Original Research

Outcome of Patients with Haemodynamically Stable Ventricular Tachycardia Treated with an Implantable Cardioverter-Defibrillator

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Introduction: The benefit of implantable cardioverter defibrillator (ICD) therapy in patients with haemodynamically stable ventricular tachycardia (VT) is not well documented.

Methods: In this single-centre observational study, we examined the medical records of 53 patients (48 men, mean age 66 ± 1 years) treated with an ICD. The patients were classified into four groups with comparable clinical and electrophysiological characteristics, as follows: patients presenting with (a) stable VT, (b) unstable VT, (c) cardiac arrest, and (d) non-sustained VT and induced sustained VT or ventricular fibrillation (VF) on electrophysiological study. Kaplan-Meier event-free survival curves were constructed and the incidence of appropriate device therapy was compared among the four groups.

Results: All patients had structural heart disease with a mean ejection fraction of 32.5 ± 1.3%. During a mean follow-up period of 35.5 ± 2.7 months, event-free survival was similar in the four groups. However, appropriate device therapy occurred in 9 (81.8%) patients with stable VT, in 6 (44.4%) patients with unstable VT, in 2 (33.3%) patients with cardiac arrest and in 6 (33.3%) patients with non-sustained VT and induced sustained VT/VF. Compared to the total patient cohort, appropriate therapy was significantly (p=0.024) more common in patients presenting with stable monomorphic VT. In 2 (22.2%) of these patients, the tachycardia rate was faster than the presenting VT.

Conclusions: High recurrence rates are observed in patients with structural heart disease and stable VT, with a considerable proportion being faster than the presenting VT. ICD therapy is beneficial and should be offered in these patients.

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Ventricular tachyarrhythmias often lead to sudden cardiac death, constituting a major health-related problem worldwide.[1] These arrhythmias can be classified as ventricular fibrillation (VF), polymorphic ventricular tachycardia (VT) and monomorphic VT. Substantial differences exist between these arrhythmias, not only in the underlying electrophysiological mechanisms but also in their clinical presentation and outcome. In contrast to VF and sustained polymorphic VT, which lead to cardio-respiratory arrest, the haemodynamic stability of sustained monomorphic VT varies widely, ranging from mild symptoms to haemodynamic collapse and death.[2-4]

Observational studies have demonstrated that clinical presentation with VF or haemodynamically unstable VT is a major risk for sudden and total mortality.[5-7] However, conflicting evidence exists with respect to the long-term outcome of patients who present with haemodynamically tolerated, sustained monomorphic VT.

Although earlier studies indicated low sudden death rates in these patients,[5] this view was challenged by subsequent reports.[8,9] Thus, the clinical management of patients with haemodynamically tolerated VT continues to be a matter of considerable controversy,[10-12] as exemplified in current practice guidelines.[13]

The introduction of the implantable cardioverter-defibrillator (ICD) by Michel Mirowski in 1980 was a major milestone in the development of the antiarrhythmic armamentarium.[14] Compared to pharmacological antiarrhythmic therapy, several clinical trials have shown improved survival after device implantation in patients experiencing VT/VF.[15-17] Based on these findings, ICDs have become the standard of care for these patients. However, in most major clinical trials evaluating the efficacy of ICD therapy[15-17] patients presenting with VF, polymorphic VT and monomorphic VT were grouped together. Consequently, data concerning patients with sustained monomorphic VT are available only from *post hoc* analysis of patient subgroups and, as such, are more likely to be biased by confounding factors. Moreover, since most prospective randomized trials[15-17] excluded patients with haemodynamically stable sustained monomorphic VT, information about the clinical outcome of such patients originates mostly from non-randomised studies.[5,8,9]

Based on the above considerations, the benefit of ICD implantation in patients with sustained, haemodynamically stable, monomorphic VT has not been clearly demonstrated. In the present study, we aimed to provide further information about the long-term outcome of patients with various presentations of ventricular tachyarrhythmias treated with an ICD. In this single-centre observational study, we evaluated the efficacy and safety of ICD therapy in patients with a history of haemodynamically tolerated, sustained monomorphic VT, compared to patients treated with a device for other indications. In addition, we assessed the prognostic value of several clinical variables in relation to survival and appropriate ICD therapy in this patient cohort.

