Incidence, Determinants and Prognostic Implications of True Pleomorphism of Ventricular Tachycardia in ICD Patients: A Substudy of the DATAS Trial

Running title: Hadid et al.; Pleomorphism and Multiple Morphologies of VT

Claudio Hadid, MD¹; Jesus Almendral, MD, PhD¹; Mercedes Ortiz, PhD¹; Joerg Otto Schwab, MD FESC²; Sabine Janko, MD³; Karl Mischke, MD⁴; Fernando Arribas, MD⁵; Christian Wolpert, MD⁶; Renato Ricci, MD⁷; Pedro Adragao, MD⁸; Erik Cobo, MD⁹; Xavier Navarro, MD¹⁰; Aurelio Quesada, MD¹¹

¹Hospital Gregorio Marañon, Madrid, Spain; ²University of Bonn, Bonn; ³Ludwig-Maximilians-University Munich, Munich; ⁴RWTH Aachen University, Aachen, Germany; ⁵Hospital 12 de Octubre, Madrid, Spain; ⁶University of Mannheim, Mannheim, Germany; ⁷Hospital San Filippo Neri, Rome, Italy; ⁸Hospital Santa Cruz, Carnaxide, Portugal; ⁹Universidad Politecnica de Cataluña, Barcelona; ¹⁰Medtronic, Barcelona; ¹¹Hospital General Universitario, Valencia, Spain

Correspondence:
Jesus Almendral, MD, PhD
Electrophysiology Unit
Hospital Madrid Norte Sanchinarro
Oña, 10. Madrid-28050, Spain.
Telephone: 917567800 Ext. 4146-7.
Fax: +34917500203
E-mail: almendral@secardiologia.es

Abstract:

**Background** - The occurrence of monomorphic ventricular tachycardia (M-VT) with more than one QRS morphology during the same episode (pleomorphism, PL) or in different episodes (multiple morphologies, MM) has been described on an ECG basis. ICD electrograms (ICD-EG) 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 ICD patients.

**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-up for 17 months. PL and MM occurred in 6% and 19% 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% vs. 15%; p<0.001), as compared to patients without PL. Total mortality (5%) was significantly higher in patients with PL (20%), with MM (11.5%) and women (12%). In multivariate analysis, only PL (OR 5.33, p=0.009) and female gender (OR 3.1, p=0.038) predicted mortality.

**Conclusion** - In a prospective series of ICD patients, mostly indicated for secondary prevention, both pleomorphism and multiple morphologies of VT, as judged by ICD-EG, were not uncommon and were strongly associated. Female gender and the development of pleomorphic VT were the only independent predictors of mortality.

**Key words:** ventricular tachycardia; ICD; tachycardia morphology; pleomorphism; ICD electrograms
Sustained 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.\textsuperscript{1,2} Recurrent M-VTs with different QRS morphologies in different episodes, is a common phenomenon in post-MI M-VT patients.\textsuperscript{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”.\textsuperscript{9} The term multiple morphologies (MM) or Multiple monomorphic VTs refers to “more than one morphologically distinct M-VT, occurring as different episodes”.\textsuperscript{9} Since the original description of pleomorphic VT,\textsuperscript{3} its characterization in terms of clinical consequences has been limited. The development of VT with MM has been associated to failure of antiarrhythmic drug therapy, lower acute radiofrequency catheter ablation success and higher rates of VT recurrence.\textsuperscript{7,8,10} 

All previous reports evaluated MM and PL on an ECG basis. With the increase in the use of implantable cardioverter defibrillator (ICD) therapy in patients with severe structural heart disease\textsuperscript{11-17} the opportunity to observe 12-lead ECG of M-VT episodes is decreasing, while that to observe ICD stored electrograms (EG) is increasing. Unlike ECG, ICD-EG allows the analysis of all spontaneous VT episodes, and usually from the beginning of the VT episode. ICD-EG have been shown to be useful in discriminating different M-VTs and sites of ventricular impulse formation.\textsuperscript{18,19} Thus, in the present study we used ICD-EG morphology as indicative of a M-VT morphology in order to identify distinct M-VT morphologies.
The aim of the present study is to evaluate the incidence, determinants and prognostic
significance of PL and MM as assessed by ICD-EG in a prospective series of ICD patients, those
included in the DATAS Trial.\textsuperscript{20}

