Ventricular arrhythmias remain a common problem in everyday practice for the clinical cardiologist. Most concerns are related to the fact that sustained ventricular tachyarrhythmias represent a major cause of sudden cardiac death (SCD) and morbidity in patients with various types of heart disease, and in some cases even in patients with structurally normal hearts. Therefore, risk stratification should be among the first priorities for all patients presenting with ventricular arrhythmias. Recent research developments and technological achievements have resulted in a remarkable increase in the number of diagnostic and prognostic tools for non-invasive risk stratification, providing a multitude of echocardiographic and electrocardiographic markers. On the other hand, the electrophysiology laboratory provides us with great opportunities in terms of completing the risk stratification and implementation of a number of interventional therapies, such as catheter ablation and implantation of the life-saving automatic implantable cardioverter defibrillators (AICD). In this review we present the different electrophysiologically-guided approaches for investigating the great variety of ventricular arrhythmias, ranging from the benign to potentially malignant.

Potentially malignant ventricular arrhythmias

In this group of patients, the study of the cardiac substrate is fundamental. Attempts to empirically suppress ventricular arrhythmias, without any further risk stratification, by means of potent antiarrhythmic medication have failed or, as in the case of amiodarone, have shown only marginal benefits. It is thus reasonable to suggest that all patients who present with complex ventricular arrhythmias should receive a complete assessment using all available electrophysiological means, non-invasive and/or invasive, in order to identify those who would benefit from the administration of the appropriate antiarrhythmic therapy, pharmacological or not. Our strategy should be individualized, according to the nature and the severity of the underlying structural heart disease.

Coronary heart disease (CHD)

It has previously been shown by many
studies that risk factors predicting the development of severe ventricular arrhythmias can be determined from medical history, non-invasive electrocardiography, and echocardiography. These risk factors include a history of multiple myocardial infarctions (MI), syncope, complex ventricular ectopy, activation of the sympathetic nervous system, detection of sites of slow ventricular conduction or ventricular conduction abnormalities, presence of ventricular aneurysm, and left ventricular (LV) dysfunction. The more the risk factors revealed in non-invasive studies, the higher the probability of either triggering sustained ventricular tachyarrhythmia during an electrophysiological study (EPS) and/or the patient presenting with such an episode during the next 3 years of follow up.10-14

Based on the design and the results of 3 out of 4 major primary trials for the prevention of SCD with an AICD, we know that post-infarction patients with non-sustained ventricular tachycardia (VT) and LV dysfunction (LV ejection fraction, EF ≤ 40%) in whom VT and/or ventricular fibrillation (VF) is induced by programmed ventricular stimulation (PVS) have a better life expectancy when treated with an AICD (MA-DIT-I, MUSTT).11,15 Furthermore, even the simple presence of significant LV dysfunction (LVEF ≤ 30%) defines a high risk group of post-MI patients who may also benefit from AICD implantation (MADIT II).16-18 In contrast, when coronary surgical revascularisation is performed in post-MI patients associated with LV dysfunction, with or without the presence of “soft” criteria of late potentials, there is no additional benefit from AICD implantation (CABG-PATCH).19 Thus, before we risk stratify the post-MI patient with the AICD in mind, we should first exhaust all coronary revascularisation procedures available in order to reduce coronary ischaemia and potentially improve the LV function. There is evidence to support the late application of the risk stratification approach after the acute MI phase. Indeed, there was no additional AICD benefit from the early device implantation in the first month post-MI (DYNAMIT, IRIS).20-22 However in a recent retrospective review of the MUSTT trial with EP-guided selection of AICD recipients, the risk of arrhythmic death did not vary as a function of time from the most recent MI.23 The LVEF has emerged as the simplest and most important risk stratifier after the results of the MADIT-II trial. Until more reliable tools for identifying a high risk for SCD are recognised, a low threshold for AICD implantation for primary prevention in patients with significant LV dysfunction should be applied.16,17,24-26 Attempts to introduce scoring systems that include clinical, laboratory and electrocardiographic parameters (e.g. New York Heart Association, NYHA class > II, QRS duration > 120 ms, age > 70 years, presence of atrial fibrillation, and blood urea nitrogen > 9 mmol/L) have been made, but experience is still limited.27,28

