Incidence, Determinants, and Prognostic Implications of True Pleomorphism of Ventricular Tachycardia in Patients With Implantable Cardioverter-Defibrillators
A Substudy of the DATAS Trial

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Background—The occurrence of monomorphic ventricular tachycardia (M-VT) with >1 QRS morphology during the same episode (pleomorphism [PL]) or in different episodes (multiple morphologies [MM]) has been described through ECG. Implantable cardioverter-defibrillator (ICD) electrograms (EGs) provide the opportunity to analyze virtually all spontaneous M-VT episodes. We sought to study the incidence, determinants, and prognostic significance of PL and MM as assessed by ICD-EG in a prospective series of patients with ICDs.

Methods and Results—Spontaneous episodes of M-VT were analyzed before ICD intervention. PL was defined as >1 ICD-EG morphology, each having ≥6 consecutive identical beats during the same VT episode, and MM as >1 ICD-EG morphology in different M-VT episodes in the same patient. We analyzed 1881 M-VT episodes from 315 patients followed for 17 months. PL and MM occurred in 6% and 19%, respectively, of the total population (16% and 62% of patients with M-VT). Recurrent M-VT as diagnosis for ICD indication predicted PL and MM. Patients with PL more frequently developed MM (85% versus 15%; P < 0.001) compared to patients without PL. Total mortality (5%) was significantly higher in patients with PL (20%), in patients with MM (11.5%), and in women (12%). In multivariate analysis, only PL (odds ratio, 5.33; P < 0.009) and female sex (odds ratio, 3.1; P = 0.038) predicted mortality.

Conclusions—In a prospective series of patients with ICDs, mostly indicated for secondary prevention, both PL and MM of VT, as judged by ICD-EG, were not uncommon and were strongly associated. Female sex and the development of PL VT were the only independent predictors of mortality. (Circ Arrhythm Electrophysiol. 2011;4:33-42.)

Key Words: tachycardia ventricular ■ cardioverter-defibrillators implantable ■ mortality ■ intracardiac electrogram

S ustained monomorphic ventricular tachycardia (M-VT) occurring spontaneously in patients with prior myocardial infarction (MI) is associated with high rates of arrhythmia recurrence and total mortality.1-3 Recurrent M-VTs with different QRS morphologies in different episodes is a common phenomenon in patients with post-MI M-VT.3-8 Although the term pleomorphic VT has been used several times to describe this situation, the recent consensus document on VT ablation recommends to restrict the term pleomorphic (PL) to a VT that has “more than one morphologically distinct QRS complex during the same episode of VT, but the QRS is not continuously changing.”9,10 The term multiple morphologies (MM), or multiple monomorphic VTs, refers to “more than one morphologically distinct M-VT, occurring as different episodes.”9 Since the original description of PL VT,3 its characterization in terms of clinical consequences has been limited. The development of VT with MM has been associated with failure of antiarrhythmic drug therapy, low acute radiofrequency catheter ablation success, and high rates of VT recurrence.7,8,10

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All previous reports have evaluated MM and PL by ECG. With the increase in the use of implantable cardioverter-defibrillator (ICD) therapy in patients with severe structural heart disease,11-17 the opportunity to observe 12-lead ECG of
M-VT episodes is decreasing, whereas that to observe ICD-stored electrograms (EGs) is increasing. Unlike ECG, ICD-EG allows the analysis of all spontaneous VT episodes and usually from the beginning of the VT episode. ICD-EGs have been shown to be useful in discriminating different M-VTs and sites of ventricular impulse formation. Thus, in the present study, we used ICD-EG morphology as indicative of an M-VT morphology to identify distinct M-VT morphologies. The aim of the study was to evaluate the incidence, determinants, and prognostic significance of PL and MM as assessed by ICD-EG in a prospective series of patients with ICDs, those included in the Dual Chamber and Atrial Tachyarrhythmias Adverse Events Study (DATAS).20

Methods

The design and results of the DATAS trial have been described previously. Briefly, the trial was a prospective, multicenter, randomized study that included patients with ICD indication and compared single- and dual-chamber ICD in clinically significant adverse effects. Inclusion criteria were cardiac arrest due to VT or ventricular fibrillation (VF); spontaneous recurrent sustained M-VT; unexplained syncope with induced VT/VF; and post-MI unsustained VT with inducible sustained VT/VF. All devices implanted were provided by Medtronic Inc (Minneapolis, MN). ICD devices implanted were 7223, 7227, 7229, 7230, 7231, 7250, and 7276. All study patients were followed up at 1, 4, 8, 9, 13, and 17 months. Follow-up period was 17 months for all patients.

