Differences in Mode of Onset of Ventricular Tachyarrhythmias in Dilated Cardiomyopathies and Coronary Artery Diseases

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Abstract

This explorative study focuses on differences between the onset of spontaneous ventricular tachyarrhythmias (VT) of patients with implantable cardioverter defibrillator (ICD) and affected by coronary artery disease (CAD) or dilated cardiomyopathy (DCM). From 57 patients (40 CAD and 17 DCM), 35 (24 CAD and 11 DCM) we retrieved a total of 154 spontaneous VTs (72 CAD and 82 DCM). Three modes of VT onset are observed: (i) premature ventricular contraction (PVC); (ii) PVC preceded by a short-long-short cycle; (iii) PVC preceded by a paced beat immediately after PVC pause.

The analysis indicates that (i) average number of spontaneous VTs is much higher in DCM than CAD (7.5 vs. 3 VTs per patients in patient with VTs); (ii) modes of onset are more variable in DCM (1 patient experienced all 3 modes, 5 experienced 2 modes,) than CAD (only 2 patients experienced 2 modes) patients.

1.   Introduction

The mechanisms of onset of spontaneous ventricular tachyarrhythmia (VT) have been the object of several electrocardiography studies often limited by the unpredictable occurrence of arrhythmia episodes. More recently, new generation of implantable cardioverter defibrillators (ICDs) have stored growing amount of intracardiac electrograms (EGMs) immediately before the onset of the VT episode and during its course [1]. Nowadays the availability of the EGM in critical period of the cardiac electrical activity is allowing detailed data analyses of spontaneous VT onset [2, 3].

This retrospective study is aimed to further examine modes of VTs onset treated by ICD shocks. In particular it focuses differences between modes of spontaneous VT onset observed in patients with coronary artery disease (CAD) and dilated cardiomyopathy (DCM). The analysis includes clinical information about the considered patients, investigation of the EGMs morphology and quantification of signal energy during VTs. This preliminary study attempts to make a coarse grain analysis of the differences between VTs generated by CAD and DCM patients in order to get an insight on the different mechanisms of VT onset that may be involved in these cardiac illnesses.

2.   Methods

Patients and signals

The analysis is based on data retrieved from the memories of St Jude Medical – Ventritex ICD devices (Angstrom V-190HV3, Contour V-175AC and Profile V-186HV3) which can be programmed to store up to 3 EGM episodes of 2 minutes each in high resolution mode. They allow two modes of recordings: Bipolar (BIP) and Far-Field (FF). In previous studies we investigated differences between bipolar and far-field signals obtained from ICDs, and we observed that, for the purpose of characterizing dynamics of the cardiac electrical activity, it is more productive to consider far-field signals. In addition BIP signals are filtered in the low-frequency range up to about 10 Hz or slightly more, while FF don't [4]. For these reasons the EGMs used in this paper are recorded in far-field mode.

A total of 57 are considered. Aetiology is CAD in 40 patients (average EF: 35%, average age is 71, average NYHA class II), while it is DCM in 17 subjects (average EF: 34%, average age is 67, average NYHA class II)). The mean follow-up is 20 months.

The pattern of initiation of the VTs has been carefully examined by a cardiologist that found three different modes of VT onset: (i) premature ventricular contraction (PVC group); (ii) PVC preceded by a short-long-short cycle (SLS group); (iii) PVC preceded by paced beats immediately after PVC pause (PM group).