Methods

The design and results of the DATAS Trial have been previously described.\textsuperscript{20,21} Briefly, it was a
prospective, multicentre, randomized study that included patients with ICD indication, and
compared single and dual chamber ICD in clinically significant adverse effects.\textsuperscript{20} Inclusion
criteria were: cardiac arrest due to VT or ventricular fibrillation (VF); spontaneous recurrent
sustained M-VT; unexplained syncope with induced VT/VF; post-MI unsustained VT with
inducible sustained VT/VF. All devices implanted were provided by Medtronic Inc.
(Minneapolis, MN, USA). 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: 2 zones of
tachyarrhythmia detection: VT<380ms (antitachycardia pacing + shocks) and VF<300ms
(shocks only); number of intervals needed to detect (NID) VT:16, and VF:18/24. These
parameters as well as all arrhythmic events were stored in floppy discs at each visit,\textsuperscript{22} allowing
subsequent analysis. Patients in whom ICD-EG were not available for at least three months of
follow-up were excluded.

We prespecifically sought to determine the incidence and implications of PL and MM by
analyzing ICD-EG 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 supraventricular,\(^23-26\) 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 more than one stable ICD-EG morphology each having \(\geq 6\) consecutive beats with identical EG morphology during the same VT episode. MM was defined as more than one 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 were expressed as mean ± standard deviation, while those with nonparametric distribution were presented as median and interquartile range (IR). For statistical analysis we used Student t Test for continuous variables with parametric distribution, Mann-Whitney Test for those with nonparametric distribution and Chi2 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 included age, gender, left ventricular ejection fraction (LVEF), coronary heart disease, functional
class, met inclusion criteria and class III antiarrhythmic drug therapy evaluated at hospital discharge, as well as number of VT episodes and shock therapy during follow-up. These variables were included in the model regardless of their statistically significance (although not all presented in the tables). SPSS version 16.0 (SPSS Inc., Chicago, Illinois) was used. All probability (p) values were two-sided and statistical significance was established at p<0.05.

**Interobserver agreement assessment:** Interobserver variability of ICD-EG morphologic analysis was studied by an independent analysis of all PL and MM episodes, and a random subset of similar number of single morphology cases, blindly performed by 3 investigators. Since this analysis was performed by three investigators and both variables are dichotomic (only two categories), free-marginal multi-rater kappa coefficient was calculated for interobserver agreement assessment.

**Results**

The DATAS Trial analyzed 334 patients, 90% of which received an ICD for secondary prevention of arrhythmic death. There were no ICD-EG available for a period of at least 3 months in 19 patients. The remaining 315 patients composed our study population (Figure 3).

Patients’ mean age was 64±10 years old and 265 (84%) were male. Median LVEF was 35% (IR 27-45), 85% had coronary heart disease (74% had 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 patients (38%) who had ≥1 episode of M-VT (median 4 [IR 2-18] episodes per patient). Twenty patients (6% [CI95% 4-9%] of the total population, 16% [CI95% 10-24%] of patients with M-VT) had ≥1 episodes of PL. Analyzing VT
cycle length as the median cycle length of each episode, it was shorter in PL than in non-PL episodes (median 330ms[IR 287-392] vs. 350ms[IR 310-420]; p=0.044). MM were found in 61 patients (19%[CI95% 15-24%] of the total population, 62%[CI95% 52-72%] of the 98 patients with >1 M-VT episode). Interobserver agreement coefficient (kappa) was 0.825 for PL assessment and 0.864 for MM assessment.