Some specific ICD programming parameters were strongly recommended, including 2 zones of tachyarrhythmia detection (VT/380 ms [antitachycardia pacing+shocks] and VF/240 ms [shocks only]) and number of intervals needed to detect (NID) VT (16) and VF (18/24). These parameters as well as all arrhythmic events were stored on floppy discs at each visit, allowing subsequent analysis. Patients in whom ICD-EGs were not available for at least 3 months of follow-up were excluded.

We specifically sought to determine the incidence and implications of PL and MM by analyzing ICD-EGs of all spontaneous M-VT episodes that required ICD therapy. For morphology analysis, we used an HVA/HVB and an Atip/Vring EG-configuration in single- and dual-chamber ICDs, respectively.

Analysis of Arrhythmic Episodes

Only spontaneous M-VT episodes were analyzed, always before ICD intervention. Episodes of polymorphic VT and VF and those considered to be supraventricular23–26 were excluded from the analysis.

Definitions

A new ICD-EG morphology was said to be present when a significant and sustained change in morphology occurred, including changes in polarity of the initial deflection, addition or loss of a deflection, shifts in the dominant polarity of the ICD-EG, and important changes in voltage of a deflection (Figures 1 and 2). Minor changes in voltage of deflections were ignored. PL was defined as 1 stable ICD-EG morphology, each having ≥6 consecutive beats with identical EG morphology during the same VT episode. MM was defined as >1 ICD-EG morphology in different M-VT episodes in the same patient.

Statistical Analysis

Continuous variables were assessed for normality using the Wilk-Shapiro test. Variables with parametric distribution are expressed as mean±SD, whereas those with nonparametric distribution are presented as median and interquartile range (IQR). For statistical analysis, we used Student t test for continuous variables with parametric distribution, Mann-Whitney U test for those with nonparametric distribution, and χ2 test or Fisher exact test for categorical data. For the comparison of paired data, we used Wilcoxon signed rank test. The results from bivariate analyses were used to select variables for the multivariable logistic regression analysis of PL, MM, and mortality. Clinically meaningful potential confounders were age, sex, left ventricular ejection fraction (LVEF), coronary heart disease, New York Heart Association (NYHA) functional class, met inclusion criteria, class III antiarrhythmic drug therapy evaluated at hospital discharge, and number of VT episodes and shock therapy during follow-up. These variables were included in the model regardless of their statistical significance (although not all are presented in the tables). SPSS version 16.0 (SPSS Inc; Chicago, IL) was used. All P values are 2 sided, and statistical significance was established at P<0.05.

Interobserver Agreement Assessment

Interobserver variability of ICD-EG morphological analysis was studied through a blinded independent analysis of all PL and MM

Figure 1. PL VT in 2 different patients. Two distinct ICD-EG morphologies during M-VT can be noted (A and B). *The changing beat.
episodes and a random subset of a similar number of single morphology cases by 3 investigators. Because this analysis was performed by 3 investigators and both variables are dichotomic (only 2 categories), a free-marginal, multirater $k$ coefficient was calculated to assess interobserver agreement.

**Results**

The DATAS trial analyzed 334 patients, 90% of whom received an ICD for secondary prevention of arrhythmic death. There were no ICD-EGs available for a period of at least 3 months in 19 patients. The remaining 315 patients comprised our study population (Figure 3). Patient mean age was 64±10 years, and 265 (84%) were men. Median LVEF was 35% (IQR, 27% to 45%), 85% had coronary heart disease (74% prior MI and 28% prior surgery), and 69% were in NYHA functional class ≥2. Follow-up was complete in 97%.

We reviewed 1881 M-VT episodes from the 121 (38%) patients who had ≥1 episode of M-VT (median episodes per patient, 4; IQR, 2 to 18). Twenty patients (6% of the total population [95% CI, 4% to 9%] and 16% of patients with M-VT [95% CI, 10% to 24%]) had ≥1 episode of PL. Analyzing VT cycle length as the median cycle length of each episode, it was shorter in PL (median, 330 ms; IQR, 287 to 392 ms) than in non-PL (350 ms; IQR, 310 to 420 ms) episodes ($P=0.044$). MM was found in 61 patients (19% of the total population [95% CI, 15% to 24%] and 62% of the 98 patients with >1 M-VT episode [95% CI, 52% to 72%]). Interobserver agreement coefficient ($k$) was 0.825 for PL assessment and 0.864 for MM assessment.