However not all post-MI patients with LVEF ≤ 30% are at risk of SCD. It is estimated that 25% of this patient population are at low risk, based on the absence of complex ventricular ectopy, inducibility of VT/VF on PVS, prolongation of the QRS complex, and symptoms of advanced congestive heart failure.29,30 In such patients the risk stratification process, including PVS, could be repeated periodically, every 2 to 3 years, given its high negative predictive value. A high negative predictive value has also been claimed when no late potentials are found on the signal-averaged ECG (SAECG), whereas the positive predictive value is relatively low (<30%).31 The SAECG is thus considered a strong predictor of arrhythmic death and total mortality. Most of these studies excluded post-MI patients with significant prolongation of the unfiltered QRS complex on the standard 12-lead ECG.31-36 a condition frequently met among high-risk post-MI patients with potentially malignant ventricular arrhythmias. There is evidence that late potentials could be identified even among these patients, provided that modified criteria are applied. When non-conventional criteria of a very long filtered QRS duration (fQRS ≥ 145 ms) with a low amplitude signal in its terminal portion (LAS ≥ 55 ms) and a significant depression of its voltage (RMS ≥ 17.5 μV) are found, there is a high likelihood of inducing VT on PVS.36 A series of studies demonstrated a very high negative predictive value for predicting ventricular arrhythmias for microvolt T-wave alternans (MTWA) in the post-MI (and non-CHD) population, regardless of the severity of LV dysfunction.37-40 We previously demonstrated that an inverse spatial QRS-T angle circadian variation is associated with an adverse outcome in post-MI patients, whereas a normal pattern is associated with a favourable outcome.31 However, the prognostic value of heart rate variability, baroreflex sensitivity, heart rate turbulence, and deceleration capacity of heart rate, which reflect the function of the autonomic nervous system and of repolarisation parameters such as QT dispersion, QT dynamicity and QT variability, remains controversial.16,17,24,25

It should be mentioned that 2 out of 3 SCD vic-
tions with CHD have LVEF ≥ 35%. Among post-MI patients with no severe LV dysfunction (LVEF in the 30% to 40% range) or even mild LV dysfunction (LVEF ≥ 40%), one can meet patients at increased risk of SCD when indices such as non-sustained VT, inducibility of sustained ventricular tachyarrhythmia on PVS and/or prolongation of the QRS complex are present. Furthermore, beyond the LVEF there are a number of other non-invasively derived ECG indices, including heart rate variability, QTc duration, late ventricular potentials, and T-wave alternans, all of which have been associated with an increased risk of SCD. These additional non-invasive ECG risk stratifiers have a low positive predictive value when examined alone, and thus have not been thoroughly investigated in prospective primary prevention AICD trials. However, the positive predictive value is markedly increased in subpopulations of post-MI patients when multiple risk factors are present. In a recent observational study of 1041 post-MI patients with well preserved LVEF ≥ 40% (average 55 ± 10%), the incidence of non-invasively derived ECG indices of risk, such as non-sustained VT, late potentials and T-wave alternans, was estimated at about 10%. The presence of such risk factors was associated with a higher incidence of major arrhythmic events during the long-term follow up. It is unknown how many of these post-MI patients would have had inducible VT/VF on EPS. Other electrocardiographic predictors of cardiovascular events and SCD recently identified in this group of patients include the fragmented QRS complexes (notched QRS complexes unrelated to bundle-branch block) and early repolarisation (defined as an elevation of the QRS-ST junction of at least 0.1 mV from baseline in inferior or lateral leads), respectively. Indices of autonomic function (heart rate variability, baroreflex sensitivity, heart rate turbulence) may also predict VT/VF. Recently, a scoring system was proposed for patients with stable CHD and relatively preserved LVEF (>40%), based on a number of clinical factors predicting SCD risk. Induction of VT or VF with PVS is a stronger predictor of risk for ventricular tachyarrhythmias in patients with well preserved, than in those with moderately to severely reduced ventricular function. Although it is unknown whether AICD therapy may offer a significant survival benefit in such CHD patients, one can argue to follow a more aggressive risk stratification approach, including PVS, in all of these patients, implementing a device in those with inducible sustained ventricular tachyarrhythmias.

