Differences between Ventricular Tachyarrhythmias for Patients with Coronary Artery Disease and Dilated Cardiomyopathy

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Abstract

Aim: Coronary Artery Disease (CAD) and Dilated Cardiomyopathy (DCM) are structurally different heart diseases. Spontaneous ventricular tachyarrhythmias (VT) from implantable cardio-defibrillators (ICD) are studied to explore clinical differences between CAD and DCM.

Methods: The analysis is focused on: number of VT episodes, variability of the VT onset (three modes are considered), VT-rate, coupling interval, prematurity index, median heart cycle of the 20 sec. preceding VT onset and circadian distribution of VT-onset. Significant differences are evaluated with p<0.05.

Results: 165 VT episodes among 37 patients (79 from 26 CAD and 86 from 11 DCM) are studied. DCM patients have more VT episodes (p<0.02) and greater variability of VT-onset (p<0.01) than CAD. Circadian distribution in CAD has peaks in morning and afternoon, while in DCM it is almost uniform during light hours.

Conclusion: DCM patients have more VT, greater VT-onset variability and different circadian distributions.

1. Introduction

The progress in implantable cardioverter defibrillator (ICD) technology has improved diagnostic and therapeutic efficacy of these devices in the management of malignant ventricular tachyarrhythmias [1,2]. Moreover, extended recording of electrical cardiac activity surrounding delivered device therapy provides documentation of electrical events immediately preceding the arrhythmia onset and during its course. This progress has opened up the possibility to investigate: (i) the mechanisms of initiation of spontaneous ventricular tachyarrhythmias; (ii) peculiar features extracted from intracardiac electrograms (EGMs) retrieved from the ICD device [3-5]; (iii) circadian distribution of the VT initiation [6-9].

This evolution facilitates a deeper characterization of cardiac activity through the analysis of the EGMs, thus differences between structurally different cardiac diseases such as coronary artery disease (CAD) or non-ischemic dilated cardiomyopathy (DCM) can more easily come out. This study investigates the differences between CAD and DCM. The classification is based on simple clinically features: on one side, it is focused on overall clinical features such as: (i) the frequency of spontaneous ventricular tachyarrhythmias (VT) measured from CAD or DCM patient; (ii) the variability of VT-initiation in the two etiologies; (iii) the circadian distribution of VT-onset. On the other side the study explores the differences in time-domain features that can be easily obtained from the intracardiac electrogram (EGM) measured on CAD or DCM patients.

2. Methods

This retrospective study is based on spontaneous VT episodes from patients that received a St Jude Medical – Ventritex ICDs (model Angstrom, Contour or Profile) in the framework of the ELECTA (ELECTrogram Analysis) protocol which run at our institutions between December 1998 and October 2002. Visual inspection of the cardiologist identified VT by a sudden increase in heart rate along with a change in EGM morphology from the baseline rhythm. Supraventricular tachycardia and atrial fibrillation recordings are not consider.

For this study both VT episodes requiring ICD therapy (with antitachycardia pacing or shock cardioversion) and non-sustained VT that spontaneously recovered are included. Exclusion criteria is the absence of a minimum of 20 seconds of the EGM basal rhythm before the onset of the VT and, following the outcomes of our previous study [10], only EGMs stored with far-field mode of recording are analyzed.

The following modes of VT onset are visually classified by the electrophysiologist: (i) PVC onset when
VT initiates with a premature ventricular contraction (PVC) as shown in Fig. 1A; (ii) Short-long-short (SLS) onset when VT initiation is preceded by a short-long-short cycle (Fig. 1B); (iii) Pacemaker (PM) onset when VT initiates immediately after a paced beat (Fig. 1C). In PM-onset the pause preceding paced beat is appropriate if it correlates to the programmed lower rate interval of the anti-bradycardia system, otherwise it is not considered PM-onset being ICD undersensing.

![Fig. 1: VT initiation: (A) PVC onset, (B) SLS onset, (C) PM onset; RR intervals preceding VT onset in msec.](image)

For each considered VT episode the following EGM features are analysed: (i) VT-cycle defined as the median value of the VT cycles (in msec); (ii) Coupling interval (CI) taken as the interval between the first beat of VT and the previous baseline beat, in msec; (iii) Prematurity index (PI) calculated by normalizing the coupling interval to the preceding RR interval; (iv) Median heart rate of the 20 sec. immediately preceding VT onset (HR-PreVT), in beats per minute (bpm).