**Patients With PL**

All 20 patients with PL had 2 different ICD-EG morphologies in the PL episode (Figure 1). None had ≥3 morphologies. Patients with PL had more episodes of M-VT than those without PL (median, 17 versus 0; $P<0.001$). This difference

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**Figure 2. MM of VT. Illustrative example of a patient with 4 different M-VT episodes having 4 different morphologies of the ICD-EG (A to D).**
remained significant (P=0.007) when only patients with M-VT were considered. Patients enrolled in the study for recurrent sustained M-VT (as opposed to other inclusion criteria) more frequently developed PL (9.7% versus 3.1%; odds ratio [OR], 3.32; 95% CI, 1.2 to 9.4; P=0.02) (Table 1). M-VT as the inclusion criteria was the only independent predictor of PL (OR, 3.3; 95% CI, 1.1 to 9.3; P=0.02) (Table 2). There were no significant differences in other clinically relevant variables between patients with and without PL. Type of ICD-EG configuration did not influence detection of PL. No patient underwent VT ablation before the development of PL, although 5 did after PL.

Patients With MM
Forty-three (70%) of the 61 patients with MM had only 2 different M-VT morphologies. The remaining had 3 (20%), 4

Table 1. Baseline Characteristics of Patients According to the Presence or Absence of PL and MM

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>With PL</th>
<th>Without PL</th>
<th>P</th>
<th>With MM</th>
<th>Without MM</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>315</td>
<td>66±10</td>
<td>64±10</td>
<td>0.211</td>
<td>66±10</td>
<td>64±10</td>
<td>0.076</td>
</tr>
<tr>
<td>Male sex</td>
<td>315</td>
<td>16 (80)</td>
<td>249 (84)</td>
<td>0.537</td>
<td>53 (87)</td>
<td>212 (84)</td>
<td>0.503</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>313</td>
<td>16 (80)</td>
<td>252 (86)</td>
<td>0.506</td>
<td>48 (79)</td>
<td>220 (83)</td>
<td>0.085</td>
</tr>
<tr>
<td>Previous MI</td>
<td>268</td>
<td>13 (81)</td>
<td>185 (73)</td>
<td>0.769</td>
<td>39 (81)</td>
<td>159 (72)</td>
<td>0.20</td>
</tr>
<tr>
<td>NYHA functional class ≥2</td>
<td>308</td>
<td>17 (85)</td>
<td>197 (68)</td>
<td>0.138</td>
<td>45 (74)</td>
<td>169 (68)</td>
<td>0.416</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>315</td>
<td>30 (20–48)</td>
<td>35 (27–45)</td>
<td>0.272</td>
<td>30 (22–40)</td>
<td>35 (28–45)</td>
<td>0.024</td>
</tr>
<tr>
<td>LVESD, mm</td>
<td>315</td>
<td>54 (42–64)</td>
<td>47 (40–57)</td>
<td>0.08</td>
<td>56 (47–62)</td>
<td>46 (38–56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDD, mm</td>
<td>315</td>
<td>60 (57–70)</td>
<td>60 (54–66)</td>
<td>0.203</td>
<td>63 (56–70)</td>
<td>59 (54–66)</td>
<td>0.056</td>
</tr>
<tr>
<td>Class III antiarrhythmic drugs</td>
<td>315</td>
<td>4 (20%)</td>
<td>98 (33%)</td>
<td>0.323</td>
<td>11(18%)</td>
<td>91(36%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Cardiac arrest*</td>
<td>315</td>
<td>7 (35)</td>
<td>108 (37)</td>
<td>0.885</td>
<td>13 (21)</td>
<td>102 (40)</td>
<td>0.006</td>
</tr>
<tr>
<td>Sustained VT*</td>
<td>315</td>
<td>15 (75)</td>
<td>140 (47)</td>
<td>0.02</td>
<td>42 (69)</td>
<td>113 (44)</td>
<td>0.001</td>
</tr>
<tr>
<td>Atrial arrhythmias</td>
<td>315</td>
<td>1 (5)</td>
<td>59 (20)</td>
<td>0.14</td>
<td>13 (21)</td>
<td>47 (19)</td>
<td>0.626</td>
</tr>
<tr>
<td>PVCs</td>
<td>294</td>
<td>8 (42)</td>
<td>129 (47)</td>
<td>0.813</td>
<td>28 (48)</td>
<td>109 (46)</td>
<td>0.775</td>
</tr>
<tr>
<td>NSVT</td>
<td>294</td>
<td>6 (32)</td>
<td>104 (38)</td>
<td>0.635</td>
<td>22 (38)</td>
<td>88 (37)</td>
<td>0.928</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD, median (IQR), or no. (%). LVESD indicates LV end-systolic diameter; LVEDD, LV end-diastolic diameter; NSVT, nonsustained ventricular tachycardia; PVC, premature ventricular complex.

