Spectral and Nonlinear Analysis of Surgical Ventricular Fibrillation

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Abstract

Most studies about ventricular fibrillation (VF) in humans have attempted to analyze the first minute of its evolution. However, longer duration studies or VF complete evolution (from onset to end) have been scarcely reported. Our aim was to study the complete evolution of VF signal, until asystolia, in a heart surgical VF model in humans using frequency and nonlinear parameters.

We recorded ECG signals during VF from 30 patients underwent heart surgery under cardiopulmonary bypass (CPB). Two types of VF could be present, before surgery and after surgery. We characterized VF using dominant frequency (f_d) and regularity index (ri), and the nonlinear parameter sample entropy ($SampEn$) on the first and the last 5-sec segment before and after surgery. The goal was to analyse the temporal evolution of the VF, and also to compare the beginning and end of both VF before and after surgery. We used a nonparametric resampling statistical hypothesis test.

We found an inverse temporal evolution before and after surgery, so that f_d and $SampEn$ decreased before (2.95 to 2.51 Hz; 0.36 to 0.32) and significantly increased after surgery (2.68 to 3.50 Hz; 0.33 to 0.37). The onsets of the VF were significantly different only on ri, whereas the end of the VF were significantly different on f_d and $SampEn$

The results are in agreement with studies with animal models, and might help to better understand the driven mechanisms of the VF and its temporal evolution.

1. Introduction

Ventricular fibrillation (VF) is one of the major arrhythmias associated with cardiac arrest [1]. During VF, the ventricles do not beat in a coordinated way, leading to inefficient beats, so that there is no cardiac output leading rapidly to death. However, the mechanism of VF are not well known. VF is a very irregular cardiac electrical activity that produces the impossibility of the myocardium to contract.

Some studies about VF in humans aimed to analyze early stages of its evolution. However, few studies had analyzed the complete evolution of the VF, from the beginning to the end, because of its complexity and hemodynamic instability [2, 3]. There has been some studies of the complete evolution of the VF but in animals models [4–6]

The aim of this work is to study the complete evolution of the VF signal from the beginning until the asystolia. VF ECG signals are recorded from patients underwent heart surgery under cardiopulmonary bypass (CPB) with a Holter device. VF might occur before the surgery and after the surgery. Therefore, there are VF with two different onset mechanisms, before surgery the VF occurs from a beating situation, whereas after surgery the VF occurs from the asystole. We aim to study whether there exist differences between both VFs by comparing the beginnings, the ends and the temporal evolution.

We characterize VF signals using indices from the frequency domain, namely the dominant frequency (f_d), related with the periodicity of the signal, and the regularity index (ri), which characterizes how different is the VF signal from a pure sinusoidal [7, 8]. We also characterize VF signals using complexity measures, namely the Sample Entropy ($SampEn$) which is a nonlinear index that characterizes the complexity of a time series [9]. SampEn is widely used in the analysis of biomedical time series [10].

The structure of the paper is as follows. In Section 2 the VF signal preprocessing, spectral analysis, and nonlinear VF analysis methods are described. In Section 3 the database and statistical analysis are described. In Section 4 the results are presented, and finally, in Section 5, conclusions are presented.

2. Methods

2.1. VF Signal pre-processing and spectral analysis

Two cardiologists identified the onset and the end of each VF recorded in Holter, and manually excluded segments with noise by visual inspection. Then, each VF episode was segmented in 5-sec segments. We prepro-