The cost effectiveness of AICD therapy for the primary prevention of SCD in the post-MI patient has been a matter of discussion. When the device is used based on more stringent risk stratifiers, including PVS induction of VT/VF (MADIT-I, MUSTT patient population) with the concurrent presence of complex ventricular ectopy and/or late potentials, the incidence of appropriate AICD activation during the short-term follow up is high. In contrast, the corresponding incidence of appropriate AICD activation is lower among the MADIT-II patient population, especially when no late potentials or significant QRS prolongation are detected. It could be argued that the device therapy can safely be postponed until the repeat risk stratification approach identifies a higher risk among post-MI patients with LV dysfunction in whom no significant ventricular ectopy, QRS prolongation, late potentials, T-wave alternans or inducible sustained ventricular arrhythmias are found. Provided that the underlying CHD remains stable, the PVS could be repeated after 3 years if in the meantime no additional non-invasive risk stratifiers emerge. This strategy may be more realistic in a world basis application given the economic and logistic constraints, as well as a non-insignificant incidence of late complications associated with the current AICD technology as it is applied today. Indeed, AICD research and technology has a long way to go before it can be uniformly applied to lower risk CHD patients. The devices have to be markedly reduced in size and weight, have to be of longer duration, limiting the need of replacement, to be smarter in recognising truly life-threatening ventricular arrhythmias; the electrodes have to be smaller in size and more resistant to time, and the risk of device-related infection has to be better controlled.

**Idiopathic hypertrophic cardiomyopathy (IHCM)**

Sudden death accounts for 50% to 70% of deaths associated with IHCM and can potentially affect anyone with the disease, although it is more common in younger age groups. Thus, a non-invasive risk stratification strategy is an issue of fundamental clinical importance and should be adopted for every patient with this entity, especially in the young. Moreover, there is a proven high impact of protection offered by AICDs to high-risk individuals with IHCM.

Major risk factors associated with higher rates of SCD have been identified; however, there are
still doubts regarding the individual predictive value of each of them and so risk stratification has not yet been completely systematised. Additionally, it seems that there is an association of certain genetic defects with SCD, even when the presence of hypertrophy is minimal or absent. Risk predictors include:

a. The detection of complex ventricular arrhythmias on ambulatory electrocardiography. The risk for SCD is higher with frequent, repetitive and prolonged episodes, whereas when sporadic and transient the prognosis is benign. A high negative and a low positive predictive value is suggested, with a favourable prognosis and mortality rates lower than 1.5% per year in asymptomatic patients with brief and infrequent episodes of non-sustained VT on 24-hour ECG ambulatory monitoring. On the other hand, children and young adults rarely have ventricular arrhythmias, but when these are present the positive predictive value is high.

b. A history of aborted SCD defines the clinical group with the highest risk for SCD, since the possibility to develop a new sustained VT/VF episode is as high as 10% per year.

c. A history of syncope, which might be due to ventricular or supraventricular tachy- or bradyarrhythmias, has been recognised as an independent risk factor for SCD. Syncope associated with massive LV hypertrophy usually requires prophylactic treatment, especially in the young.

d. A family history of SCD in first-degree family members under 40 years old.

e. Excessive hypertrophy of the interventricular septum (>30 mm). An association between the echocardiographically determined extent of LV hypertrophy and mortality has been identified. In a later study, however, the risk of SCD and AICD activation appears to depend more on the number of risk factors for SCD than on the severity of hypertrophy alone. In very young patients, the risk is higher and justifies the implantation of an AICD.

f. An abnormal blood pressure response to exercise testing is associated with SCD, especially in young individuals, where a high negative predictive value is reported. However, when it is an isolated abnormality, not associated with other risk markers, no prophylactic treatment is required.