Methods

Patient population and data collection

We have constructed a database for every patient undergoing initial ICD implantation. All implantations performed from October 2001 until the end of December 2007 were included in the present analysis. In-

formed consent was obtained from all patients and the study complied with the Helsinki Declaration of 1975, as revised in 2000.[18]

Baseline data were collected on standardised implant forms and entered into the database prospectively at the time of device implantation. The obtained variables included patient demographics, implant indication, primary cardiac diagnosis and antiarrhythmic treatment. In addition, clinical presentation was recorded, based on the information provided by the patients, their relatives and the medical records of the hospital to which the patient was admitted during the index ventricular arrhythmia. Haemodynamically unstable VT was defined as monomorphic VT requiring immediate cardioversion due to pre-syncope or syncope, associated with a systolic blood pressure below 70 mmHg. Haemodynamically stable VT was defined as monomorphic VT, associated with a systolic blood pressure above 80 mmHg and an adequate level of consciousness. The patients were grouped according to their clinical presentation as follows: (a) haemodynamically stable VT; (b) haemodynamically unstable VT; (c) resuscitated cardiac arrest; and (d) non-sustained VT on 24-hour electrocardiographic (ECG) Holter monitoring and inducible VT/VF on electrophysiological study, in the presence of significant structural heart disease. It should be noted that, as is the general policy in our centre, no implantations were performed in post-myocardial infarction (MI) patients with the indication of poor left ventricular (LV) function alone, i.e. the so-called 'MADIT-II' indication. This is in accordance with national healthcare guidelines, mainly due to socioeconomic restrictions.

In addition to clinical presentation, the following clinical data were collected: New York Heart Association (NYHA) functional class, history of MI, and medical treatment. In patients with coronary artery disease (CAD), the following supplementary variables were recorded: coronary anatomy, history of revascularisation procedures, and the presence of residual ischaemia after revascularisation, based on exercise stress test or thallium scintigraphy. Further information comprised echocardiographic assessment, including measurement of LV ejection fraction (EF) and findings from continuous 24-hour ECG monitoring. During the electrophysiological study, every attempt was made to induce monomorphic VT with similar features to those of the clinical VT. For

the purposes of the present study, detailed information derived from the electrophysiological study was recorded for each patient.

Device programming

All implanted devices were capable of storing intracardiac electrograms. Programming of the device was performed immediately after device implantation by the implanting physician (TMK) and a certified pacemaker/ICD technician (DA). Low basic rate and long atrioventricular (AV) delay values were programmed for bradycardia pacing, aiming at the maintenance of a normal activation sequence. In general, the detection zone for VT was programmed at a cycle length approximately 50 ms higher that the documented VT; VF detection was programmed at a cycle length shorter than 300 ms, invariably at 270-280 ms. Four to ten sequences of antitachycardia pacing were programmed in all patients, irrespective of the presenting arrhythmia. Programming was based on clinical information, as well as on the results of the electrophysiological study and the preceding exercise tolerance testing. Device algorithms discriminating supraventricular from ventricular arrhythmias, namely interval stability and tachycardia sudden onset, were programmed 'on' in all patients. Ventricular electrogram morphology was programmed 'on' during follow-up visits, only in patients classified as having experienced an inappropriate device discharge for supraventricular rhythm(s).

Follow up

Follow-up evaluation was accomplished by outpatient clinical visits, attended by the same physician (TMK) and technician (DA). All follow-up data were recorded on a standardised form. Every patient was seen regularly every 6 months, or at shorter intervals in case of clinical deterioration, device therapy, or substantial device reprogramming. Follow-up data included clinical status and information on ICD therapy, obtained by device interrogation. If the patient experienced an arrhythmic episode, details on ICD therapies were carefully assessed by the implanting physician and the certified technician. ICD therapies were classified as 'appropriate' or 'inappropriate', based on patient symptoms and the analysis of stored electrograms, including the results of antitachycardia pacing. At the end of the study, all data were reviewed independently by four authors. In

case of disagreement between the reviewers, two further authors adjudicated.

If monomorphic VT episodes occurred during follow-up, the tachycardia cycle length was recorded and compared to the cycle length of the presenting arrhythmia. The two cycle lengths were classified as similar, if they differed by <50 ms or as dissimilar, if they differed by ≥50 ms. Mortality data were obtained from the family or from the following physicians. Follow-up data collection was completed by the end of January 2008.

Statistical analysis

All values are given as mean ± standard error of the mean, unless stated otherwise. Cumulative event-free survival rates were estimated using the Kaplan-Meier method. Each patient was censored in case of death or appropriate therapy by the device. Differences in event-free survival between groups were assessed by the generalised log-rank test. In particular, a score was assigned to each event-free survival time using Mantel's procedure[19] and a chi-square value was computed based on the sums (for each group) of this score. Differences in continuous variables were assessed with the use of one-way analysis of variance; in case of significant variance, differences between groups were assessed with the use of the *post hoc* Tukey HSD multiple comparisons test. Differences in categorical variables between two groups were assessed using chi square, after Yates' correction. Differences in categorical variables between three or more groups were assessed with the use of Kruskal-Wallis analysis of variance by ranks; in case of significant variance, differences between groups were assessed using median test. Univariate analysis assessed a large number of clinical and electrophysiologic parameters. After such analysis, those parameters with a p-value ≤0.10 were entered into the multivariate analysis, which was performed using a Cox proportional hazards model. Statistical significance was defined at an alpha level of <0.05.

