Ventricular Tachyarrhythmia Onset in Patients with Implantable Cardioverter Defibrillators

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Abstract

Ventricular tachyarrhythmia (VT) onset is studied by reviewing spontaneous intracardiac electrograms (EGMs) from coronary artery disease (CAD) and dilated cardiomyopathies (DCM) patients with implantable cardioverter-defibrillators (ICD).

A total of 165 VT episodes (79 CAD and 86 DCM) from 37 patients (26 CAD and 11 DCM) are analysed. Modes of VT onset are divided into: (i) premature ventricular contraction (PVC); (ii) PVC preceded by a short-long-short cycle (SLS); (iii) PVC preceded by a pacing beat after a post-ectopic escape interval (PM).

VT cycle, median RR cycles of 4 (LastRR4s) and 20 sec (LastRR20s) immediately before VT onset, coupling interval and prematurity index are examined. Significant differences are assessed by Student T-test with $p < 5\%$.

DCM patients have more VT episodes and a greater variability of the VT initiation patterns than CAD. We observed, both in DCM and CAD, that PVC onset is the most frequent initiation pattern, while LastRR4s and LastRR20s are significantly higher in PM than PVC or SLS onset. This indicates importance of proper ICD setup on the patients, and it may be useful to predict the risk of experiencing VTs with PM onset of the patients.

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 [1-4].

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 opens up new possibilities to explore the mechanisms of initiation of spontaneous ventricular tachyarrhithmias [5-8].

The present study resumes our results to gain insight into the initiation of spontaneous ventricular tachyarrhythmias (VT) by analyzing stored intracardiac electrograms from patients that received an ICD as secondary prevention.

The analysis is separately carried on for coronary artery disease (CAD) and dilated cardiomyopathy (DCM) aetiologies, and tries to investigate if the different patterns of VT initiation correlate with the presence of various clinical features and intracardiac electrograms (EGMs) characteristics .

We believe that recognition of specific EGM patterns occurring at the time of VT initiation can help in understanding the electrophysiologic mechanisms responsible for arrhythmia initiation and may lead to better diagnostic and therapeutic interventions.

2. Methods

All spontaneous VT episodes (including ventricular tachycardia and fibrillation) from patients with third-generation ICD devices placed at our institutions between December 1998 and October 2002 were reviewed. Visual inspection of the cardiologist identified VT by a sudden increase in heart rate (automatically computed) along with a change in EGM morphology from the baseline rhythm; we did not consider supraventricular tachycardia nor atrial fibrillation episodes.

We included VT episodes requiring ICD therapy (with antitachycardia pacing or shock cardioversion) as well as non-sustained VT that spontaneously recovered. We used St Jude Medical – Ventritex ICDs (model Angstrom, Contour or Profile) because we have the possibility to retrieve and convert internally stored EGMs from those devices. Only events that had a minimum of 20 seconds before the onset of the VT were selected for further analyses and, following the outcomes of our previous study [9], we analyzed only EGMs stored with far-field mode of recording. We defined the following modes of VT onset: (i) *PVC onset* when VT initiates with a PVC (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 with a PVC immediately after a paced beat (Fig. 1c); in these cases each pause preceding the paced beat was considered appropriate if it correlated to the programmed lower rate interval of the anti-bradycardia system, while we neglected the cases with pause less than the escape interval because representing an ICD undersensing.

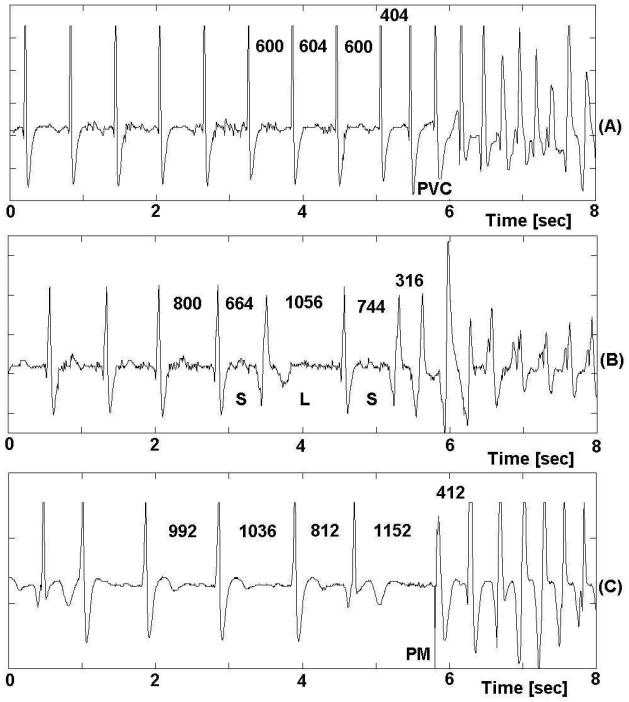

Figure 1: Tachyarrhythmias initiation: (A) PVC onset, (B) SLS onset, (C) Pm onset; RR intervals immediately preceding VT onset in msec.