The probability of SCD is significantly higher when multiple risk factors are detected during non-invasive assessment and, in general, the more the risk predictors present, the higher the risk. Individuals with one marker are considered to be at intermediate risk, with an annual incidence of sudden death ranging from 1% to 1.5%, whereas the presence of two or more markers increases the annual mortality rate to more than 3%. The group of patients manifesting the lowest risk for SCD (less than 1% per year) consists of adults in NYHA functional class I/II, without a family history of SCD, who do not present with syncope, non-sustained VT on 24-hour Holter monitoring, or abnormal blood pressure response during exercise, and who additionally exhibit a pressure gradient ≤30 mmHg, maximum LV wall thickness ≤20 mm and left atrial diameter ≤45 mm. These patients can be strongly reassured. In individuals at low or intermediate risk for SCD, the risk stratification process should be repeated every 3-5 years.

Other markers related to a high risk for SCD in patients with IHCM are: myocardial ischaemia, obstruction of the LV outflow tract, paroxysmal atrial fibrillation, conduction system disease, accessory pathway, and over-activation of the sympathetic nervous system. The predictive value of markers such as the presence of late potentials on SAECG, heart rate variability, and QT dispersion has been debated. Additionally, other risk factors, such as fractionation of paced RV electrograms, late gadolinium enhancement on magnetic resonance, and genotyping, have been investigated, but to date the results are contradictory or preliminary.

Implantation of AICDs in patients with IHCM is a safe and effective preventive therapy marked with a class I indication for secondary and class IIB for primary prevention. The criteria used for AICD implantation are still empirical, based on clinical experience. Thus, it has been currently suggested that an AICD should be implanted for primary prevention in cases where two or more of the previously described risk factors are present. There is no real consensus regarding patients with just one risk factor and treatment decisions should thus be individualised, considering the person’s age, the quantitative aspects of the risk factor involved, and the desires of the fully informed patient. Even a single marker of high risk may represent sufficient evidence to justify prophylactic AICD insertion in selected patients with IHCM. Interestingly, a recent study showed that percutaneous alcohol septal ablation, a relatively new therapeutic strategy in IHCM, results in a transmural scar in the hypertrophied proximal ventricular septum and actually increases the risk for SCD, given...
that AICD shocks were 4-fold more common compared to surgical myectomy.73

The role of the EPS in IHCM is under investigation and still remains a matter of debate, with older studies supporting an excellent long-term prognosis in cases where sustained ventricular tachyarrhythmias are not induced.57 It can be used in borderline cases with one risk factor present, such as non-sustained VT, history of unexplained syncope, family history of SCD, or an abnormal response to exercise. Induction of sustained ventricular arrhythmias on PVS could facilitate the decision-making process for the AICD implantation. It could also be useful in cases where permanent antibradycardia pacing is considered due to coexisting sinus node dysfunction or/and significant conduction defects.

It should be mentioned that AICD therapy in high risk IHCM patients has not been tested in a prospective controlled fashion. Based on a multi-centre retrospective collection of cases, we know that AICD implantation is effective for subjects considered as “high-risk”, although the long run AICD appropriate activation rate for the primary prevention of SCD is lower than in other disease states such as CHD and idiopathic dilated cardiomyopathy (Figure 1).58 Whether PVS results might have improved the selection process of those IHCM patients who will get the most from the AICD therapy remains unknown.

Idiopathic dilated cardiomyopathy (IDCM)

The risk of SCD in patients with IDCM is known to be significant.17 A risk stratification approach, however, that would include the history, electrocardiographic and echocardiographic findings has not been sufficiently investigated and evaluated in large prospective trials.

The presence of complex ventricular arrhythmias, such as non-sustained VT in 24-hour ambulatory ECG monitoring, is common in patients with IDCM and has been associated not only with a higher risk for SCD but also with an increased overall mortality.75,76 Moreover, it has been reported that LVEF is a significant risk predictor for severe arrhythmias.26,75,77