Clinical information for each patient including age, gender, heart disease, left ventricular ejection fraction, and antiarrhythmic drug at the time of ICD implant date were documented by review of clinical records.

Time of VT events for circadian distribution analysis was retrieved from the log file of ICD device. Circadian distribution analysis was made with 3-hour time-interval which is a good compromise between the need of reducing time interval to construct detailed distribution, and the need of having enough VT episodes in each time-interval.

### 2.1. Statistical analysis

Interval and normal variables are expressed as mean ± standard deviation. Mean between groups of these variables were compared using Student T-test, while Chi-square test was used with nominal variables. Statistical significance is assumed when $p<0.05$.

Circadian distributions has been modelled by polynomial (fifth order polynomial model) and harmonic regression (two harmonics with greater energy model). It is expected that distributions with peaks and dumb-peaks can be better fitted by harmonic models, while polynomials regression might better approximate smoother distributions.

Goodness of fit of the regression models is tested using coefficient of determination $R^2$, defined as in equation (1):

$$R^2 = 1 - \frac{\sum (y_i - \hat{y}_i)^2}{\sum (y_i - \bar{y})^2}$$

In (1) the value of $y_i$ represents the measured variable for each 3-hour interval, $\bar{y}_i$ is its mean value, and $\hat{y}_i$ is the approximation obtained by the regression model. $R^2$ typically assumes values between 0 and 1, and it is often interpreted as the fraction of variation explained by the regression model. Extreme cases are: $R^2 = 1$ (obtained when the approximated and the measured values equals) indicating that the fitted model describes all the variability of the data set, and $R^2 = 0$ (obtained when the model correspond to the mean value of the data set) indicating that the fitted model does not describes at all the variability of the data set. As a consequence $R^2 = 1$ indicates an excellent model, while $R^2 = 0$ reflects a poor model.

### 3. Results

From a pool of sixty-eight patients implanted with a St Jude Medical – Ventritex ICD device for secondary prevention, a total number of 165 VT episodes from 37 patients are considered. Among them, 79 episodes are retrieved from 26 CAD patients and 86 VT are obtained from 11 DCM. Baseline characteristics of patient population are shown in Table 1.
Table 1. Baseline characteristics of the patients.

<table>
<thead>
<tr>
<th></th>
<th>CAD</th>
<th>DCM</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td># of pts with VT</td>
<td>26</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td># of VT episodes</td>
<td>79</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>70±10</td>
<td>64±12</td>
<td>n.s.</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>23/3</td>
<td>10/1</td>
<td>n.s.</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>33±10</td>
<td>24±13</td>
<td>&lt; 0.03</td>
</tr>
<tr>
<td>Ejection Fraction</td>
<td>35±8</td>
<td>31±9</td>
<td>n.s.</td>
</tr>
<tr>
<td>NYHA Class: I/II+III</td>
<td>2/24</td>
<td>2/9</td>
<td>n.s.</td>
</tr>
<tr>
<td>Treatment at implant:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated / Non-treated</td>
<td>18/8</td>
<td>5/6</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Table 2 reports, for the different modes of onset, the number of VT episodes and the mean values of the EGM features, separately for CAD and DCM populations. Although no significant differences are observed between CAD and DCM groups, intra-group analysis showed that PI is significantly higher in PVC onset than in SLS and PM (in DCM even SLS significantly higher than PM), and HC_PreVT is significantly higher in PM than PVC and SLS onsets.

Table 2. Analysis of PVC, SLS and PM VT-onset. In intra-set analysis the * indicate significantly higher values.

<table>
<thead>
<tr>
<th>Feature</th>
<th>PVC</th>
<th>SLS</th>
<th>PM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>59</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>VT-rate</td>
<td>356</td>
<td>325</td>
<td>298</td>
</tr>
<tr>
<td>CI</td>
<td>497</td>
<td>515</td>
<td>600</td>
</tr>
<tr>
<td>PI</td>
<td>0.75*</td>
<td>0.56</td>
<td>0.5</td>
</tr>
<tr>
<td>HC-preVT</td>
<td>697</td>
<td>663</td>
<td>1018*</td>
</tr>
<tr>
<td>Number</td>
<td>51</td>
<td>22</td>
<td>13</td>
</tr>
<tr>
<td>VT-rate</td>
<td>323</td>
<td>343</td>
<td>332</td>
</tr>
</tbody>
</table>

Table 3 shows that DCM patients present more VT episodes and a more variable pattern of initiation of the episodes compares to CAD.