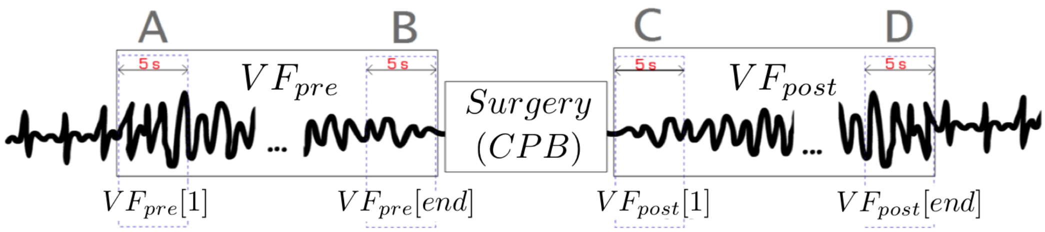

Figure 1. VF signals are split into 5sec segments. To study the difference between VF before surgery (VF_{pre}) and after surgery (VF_{post}), we compute spectral and nonlinear indices on the first ($VF_{pre}[1]$, $VF_{post}[1]$) and on the last ($VF_{pre}[end]$, $VF_{post}[end]$) segment.

cessed each 5-sec segment to remove high frequency noise (50 Hz) by using a moving average filter. Then, we removed the wander base line using a high pass filter with a cut-off frequency of 1 Hz first. Finally, high frequency content was removed by using a Butterworth filter with a cut-off frequency of 30 Hz.

Spectrum was estimated for each EGM segment using a Welch periodogram, with Hamming window of 128 samples, and 50% overlap, and spectral resolution of 1.024 samples. We computed the following indices from the spectrum estimation:

Dominant frequency, f_d, defined as the frequency at which the absolute spectral maximum occurs. The f_d is related with the periodicity of the VF signal.

Regularity index, ri, defined as the ratio of the power in a 75% bandwidth around the f_d, to the power of the $[1, 15]\ Hz$ band [7]. The power band used in this work is different than the usual in other works (usually $[3, 15]\ Hz$) since the lower dominant frequency of VF signal is approximate $\approx 1.3\ Hz$. This index aims to quantify how close to a pure sinusoidal is the VF signal.

2.2. Nonlinear VF analysis

Entropy-based methods provide a quantification of the complexity of a time series. Among them, $SampEn$ [9], which is a modification of the Approximate Entropy [11], holds some properties which are appropriate for the study of physiological signals. The $SampEn$ is the negative natural logarithm of the conditional probability that two sequences which are similar for m points remain similar for $m + 1$ points. Thus, a lower value of SampEn indicates more self-similarity in the time series. In order to compute the $SampEn$, the specification of two parameters is previously required, namely, the embedded dimension m, that is, the length of the vectors to be compared, and a noise filter threshold r.

The procedure for *SampEn* calculation given a time series with N data points is as follows

- $B_i^m(r)$ is defined as $(N-m-1)^{-1}$ times the number of template vectors $\mathbf{x}_m(j)$ similar to $\mathbf{x}_m(i)$ (within *r*) where $j = 1...N - m$ with $j \neq i$.
- The average of $B_i^m(r)$ for all i is calculated as

$$B^m(r) = \frac{1}{N-m} \sum_{i=1}^{N-m} B_i^m(r)$$

- Similarly $A_i^m(r)$ is defined as $(N - m - 1)^{-1}$ times the number of template vectors $\mathbf{x}_{m+1}(j)$ similar to $\mathbf{x}_{m+1}(i)$ (within *r*) where $j = 1...N - m$ with $j \neq i$.
- The average of $A_i^m(r)$ for all i is calculated as

$$A^m(r) = \frac{1}{N-m} \sum_{i=1}^{N-m} A_i^m(r)$$

- *SampEn(m,r)* and its statistic *SampEn(m,r,N)* are defined as follows

$$SampEn(m, r) = \lim_{N\to\infty} \{-\ln [A^m(r)/B^m(r)]\}$$

$$SampEn(m, r, N) = -\ln [A^m(r)/B^m(r)]$$

3. Data base and analysis

We recorded ECG signals during VF, using a Holter device, from 30 patients underwent heart surgery under cardiopulmonary bypass (CPB) in the Hospital Virgen de Arrixaca (Murcia, Spain). The electrodes were placed on the back of the patient to avoid interferences with the surgery monitorization.