Results

Patient characteristics

A total of 53 patients (48 men, age 66 ± 1 years) were included in the study. The follow up duration was 35.5 ± 2.7 months (range 1-75 months). Complications of

Table 1. Patient characteristics.

Characteristic	All patients	Stable VT	Unstable VT	Cardiac arrest	Non-sustained VT
n (%)	53 (100)	11 (20.7)	18 (33.9)	6 (11.3)	18 (33.9)
Age (years)	66 ± 1	64 ± 3	67 ± 2	66 ± 2	67 ± 1
Sex (M/F)	48/5	11/0	16/2	5/1	16/2
CAD n (%)	40 (75.4)	6 (54.5)	15 (83.3)	5 (83.3)	14 (77.7)
CABG	15	2	5	1	7
PCI	22	5	7	4	6
Residual ischaemia	8	3	3	0	2
DCM	10 (18.8)	4 (36.3)	1 (5.5)	1 (16.6)	4 (22.2)
Other	3 (5.6)	1 (9.0)	2 (11.1)	0	0
VT ablation	2 (3.7)	1 (9.0)	1 (5.5)	0	0
LVEF (%)	32.5 ± 1.3	29.4 ± 2.1	33.4 ± 3.0	32.5 ± 4.2	33.2 ± 1.7
NYHA:					
I or II	47	10	16	5	16
III or IV	6	1	2	1	2

CABG – coronary artery bypass grafting; CAD – coronary artery disease; DCM – dilated cardiomyopathy; LVEF – left ventricular ejection fraction; NYHA – New York Heart Association; PCI – Percutaneous coronary intervention; VT – ventricular tachycardia.

the implantation included lead dislodgement in one patient, requiring lead repositioning, and pocket erosion in another patient, successfully managed by device generator repositioning. Baseline characteristics of the total patient population are given in Table 1. Ischaemic heart disease was the primary cardiac diagnosis in 75.4%, followed by dilated cardiomyopathy in 18.8%. Hypertrophic cardiomyopathy, hypertensive heart disease and valvular heart disease accounted for the remaining small percentage of implants. All patients with ischaemic heart disease had a history of MI, 8.4 ± 1.2 years prior to the index arrhythmia that led to device implantation. In the total patient cohort, there were 1.7 ± 0.7 episodes prior to the index arrhythmia, without significant differences between groups (F=0.30, p=0.82). Four patients presented with electrical storm, unresponsive to medical treatment in two, and were successfully managed with radiofrequency catheter ablation. One of these cases has been reported previously.[20]

Table 1 also displays patient characteristics of the four groups. No significant differences were found with respect to age (F=0.25, p=0.85), sex (H=1.65, p=0.64), primary diagnosis (H=2.91, p=0.40) or ICD type (H=1.03, p=0.79). Similarly, no significant differences were found in LVEF (F=0.38, p=0.76) and NYHA class (H=0.22, p=0.97). Table 2 shows the antiarrhythmic treatment at the time of the index arrhythmia. No significant differences were found in beta-blockade (H=4.5, p=0.21), or treatment with either amiodarone (H=4.4, p=0.21) or sotalol (H=3.5, p=0.31). No patient was on mexiletine at the time of presentation. These differences remained non-significant, when patients presenting with stable VT were directly compared with those presenting with unstable VT (p=0.30 for beta-blockers, p=0.98 for amiodarone and p=0.80 for sotalol).

Table 3 shows the implanted ICD type and the medical therapy during the follow-up period in the four groups. No significant differences were found in the

Table 2. Antiarrhythmic treatment at presentation.

	All patients	Stable VT	Unstable VT	Cardiac arrest	Non-sustained VT
β-blocker, n (%)	43 (81.1)	10 (90.9)	12 (66.6)	6 (100)	15 (83.3)
Amiodarone, n (%)	10 (18.8)	2 (18.1)	2 (11.1)	0	6 (33.3)
Sotalol, n (%)	4 (7.5)	0	1 (5.5)	0	3 (16.6)
Mexiletine, n (%)	0	0	0	0	0

No significant differences were found. Abbreviations as in Table 1.

Table 3. ICD type and medical therapy during follow-up.