Figure 1. Ventricular tachycardia recorded during interrogation of an automatic implantable cardioverter defibrillator (AICD) in a patient with idiopathic hypertrophic cardiomyopathy. Interrogation of an AICD in a 14-year-old patient with idiopathic hypertrophic cardiomyopathy and multiple risk factors, who underwent device implantation for the primary prevention of sudden cardiac death. Although in the first strip it remains unclear whether the cause of the AICD activation was atrial fibrillation or non-sustained VT, in the second strip the device intervention successfully interrupted an episode of ventricular flutter accompanied with severe dizziness. (From: Gatzoulis K, Gialafos J. Dual Chamber Antitachycardia Cardioverter Defibrillators. Another Step in the Treatment of High Risk Patients. Hellenic J Cardiol 2003; 44: 71-9.)
In general, patients presenting with severe LV dysfunction, a history of syncope and recorded episodes of non-sustained VT are considered to be at high risk for sustained VT and SCD, although these risk factors are less well defined in this case than in CHD.20 The role of PVS in IDCM remains unclear.78-81 Many authors believe that the induction of polymorphic VT or VF represents a non-specific response.82-85 However, it was recently shown that induction of polymorphic VT/VF is related to more AICD interventions over the long term than induction of sustained monomorphic VT or non-induction of VT.86 It is also believed that, among asymptomatic patients, PVS does not have a place in risk stratification, although in some studies the incidence of appropriate AICD shocks during follow up in inducible patients was found to be higher than in non-inducible.73,84,85,87 The type of induced ventricular arrhythmia depends on the type of presenting clinical tachyarrhythmia.78,88-92 Indeed, in cases of IDCM patients presenting with sustained VT, the induction of sustained ventricular tachyarrhythmias on PVS is extremely high, falling to 40% when the index arrhythmia is cardiac arrest and to 25% when it is non-sustained VT.78,88-92 In summary, although induction of sustained VT during PVS is generally associated with a poor prognosis, in IDCM patients it is considered to be of minor value for predicting subsequent arrhythmic events.78-81,93 Contrary to this so far prevailing view, there is old as well as recent evidence that the induction of sustained VT/VF among either asymptomatic or syncopal patients is the strongest predictor of future malignant ventricular arrhythmia events and thus might have a potential role in the primary prevention of SCD in this population.92-94 Such information might be particularly important for the management of IDCM patients at earlier stages of heart failure, with better preserved LVEF, when presenting with complex ventricular ectopy.91 Thus, prospective studies are necessary for precise risk stratification.

On the other hand, magnetic resonance imaging showing areas of delayed gadolinium enhancement might be helpful in identifying patients with IDCM or other non-ischaemic cardiomyopathies at risk, but this issue is still under investigation.95

Although two of the early studies have failed to demonstrate any improvements in survival after AICD implantation in patients with IDCM, more recent data revealed a protective effect in terms of SCD prevention and reduction of total mortality.17,87,96-98 In a randomised multi-centre trial including 458 patients with IDCM, LV dysfunction and non-sustained VT, prophylactic AICD implantation showed a tendency to better long-term prognosis, although not reaching the levels of statistical significance.97 Similarly, a borderline trend for improved survival with an AICD among IDCM patients with LV dysfunction was well documented in the SCD-HeFT population.17 Additionally, a high incidence of appropriate shocks in AICD recipients with significant LV dysfunction for both primary and secondary prevention was recently documented.74,77,99-101

It appears that the combination of complex ventricular ectopy with significant LV dysfunction defines a high-risk group of symptomatic heart failure IDCM patients who may be protected by an AICD regardless of the results of PVS. Whether this is true in asymptomatic heart failure IDCM patients, with better preserved LV function, remains unknown. In summary, until ambiguous aspects are resolved in the light of newer data, it is recommended that all invasive and non-invasive diagnostic information should be collected and every case should be individualised before deciding what the proper therapy should be (Figure 2A & B).

### Arrhythmogenic right ventricular cardiomyopathy/ dysplasia (ARVC/D)

A common limitation of the studies investigating ARVC/D is the small number of patients included, due to logistical difficulties in enrolling subjects with this unusual form of cardiomyopathy. Underpowered studies often prohibit investigators from drawing safe conclusions about the best approach for primary prevention of SCD in individuals with ARVC/D presenting with complex ventricular arrhythmias. In general, young age, a family history of ARVC/D or SCD, syncope or aborted SCD, recorded episodes of VT, QRS dispersion ≥ 40 ms, T-wave inversion beyond V1 and LV involvement are considered to be the major determinants for adverse prognosis and impending sudden death.102,103