Myocardial protection was achieved using antegrade and retrograde hyperkalemic cold blood cardioplegia. VF might occur in two situations: before the surgery, during aortic cross-clamping and perfusion; and after the surgery, right after realising aortic cross-clamp. Therefore, VF n these situations have two sources: VF before the surgery (VF_{pre}), which is secondary to the cardioplegia, and VF after the surgery (VF_{post}), which begging from asystole.

The aim of this work is study whether there are differences in the beginning, end, and evolution between VF_{pre}

	$VF_{pre}[1]$	$VF_{post}[1]$	p-value
f_d (Hz)	2.95 ± 0.84	2.68 ± 0.95	n.s
$\boldsymbol{ri}$	$\mathbf{0.60 \pm 0.19}$	$\mathbf{0.68 \pm 0.14}$	$\mathbf{p < 0.1}$
$SampEn$	0.36 ± 0.10	0.33 ± 0.09	n.s.

Table 1. Mean$\pm$standard deviation of spectral and nonlinear indices computed on the first 5-sec segment in VF_{pre} and VF_{post}. $P - value < 0.1$ is considered a statistically significant difference.

	$VF_{pre}[end]$	$VF_{post}[end]$	p-value
$\boldsymbol{f_d}$ **(Hz)**	$\mathbf{2.51 \pm 0.9}$	$\mathbf{3.50 \pm 1.0}$	$\mathbf{p < 0.1}$
ri	0.61 ± 0.22	0.71 ± 0.19	n.s.
$\boldsymbol{SampEn}$	$\mathbf{0.32 \pm 0.11}$	$\mathbf{0.37 \pm 0.09}$	$\mathbf{p < 0.1}$

Table 2. Mean$\pm$standard deviation of spectral and nonlinear indices computed on the first 5-sec segment in VF_{pre} and VF_{post}. $P - value < 0.1$ is considered a statistically significant difference.

and VF_{post}. To study this differences, we split the VF signals in 5-sec segments, and compute the spectral and nonlinear parameters on the first and last segments in both $VF_{pre}$and VF_{post}.

To test whether exists statistically significant differences on spectral and nonlinear indices we performed statistical hypothesis tests based on bootstrap resampling. The null hypothesis (H_0) represents no difference between two groups of data, that is, to test differences on the beginning we compare the indices computed on $VF_{pre}[1]$ vs. indices computed on $VF_{post}[end]$. The alternative hypothesis (H_1) implies that there exist significant differences. We used the mean difference between each indices as the statistic to summarize our data. Bootstrap hypothesis test is based on the idea of building an empirical distribution of the statistic, under H_0, by computing the statistic on B different resamplings. Assuming that H_0 is true, bootstrap statistics are computed on resamplings from a population which is the concatenation of the indices from the groups that we want to compare. We computed the p-value as the fraction of the points on the distribution (probability) that are more extreme than the actual statistic value [12, 13].

4. Results

Comparison of the beginning. $VF_{pre}[1]$ *vs.* $VF_{post}[1]$. Table 2 shows the mean and standard deviation values for spectral and nonlinear indices. Statistically significant differences between $VF_{pre}[1]$ and $VF_{post}[1]$ are highlighted.

f_d was lower, on average, after surgery but without a statistically significant different. Only the spectral index ri showed a significantly increasing before and after surgery, meaning that VF_{post} might be more irregular in the sense of being less pure sinusoidal.

Comparison of the end.$VF_{pre}[end]$ *vs.* $VF_{post}[end]$. Table 2 shows the mean and standard deviation values for spectral and nonlinear indices. Statistically significant differences between $VF_{pre}[end]$ and $VF_{post}[end]$ are highlighted.

f_d showed a statistically increase after surgery, actually it was 1 Hz on average. Also, the last 5-sec segment after surgery ($VF_{post}[end]$) was more complex than the last 5-sec segment before surgery ($VF_{pre}[end]$), showing a difference statistically significant.