Figure 1 shows short intervals of 8 seconds each of

intracardiac electrograms with VTs that spontaneously onset with these modes.
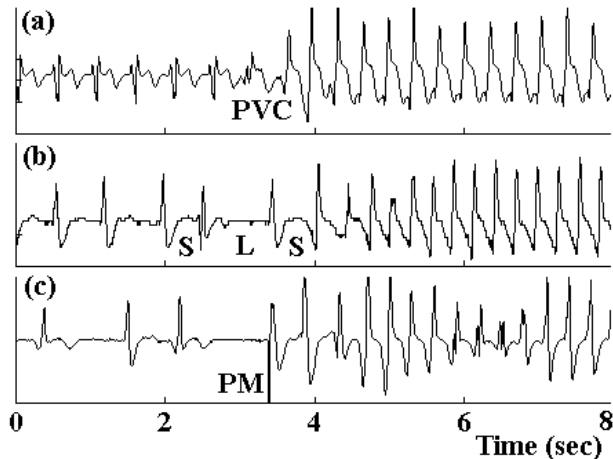

Figure 1: Examples of spontaneous VT started with (a) premature ventricular contraction (PVC), (b) short-long-short cycle (SLS); (c) PVC preceded by a paced beat after a previous PVC pause (PM).

Method of analysis

Besides clinical information on the patients, we explore heart rates automatically extracted from the EGMs and we quantify the characteristics of the power spectral density (PSD) of the VT interval extracted from the intracardiac electrograms retrieved from the ICDs. In particular we consider the frequencies of the 25th, 50th and 75th percentile of the signal energy, namely F25, F50 and F75 to classify PSD of every VT; from the clinical view, severity of the VTs is classified according to their heart rates: we consider as less severe VTs with rate lower than 160 beats per minute (slow VTs), intermediate severity has been assigned to VTs with rates between 160 and 210 (mid VTs), and the most severe tachyarrhythmias are classified for rates overwhelming 210 beats per minute or ventricular fibrillation (fast VTs).

To this purpose a proper software is implemented in which PSD is determined using MATLAB routines.

No sophisticated statistical analysis are performed in this study, we present our results explicating mean and standard deviation values.

3. Results

Table 1 show the outcomes obtained from CAD group. This tables resume, for every mode of onset, the corresponding number of patients, average ejection fraction and age. In addition it reports the number of EGMs and, in brackets, the number of patients from which these EGMs are retrieved, separated for three level of severity of the tachyarrhythmias according to their beat rates.

Table 1: clinical characteristics of the VTs extracted from the CAD group (see text for explanation).

Onset	Pats	Mean EF%	Mean Age	Type of VTs Slow	Mid	Fast
PVC	20	34.3	76	25 (7)	26 (13)	4 (3)
SLS	2	40	71	3 (2)	4 (1)	0
PM	4	40	69	4 (2)	4 (2)	2 (2)

Although details are not reported in Table 1, it should be added that the ejection fraction of the PM group patient is extremely variable: we have 1 female subject that experienced cardiac heart failure whose EF% is 20%. This patient experienced 6 VTs with PM onset. This patients should be analyzed as a case study, this will not be done here, we just like to stress this information to allow better understanding of Table 1.

Table 2 show corresponding results obtained from the DCM groups. Legend is the same as for Table 1.

Table 2: characteristics of the VTs extracted from the DCM group.

Onset	Pats	Mean EF %	Mean Age	Type of VTs Slow	Mid	Fast
PVC	11	31.1	64	11 (5)	35 (9)	8 (5)
SLS	4	36.3	69	5 (1)	12 (4)	0
PM	3	25.3	68	4 (2)	2 (1)	5 (2)

We report a few comments about these first two tables.
1. Our data set, composed of patients that received an ICD as secondary prevention, indicates that the average age of DCM patients is slightly lower than CAD ones. This difference is not statistically significant.
2. Focusing on severity of VTs types, we observe that CAD group has 44.5% slow-VTs, 47.2% mid-VTs and 8.3% fast-VTs. DCM group includes 24.4 % slow-VTs, 59.8 % mid VTs and 15.9 % fast-VTs. Thus DCM patients seems to have spontaneous malignant VTs more severe than CAD ones.
3. Although in the literature the short-long-short mode of onset has been associated to more severe VTs (cita Taylor) our results indicate the opposite: no fast-VTs, onset with SLS mode, independently from the aetiology of the patient.
4. Modes of onset are more variable in DCM patients then in CAD group. Only two patients of the CAD group presents 2 modes of onset: PVC and PM. One of them is the female subject with EF%=20. She is extremely sensitive to pacing in some cases. Indeed she is the only patient that switched a mid VT into VF after anti-tachycardia pacing. This is a unique case since in our experience anti-tachycardia pacing