Therapy with AICD implantation has been proven to be life-saving in ARVC/D.104 Implantation for secondary prevention is strongly recommended. Indications for primary prevention are documented non-sustained VT and/or syncope, in the presence of risk factors such as extensive, progressively worsening RV dysfunction, LV involvement, polymorphic VT, late potentials on SAECG, epsilon wave and a family history.102,105,106 Moreover, in asymptomatic patients
without a family history, if ARVC/D is severe PVS is recommended. If negative, conservative treatment with β-blockers and follow up should be preferred. In cases where sustained VT is triggered, the possibility of prophylactic implantation of an AICD in combination with antiarrhythmic drugs should be considered. In asymptomatic patients with a family history, it is controversial whether an EPS should be carried out, even in patients at low risk. On the other hand, in asymptomatic patients without a family history and a mild form of ARVC/D, as well as in cases presenting with sustained VT and palpitations but with a low risk profile (e.g. none of the previously mentioned risk factors), medical treatment and/or ablation is recommended (Figure 3).102-118

Catheter VT ablation has been proposed in drug-refractory cases and, although effective in the short term, has been associated with a high rate of recurrence.102,117

In patients with ARVC/D the right ventricle is globally affected and thus AICD implantation is technically challenging. Additionally, there is a probability of gradual deterioration of both pacing and sensing thresholds of the defibrillator lead over time. However, it is possible that this type of treatment results in a better long-term prognosis in ARVC/D compared to patients with CHD or IDC and severe LV dysfunction.

**Congenital heart disease**

Sudden cardiac death, of presumed arrhythmic aetiology, remains a leading cause of mortality in patients with congenital heart disease, showing an increased incidence as the patient ages.119-121 Furthermore, the number of adults with surgically corrected congenital heart disease has been increasing in the last years. Although recent data demonstrate an increased risk of SCD in surgically corrected tetralogy of Fallot, great vessels transposition (Mustard or Senning operation), patients after the Fontan procedure, coarctation of the aorta, and aortic stenosis, it remains unclear how these patients should be approached when they present with complex ventricular arrhythmias.122-126

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**Figure 2.** A: A 12-lead Electrocardiogram (ECG) and signal averaged electrocardiogram (SAECG) of a 72-year-old patient with idiopathic dilated cardiomyopathy at an early stage (left ventricular ejection fraction 45%, New York Heart Association class I). Non-invasive assessment revealed intermittent complete heart block, frequent episodes of non-sustained ventricular tachycardia and positive late potentials. B: The subsequent EPS performed in the same patient documented the presence of high-degree atrioventricular block. Additionally, sustained monomorphic ventricular tachycardia was easily induced. The patient remains alive 7.5 years later with the automatic implantable cardioverter defibrillator (AICD) interrupting 6 episodes of sustained VT and ventricular flutter.
Adults with unoperated aortic stenosis represent the highest-risk subgroup for SCD and ventricular arrhythmias in patients with congenital heart disease that unfortunately persists despite surgical repair.\textsuperscript{125} It has been suggested that, similarly to other pathological conditions affecting the left or right ventricle, diagnostic techniques like ambulatory electrocardiography, SAECG and EPS should be used in order to determine the risk of SCD and subsequently administer an efficient antiarrhythmic treatment.\textsuperscript{127} In terms of selection of the most effective methods for SCD prevention, radiofrequency catheter ablation of the site of VT origin and AICD implantation have been proposed (Figure 4).\textsuperscript{127-131} The former is a promising therapy but experience is still limited, whereas AICDs are considered to have a favourable impact on long-term outcome.\textsuperscript{132} The latest guidelines for the management of patients with congenital heart disease, suggest the use of AICDs in SCD survivors, those with spontaneous sustained VT not successfully ablated, and those with inducible VT with unexplained syncope and impaired RV or LV function.\textsuperscript{133}