Temporal evolution of VF_{pre} *and* VF_{post}. Figure 2 shows boxplots of the spectral and nonlinear parameters computed before (VF_{pre}) and after surgery (VF_{post}). We tested whether there existed a significant difference between the parameters computed on the first (noted by [1]) and the last (noted by $[end]$) 5-sec segment. Only the f_d and $SampEn$ after surgery (VF_{post}) parameters showed a statistically significant difference between the onset of the VF and the end. f_d showed a non-significant decrease before surgery from 2.95 Hz to 2.51 Hz before surgery, which contrasted with the significant increase showed after surgery going from 2.68 Hz to 3.50 Hz. The nonlinear parameter $SampEn$ presented a similar behaviour, showing a decreasing complexity before surgery from 0.36 to 0.32, and a significant increasing complexity after surgery from 0.33 to 0.37. Regarding ri, it showed a steady behaviour but with clear differences before and after surgery.

5. Conclusions

The mechanisms of the onset of the VF are currently under study. There have been some studies stating that arrhythmics storms in different cardiopathies, the onset of the VF are driven by ventricular extrasytoles. In this work we studied the onset, end, and temporal evolution of VF with very different underlying situations at the beginning. VF signals were recorded on patients underwent heart surgery under cardiopulmonary bypass. In this type of surgeries, VF might occur before and after the surgery. This allowed us to record the VF from the beginning until the end, which are different before and after the surgery. Before the surgery the beginning is from a heart beating until the asystolia, whereas after the surgery the beginning is converse.

We characterized VF signals by spectral indices, dominant frequency (f_d) and regularity index (ri), and by nonlinear index sample entropy ($SampEn$). The results showed that there is a complete inverse temporal evolution before and after surgery on f_d and $SampEn$ indices. They also showed a significant difference of parameters f_d and $SampEn$ at the end of both VF. Parameter ri was significantly different on the beginning of the VF.

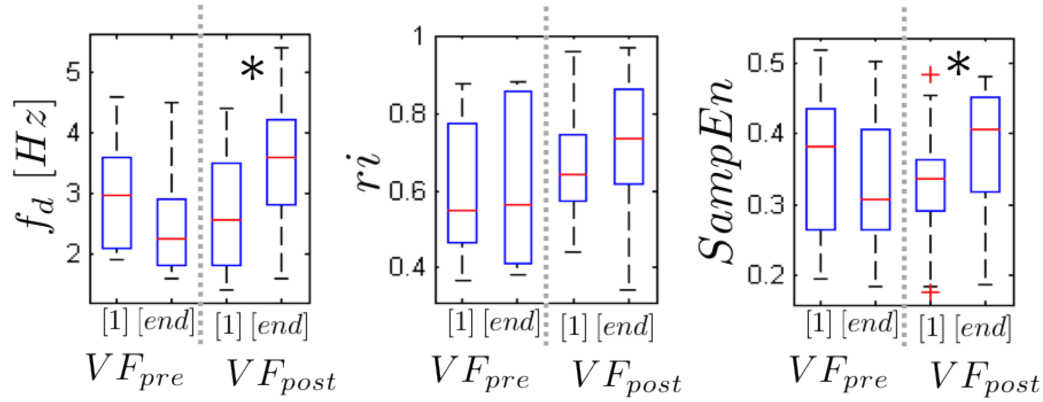

Figure 2. Temporal Evolution of spectral and nonlinear indices of VF before (VF_{pre}) and after (VF_{post}) surgery. Boxplots shows the distribution of the parameters computed on the firsts 5-sec segments ($VF_{pre}[1]$ and $VF_{post}[1]$) and on the lasts 5-sec segments ($VF_{pre}[1]$ and $VF_{post}[1]$). An asterisk indicates a significant difference between the parameter computer on the first and the last 5-sec segment.

The dataset was small to derive conclusive results (12 patients with VF before surgery and 18 with VF after surgery). These results are in agreement with previous results in animal models, and might will allow to better understand the mechanisms of VF.

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