*Cardiac arrest and sustained VT refer to inclusion criteria.
(5%), 5 (3%), and 6 (2%) VT morphologies (Figure 2). Patients with MM had more episodes of M-VT than those without MM (median, 9 versus 0; \( P < 0.001 \)). This difference remained significant (\( P < 0.001 \)) when only patients with M-VT were considered. Patients enrolled in the study for recurrent sustained M-VT (as opposed to other inclusion criteria) more frequently developed MM (27% versus 12%; OR, 2.76; 95% CI, 1.5 to 5; \( P = 0.001 \)) (Table 1). Conversely, patients with ICD intervention for cardiac arrest were less likely to develop MM (11% versus 24%; OR, 0.4; 95% CI, 0.2 to 0.78; \( P = 0.006 \)). Patients with MM had significantly lower LVEF, significantly larger LV end-systolic diameters, and nonsignificantly larger LV end-diastolic diameters than those without MM (Table 1). Patients on class III antiarrhythmic drugs had significantly less MM. There were no significant differences in other clinically relevant variables between patients with and without MM. Type of ICD-EG configuration did not influence detection of MM. No patient underwent VT ablation before MM, although 6 did after MM. Recurrent M-VT as diagnosis for ICD indication and low LVEF were the only independent predictors of MM in logistic regression analysis (Table 2).

The occurrence of MM was more frequently observed in patients with PL (17/20; 85%) than in those without PL (44/295; 14.9%) (Figures 4 and 5). There was a strong association between these 2 findings (OR, 32.3; 95% CI, 9 to 115; \( P < 0.001 \)).

Mortality
Seventeen (5%; 95% CI, 3% to 8%) patients died. Mean survival time to death was 9 ± 5 months. Mortality was significantly higher in patients with PL (20%) than in those without PL (4.4%) (Figure 6, Table 3). Patients with MM also had higher mortality (11.5%) than those without MM (3.9%) (Figure 6, Table 3). Mortality was higher in women (12% without PL (4.4%) (Figure 6, Table 3). Patients with MM also had significantly higher mortality than in those without PL (20%) than in those with PL (4/17) compared to 6.8% (3/44) in patients with MM but without PL, which was quite similar to the overall mortality of the study group (5.4%), suggesting that mortality rate of the MM subgroup was driven by patients with PL. Other baseline conditions, such as age, qualifying event considered for enrollment (ie, cardiac arrest, recurrent M-VT), coronary heart disease, LVEF, NYHA functional class, and antiarrhythmic drug therapy, did not have an impact on survival. Having episodes of VT/VF or shock therapy did not increase mortality either. Two patients with PL and 3 with MM who underwent VT ablation died during follow-up. In no case was death related to the procedure. Cardiac mortality was significantly increased in patients with PL but not so in those with MM (Table 3). No differences were found in arrhythmic mortality (Table 3).

Time from the development of PL VT to death was markedly short (median, 1.5 months; IQR, 1.4 to 4.9 months). In contrast, median time from implant to PL VT was 6.9 months (IQR, 3.6 to 11.1 months). Rather similar findings were observed regarding MM VT (median time from the development of MM VT to death, 2.3 months; IQR, 0.7 to 6 months; median time from implant to MM VT, 4.3; IQR, 3.3 to 10 months).

In multivariate regression analysis, PL and female sex were the only predictors of all-cause mortality (Table 4). Inclusion of clinically relevant variables (eg, age, LVEF, coronary heart disease, NYHA functional class, qualifying arrhythmic event considered for enrollment, antiarrhythmic drug therapy, number of VT episodes, shock therapy) in the logistic regression model did not affect this result.

