Mode of Onset of Spontaneous Ventricular Tachyarrhythmias from Implantable Cardioverter Defibrillator Electrograms

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Abstract

Aim: This work investigates the correlation between the cardiac electrical activity underlying spontaneous ventricular tachyarrhythmias and their modes of onset.

Signals: We analyzed 81 episodes of spontaneous ventricular tachycardia (VT) and ventricular fibrillation (VF) lasting at least 5 seconds from 17 patients. The cardiologist classified VT/VF malignancy by considering fast VT as more malignant. We study 3 modes of onset: (i) premature ventricular contraction (PVC group); (ii) PVC preceded by a short-long-short cycle (SLS group); (iii) PVC preceded by a paced beat after a previous PVC compensatory pause (PM group). In 4 patients more than one mode of VT/VF onset is present, in the other 13 patients VT/VF always started with the same mode.

Mathematical methods: Cardiac electrical activity is characterized by power spectral density and correlation dimension analyses; statistical analysis is carried on using one way ANOVA in order to test significant differences among the mean values of PVC, SLS and PM populations.

Results: Preliminary results shows significant differences at 5% level in two of the considered quantitative parameters.

Conclusion: Although initial significant differences have been obtained, the limited number of ICDs and the small variability of the intra-subject characterization suggest that further research is needed to conclude that dynamics underlying VT/VF and the VT/VF mode of onset are strictly related.

1. Introduction

Prediction and prevention of the events leading to sudden cardiac death (SCD) is a growing field of research [1]. It is known that implantable cardioverter defibrillators (ICDs) provide a mortality benefit compared with conventional drug therapy [2]. It is also known that SCD is generated by malignant tachyarrhythmia events such as ventricular tachycardia (VT) and ventricular fibrillation (VF). Mechanisms underlying the onset of spontaneous VT/VF have become an important research topic of the last decades.

The dynamical model, generally accepted in the literature, assumes that the spontaneous tachyarrhythmia starts because of the beginning of a spiral wave originating in the ventricle able to drive the whole heart to a sudden, fast activity by starting a re-entrant dynamical phenomenon. Cardiac clinical electrophysiology supports the re-entry model by showing how the cardiac substrate could be modified by the presence of an infarct in such a way to make possible the initiation of the re-entry [3]., in non infarcted patients the re-entry in the ventricle has not always been shown and likely other mechanisms could be responsible of ventricular tachyaarhythmias.

The biological model of the onset of tachyarrhythmia considers three elements as necessary to bring the cardiac activity to the transition between the sinus rhythm (SR) and the VT/VF: (i) a control activity from the autonomous system and the metabolism, (ii) a triggering activity as a Premature Ventricular Contraction (PVC), and (iii) a substrate condition able to maintain the tachyarrhythmia.

Recently the study of the differences between the modes of VT/VF onset is increasing [4, 5] also because it is still unexplained the reason why some patients may have thousands of PVC before one of them might start a tachyarrhythmia, while in other presenting frequent PVC the spontaneous tachyarrhythmia never occurs.

In this work we study intracardiac electrograms obtained from 17 patients underwent to St Jude medical – Ventritex ICD implantation, and we consider spontaneous VT/VF originated from three different mode of onset: (i) the single premature ventricular contraction (PVC); (ii) the PVC preceded by a short-long-short cycle; (iii) a PVC preceded by a paced beat immediately after a PVC compensatory pause.

Our aim is to get an insight on possible correlation between the mode of VT/VF onset and the cardiac electrical activity underlying the same VT/VF.

The statistical parameters that we use to characterize VT/VF from the electrograms (EGM) analysis are obtained from spectral density or correlation dimension estimation. Clinical markers are the cardiac VT rate and the VT termination therapy intervention automatically applied by the ICDs.

This paper is a part of the ElectA (Electrogram Analysis) study, already presented in a previous work [6].

2. Signals and methods

The ICDs used for this study are 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 a very high resolution mode. Moreover they allow two types of recordings: Bipolar (BIP) and Far-Field (FF). In a previous paper [6] we studied the 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 this paper all the intracardiac electrograms are obtained using the far-field mode of recording, and we selected all the VT/VF electrograms lasting at least 5 seconds. From a pool of 70 patients undergone to ICD implantation, we have 17 subjects with VT/VF episodes (from which the VT/VF onset is available) recorded in Far-Field. From these 17 subjects we collected 81 intracardiac electrograms of spontaneous VT/VF. These EGMs have been divided in 3 groups:

A) Premature Ventricular Contraction (PVC) group composed by 50 EGMs from 14 patients. Tachyarrhythmias from this group starts with a PVC beat.
B) Short-long-short (SLS) group composed by 20 EGMs from 5 patients. In this case VT/VF starts with a PVC preceded by a short-long-short cycle.
C) Pacemaker (PM) group composed by 11 EGMs obtained from 3 patients. The VT/VF onset with a PVC preceded by a paced beat after a previous PVC compensatory pause.