**Patients with PL:** All 20 patients with PL had two 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 vs. 0; p<0.001). This difference 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% vs. 3.1%, OR 3.32[1.2-9.4]; p=0.02, Table 1). M-VT as the inclusion criteria was the only independent predictor of PL (OR 3.3[CI95% 1.1-9.3], 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 prior to the development of PL, although 5 did after PL.

**Patients with MM:** Forty-three of the 61 patients with MM (70%) had only two different M-VT morphologies. The remaining had three (20%), four (5%), five (3%) and six (2%) VT morphologies (Figure 2). Patients with MM had more episodes of M-VT than those without MM (median 9 vs. 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% vs. 12%, OR 2.76[1.5-5]; p=0.001, Table 1). Conversely, patients with ICD implantation for cardiac arrest were less likely to develop MM (11% vs. 24%, OR 0.4[0.2-0.78]; p=0.006). Patients with MM had
significantly lower LVEF, significantly larger left ventricular end-systolic diameters and non-significantly larger left ventricular 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 prior to 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 two findings (OR 32.3[CI95% 9-115]; p<0.001).

**Mortality:** Seventeen patients died (5% [CI95% 3-8%]). 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%) (Table 3, Figure 6). Patients with MM also had higher mortality (11.5%) compared to those without MM (3.9%) (Table 3, Figure 6). Mortality was also higher in women (12% vs. 4.2%, OR 3.15[CI95% 1.10-8.95]; p=0.036). Patients with both MM and PL had a mortality rate of 23.5% (4/17) compared to 6.8% (3/44) of patients with MM but without PL, 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 (i.e. cardiac arrest, recurrent M-VT), coronary heart disease, LVEF, NYHA functional class and antiarrhythmic drug therapy did not have 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 [IR 1.4-4.9] months). In contrast, median time from implant to PL VT was 6.9 [IR 3.6-11.1] months. Rather similar findings were observed regarding MM VT: median time from the development of MM VT to death was 2.3 [IR 0.7-6] months and that from implant to MM VT was 4.3 [IR 3.3-10] months.

In multivariate regression analysis PL and female gender were the only predictors of all cause mortality (Table 4). Inclusion of clinically relevant variables (such as age, LVEF, coronary heart disease, NYHA functional class, qualifying arrhythmic event considered for enrollment, antiarrhythmic drug therapy, number of VT episodes and 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 Consensus document) is not a rare finding in ICD patients (6% of the total population and 20% of those with M-VT during follow-up), and is associated with MM. Although MM were predicted by a low EF and an ICD indication for M-VT, PL was only predicted by the latter. In this prospective series of ICD patients, mostly indicated for secondary prevention, PL predicted total mortality and cardiac mortality and, along with female gender, was the only independent predictor of total mortality in the multivariate regression analysis. These findings suggest that PL, as used in the Consensus document, merits further attention as a prognostic determinant in ICD patients with M-VT.
Incidence of PL and MM

Most of the published reports consider both phenomena together, and in fact the term pleomorphism has been frequently used instead of MM, but referring mostly to MM as defined in the Consensus document. As such, MM has been shown to occur spontaneously in 25-40% and induced at electrophysiological (EP) testing in 25-67% of patients with post-MI VT. The 12 lead QRS configuration has been used as the standard tool to assess VT morphology, and it is generally assumed that using less number of ECG leads may lead to an underestimation of both PL and MM.

For the assessment of VT morphology we used intracardiac signals recorded by ICD leads. As mentioned above, ICD-EG help to identify two 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. It has also been demonstrated that standard ICD-EG morphology can accurately distinguish between two different sites of ventricular impulse formation, as long as they are >2 cm apart. Indeed, ICD-EG morphology has been used to distinguish between two different M-VTs in previous reports such as in a patient with Brugada syndrome or in patients with Chagas disease. Although a 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 is due to a higher discriminating capability of ICD signals as compared to 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 was originally described by Josephson et al, occurring spontaneously in four patients and induced during EP study in ten additional patients. However, to the best of our knowledge, this is the first report regarding incidence or prognostic implications on this specific phenomenon. 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 due to 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 that study, “VT was documented during a mean of 3.1 antiarrhythmic drug treatments in each patient”. In our series, only 34% of patients received antiarrhythmic drug therapy (amiodarone in almost all) and no one received a combination of drugs. This can probably explain why the use of antiarrhythmic drugs was not a determinant of MM or PL in our series in 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, could also 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-VT during follow-up and eventually MM and/or PL than other high-risk arrhythmic populations.

