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CLINICAL RESEARCH

Spectral analysis of intracardiac electrograms during induced and spontaneous ventricular fibrillation in humans

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Aims Very limited data are available on the differences between spontaneous and induced episodes of ventricular fibrillation (VF) in humans. The aim of the study was to compare the spectral characteristics of the electrical signal recorded by an implantable cardioverter defibrillator (ICD) during both types of episodes.

Methods and results Thirteen ICD patients with at least one spontaneous and one induced VF recorded by the device were included in the study. A spectral representation was obtained for the first 3 s of the intracardiac unipolar electrogram during VF. The dominant frequency (f_d), the peak power at f_d, an organization index (OI), a bandwidth measurement, and an estimate of the correlation with a sinusoidal wave (leakage) were estimated for each episode. The f_d was higher in induced episodes (4.75 $\pm$ 0.57 vs. 3.95 $\pm$ 0.59 Hz for the spontaneous episodes, $P = 0.002$), as well as the degree of organization assessed by the OI, bandwidth, and leakage parameters.

Conclusion Clinical and induced VF episodes in humans have different spectral characteristics. Changes in the electrophysiological substrate or in the location of the arrhythmia wavefront at onset could play a role to explain the observed differences.

Keywords Ventricular fibrillation • Spontaneous onset • Spectral analysis • Electrogram • Implantable cardioverter defibrillator

Introduction

The aim of the automatic implantable cardioverter defibrillator (ICD) is to provide an effective therapy for spontaneous ventricular arrhythmias. The testing protocol during the device implant is based on the adequate sensing and termination of induced ventricular fibrillation (VF), with the assumption that the induced arrhythmia mimics the clinical arrhythmia and has similar electrophysiological characteristics. However, available data to substantiate this hypothesis are scarce. The analysis of intracardiac electrograms (EGMs) recorded by an ICD may provide an opportunity to compare both types of episodes in the same patient. Several methods have been proposed to assess the cycle length (CL) and the organization patterns of the fibrillatory rhythms, using time- and frequency-domain techniques.[1–3] Specifically, the spectral analysis of optical or electrical signals allows a reliable quantification of the rate and organization properties of the VF process and has been extensively used in experimental and clinical conditions. Only one previous study including nine patients has assessed the electrical characteristics of spontaneous and induced VF events in patients with ICD.[4] The aim of the study was to compare the electrophysiological characteristics of both VF episodes using a spectral analysis of the EGMs recorded by an ICD device.

Methods

Patients and episodes

The patient files stored in the ICD follow-up units of two tertiary hospitals were reviewed. Patients with at least one spontaneous and one

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induced episode of VF recorded by the device with the same unipolar lead configuration were included in the study. Clinical and demographic data and ICD recordings were transferred to a database for further analysis. Patients' data were kept completely anonymous, consistent with the ethical policy of our centre. Ventricular fibrillation was defined as a fast irregular ventricular rhythm with a continuously changing morphology and CL <200 ms.[5] Ventricular fibrillation induction was performed in all cases with 50 Hz alternate current. Intracardiac EGMs were recorded during VF in a unipolar configuration using the defibrillation coil in the right ventricle and the can as the indifferent electrode. Patients were implanted Guidant and Medtronic devices (9 Mini 840 model, 3 Prizma 1860 model, and 1 Medtronic 7227 model). Sampling rate was 128 Hz for 840 and 7227 models and 200 Hz for 1860 models. Device internal filtering settings were not available for us. Storage accuracy was also unknown, but no significant quantification noise could be observed in any of the recordings, so we considered that the number of quantification levels was being used which was enough to avoid spectral distortion. The recorded EGMs were saved in a digital format for further analysis. Each episode detected in the VF zone by the device was visually tested to exclude fast ventricular tachycardias. The onset of each VF episode was manually annotated, and the following 3 s was selected for processing. An automatic cancellation of low-frequency baseline trend was implemented using a 250 ms median filter and spline interpolation.[6] A (normalized to unit area) spectral representation $P_n(f)$ was obtained for each EGM segment with a Welch periodogram, with a Hamming window of 128 samples, 50% overlap. Actual spectral resolution was 128 Hz/384 samples/2 = 0.166 Hz (200 Hz/384 samples/2 = 0.10 Hz), but zero padding to 1024 samples was used in order to work with all the information conveyed in the spectral profile in similar conditions for sampling rates and with more numerically stable estimations of spectral parameters.