Characteristic	All patients	Stable VT	Unstable VT	Cardiac arrest	Non-sustained VT
n (%)	53 (100)	11 (20.7)	18 (33.9)	6 (11.3)	18 (33.9)
ICD type					
DDD	37	9	12	4	12
VVI	16	2	6	2	6
β-blocker, n (%)	45 (84.9)	11 (100)	13 (72.2)	6 (100)	15 (83.3)
Amiodarone, n (%)	41 (77.3)	10 (90.9)	15 (83.3)	6 (100)	10 (55.5)
Sotalol, n (%)	2 (3.7)	1 (9.0)	1 (5.5)	0	0
Mexiletine, n (%)	7 (13.2)	3 (27.2)	4 (22.2)	0	0
ACEI, n (%)	43 (81.1)	9 (81.8)	15 (83.3)	6 (100)	13 (72.2)
ARB, n (%)	6 (11.3)	1 (9.0)	2 (11.1)	0	3 (16.6)

ACEI – angiotensin converting enzyme inhibitors; ARB – angiotensin receptor blockers. Other abbreviations as in Table 1.

treatment with beta-blockers (H=4.44, p=0.21), angiotensin converting enzyme (ACE) inhibitors (H=2.11, p=0.54), or angiotensin receptor antagonists (H=1.39, p=0.70). During the follow-up period, antiarrhythmic treatment was more frequently used, compared to the period prior to the index arrhythmia. This was evident in the use of amiodarone (18.8% versus 77.3%, χ^2=34.01, p<0.001) and mexiletine (0% versus 13.2%, χ^2=5.51, p=0.01). During the follow-up period, a nearly significant variance (H=7.76, p=0.051) was observed in antiarrhythmic treatment with amiodarone, with patients presenting with non-sustained VT being less likely to receive amiodarone. Similarly, a trend towards a significant variance (H=6.61, p=0.085) was observed in the antiarrhythmic treatment with mexiletine, with patients presenting with monomorphic VT (either stable or unstable) being more likely to receive such treatment.

Electrophysiological study

Of the total study population, 47 patients (88.6%) underwent electrophysiological study. This percentage was comparable in the four patient groups (H=3.32, p=0.34). The results of the electrophysiological study are displayed in Table 4. No significant differences were found in the underlying rhythm between the four groups (H=2.08, p=0.55). Similarly, comparable percentages of patients with sinus nodal dysfunction (H=3.14, p=0.37), AV-nodal dysfunction (H=0.31, p=0.95) and intra- or infra-His conduction disturbances (H=2.73, p=0.43) were found in the four patient groups.

As expected, the percentage of patients with induced monomorphic VT during the electrophysiological study was higher (χ^2=9.02, p=0.0027) in patients who had presented with monomorphic VT (either stable or unstable), compared to patients presenting with either VF or non-sustained VT (either monomorphic or polymorphic). Of the 25 patients who had presented with monomorphic VT and underwent electrophysiological study, the induced monomorphic VT had similar features to the clinical VT in 18 patients, albeit generally faster. In 6 patients the induced VT had 2 or more morphologies, one of which had similar features to the clinical VT. In one further patient who had presented with haemodynamically stable monomorphic VT, only polymorphic VT could be induced during the electrophysiologic study.

Follow-up data

Inappropriate therapy

During the follow-up period, 8 (15.0%) patients had one or more inappropriate therapies delivered by the device, due to atrial fibrillation. Inappropriate shocks occurred in 1 (9.0%) patient who had presented with stable monomorphic VT, in 2 (11.1%) patients who had presented with unstable monomorphic VT, in 1 (16.6%) patient with resuscitated cardiac arrest and in 4 (22.2%) patients with non-sustained VT and induced sustained VT/VF. The occurrence of inappropriate device therapy was not significantly different in the four patient groups (H=1.23, p=0.74).

Table 4. Electrophysiological study results.

Characteristic	All patients	Stable VT	Unstable VT	Cardiac arrest	Non-sustained VT
n (%)	53 (100)	11 (20.7)	18 (33.9)	6 (11.3)	18 (33.9)
EPS	47 (88.6)	10 (90.9)	15 (83.3)	4 (66.6)	18 (100)
Basic rhythm (SR/AF)	45/8	10/1	16/2	4/2	15/3
SN function (normal/abnormal)	34/4	8/2	9/2	2/0	15/0
AVN function (normal/abnormal)	23/15	6/4	6/5	1/1	10/5
Intra- or infra-His block	4	2	0	0	2
Induced arrhythmia, n (%):					
VF	5 (10.6)	0	0	2 (50.0)	3 (16.6)
sust mono VT	36 (76.5)	9 (90.0)	15 (100)	1 (25.0)	11 (61.1)
morphologies (mean ± SD)	1.2 ± 0.6	1.5 ± 1	1.2 ± 0.4	1	1.0 ± 0.2
sust poly VT	4 (8.5)	1 (10.0)			3 (16.6)
non-sust poly VT	1 (2.1)	0	0	1 (25.0)	0
Induced arrhythmia CL (ms)	296 ± 11	325 ± 25	303 ± 19	280 ± 47	252 ± 13
Number of ES (mean ± SD)	2.5 ± 0.6	2.4 ± 0.5	2.5 ± 0.7	2.7 ± 0.5	2.8 ± 0.4
Termination, n (%):					
Shock	22 (46.8)	4 (40.0)	6 (40.0)	2 (50.0)	10 (55.5)
ATP	21 (44.6)	6 (60.0)	9 (60.0)	1 (25.0)	5 (27.7)
Spontaneous	4 (8.5)	0	0	1 (25.0)	3 (16.6)