Prognostic implications

Inducing MM has been shown to predict lower catheter ablation success and higher failure rate of surgery. Della 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
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 > 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 represents the first study reporting increased mortality associated with PL VT. PL was also associated with a significantly higher cardiac mortality and with a non-significantly 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 2[0.3-4.3] vs. 21.4[3.3-32.4]). Second, the development of PL resulted in a subsequent increase in the number of appropriate ICD shocks: 0.4 (0-2.4) shocks per month before vs. 5.3 (0.4-7) after PL. 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 PL patients. Third, it is conceivable that this increased arrhythmic activity could add, per se, a certain degree of damage to myocardial function since the prognostic implications are over a short-term. Finally, PL could be, instead, a consequence of deterioration in the clinical condition and/or ventricular function.

In any case, our data pictures 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%-21% of women included in other secondary prevention ICD trials and to the 8%-23% in primary prevention trials.11,13-16,35,36 Our data show that women had reduced survival and that gender 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 patients, female gender was the only predictor of all cause mortality.32 As in ours, this study found nonsignificant differences in baseline clinical characteristics according to gender. In two other studies, female sex has been demonstrated to be an independent predictor of ICD shocks.37,38 Similarly, in SCD-HeFT ICD benefit was smaller among women.39 Indeed, reduction in mortality with ICD therapy was nonsignificant in women. On the other hand, two other studies found comparable outcome between men and women implanted with an ICD.40,41 In the first one, a MADIT-II substudy, men and women randomized to the ICD arm had equal mortality. Despite this, women tended to have a higher rate of the combination of hospitalization for heart failure or death (41% vs. 31%). The second study was a retrospective series of secondary prevention ICD patients, in which women were younger and had higher LVEF than men. Due to these baseline differences, the comparison with our findings may not be appropriate.

**Limitations**

All morphologic analyses were performed based on one intracardiac recording. As mentioned above, this could lead to an underestimation of both PL and MM, since 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 detection the longer the time for the VT episode to develop morphologic 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=NS), made 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 arrhythmic patients since serial laboratory findings are difficult to perform.

The findings of this study may not be applicable to all patients with ICD, since 90% of indications were for secondary prevention of death.

**Conclusion and Clinical Implications**

In a prospective series of patients implanted with an ICD, mostly for secondary prevention of death, pleomorphism and multiple morphologies of ventricular tachycardia, as judged by ICD-
EG, were not uncommon findings and were strongly associated. Both occurred more frequently in patients with previous recurrent sustained ventricular tachycardia. The development of pleomorphic VT, but not multiple morphologies, and female gender 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.

**Acknowledgement:** The authors acknowledge Daniel Hadid for his technical support.


**References.**


Table 1. Baseline characteristics of patients according to the presence or absence of Pleomorphism and Multiple Morphologies.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pat. with PL</th>
<th>Pat. without PL</th>
<th>( p ) value</th>
<th>Pat. with MM</th>
<th>Pat. without MM</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y) (n=315)</td>
<td>66±9</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 gender (n=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 (n=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 (n=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 (n=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 (%) (n=315)</td>
<td>30 (IR 20-48)</td>
<td>35 (IR 27-45)</td>
<td>0.272</td>
<td>30 (IR 22-40)</td>
<td>35 (IR 28-45)</td>
<td>0.024</td>
</tr>
<tr>
<td>LVESD (mm) (n=315)</td>
<td>54 (IR 42-64)</td>
<td>47 (IR 40-57)</td>
<td>0.08</td>
<td>56 (IR 47-62)</td>
<td>46 (IR 38-56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDD (mm) (n=315)</td>
<td>60 (IR 57-70)</td>
<td>60 (IR 54-66)</td>
<td>0.203</td>
<td>63 (IR 56-70)</td>
<td>59 (IR 54-66)</td>
<td>0.056</td>
</tr>
<tr>
<td>Class III Antiarrhythmic Drugs (n=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* (n=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* (n=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 (n=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 (n=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 (n=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>