The frequency at which the absolute spectral maximum occurs was considered as the dominant frequency (f_d). The peak of the normalized power spectrum at f_d was denoted by P_n (f_d). The organization index (OI) was defined as follows. Given that the EGM spectra were mostly contained in the band from 4 to 30 Hz, we first obtained the total power in this band. Then, for the spectral peaks corresponding to f_d and to every harmonic peak within this band, their power in a bandwidth, given by the 75% decrease in amplitude in each peak, was obtained and added up. Accordingly, the OI was calculated as the ratio between the power in the bandwidth of the fundamental and harmonic peaks and the total power in the band from 4 to 30 Hz.[7] The bandwidth of the component f_d was used as a parameter and denoted just by bandwidth. Leakage is the correlation coefficient between the EGM recording and a sinusoidal function with the same fundamental period (and adjusted phase). Therefore, this parameter measured the similarity between the EGM and a phase-adjusted, purely sinusoidal signal.[8] Given the low-pass spectral profile of the unipolar ICD-stored EGM, that the spectrum usually contains some few peaks, and that the fundamental frequency usually contains most of the spectral energy, the leakage can be seen as a measurement of the narrow-band character of a near-to-periodic signal. It also represents a regular measurement in the time domain, and hence, the higher its value, the more organized the signal.

Statistical analysis

Values are presented as mean ± SD. The significance of the mean differences between spontaneous and induced episodes was assessed by a Student's *t*-test for paired observations. A value $P < 0.05$ was considered statistically significant.

Results

Two hundred and forty-three patients undergoing routine follow-up in an outpatient ICD unit were evaluated. Thirteen of them (12 men, age: 65.5 ± 7.4 years) had at least one episode of spontaneous and one episode of induced VF recorded by the device with a mean of 4 (range 0.07–15) months between them. Eleven subjects (85%) had a history of coronary artery disease with ($n = 10$) or without ($n = 1$) previous myocardial infarction, one had a dilated cardiomyopathy, and one had a structurally normal heart. The left ventricular ejection fraction (LVEF) was severely depressed (<30%) in five patients (38%). The ICD was implanted for primary prevention of sudden death in four subjects (31%). The rest had a history of monomorphic VT ($n = 5$), VF ($n = 2$), or syncope ($n = 2$). The mean duration was 8.2 ± 1.7 s for the induced and 9.1 ± 5.2 s for the spontaneous episodes ($P = 0.6$). The spectral characteristics of both types of arrhythmias are shown in Table *1*. Induced arrhythmias had a higher f_d (4.75 ± 0.57 vs. 3.95 ± 0.59 Hz, $P = 0.002$) and seem to be more organized, as shown by the thinner bandwidth and higher values of OI and leakage. The peak power at f_d was also higher in induced VFs. Figure *1* shows an example of two VF episodes, induced and spontaneous, in the same patient, and illustrates the differences that have been obtained in the spectral domain.

Discussion

Our results show that the spectral characteristics of the electrical signal are significantly different in induced and spontaneous VFs. The dominant frequency, the power at f_d, and the degree of organization are higher in induced episodes.

The characteristics of the electrical signal recorded by ICDs during VF in humans have been analysed in several studies and have been related to the mode of induction,[9] duration of the arrhythmia,[5] probability of recurrence,[10] or location of the scar in patients with myocardial infarction.[11] Few data are reported on the differences of the electrophysiological characteristics of the VF signal between induced and spontaneous episodes. In a study by Lever *et al.*,[4] nine ICD patients had available paired data sets of spontaneous and induced VF events. The indications for the device were heterogeneous (four ischaemic heart disease, three long QT syndrome, two dilated cardiomyopathy), and the mean LVEF was 36%. The EGMs recorded by the device were

Table 1 Spectral parameters in induced and spontaneous episodes of ventricular fibrillation

	Induced VF	Spontaneous VF	*P*-value
f_d	4.75 ± 0.57	3.95 ± 0.59	0.002
$P_n(f_d)$	0.12 ± 0.03	0.06 ± 0.03	0.001
Bandwidth	0.67 ± 0.13	0.80 ± 0.24	0.05
OI	0.81 ± 0.10	0.65 ± 0.15	0.02
Leakage	0.94 ± 0.03	0.85 ± 0.08	0.004

f_d, dominant frequency; $P_n(f_d)$, peak power at f_d; OI, organization index.