Typical electrograms from the different populations are shown in Figure 1.

The considered clinical parameters are the VT/VF rate and the interruption therapies. The cardiac rate of VT/VF is measured in beat per minute (BPM) and it is obtained from the median interval between beats of the VT/VF. As a preliminary method to evaluate the interruption therapy we used the number of therapies needed to interrupts the tachyarrhythmias. The considered devices can interrupt the VT/VF using Anti-Tachycardia Pacing (ATP) therapy or shocks. In the first case the method is based on entrainment of the VT by fast pacing [7], in the second a shock is characterized by the energy which has been delivered between the intracardiac coils and the active can of the ICD device.

The parameters used to characterize the underlying cardiac activity are obtained from power spectral density and correlation dimension analyses.

In order to quantify frequency domain characteristics we defined 2 parameters. The first is the fraction of the signal power in the low frequency bandwidth – R_{LF} – defined as the ratio between the signal power in the 0-6 [Hz] bandwidth and the total power of the signal. The second parameter is the value of the frequency corresponding to the 50% of the signal power, and it is denominated F_{50}.

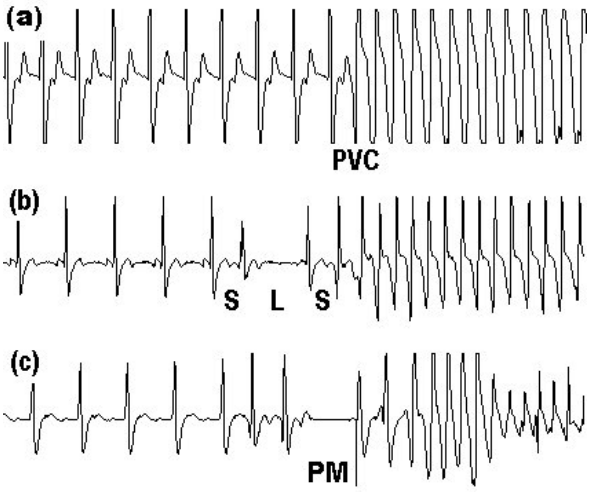

Figure 1: Examples of spontaneous tachyarrhythmias started with (a) premature ventricular contraction (PVC), (b) short-long-short cycle (SLS); (c) PVC preceded by a paced beat after a previous PVC pause (PM).

The correlation dimension estimation is computed using two different algorithms already presented in [8, 9]. From the correlation integral function which is estimated with the known procedure [10, 11, 12], two independent automatic dimension estimation are obtained using the Most Flat scaling Interval (MFI) and the Most Probable Dimension Value (MPDV) algorithms. Note that, since MFI and MPDV are dimension estimates obtained from the same signal, they should not be too different in between: in other words, if MFI and MPDV lead to differing conclusions, the results might be wrong. The scaling region required for MFI estimation (1/4 of decade) is smaller than the scaling region usually accepted (1/2 decade), and which allows to obtain results about the presence of a low dimensional dynamical activity underlying the investigated signal. For this reason in this paper we are considering dimension estimates as statistical parameters, and as indication of a possible underlying dynamical classification. This limit is required

because, with the scaling region width of half a decade, the automatic MFI algorithms leaded to obtain a number of reliable dimension estimates very small (below 40%), while with only ¼ of decade we ca reach about 65% of acceptable dimension estimates.

The statistical analysis consists of group statistic (mean, and standard deviation for each statistical parameter and each group), and one way ANOVA analysis to test the presence of significant difference among the mean value of the three groups (PVC, SLS and PM). The statistical element is the single patient, thus all the statistical parameters (R_{LF}, F_{50}, MFI, MPDV) obtained from all the VT/VF of each single patient are averaged before making statistical analysis.

3. Results

The following tables resume our results: Table 1 compares the clinical data obtained from the three groups; Table 2 resumes results of spectral analysis and Table 3 is related to dimension estimates.

Table 1: Mean values and standard deviations of the clinical information: VT/VF rate (in beats per minute – BPM) and number of therapies needed to interrupt VT/VF. "# Pts" indicates the number of patients from that group. Abbreviations as in Figure 1.

		VT/VF rate		# of Therapies	
	# Pts	Mean	St Dev	Mean	St Dev
PVC	14	182	33	1.17	0.44
SLS	5	180	20	1.06	0.13
PM	3	220	72	1	0

One way ANOVA analysis shows that the mean values of the three groups are not significantly different at a level of 5% neither for the "VT/VF rate", neither for the "# of therapies". Although one way ANOVA test does not prove that the mean values of the three groups are significantly different, we note that the PM group has a mean VT/VF rate faster than the one observed in the PVC and SLS groups.