AF – atrial fibrillation; ATP – antitachycardia pacing; AVN – atrioventricular node; CL – cycle length; EPS – electrophysiological study; ES – extrastimuli; mono – monomorphic; poly – polymorphic; SD – standard deviation; SN – sinus node; SR – sinus rhythm; sust – sustained; VF – ventricular fibrillation; VT – ventricular tachycardia.

Appropriate therapy

During the follow-up period, 25 (47.1%) patients had one or more appropriate therapies delivered by the device. The respective data in the four groups are depicted in Figure 1. Compared to the total pa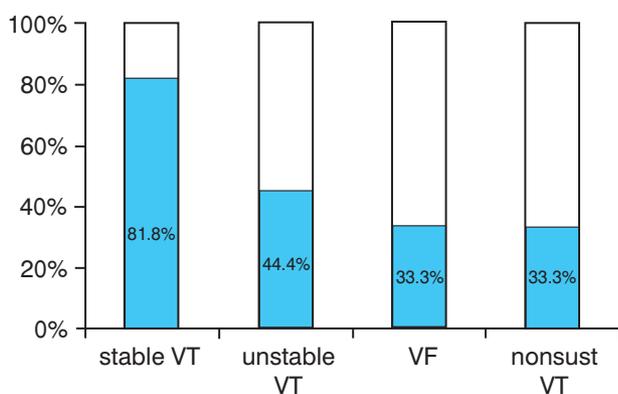tient cohort, appropriate therapy was significantly more common in patients presenting with stable monomorphic VT (χ^2=5.0, p=0.024). In contrast, the occurrence of appropriate therapy by the device was similar in patients presenting with unstable VT (p=0.99), in patients presenting with cardiac arrest (p=0.77) and in patients with non-sustained VT and induced sustained VT/VF (p=0.24), when compared to the total patient cohort.

There was a significant variance (F=3.23, p=0.031) in the total number of VT/VF episodes in the four groups. This was due to significantly (p=0.030) more episodes in patients presenting with stable monomorphic VT, compared to patients with non-sustained VT and induced sustained VT/VF. More specifically, in the 9 (81.8%) patients presenting with stable monomorphic VT who had an appropriate therapy, a total of 448 episodes were successfully treated by the device. The mean number of episodes per patient in this subgroup was 49.7 ± 26.9, with a median value of 20 episodes per patient. Of the total number of episodes, 422 (94.1%) were treated by antitachycardia pacing and the remaining 26 (5.8%) were treated by shocks. The first episode occurred 9.6 ± 5.0 months after device implantation.

In the 8 (44.4%) patients presenting with unstable monomorphic VT who had an appropriate therapy, a

Figure 1. Appropriate device therapy. Compared to the total patient cohort, appropriate device therapy was more common in patients presenting with stable ventricular tachycardia. nonsust – non-sustained; VF – ventricular fibrillation; VT – ventricular tachycardia.

total of 87 episodes were successfully treated by the device. Of these episodes, 76 (87.3%) were treated by antitachycardia pacing and the remaining 11 (12.6%) were treated by shocks. There were 10.8 ± 4.5 episodes per patient in this group, with a median value of 6.5 episodes per patient. The first episode occurred a mean of 9.6 ± 3.6 months after device implantation.

Of the 2 (33.3%) patients presenting with cardiac arrest who had appropriate therapies by the device, one patient had 3 appropriate shocks and the remaining patient had one appropriate shock. In the 6 (33.3%) patients with non-sustained VT and induced sustained VT/VF that had appropriate therapy by the device, there were a total of 15 episodes, of which 7 (46.6%) were treated by antitachycardia pacing and the remaining 8 (53.3%) were treated by shocks. The mean number of episodes per patient was 2.5 ± 0.6, with a median value of 2.0 episodes per patient. The first episode occurred a mean of 15.1 ± 2.8 months after device implantation.