Significant progress has been made in recent years in the risk stratification process of patients with surgically corrected tetralogy of Fallot.\textsuperscript{124,134-139} High-risk patients are those who had the operation at an older age with several years of postoperative follow up, with right ventricular dysfunction and dilatation, as well as significant pulmonary valve regurgitation.\textsuperscript{124,134-139} The 12-lead ECG shows marked prolongation of the QRS complex $\geq$180 ms, and an annual increase in QRS duration with right bundle branch block.\textsuperscript{124,134-139} Other recognised non-invasive risk factors are: increased cardiothoracic ratios,\textsuperscript{139} at least moderate tricuspid valve regurgitation and peripheral pulmonary stenosis,\textsuperscript{139} a higher QT dispersion,\textsuperscript{139} impaired heart rate variability,\textsuperscript{140} frequent ectopic beats,\textsuperscript{134} increased RV systolic pressures,\textsuperscript{141} complete heart block,\textsuperscript{141,142} increased JT dispersion,\textsuperscript{143} late gadolinium enhancement on MRI scan,\textsuperscript{144} and LV dysfunction.\textsuperscript{145} In the early stages, on the other hand, high-risk patients might be recognised by positive late potentials on the SAECG, in addition to mild RV dilatation and non-sustained VT on the ambulatory ECG.\textsuperscript{146} A scoring system derived from surgical, haemodynamic, electrocardiographic and electrophysiological factors, categorising patients as low, intermediate and high-risk has been reported.\textsuperscript{147} In patients with moderate risk, further stratification by means of PVS may be helpful.\textsuperscript{148-149} In patients demonstrating a high risk, AICDs are increasingly utilised in primary and secondary prevention; however, further research is essential.\textsuperscript{147-150}

Finally, in patients who have undergone the Mustard or Senning operation, atrial tachyarrhythmias\textsuperscript{151} and systemic RV dysfunction\textsuperscript{152} have also been identified as important contributors to SCD. In a retrospective study, risk markers included the presence of symptoms related to arrhythmia or cardiac failure and a history of documented atrial fibrillation or flutter, whereas the electrocardiogram, chest X-ray, and Holter findings were not predictive of SCD.\textsuperscript{153} The role of AICDs in such patients remains unclear.\textsuperscript{153}

**Patients without underlying heart disease**

Complex ventricular arrhythmias, such as frequent ventricular ectopic beats, ventricular couplets and non-sustained VT, are considered to be of favourable prognosis in patients without structural heart disease,
provided that conditions like Brugada syndrome, long-QT syndrome, idiopathic ventricular tachycardia, or subclinical forms of ARVC/D are excluded. The diagnosis of Brugada and long-QT syndromes is established from the characteristic ECG changes in addition to the clinical presentation and a positive family history. On the other hand, further investigation for idiopathic ventricular tachycardia and ARVC/D should take place in patients presenting with ventricular arrhythmias originating from the RV.

In a series of 37 patients without underlying structural heart disease, who presented in our department with a complex ventricular arrhythmia that was originally classified as “idiopathic ventricular arrhythmia from the right ventricle”, changes in the 12-lead ECG and the SAECG, as well as minor abnormal findings in echocardiography—especially in the RV—were indeed not infrequently recorded. Furthermore, sustained ventricular tachyarrhythmia was occasionally triggered on PVS. The prognostic value of these findings, as well as the possibility that they could be related to subclinical forms of RV cardiomyopathy, are currently under investigation.

Another group of patients that requires further investigation when presenting with non-sustained VT without detection of underlying structural heart disease, are the elderly. It is possible that, besides the well known conduction abnormalities often recognised in these patients, degeneration of the Purkinje fibres leading to organised re-entry circuits may also develop (Figure 5).

Finally, patients with multiple risk factors for CHD who present with non-sustained VT should be further investigated to exclude CHD, even when exercise testing is normal.

In general, patients without apparent heart disease who present with complex ventricular arrhythmias should be thoroughly examined. In a retrospective study of 270 patients who presented with sudden cardiac arrest in the “absence” of heart disease, careful examination revealed structural disease in 95% of them.

**Congestive heart failure (CHF)**

The detection of complex ventricular arrhythmias in patients with CHF of any aetiology is not rare, and is related to an increased cardiac mortality and a high incidence of SCD.

In addition, AICD implantation in these patients was recently proven efficacious, resulting in reduced incidence of SCD and prolonged life expectancy. Results from the MADIT II trial revealed that implantable defibrillators should be considered in all post-MI patients with severe ventricular dysfunction. In addition, SCD-HeFT, a study recruiting patients with NYHA class II/III and LVEF<35% to receive placebo, amiodarone, or an AICD, demonstrated an absolute mortality reduction of 7.2% after five years in patients who received an AICD. This evidence led the US Centre for Medicare & Medicaid Services to conclude that an AICD is “reasonable and necessary”.