Table 2: Mean value and standard deviation of the spectral density analyses quantified by R_{LF} and F_{50} statistical parameters. Abbreviations as in Figure 1.

		R_{LF} [%]		F_{50} [Hz]	
	# Pts	Mean	St Dev	Mean	St Dev
PVC	14	56	13	5.6	1.7
SLS	5	63	8	3.4	0.6
PM	3	63	9	4.9	0.8

Next results regards the cardiac activity characterization by means of spectral density and correlation dimension analyses.

We first consider the spectral density analyses and thus R_{LF}, and F_{50} quantitative parameters. In the Table 2 intra-group statistics (mean and standard deviation) are presented.

One way ANOVA analysis indicates that R_{LF} mean values of the three groups are not significantly different, but F_{50} mean values are significantly different at the level of 5% with P = 3.1%. This may lead to the conclusion that tachyarrhythmias from SLS group are more synchronized than VT/VF of PVC or PM populations. At this stage, with only a few ICDs, we prefer to stress that further research is needed to make any remarkable conclusion.

Finally we use correlation dimension to quantify the presence of a scaling in the reconstructed phase space and to better classify the low-dimensional dynamics underlying the studied cardiac activity. Results are shown in Table 3.

Table 3: Mean values and standard deviations of the correlation dimension estimated using MFI and MPDV automatic methods. Abbreviations as in Figure 1.

		MFI		MPDV	
	# Pts	Mean	St Dev	Mean	St Dev
PVC	13	1.33	0.27	1.32	0.16
SLS	5	1.45	0.24	1.46	0.3
PM	2	1.67	0.03	1.89	0.01

One way ANOVA analysis indicates that dimensions estimated using MFI algorithm do not have significantly different mean values at the 5% level, but the MPDV estimated values presents significant difference between the mean values of the PVC, SLS and PM groups with a probability P = 0.7 %. As we observed in the previous section MFI and MPDV are two independent algorithms to estimate the correlation dimension. Indeed similar results are obtained with them in the dimension estimates of the PSV and SLS groups. The result of MFI and MPDV significantly different (as in the PM group) indicates by itself that the correlation dimension estimation might not be reliable. For this reason, in this case, we prefer not to make any conclusive comment about the results obtained with one way ANOVA.

4. Discussion

Among several topics that could be focused on (correlation with the aethiology of the cardiac disease, or the pharmacological therapy, or the ejection fraction; existence of a qualitative typical pattern in the cardiac characterization of SLS, PM or PVC groups, etc), we like to stress only two comments about: (i) the intra-subject tachyarrhythmias variability; and (ii) the total number of EGMs considered for this work and the number of ICDs from which they are collected.

The first comment regards the possibility that the

mode of VT/VF onset might potentially be patient-specific. Our experience let us to conclude that the mode of VT/VF onset should not always be patient-specific. This conclusion arises from the observation that one patient starts spontaneous tachyarrhythmias with all the three different modes of onset, another subject has VT/VF onset with PM or PVC; and 2 patients start VT/VF with PVC or SLS. On the other hand we have 13 patients in which VT/VF always start with the same mode: 1 with PM, 2 with SLS, and 10 with PVC.

The second comment is related to the known problem that many EGMs are often collected from a few patients, while other patients have a few tachyarrhythmia episodes. This is true also in our data base. Of the whole data base composed of 70 patients, only 17 have spontaneous VT/VF episodes (24 %), and the ICDs with 5 or more VT/VF episodes are 6 over 70 (9 %). In one patient, which presents 20 VT episodes, we found all the three types of VT/VF onset. Moreover this patient very often resolves its spontaneous VT by means of ATP cycles.

5. Conclusion

In this paper we studied three different modes of onset of spontaneous VT/VF: the premature ventricular contraction (PVC), the short-long-short cycle preceding a PVC (SLS), and the PVC preceded by a paced beat immediately after PVC pause (PM). 81 electrograms obtained from ICD implanted in 17 patients are analysed. Cardiac electrical activity characterization is quantified by means of spectral density and correlation dimension measures.

The statistical analysis with one way ANOVA shows that the three groups (PVC, SLS, and PM) are significantly different with respect to 2 of the 4 defined statistical parameters. Our conclusion is that further research is needed to demonstrate that there is a link between the mode of VT/VF onset and the type of spontaneous tachyarrhythmia which is developed. This conclusion is based on considerations related to the small variability in the intra-subject cardiac characterization, as we see in patients with more than one mode of VT/VF onset.

Another indication of this paper regards the presence of a pacing beat closed to the onset of spontaneous ventricular tachyarrhythmias. This observation, at present not widely reported in the literature, if confirmed by other studies suggest that, in patients with ventricular disorders such as those undergone to ICD implantation, might be useful to see the whole intracardiac electrogram at the onset of the tachyarrhythmia events.

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