With respect to tachycardia rate during follow up, no significant differences ($\chi^2=0.19$, p=0.66) were found in the comparison of patients who received appropriate therapy from the device in the groups of patients presenting with haemodynamically stable and unstable VT (Figure 2). The tachycardia rate during follow-up was similar to the presenting arrhythmia in 6 (66.6%) patients in the group presenting with haemodynamically stable VT, while in 1 (11.1%) patient the rate was slower. However, in 2 patients (22.2%), the tachycardia was faster; one patient had a faster monomorphic VT, terminated by antitachycardia pacing, and the second patient had VF that was successfully defibrillated by the device. Corrected for the mean follow-up period for the group of patients pre-
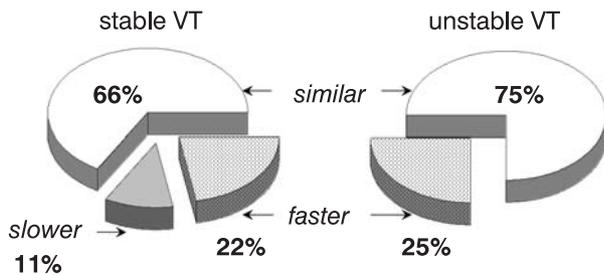
senting with stable monomorphic VT, the incidence of a tachycardia of similar rate was 15.5% per year and the incidence of a faster tachycardia was 5.2% per year. In patients who had presented with haemodynamically unstable VT the tachycardia rate during follow-up was similar to the presenting arrhythmia in 6 (75.0%) patients. In 2 patients (25%) the tachycardia was faster and was terminated by antitachycardia pacing in one and by a shock in the remaining patient.

Event-free survival analyses

During the follow-up period, 5 patients died. The Kaplan-Meier event-free survival curves of the four patient groups are depicted in Figure 3. Event-free survival probability was comparable in the four patient-groups ($\chi^2=4.22$, degrees of freedom=4, p=0.23).

Predictors of event-free survival

The following variables were entered into the univariate analysis (Table 5): age; sex; arrhythmia presentation; primary cardiac diagnosis; LVEF; rate and mode of termination of the presenting arrhythmia; history of revascularisation with either bypass grafting (CABG), percutaneous coronary intervention (PCI), or both, as well as the presence of residual ischaemia (in patients with CAD); basic rhythm during the electrophysiological study, sinus and AV nodal function, presence of intra- or infra-His block, type, rate and mode of termination of the induced arrhythmia, number of ex-
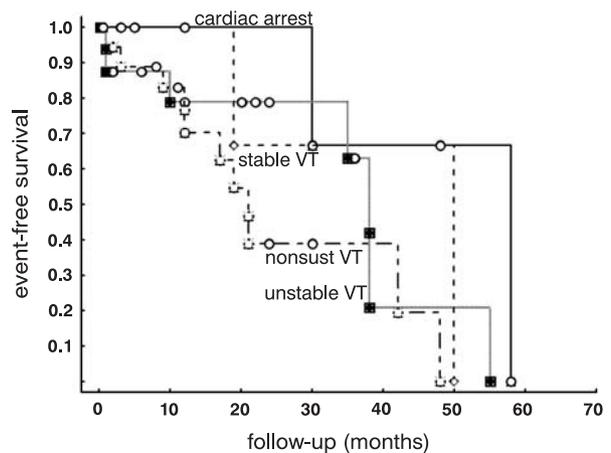

Figure 2. Ventricular tachycardia rate. The incidence of faster arrhythmia recurrences during follow-up was similar in patients with stable and unstable ventricular tachycardia.

Figure 3. Kaplan-Meier event-free survival. Event-free survival was similar in the four groups.

Table 5. Univariate analysis.

Characteristic	Death or appropriate therapy	Event-free survival	p-value
n (%)	30 (56.6%)	23 (43.3%)	
Age	67.0 ± 1.7	66.0 ± 1.8	0.70
Sex (M/F)	26/4	22/1	0.52
stVT/unstVT/CA/nonsustVT	9/11/3/7	2/7/3/11	0.37
CAD/DCM/other	22/5/3	18/5/0	0.55
LVEF	30.1 ± 1.7	35.4 ± 1.9	0.047
NYHA class (I or II/III or IV)	27/3	20/3	0.92
Presenting tachycardia rate	342 ± 15	324 ± 12	0.39
Termination (shock/medical)	14/5	6/3	0.68
Revascularisation (CABG/PCI)	9/12	6/10	0.99
Residual ischaemia (yes/no)	1/20	4/11	0.16
EPS (yes/no)	27/3	19/4	0.70
Basic rhythm (SR/AF)	27/3	18/5	0.42
SN function (normal/abnormal)	19/4	13/1	0.69
AVN function (normal/abnormal)	14/10	9/5	0.98
Intra- or infra-His block (yes/no)	3/21	1/13	0.97
Induced arrhythmia (VT/VF-poly VT/nonsust VT)	23/2/2	13/6/0	0.01
Induced arrhythmia CL	311 ± 15	268 ± 15	0.06
Termination (shock/ATP/spont)	12/11/2	9/7/2	0.98
Number of ES	2.7 ± 0.1	2.5 ± 0.1	0.22
ICD type (DDD/VVI)	22/8	15/8	0.73
VT ablation	1/24	1/17	0.62
β-blockers (yes/no)	25/5	20/3	0.98
Amiodarone (yes/no)	25/5	17/6	0.61
Sotalol (yes/no)	1/29	1/22	0.59
Mexiletine (yes/no)	6/24	1/22	0.20
ACEI or ARB (yes/no)	27/3	22/1	0.80