Discussion
The results of the present study show that true PL (as defined in the Expert Consensus on Catheter Ablation of Ventricular Arrhythmias)\(^9\) is not a rare finding in patients with ICDs (6% of the total population and 20% of those with M-VT during follow-up) and is associated with MM. Although MM was predicted by a low LVEF and an ICD indication for M-VT, PL was only predicted by the latter. In this prospective series of patients with ICDs, mostly indicated for secondary prevention, PL predicted total mortality and cardiac mortality and along with female sex, was the only independent predictor of total mortality in the multivariate regression analysis. These findings suggest that PL, as used in the consensus document,\(^9\) merits further attention as a prognostic determinant in patients with ICDs and M-VT.

Incidence of PL and MM
Most of the published reports consider both phenomena together, and in fact, the term pleomorphic has frequently been used instead of multiple morphologies but mostly in reference to MM as defined in the consensus document.\(^8,10,27,28\) As such, MM has been shown to occur spontaneously in 25% to 40% and induced at electrophysiological testing in 25% to 67% of patients with post-MI VT.\(^3\)–\(^8\) The 12-lead QRS configuration has been used as the standard tool to assess VT morphology, and it generally is assumed that using a fewer number of ECG leads may lead to an underestimation of both PL and MM.\(^5\)\(^29\)

For the assessment of VT morphology, we used intracardiac signals recorded by ICD leads. As mentioned previously, ICD-EGs help to identify 2 M-VTs as different by assessing morphology. Changes in ICD-EG shape in morphologically distinct M-VTs led to a correct identification of a specific VT morphology.\(^18\) It also has been demonstrated that standard ICD-EG morphology can accurately distinguish between 2 different sites of ventricular impulse formation as long as they are >2 cm apart.\(^19\) Indeed, ICD-EG morphology has been used to distinguish between 2 different M-VTs in previous reports, such as in a patient with Brugada syndrome\(^30\) or in patients with Chagas disease.\(^31\) Although a

### Table 2. Logistic Regression Analysis for PL VT and MM of M-VT

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>PL VT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustained VT</td>
<td>3.3 (1.1–9.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>MM of M-VT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustained VT</td>
<td>2.89 (1.57–5.32)</td>
<td>0.001</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.97 (0.94–0.99)</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Sustained VT refers to inclusion criteria.
single ICD signal could be considered equivalent to a single ECG lead, the incidence of MM found in our study (62% of the 98 patients who had >1 episode of M-VT, using the same denominator as in previous studies) is as high as that previously reported in ECG-based studies. Whether this finding is due to a higher discriminating capability of ICD signals compared with the ECG, to a higher incidence of MM at the onset of VT episodes, or to the ability to record most VT episodes cannot be determined.

PL originally was described by Josephson et al., occurring spontaneously in 4 patients and induced during an electrophysiology study in 10 additional patients. However, to the best of our knowledge, this report is the first regarding incidence or prognostic implications on this specific phenom-

![Figure 4. PL and MM of VT in the same patient. A, A PL VT episode is shown. B to E, Four different M-VT episodes from the same patient are shown. Note that VT morphologies in B and C match those of the PL episode in A.](image-url)
The incidence of PL found in the present study may have underestimated the true incidence of PL by restricting the analysis to the period preceding ICD therapy. However, we wanted to avoid the potential overestimation of PL because of changes in morphology after ICD therapy.

Determinants of PL and MM
Wilber et al. identified the number of antiarrhythmic drug treatments and the presence of multiple MIs as predictors of spontaneous MM. In their study, “VT was documented during a mean of 3.1 antiarrhythmic drug treatments in each patient.” In the present series, only 34% of patients received antiarrhythmic drug therapy (amiodarone in almost all), and no patient received a combination of drugs, which probably explains why the use of antiarrhythmic drugs was not a determinant of MM or PL in the multivariate analysis.

We could not analyze multiple infarctions because this variable was not recorded in the DATAS database, but a low LVEF, found to be a determinant of MM in our study, also could be an expression of a more-extensive substrate. It is also conceivable that patients with M-VT as the index arrhythmia in an ICD population tend to have more M-VTs during follow-up and eventually MM and PL than other high-risk arrhythmic populations.