*Cardiac arrest and sustained VT refer to inclusion criteria. Pat.: patients; MI: myocardial infarction; NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVEDD: left ventricular end-diastolic diameter; PVCs: premature ventricular complexes; NSVT: non-sustained ventricular tachycardia.

Table 2. Logistic Regression Analysis for Pleomorphic VT and for Multiple Morphologies of M-VT. Sustained VT refers to inclusion criteria.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (CI 95%)</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pleomorphic VT</strong></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><strong>Multiple Morphologies of M-VT</strong></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>LV Ejection Fraction</td>
<td>0.97 (0.94-0.99)</td>
<td>0.012</td>
</tr>
</tbody>
</table>
Table 3. Causes of death of patients with pleomorphism and multiple morphologies 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><strong>PLEOMORPHIC VT</strong></td>
<td>OR 5.42(1.59-18.53), p=0.017</td>
<td>OR 5.03(1.27-20), p=0.041</td>
<td>OR 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>
</tbody>
</table>

| **MULTIPLE MORPHOLOGIES OF M-VT** | OR 3.16(1.15-8.68), p=0.028 | OR 1.91(0.57-6.42), p=0.471 | OR 0.46(0.46-17.36), p=0.25 |
| Yes                       | 7/61 (11.5%)        | 4/61 (6.56%)       | 2/61 (3.28%)         |
| No                        | 10/254 (3.9%)       | 9/254 (3.54%)      | 3/254 (1.18%)        |

Table 4. Logistic Regression Analysis for All Cause Mortality.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (CI 95%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleomorphic VT</td>
<td>5.33 (1.52-18.66)</td>
<td>0.009</td>
</tr>
<tr>
<td>Female Gender</td>
<td>3.10 (1.07-9.01)</td>
<td>0.038</td>
</tr>
</tbody>
</table>
Figure Legends:

**Figure 1.** Pleomorphic VT in two different patients. On both panels two distinct ICD electrogram morphologies during M-VT can be noted (the changing beat marked by*).

**Figure 2.** Multiple Morphologies of VT. Illustrative example of a patient with 4 M-VT morphologies. A to D: four different M-VT episodes having four different morphologies of the ICD electrogram.

**Figure 3.** Summary of patients included and arrhythmic events.

**Figure 4.** Pleomorphism and Multiple VT Morphologies in the same patient. A shows a pleomorphic VT episode. In 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 pleomorphic episode (A).

**Figure 5.** Association between Pleomorphism and Multiple Morphologies of VT.

**Figure 6.** Variables associated with increased mortality in univariate analysis.
All Cause Mortality

- Pleomorphism: 20% Yes, 4.4% No, p = 0.017
- Multiple Morphologies: 11.5% Yes, 3.9% No, p = 0.028
- Female Gender: 12% Yes, 4.2% No, p = 0.036

Circulation: Arrhythmia and Electrophysiology
Incidence, Determinants and Prognostic Implications of True Pleomorphism of Ventricular Tachycardia in ICD Patients: A Substudy of the DATAS Trial
Claudio Hadid, Jesus Almendral, Mercedes Ortiz, Joerg Otto Schwab, Sabine Janko, Karl Mischke, Fernando Arribas, Christian Wolpert, Renato Ricci, Pedro Adragao, Erik Cobo, Xavier Navarro and Aurelio Quesada

Circ Arrhythm Electrophysiol. published online November 13, 2010;
Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circep.ahajournals.org/content/early/2010/11/13/CIRCEP.110.957068