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**Figure 4.** A 12-lead electrocardiogram (ECG) and electrophysiological study (EPS) performed in a 38-year-old patient with a surgically repaired atrial septal defect 12 years ago. For the last 4 years the patient presented with multiple episodes of paroxysmal atrial flutter and wide-complex tachycardia (WCT). Figure 4A shows WCT reproduced during EPS. Atrioventricular dissociation can be observed, indicating the presence of sustained ventricular tachycardia (VT). In figure 4B entrainment of sustained VT can be observed during pacing from the successful ablation VT site in the right ventricle. Presystolic electrograms were also recorded at this site.
for “patients with ischemic cardiomyopathy, prior MI, NYHA Class II/III, and measured LVEF<35%.” Furthermore, according to the current guidelines, in patients with CHD, LVEF≤35%, NYHA Class II/III and LVEF≤30%, or NYHA Class I, 40 days post-MI, are all indications for AICD implantation (Class IA), whereas in patients with LVEF≤40% plus the presence of non-sustained VT on Holter monitoring and inducible VT on PVS, the indication for AICD insertion is classified as IB. In cases of LVEF in the range 30-35% and NYHA class I, the indication is not specified. On the other hand, in IDCM patients with LVEF<35%, in NYHA class II/III and LVEF<35% in NYHA class I, the indications for AICD implantation are I (level of evidence B) and IIb (level of evidence C), respectively.

The appropriate AICD activation rate during the long-term follow up is higher when the risk stratification process is EP guided and clearly ventricular arrhythmia oriented. We previously demonstrated that induction of sustained VT on EPS predicted appropriate AICD activation in biventricular AICD recipients. This implies that better risk stratification tools, beyond the degree of LV dysfunction, are needed if the number of patients likely to benefit from an AICD is to be maximised.

The same approach should also be used for candidates for biventricular pacing in an advanced stage of CHF, with intraventricular conduction abnormalities, and in patients who show a delay in LV contraction, even at earlier stages of heart failure (Figure 6). Indeed, patients with CHF treated with biventricular pacing plus an AICD not only demonstrated a significant clinical improvement, but also showed the longest life expectancy.

Benign ventricular arrhythmias

The long-term prognosis of patients presenting only with single ventricular ectopic beats, without complex forms of ventricular arrhythmia recorded on the ambulatory ECG, and when underlying structur-
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al heart disease is not detected, is excellent. Occasionally, in addition to the regular clinical follow up, such benign forms of ventricular arrhythmias may require suppression. In these cases, the effectiveness of the antiarrhythmic medication administered is clinically assessed, while the cost of possible side effects should be taken under consideration. Endocardial radiofrequency catheter ablation of the site of origin of the ventricular ectopic beats has been reported to be effective, and should be reserved for only those rare cases that do not respond to medical treatment.154,173-179

References


Figure 6. A 12-lead electrocardiogram (ECG), signal averaged electrocardiogram (SAECG) and electrophysiological study (EPS) in a 65-year-old patient with a history of myocardial infarction, left bundle branch block (LBBB) and congestive heart failure (New York Heart Association, NYHA stage III-IV), presenting with episodes of non-sustained ventricular tachycardia (VT) and syncope. In figure 6A, LBBB can be identified on the 12-lead ECG. In addition, the SAECG shows positive late potentials when modified criteria are applied. In figure 6B, the EPS results are presented, showing an HV interval within normal limits and induction of sustained VT. The patient remains alive, in good clinical condition (no syncope, NYHA stage II) 8 years later, having had the biventricular automatic implantable cardioverter defibrillator (AICD) replaced twice after interrupting repeat episodes of sustained VT silently with antitachycardia pacing.


Ventricular Arrhythmias


European Society of Cardiology Committee for Practice Guidelines, European Heart Rhythm Association the Heart Rhythm Society. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death-executive summary: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (writing committee to develop guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death) developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Eur Heart J. 2006; 27: 2099-2140.