We also considered the following EGM features: (i) *VT-cycle* defined as the median value of the VT cycles, in milliseconds (msec); (ii) *Coupling interval* taken as the interval between the first beat of VT and the previous baseline beat, in msec; (iii) *Prematurity index* calculated by normalizing the coupling interval to the preceding RR interval; (iv) *Median cycle* of the 4 sec. immediately preceding VT onset, in msec; (v) *Median cycle* of the 20 sec. immediately preceding VT onset, in msec.

Clinical data: 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. Table 1 resumes the clinical information of CAD and DCM populations.

Statistical analysis: continuous data are expressed as mean $\pm$ SD. Mean between couple of different groups were compared by Student *T-test*. A p value <0.05 was considered statistically significant.

3. Results

Sixty-eight patients were implanted with a third-generation St Jude Medical – Ventritex ICD device between December 1998 and October 2002 for secondary prevention. Four of these patients had aetiology different from CAD or DCM, they did not have any VT episode during the follow-up, and they have been excluded from the study. Among the other 64 patients, 18 were DCM patients, while the other 46 had CAD aetiology. From these patients, 261 VT episodes occurred among 41 patients from the date of implant to December 2005.

As previously mentioned our study required the availability of the EGMs for the 20 seconds immediately proceeding VT onset: this requirement disqualified 53 sustained VT episodes (29 from DCM and 24 from CAD) for which it was not available the VT initiation from the strip stored in the ICD. Another 43 VT episodes had no far-field EGMs recording available (they were stored in the ICD as bipolar EGMs) and they have been disqualified.

Finally 165 episodes among 37 patients met study criteria. In particular 26 CAD patients had 79 episodes and from 11 DCM 86 VT have been recorded.

Table 1: Baseline characteristics of the patient (N=37).

	CAD	DCM
N of patients	26	11
Age (yrs)	70 $\pm$ 10	64 $\pm$ 12
Men/women	23/3	10/1
	⌐ p<.03 ¬	
Follow-up (months)	33 $\pm$ 10	24 $\pm$ 13
N. pats in NYHA Class I	2	2
N. pats. in NYHA Class II/III	24	9
Left Ventricular ejection fraction	35 $\pm$ 8	31 $\pm$ 9

The mean age, ejection fraction and follow up of total patient population (CAD+DCM) was 68$\pm$11 years, 34% $\pm$ 9% and 31 $\pm$ 12 months, respectively. They were 33 man and 4 women.

The number of episodes for a single patient ranged from 1 to 20 episodes/patient (mean of 4.4 $\pm$ 3.7 episodes/ patient). At time of ICD implantation, 21 patients were taking amiodarone, 6 were taking β-blockers, and 14 patients were not treated with antiarrhythmic drugs. Table 1 lists principal baseline characteristics of the study population, separately for CAD and DCM patients.

We note a significantly lower follow-up in DCM patients (p<3%), while no significant differences between the two groups are observed for age and left ventricular ejection fraction.

Table 2 reports overall number of VT episodes recorded from CAD and DCM groups. Among the CAD

group seven patients had only 1 VT episode (27% of CAD group), whereas 19 had ≥2 episodes. Among DCM group none had only 1 episode, whereas 11 patients had between 2 and 20 episodes. According to Student T-test, the mean number of VT per patient is significantly higher in DCM populations (p<2%).

Table 2: Tachyarrhythmia episodes: differences between CAD and DCM populations.

	CAD	DCM
VT range per patient	1-8	2-19
	⌐ p<.02 ¬	
# VT per patient	3 ± 2	8 ± 5

Initiation pattern was quite reproducible among CAD patients, while it is much more variable in DCM patients. Among the 19 CAD patients with multiple episodes, 15 (79%) had all subsequent episodes of VT with the same initiation pattern, whereas 4 (21%) had 2 different pattern of initiation (in 2 patients we found PVC and SLS onset, and 2 patients had PVC and PM onset). Among the 11 DCM patients with multiple episodes, 5 (45%) had all subsequent episodes of VT with the same initiation pattern, whereas 6 (55%) exhibit 2 or 3 different pattern of initiation (in 2 patients we found PVC and SLS onset, 1 patient had PVC and PM onset, and 3 patients exhibit all the 3 modes of onset).