Prognostic Implications
Inducing MM has been shown to predict a lower catheter ablation success and higher failure rate of surgery. Bella et al. showed that spontaneously occurring MM was associated with reduced acute ablation success and VT recurrence, whereas induced MM did not stand for such an adverse outcome. However, it has not been shown that MM could predict mortality. The prognostic implications of PL are unknown.

Although both PL and MM were found to be predictors of all-cause mortality in univariate analysis, only PL was identified as an independent predictor of total mortality, with a >5-fold increase in the chance of death. In fact, patients with both PL and MM had the highest mortality rate. To our knowledge, this study is the first to report increased mortality associated with PL VT. PL also was associated with a significantly higher cardiac mortality and with a nonsignificantly higher incidence of arrhythmic death (in this ICD population).

The reasons for these findings are not readily apparent, but some additional data could offer interesting suggestions. First, PL by itself may represent the development of an extremely active arrhythmic substrate; in fact, the number of M-VT episodes per month increased after the occurrence of PL in these patients (median before PL, 2 episodes per month; IQR, 0.3 to 4.3; median after PL, 21.4 episodes per month; IQR, 3.3 to 32.4). Second, the development of PL resulted in a subsequent increase in the number of appropriate ICD shocks per month (median before PL, 0.4; IQR, 0 to 2.4; median after PL, 5.3; IQR, 0.4 to 7). The relationship between ICD shocks and mortality is well recognized, and although it did not reach statistical significance in our series, we cannot exclude a role in the increased mortality of patients with PL. Third, it is conceivable that this increased arrhythmic activity could add, per se, a certain degree of damage to myocardial function because the prognostic implications are over a short term. Finally, PL instead could be a consequence of deterioration in the clinical condition and ventricular function. In any case, our data show PL as related to a rapidly worsening clinical course, with enhanced arrhythmic activity and ICD therapies leading to cardiac death within weeks.

Female patients represented 16% of our population. This proportion is similar to the 15% to 21% of women included in other secondary prevention ICD trials and to the 8% to
Table 3. Causes of Death of Patients With PL VT and MM of VT

<table>
<thead>
<tr>
<th>Variable</th>
<th>All-Cause Mortality</th>
<th>Cardiac Mortality</th>
<th>Arrhythmic Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>PL VT</td>
<td>5.42 (1.59–18.53); P = 0.017</td>
<td>5.03 (1.27–20); P = 0.041</td>
<td>3.83 (0.4–35.97); P = 0.281</td>
</tr>
<tr>
<td>Yes</td>
<td>4/20 (20)</td>
<td>3/20 (15)</td>
<td>1/20 (5)</td>
</tr>
<tr>
<td>No</td>
<td>13/295 (4.4)</td>
<td>10/295 (3.39)</td>
<td>4/295 (1.35)</td>
</tr>
<tr>
<td>MM of M-VT</td>
<td>3.16 (1.15–8.68); P = 0.028</td>
<td>1.91 (0.57–6.42); P = 0.471</td>
<td>2.77 (0.46–17.36); P = 0.25</td>
</tr>
<tr>
<td>Yes</td>
<td>7/61 (11.5)</td>
<td>4/61 (6.56)</td>
<td>2/61 (3.28)</td>
</tr>
<tr>
<td>No</td>
<td>10/254 (3.9)</td>
<td>9/254 (3.54)</td>
<td>3/254 (1.18)</td>
</tr>
</tbody>
</table>

Data are presented as OR (95% CI) or no./n (%).

23% in primary prevention trials. Our data show that women had reduced survival and that sex was an independent predictor of death. Other studies have analyzed the outcome of women treated with an ICD. In a series of secondary prevention ICD, female sex was the only predictor of all-cause mortality. As in the present series, we found nonsignificant differences in baseline clinical characteristics according to sex. In 2 other studies, female sex has been demonstrated to be an independent predictor of ICD shocks. Similarly, in the Sudden Cardiac Death in Heart Failure trial, ICD benefit was smaller among women. Indeed, reduction in mortality with ICD therapy was nonsignificant in women. On the other hand, 2 other studies found comparable outcome between men and women receiving an ICD. In the Multicenter Automatic Defibrillator Implantation Trial II substudy, men and women randomized to the ICD arm had equal mortality, but women tended to have a higher rate of the combination of hospitalization for heart failure or death (41% versus 31%). The second study was a retrospective series of secondary prevention ICD in which women were younger and had higher LVEF than men. Because of these baseline differences, the comparison with our findings may not be appropriate.