CA – cardiac arrest; nonsustVT – non-sustained ventricular tachycardia; spont – spontaneous; stVT – stable ventricular tachycardia; unstVT – unstable ventricular tachycardia; Other abbreviations as in tables 1-4.

trastimuli required for induction; ICD type; use of beta blockers and ACE-inhibitors or angiotensin receptor antagonists; additional antiarrhythmic treatment with VT ablation, or medical treatment with amiodarone, sotalol or mexiletine. Of these variables, LVEF, type of induced arrhythmia and the induced arrhythmia rate were entered into the multivariate analysis. After this analysis, none of the variables maintained statistical significance as a predictor of event-free survival. The respective p-values were 0.87, 0.17 and 0.77.

Discussion

This observational study compared the long-term outcome of patients treated with an ICD for haemodynamically stable VT with patients receiving an ICD for other indications. All patients had LV dysfunction with a mean EF of 32.5%. As in most series examining patients with malignant ventricular arrhythmias,[5,8,9] the vast majority of patients in our study had CAD, with a remote history (mean >8 years) of MI. During a mean follow-up period of approximately 3 years, nearly half of our patients had an arrhythmia recurrence and received appropriate therapy by the device. This is in agreement with recent reports,[21] indicating that the arrhythmic risk increases as a function of time in post-MI patients with poor LV function.

Main findings and comparison with previous studies

The main finding of the present study is that patients presenting with stable monomorphic VT had high recurrence rates of the arrhythmia. These recurrences were successfully treated by the implanted ICD, mostly by antitachycardia pacing. More importantly, in a substantial percentage of such patients, with an inci-

dence of around 5% per year, the tachycardia rate during follow-up was faster than the presenting arrhythmia. It should be noted that these high arrhythmia recurrence rates were observed despite intensive antiarrhythmic management, comparable with the current state of the art,[22] which includes a combination of medical treatment and ablation, with[23] or even without[20] newer mapping systems. Thus, in our patient cohort, we used antiarrhythmic class III agents in almost all patients and additional VT ablation in a few. Moreover, most patients received beta-blockade and treatment with either ACE inhibitors or angiotensin receptor blockers.

Our findings are in contrast with the long held belief that patients with haemodynamically well tolerated VT are at low risk for the future occurrence of more severe arrhythmias. This notion was based on earlier studies suggesting that arrhythmia recurrences could be predicted to be well tolerated, thus permitting patients to seek medical attention. For example, Saxon et al[5] reported significantly lower four-year sudden and total mortality in patients presenting with stable VT, compared to those presenting with cardiac arrest. Based on these considerations, altering the tachycardia cycle length with either antiarrhythmic agents or arrhythmia surgery has been regarded as an acceptable treatment endpoint, probably comparable to rendering the tachycardia non-inducible.[24]

The electrophysiological characteristics of the substrate for monomorphic VT have been examined intensively during the past years, mainly because of the refinement of catheter mapping and ablation techniques.[25] In patients with heart disease, such a substrate is formed in myocardial areas with intense fibrosis, leading to anisotropic electrical propagation, hence favouring re-entrant mechanisms. Re-entrant VT typically exists as a 'figure of eight' with rotation of wave-fronts that share a central isthmus.[25] Once the conditions for a re-entrant arrhythmia are met, high recurrence rates of the same re-entrant circuit are observed. However, the complexity of the substrate and the variability of the electrophysiological parameters that lead to re-entry may give rise to tachycardias with different morphologies and/or different rates.[25] Multiple VT morphologies, due to electrophysiological alterations in the re-entrant circuit, are commonly observed in the electrophysiology laboratory. Furthermore, the electrophysiological properties in areas with slow conduction may gradually change over long periods of time, as part of the remodelling process, and may give rise to multiple re-entrant circuits.[26]

Our results confirm the above theoretical considerations and compare favourably with recent studies.[8,9] Bocker et al[8] examined a group of 50 patients who received ICDs after presenting with haemodynamically stable monomorphic VT. They found a 22% incidence of faster VT in a follow-up period of 17 months, documented by ICD interrogation. Similarly, Glickson et al[9] reported that 12% of 82 patients treated with ICDs for haemodynamically well-tolerated VT developed unstable ventricular arrhythmias over a mean follow-up period of 23.6 months, a percentage almost identical to our findings. Our results, examined together with these studies,[8,9] imply that patients with haemodynamically stable VT are at a substantial risk for faster, potentially poorly tolerated arrhythmia recurrences.