Analysis of the initiation pattern shows that the most frequent mode of VT onset was PVC observed in 59 episodes (75%) for CAD group and in 51 episodes (59%) for DCM group; it was followed by the SLS that occurred in 13 episodes (16%) of CAD and in 22 episodes (26%) of DCM; finally pacing-induced VT happened in 7 episodes (9%) for CAD and 13 episodes(15 %) for DCM group.

We observe a significantly higher VT cycle of PVC group in CAD patients that might be explained as a consequence of the higher number of CAD patients that receive antiarrhythmic drugs at the time of ICD implant. No significant differences between CAD and DCM patients have been observed in PI, CI, median RR cycle during the 4 sec. (nor 20 sec) immediately previously VT initiation. In the literature other authors [10] found a significantly higher prematurity ratio in the ischemic heart disease group with respect to non ischemic ones. Our results do not support this conclusion.

4. Discussion and conclusions

Clinical condition of DCM and CAD groups are comparable: left ventricular ejection fraction and NYHA class of the two groups are not significantly different; similarly in DCM and CAD groups the number of patients with VT episodes are analogous: 11 of 17 for DCM and 26 of 40 for CAD, both corresponding to 65% of group population.

The number of VT episodes per patients is significantly higher in DCM then CAD patients. This result is supported by Table 2, and it is confirmed by the significantly higher follow-up of CAD with respect to DCM groups. The reason of a higher follow-up of CAD patients is principally due to the date of ICD implants: between 1998 and 2002, with MADIT I specifications [3], most of the ICDs were implanted in CAD patients, that likely were receiving drug therapy since they had previous ischemic episodes. For this reason the higher number of VT episode in DCM patients would not have been expected.

The most important difference between CAD and DCM patients, according to our results, is the variability of the modes of VT initiation that is large in DCM group, but still present in CAD patients. In particular four of the 26 CAD patients with VT episodes (15%) presented two different modes on VT onset, while among the other 22 CAD patients, 7 had a single VT episode, while all VTs of the other 15 CAD patients initiated with the same mode. On the contrary, in DCM population 6 of 11 patients with VT episodes (55%) presented at least two different modes of onset. In particular 3 of them experienced all the three modes and the other 3 experienced two different modes of VT initiation. It is widely accepted that the mechanisms thought to be responsible for the generation of ventricular arrhythmias are re-entry, triggered activity, or abnormal automaticity. Since [11] re-entry, as the mechanism for VT, was suggested because of reproducible initiation and termination of the tachyarrhythmia induced by programmed stimulation in ischemic patients. In the case of non-ischemic patients, such as DCM group, still re-entry is considered as a possible mechanism of Vt initiation. In this case cardiac substrate that determine the generation of re-entry, rather than being an ischemic area, it is supposed to be affected by conduction abnormalities of cardiac tissue [12]. Thus the mechanism of re-entry may explain the origin of VTs in CAD and DCM patients.

Although in [13] different conformations of the cardiac substrate are shown, and they support the presence of a variability of beats morphology during ventricular tachyarrhythmias, it is peculiar the large variability in the modes of VT onset that we have observed in our small collection of VTs, especially in the case of non-ischemic patients, but still present in some of the CAD.

The presence of different mode of VT onset in the same patient, and the variability in the ectopic beats morphology in other patients lead to the hypothesis that a new, more general, paradigm of the cardiac re-entry mechanism should be thought of. This new way to construct model of the heart should include other

information about cardiac substrate: rather than being based on cardiac anatomy it should take into account the functional heart dynamics; rather than assuming resistive gap junction, it should assume feedback mechanisms among cardiac cells; rather than be founded on a deeply detailed single cardiac cell activity, it should require a dramatic simplification of the single element.

In this paper we studied the differences between the modes of onset observed in coronary artery disease and dilated cardio-myopathies patients. We noted that DCM have more VT episodes per patient and a greater variability in the modes of VT initiation than CAD patients. From the analysis of the modes of VT onset we observed that a significant number of VTs (about 10 %) initiates very close to a paced beat; thus a proarrhythmic effect of pacing in some patients should not be excluded. We also observed that the RR interval immediately before VT onsets for PM mode of onset is significantly longer than the RR interval immediately before VT onset with other modes of initiation.

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