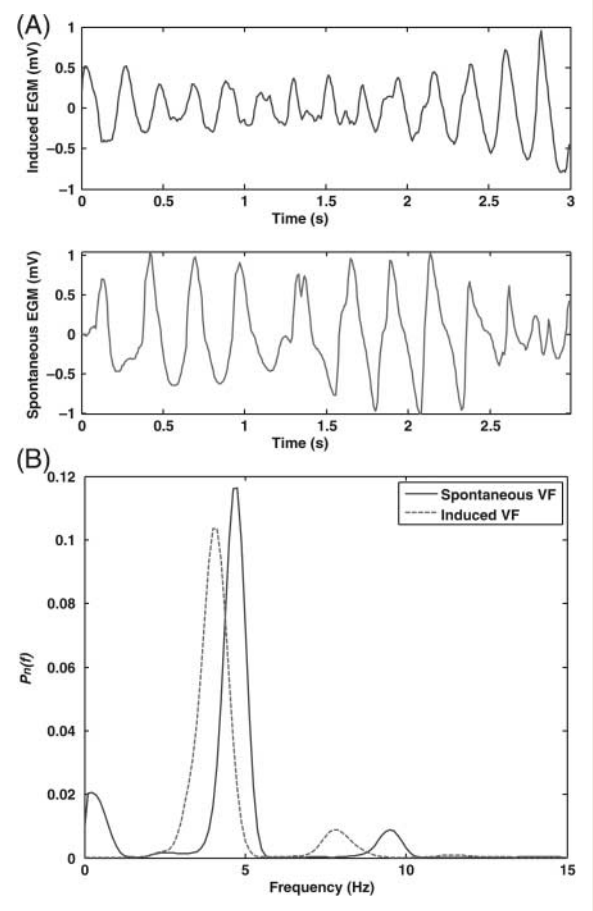

Figure 1 Example of induced and spontaneous ventricular fibrillation episodes in the same patient. Electrograms in the time (*A*) and frequency (*B*) domains. Parameters for induced (spontaneous) recording in the example were: dominant frequency 4.75 (3.8) Hz, leakage 0.96 (0.95), normalized peak 0.11 (0.10).

analysed using autocorrelation and entropy parameters to quantify the degree of organization during VF, which was higher in induced than in spontaneous episodes. The mean CL for spontaneous events was significantly shorter than for induced events, but there was no significant difference in the mean standard deviation of CL between the two types of episodes. Our results show a higher f_d in the induced episodes. As f_d is inversely related to the mean CL of the arrhythmia, the spontaneous events should have a longer CL in our series. The reason for this difference is not clear, but could be related to the analysis technique (time domain compared with frequency domain in our series) or to the method of induction (T-wave shock in Lever's study compared with 50 Hz stimulation in our series).[2] Episodes induced by external T-shock have been shown to have a shorter CL in an experimental study,[9] but not in humans.[12] Our results also suggest a higher degree of organization in induced episodes, as shown by a narrower bandwidth and a higher value of the OI. Moreover, the higher leakage parameter indicates a closer match with a sinusoidal wave in the induced episodes, which suggest a lower degree of complexity, in agreement with the lower information content of the signal in induced VF reported by Lever *et al.* using entropy analysis.[2] The reason why the spontaneous episodes have different spectral characteristics is not obvious. Most of the clinical primary VF episodes are probably associated with ischaemic conditions in some myocardial regions, leading to slower conduction velocities and decreased rotational speed of the rotors maintaining the arrhythmia. The effects of ischaemia on the spectral characteristics of the VF signal have been assessed in several experimental studies with controversial results. In canine models, f_d has been reported to be higher[13] or lower[14] during acute ischaemia than in a control group. In a recent swine model, f_d of the external VF wave was related to the existence of scars and the time from the onset of the arrhythmia,[15] which could partly explain the differences found in the literature. Regarding the organization parameters, OI was found to be higher during acute ischaemic conditions in one series[14] and did not show significant differences when compared with the control group in another.[13] We found a lower degree of organization as reflected by the OI index in spontaneous episodes. The co-existence of ischaemic and non-ischaemic areas during spontaneous arrhythmia could provide a heterogeneous electrophysiological substrate, leading to a higher degree of fragmentation and disorganization of the electrical activity when compared with the more uniform substrate present during induced VF. The area where the VF originates could also play a role to explain the differences between both types of episodes. In electrically induced VF, a local re-entrant pattern near the stimulation point has been shown to occur during the first cycles of the arrhythmia.[16] Most spontaneous episodes are probably originated in ischaemic or peri-infarcted regions of the left ventricle. If a similar mechanism is present at the onset of these episodes, the myocardium located between the site of the origin and the recording electrode could act as a low-pass frequency filter, thereby reducing the mean f_d of the detected electrical signal in spontaneous VFs.[11] Finally, the potential effects of different induction methods on the spectral characteristics of the VF have not been explored in this study, as the method of induction has been 50 Hz stimulation in all patients.

Conclusion and clinical implications

Our results show that the spectral characteristics of the electrical signal recorded by the ICD in humans are different in induced and spontaneous VF episodes. The differences can be related to the intrinsic electrophysiological properties of the arrhythmia or to its different onset location with relation to the recording electrode. Some clinical implications might derive from this fact. First, several variables have shown to affect the defibrillation threshold at the ICD implant, such as the characteristics of the defibrillation wave[17–21] or the administration of anti-arrhythmic drugs.[22–24] The extrapolation of these effects to the spontaneous VFs may not be warranted, as the electrophysiological substrate may be different in both kinds of episodes. Secondly, f_d value has been inversely correlated with the countershock success rate in various conditions.[25–27] Thus, the lower f_d in spontaneous episodes would

suggest a defibrillation threshold higher than the estimated value at the implant test, reinforcing the need for an adequate energy safety margin. However, the use of the spectral characteristics of the VF signal to predict the energy required for defibrillation has not yet been explored in humans.

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Conflict of interest: none declared.

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