Limitations

All morphological analyses were performed based on 1 intracardiac recording. As mentioned previously, morphological analysis based on 1 intracardiac recording could lead to an underestimation of both PL and MM because subtle differences in morphology could have been unmasked in the 12-lead ECG.

We could not analyze changes in antiarrhythmic drug therapy during follow-up. Thus, although antiarrhythmic drugs at study entry were not positively related to PL, MM, or death, we cannot exclude a relationship due to medication changes.

Different programming could affect PL. In principle, the longer the NID for VT, the longer the time for the VT episode to develop morphological changes. Although strong programming recommendations were made, they were not necessarily followed and could have been changed. However, both the high incidence of compliance at the end of the study (NID VT and VF met the recommendations in 80% and 95% of patients, respectively) and the lack of difference in deviation from programming recommendations between patients with and without PL (P nonsignificant) made it unlikely that a difference in programming could have influenced our findings.

We did not have longitudinal information of ventricular function status or myocardial ischemia. Thus, we could not exclude that ventricular function deterioration or active myocardial ischemia preceded PL, were its determinants, or had prognostic information per se. However, this limitation is shared by most clinical studies in patients with arrhythmia because serial laboratory findings are difficult to perform. The findings of this study may not be applicable to all patients with ICDs because 90% of indications were for secondary prevention of death.

Conclusions

In a prospective series of patients with ICDs, mostly indicated for secondary prevention of death, PL and MM of VT, as judged by ICD-EG, were not uncommon findings and were strongly associated. Both occurred more frequently in patients with previous recurrent sustained VT. The development of PL VT, but not MM VT, and female sex independently predicted all-cause mortality. If further studies confirm the ominous short-term prognostic significance of PL-VT, more-aggressive approaches, such as catheter ablation, should be explored in an attempt to improve prognosis in this patient population.

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Disclosures

Dr Almendral has received honoraria from Medtronic, Guidant (now Boston Scientific), Johnson & Johnson, and St Jude Medical for lectures and consultant fees from Johnson & Johnson. Dr Schwab has received research honoraria from Medtronic. Dr Arribas has received minor educational and consultancy fees from Medtronic, Boston Scientific, and St Jude Medical. Dr Wolpert has received speakers fees from Boston Scientific, Medtronic, Biotronik, and St Jude Medical. Dr Ricci has received minor consultancy fees from Medtronic and St Jude Medical. Dr Cobo has received consultant fees from Medtronic. Dr Navarro is an employee of Medtronic. Dr Quesada has received minor consultancy fees from Medtronic.

References

11. Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators.


The results of the present study show that pleomorphism (PL) and multiple morphologies (MM) of ventricular tachycardia (VT), as judged by implantable cardioverter-defibrillator (ICD) electrograms, are not uncommon findings in patients with ICDs, occurring in 6% and 19%, respectively. Total mortality (5%) was significantly higher in patients with PL (20%), patients with MM (11.5%), and in women (12%). In this prospective series of patients with ICDs, mostly indicated for secondary prevention, PL and MM were strongly associated and predicted all-cause mortality in univariate analysis. PL also was associated with a significantly higher cardiac mortality and with a nonsignificantly higher incidence of arrhythmic death. In multivariate regression analysis, PL, but not MM, was identified as a strong and independent predictor of total mortality, with a >5-fold increase in the chance of death. This finding affected outcome over the short term because time from the development of PL VT to death (median, 1.5 months; interquartile range, 1.4 to 4.9 months) was markedly short compared to time from ICD intervention to the occurrence of PL (median, 6.9 months; interquartile range, 3.6 to 11.1 months). In addition to the development of PL VT, female sex independently predicted all-cause mortality. These findings suggest that PL merits further attention as a prognostic determinant in patients with ICDs and recurrent VT. If further studies confirm the ominous short-term prognostic significance of PL VT, more-aggressive approaches, such as catheter ablation, should be explored in an attempt to improve prognosis in this patient population.
Incidence, Determinants, and Prognostic Implications of True Pleomorphism of Ventricular Tachycardia in Patients With Implantable Cardioverter-Defibrillators: A Substudy of the DATAS Trial

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