is extremely effective even with VTs with a beat rate around 180-200 bpm. DCM patients exhibit more heterogeneous modes of VT onset: 1 patients experienced all the three modes, 3 patients experienced SLS and PVC modes and 2 patients experienced PVC and PM modes of onset.

5. Although the average ejection fraction is similar for CAD and DCM patients, DCM patients that exhibit PM mode of onset seems to have significantly smaller EF%.

The classification of the VTs on the basis of the power spectral density is the next analysis that we performed. Examples of the power spectra obtained from the VT intervals of the EGMs presented in Figure 1 together with their F25, F50 and F75 values, are shown in Figure 2. PSD are shown in a linear-linear plot in order to make more clear the peaks of the spectra and to allow a better understanding of the F25, F50 and F75 values. The figure reports the first 15 Hz since the large majority of the signal energy is in this frequency bandwidth.
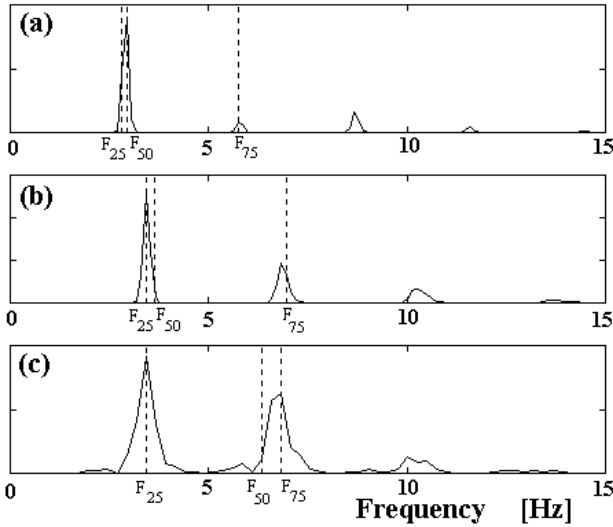

Figure 2: Examples of linear-linear plot of the power spectral density obtained from spontaneous VT of the PVC group (a); SLS group (b); PM group (c).

Plots like those of Figure 2 are quite common during spontaneous VTs. Often PSD has a clear fundamental frequency with 2 or 3 harmonics. The interpretation of this results can be drawn on the basis of the reentry model: a portion of heart ventricle becomes a fast pacemaker and the propagation wave-front spread in the ventricle always in the same way. Thus intracardiac electrograms reasonably exhibit always the same pattern and thus signals are periodical waves of slightly different shapes among each others.

The quantification of all the considered VTs is presented in the next Table. Tables 3 presents the average frequencies of the 25th, 50th and 75th percentiles of the signal energy together with their standard deviations, separately for CAD and DCM patients and for every mode of onset.

Table 3: Mean value and standard deviation of the frequency of the 25th, 50th and 75th percentile of the signal energy for the considered spontaneous VTs.

Group	Onset	Bpm	F25		F50		F75	
			Mean	SD	Mean	SD	Mean	SD
	PVC	173	3.8	1.8	6.6	3.0	9.6	4.0
CAD	SLS	176	2.9	0.3	3.8	1.4	7.2	1.2
	PM	197	3.3	1.1	4.2	1.1	6.3	1.9
	PVC	187	2.9	0.7	3.4	1.0	4.8	2.3
DCM	SLS	171	2.6	0.4	2.7	0.3	3.3	0.9
	PM	199	3.1	0.8	3.2	0.8	5.2	1.4

Table 3 indicates:
1. smaller value for F25, F50 and F75 frequencies of DCM group independently from the considered mode of onset; this means that signal energy distribution is more unfolded in CAD group.
2. smaller standard deviation of the DCM group.
3. 75 % of the signal energy lies in the 0-10 Hz frequency bandwidth.

