular tachycardia
Fascicular tachycardia is also highly amenable to curative catheter ablation. The tachycardia mechanism involves a re-entrant circuit intimately related to the posterior fascicles of the left conduction system and gives characteristic ECG features of a right bundle branch block, superior access ventricular tachycardia. It may occur in the setting of coronary or other myocardial...
Ventricular arrhythmias: key points

- Not all patients at risk of sudden cardiac death need to be seen by an electrophysiologist
- Most patients with symptomatic ventricular arrhythmias should be seen by an electrophysiologist as they may benefit from curative or ablative therapy
- Patients with “sudden death syndromes” or arrhythmias of uncertain aetiology need to be assessed by an electrophysiologist
- Complex tachycardias. Any supraventricular tachycardia may be highly successful, and an electrophysiologist is a necessary part of any adult congenital heart disease management team.

Potential Pitfalls

A series of supraventricular arrhythmias may generate broad complex tachycardias. Any supraventricular tachycardia may be associated with rate related fatigue of a bundle branch (aberrancy) which gives rise to broad complex tachycardia, then misdiagnosed as ventricular tachycardia. Careful analysis of the ECG usually determines the diagnosis although diagnostic electrophysiology study may be required. In particular, use of flecainide in the management of atrial flutter may result in paradoxical acceleration of the ventricular rate response to a slowed atrial flutter circuit, with bundle branch fatigue related both to rate and the direct effect of flecainide on the specialised conduction system. Other supraventricular tachycardia mechanisms which give rise to broad complex tachycardia include pre-excitation of Wolff-Parkinson-White syndrome with antidromic tachycardia or atrial fibrillation and the characteristic left bundle superior axis of Mahaim tachycardia.

Conclusions

The increasing breadth of cardiac rhythm management strategies requires greater referral to electrophysiologists for their involvement in the management of patients with ventricular arrhythmias. The extent of that involvement will be determined by arrhythmia mechanism, patient symptoms, co-morbidities, and resource availability.

References

2. Large scale studies of antiarrhythmic drugs, in particular the new generation of “class III” antiarrhythmics, have failed to show significant symptomatic or survival benefits in the management of ventricular arrhythmias.
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