Table 3. Differences between CAD and DCM patients

<table>
<thead>
<tr>
<th></th>
<th>CAD</th>
<th>DCM</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td># VT per pts</td>
<td>3±2</td>
<td>8±5</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td># VT-onset per pts</td>
<td>1.1±0.4</td>
<td>1.8±0.9</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

The next result regards the study of circadian distributions. In Fig. 2 it is shown, separately for CAD and DCM groups, along with corresponding polynomial (dotted line) and harmonic (solid line) regressions models. Coefficient of determination indicate that CAD patients are better fitted with harmonic model ($R^2=0.963$ vs. $R^2=0.767$ with polynomial regression), while in DCM patients polynomial regression is better ($R^2=0.997$ vs. $R^2=0.983$).

Fig. 2: Circadian distribution of CAD and DCM patients along with polynomial (dashed line) and harmonic (solid line) regression models.

4. Discussion and conclusions

Our results indicate that DCM patients have a significantly higher number of VT episodes per patients, and a significantly greater variability of the modes of VT-onset (see Table 2). To further prove this result it should be considered that CAD group has a duration of the follow-up significantly longer than DCM (see Table 1). This means that in a shorter period of time, a lower number of DCM patients (with similar ejection fraction and NYHA class as CAD) experienced a greater number of VT-episodes.

A second comment regards circadian distributions. The presence of a morning peaks (between 9 and 12 AM) and an afternoon peak (around 6 PM) is observed in CAD patients, while DCM patients present a more uniform distribution during day-light hours and a dumb peak during night. The goodness of fit for the regression that better fit the two different etiologies indicate that harmonic regression better approximate CAD distribution ($R^2=0.963$), while DCM distribution is better fitted by a polynomial model ($R^2=0.997$). In the literature CAD population has been studied and a non-uniform distribution with peaks in the morning and afternoon [7,9] has been observed. In the case of non-ischemic patients results are controversial: while in [7] non-ischemic patients presents circadian distribution with morning and afternoon peaks, in [9] non-ischemic patients rather have an almost uniformly circadian distribution along daylight hours.

The investigation of the modes of onset drive to the
the modes of onset proves also that a significant number of VTs (about 12 %) initiates immediately after a paced beat, thus a pro-arrhythmic effect of the ICD device. Indeed the study of PM-onset is an increasingly interesting topic in the literature [11] and it will be considered in a future paper. Results of the present work are in agreement with other studies in the literature [11], where a rate of PM-onset in the order of 9.4% of the VT episodes is obtained when ICD devices is set with VVI antibradyarrhythmia function (Ventricle paced, Ventricle sensed and pacing Inhibition as a response to sensing). A more detailed comparison shows a higher prevalence in DCM patients (15%), than in CAD (9%), although the difference does not reach significance (p<0.28).

Finally, the analysys of the EGM features did not evidence significant differences between the two structurally different etiologies. This lead to the hypothesys that the common parameters used to describe VT (VT-rate, CI, PI) may not be the best features for EGM characterization, when the focus is the investigation of differences between underlying structurally different cardiac disease such as CAD and DCM. Nevertheless, intra-group analysis showed a significantly higher lower PI value in PM onset. This observation needs further investigation.

5. Conclusions

In this paper the differences between coronary artery disease and dilated cardio-myopathy patients, based on simple clinical features, is studied. Results yield to the conclusion that in both groups VT-onset with a PVC is the most frequent mode of VT initiation. The analysis of the modes of onset proves also that a significant number of VTs (about 12 %) initiates immediately after a paced beat, thus a pro-arrhythmic effect of pacing in some patients should not be excluded, as it is reported in recent literature [11]. Moreover it is observed that DCM patients (15%), than in CAD (9%), although the difference does not reach significance (p<0.28).

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References


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