Two large observational studies,[27,28] examining the long-term outcome of patients presenting with various types of ventricular tachyarrhythmias, lend further support to our conclusions. Caruso et al[27] analysed the predictors of sudden cardiac death in a large cohort of patients who presented with either sustained VT or resuscitated cardiac arrest over a 6-year follow-up period. In keeping with our results, long-term outcome could not be predicted by clinical presentation on multivariate analysis. In this study,[27] 18% of patients who presented with stable VT suffered arrhythmic death or resuscitated cardiac arrest during follow-up; however, it must be acknowledged that the use of potentially harmful type I antiarrhythmic agents may have contributed to this result. Raitt et al[28] retrospectively compared total mortality in patients presenting with stable VT to those with unstable VT; EF and the extent of CAD were comparable in the two groups. Both groups were treated with ICDs, antiarrhythmic agents, catheter ablation, or a combination thereof, as determined by physician preference. Interestingly, those authors[28] found a higher total mortality at 3 years in the stable VT group, compared to the unstable VT group; multivariable analysis identified a protective effect of ICD therapy. In a similar patient population,[29] haemodynamic stability during VT had no impact on survival and ICD therapy conferred a survival benefit. Thus, it can be inferred that clinical presentation with haemodynamically stable sustained monomorphic VT does not in

itself indicate a benign prognosis in the presence of significant structural heart disease.

Predictors of event-free survival

In addition to the primary aim of the present study, we assessed a large number of variables as possible predictors of event-free survival. Univariate analysis identified low LVEF as a significant predictor of future appropriate therapy by the device, or death. This finding confirms previous reports, in which prognosis was determined predominantly by the severity of structural heart disease and the presence of heart failure.[29] Despite the well established predictive value of poor LV function on arrhythmic and total mortality, the small number of patients in our series precluded confirmation of this finding by multivariate analysis.

Inappropriate shocks

One of the biggest concerns associated with ICD therapy is the discharge of the device for supraventricular rhythms. Such inappropriate shocks may occur in as many as 30% of ICD patients.[30] In keeping with previous experience,[31] our results indicate that the frequency of inappropriate shocks can be kept low with the use of device diagnostic algorithms and proper attention to meticulous programming of the device during follow-up.

Antitachycardia pacing

In our series, the vast majority of the therapy delivered by ICDs was in the form of antitachycardia pacing. This feature was routinely programmed 'on', irrespectively of the presenting arrhythmia and the results of the electrophysiological study. In accordance with previous findings,[31] antitachycardia pacing was highly effective during follow up in our series, usually before the onset of severe symptoms. Thus, our experience suggests that antitachycardia pacing should be advocated in all ICD patients, even in patients with faster VT, which is generally regarded as less amenable to this form of therapy. Moreover, such therapy should be programmed 'on' empirically, irrespectively of the electrophysiological characteristics of the presenting or induced arrhythmias.

The avoidance of shocks by antitachycardia pacing is helpful in preventing symptoms and hospitalisations in patients presenting with either stable or unstable VT, who are at high risk of experiencing arrhythmia recurrences.

Strengths and limitations of the study

We feel that our work adds to the current understanding and management of patients with ventricular arrhythmias. The study cohort, representing a 'real-life' patient population, and the wealth of follow-up data analysed, as a result of the close follow up by a single physician, represent major strengths of the present report. The main limitation of this study is the small number of patients. The relatively long follow-up period may, in part, overcome this limitation. In light of the small number of patients no mortality analysis was attempted in this series. We assessed the event-free survival with censoring events either death or appropriate ICD therapy. However, it is well established that ICD therapy cannot be used as a surrogate for arrhythmic death,[10] mainly because of the wide variability of outcomes after an arrhythmic event in the absence of a device. Thus, mortality analysis using stored ICD electrograms was not attempted in the present study and our data should not be misinterpreted in this direction. Another limitation of the present study is the relative inhomogeneity in the underlying cardiac diagnoses, albeit similar to previous reports.[5,8,9]

Conclusions

In this small-scale observational study, high arrhythmia recurrence rates were found in patients with haemodynamically tolerated VT, in the setting of structural heart disease. These recurrences occurred despite optimal antiarrhythmic treatment complementing ICD implantation. Although most recurrences had features similar to the presenting arrhythmia, a considerable proportion of these patients experienced a faster VT during follow up. All arrhythmic episodes were successfully treated by the implanted ICD, mostly by antitachycardia pacing. Our results strongly suggest that ICD therapy is beneficial in patients with haemodynamically stable VT and should be offered in addition to other antiarrhythmic strategies.

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