The first two considerations can not be simply attributed to the higher rates of the cardiac beats during DCM. In fact lower mean values of the F25, F50 and F75 is observed also in the SLS group that presents an higher average beat rate for the CAD group. It is the opinion of the authors that this would be a consequence of the fact that the fundamental frequency is more pronounced in the DCM group than in the CAD group. On one side this may determine the lower standard deviation of the frequencies F25, F50 and F75 since they would be more closed around the peak frequency values, on the other it justify the lower importance of the harmonics, and thus the smaller values observed for F25, F50 and F75.

Third remark indicates that low frequency bandwidth contain relevant information in terms of power spectrum. This information may be due to depolarisation phase, but it might also be determined by differences in the repolarization phase.

A final comment on the major drawbacks of this study. They are surely related to:
1. Total number of considered VTs and total number of patients from which the EGMs have been collected: although we are considering more than 150 spontaneous episodes of VTs obtained from 35 patients with ICD, this study can be considered as preliminary: still there are quite large variability of the results, and these conclusion needs to be confirmed.

2. Intra-subject VTs variability is observed: often patients present a very repeatable VTs morphology, but in some cases we find quite different VT morphology from episode to episode within the same subject. We like to stress that both types of patients are present in CAD and DCM groups.

A final comment regards the importance of EGMs signal analysis as a unique path toward better understanding about the inner mechanisms involved in spontaneous malignant arrhythmia onset.

It is clear that the reentry model explains in a convincing way the VT onset mechanism when VTs are morphologically similar from episode to episode within the same patient. It is less obvious to explain as a reentry a VT that onset with a SLS mode: it is not clear why the heart should make such a kind of complication to onset VTs.

Similar surprise is justified by the effect that a single pacing can have on some patients. Sometimes we observed prolonged pause after an ectopic beat that, interrupted by a pacing, lead to a VT immediately after the paced beat. It is like the heart muscle becomes extremely sensitive to excitation after the premature ventricular contraction.

We are quite confident that further research in this field is extremely useful: it may help in the selection of those cardiac patients that might receive major benefit from the ICD implantation, and in the search of patients with higher risk of sudden cardiac death. Recent clinical findings suggested a prophylactic implantation of a defibrillator for all patients with myocardial infarction and reduced ejection fraction [5]. Nowadays this is the correct clinical practice although it has been observed that the number of patients with VTs can reach the fraction of 1 over 16 implanted ICDs. In some countries this is considered too much expensive for the national health service to implant an ICD to all people with less than 35% ejection fraction. Moreover we have observed that patients with very poor ejection fraction (in our data set mainly less then 25%) are classified as PM onset. This latter observation need further investigation and validation from the literature.

4.   Conclusions

In this paper we studied intracardiac electrograms retrieved from ICDs implanted, as secondary prevention, in patients with coronary artery disease or dilated cardiomyopathy. Our aim is to initiate a study to extract new types of information from the EGMs to increase power of methods aimed to find cardiac patient at greater risk of sudden death, and improve risk stratification. Our results show that DCM patients have more VTs than CAD. Moreover the modes of onset of the VTs is more variable in DCM than in CAD. We found a large variation in the VTs obtained from the various subjects: indeed some of them have VTs with similar morphology, while in other patients the morphology changes from episode to episode. In general we observed that the frequency of the 75th percentile of the energy of the VT signals is below 10 Hz, indicating the importance of the low frequency of the EGM. In the DCM group it is lower than in CAD. These are preliminary indications, but it is the opinion of the authors that they lead to the conclusion that much effort should be spent to obtain from the EGMs further information that they contains and we do not know how to interpret.

Acknowledgements

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