**Effects of Myocardial Stretching on Excitation Frequencies Determined by Spectral Analysis During Ventricular Fibrillation**

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**Basic research**

**Introduction and objectives.** The aim of this study was to analyze the effects of myocardial stretching on excitation frequencies, as determined by spectral analysis, during ventricular fibrillation.

**Methods.** In 12 isolated rabbit heart preparations, ventricular activation during ventricular fibrillation was recorded with multiple electrodes. Recordings were obtained before, during and after ventricular dilatation produced with an intraventricular balloon. The dominant frequency of the signals obtained with each of the electrodes was determined by spectral analysis.

**Results.** During the control phase, the mean, minimum and maximum dominant frequencies were, respectively, 14.3 ± 1.7, 12.5 ± 1.7, and 16.2 ± 1.4 Hz, and the average difference between the maximum and minimum frequencies was 3.6 ± 2.1 Hz. This difference was over 4 Hz in four cases, and in no case did it exceed 8 Hz. During ventricular stretching, the mean dominant frequency increased significantly (21.1 ± 6.1 Hz; p < 0.0001), as did the minimum values (14 ± 2.6 Hz; p < 0.05) and especially the maximum values (26.6 ± 7.7 Hz; p < 0.0001). The difference between the maximum and minimum frequencies (12.6 ± 6.4 Hz; p < 0.001) was over 4 Hz in all cases except one, and over 8 Hz in 9 cases. The maximum values were distributed heterogeneously during ventricular stretching. Upon suppressing ventricular stretching, the dominant frequency did not differ from controls.

**Conclusions.** Myocardial frequency maps during ventricular fibrillation show limited variations in the dominant frequency of the signals recorded in the lateral wall of the left ventricle. During stretching, the patterns were heterogeneous, due mainly to the marked increase in the maximum dominant frequency. In the experimental model used, the effects of stretching remitted after suppressing ventricular dilatation.

**Key words:** Electrophysiology. Ventricular fibrillation. Basic research. Mapping. Fourier analysis.

**Palabras clave:** Electrofisiología. Fibrilación ventricular. Investigación básica. Mapeo. Análisis de Fourier.

**Introduction y objetivos.** Analizar mediante técnicas espectrales los efectos del estiramiento miocárdico sobre las frecuencias de activación durante la fibrilación ventricular (FV).

**Métodos.** En 12 preparaciones de corazón aislado de conejo se ha registrado la activación durante la fibrilación ventricular utilizando un electrodo múltiple antes, durante y después de la dilatación ventricular producida con un balón intraventricular y se ha determinado (análisis espectral) la frecuencia dominante de las señales obtenidas.

**Resultados.** Durante el control, la frecuencia dominante media, minima y máxima ha sido de 14,3 ± 1,7; 12,5 ± 1,7 y 16,2 ± 1,4 Hz, y el promedio de las diferencias entre la máxima y la mínima ha sido de 3,6 ± 2,1 Hz. Esta diferencia ha sido superior a 4 Hz en 4 casos y en ningún caso ha sido superior a 8 Hz. Durante la dilatación ventricular, la frecuencia dominante media ha aumentado significativamente (21,1 ± 6,1 Hz; p < 0,0001), así como los valores mínimos (14 ± 2,6 Hz; p < 0,05) y en mayor medida los máximos (26,6 ± 7,7 Hz; p < 0,00001) y la diferencia entre máximos y mínimos (12,6 ± 6,4 Hz; p < 0,001) que ha sido superior a 4 Hz en todos los casos excepto uno y superior a 8 Hz en 9 casos. Los valores máximos se han distribuido de manera heterogénea durante la dilatación y, al suprimirla, los valores de la frecuencia dominante no han presentado diferencias con respecto al control.

**Conclusiones.** Los mapas de frecuencias durante la fibrilación ventricular ponen de manifiesto variaciones limitadas en la frecuencia dominante de las señales registradas en la pared lateral del ventrículo izquierdo. Durante la dilatación, los patrones observados se caracterizan por su heterogeneidad debido, fundamentalmente, al acen tuado incremento de las frecuencias máximas. En el modelo utilizado, los efectos del estiramiento revierten una vez suprimida la dilatación.
INTRODUCTION

Among the processes that alter cardiac electrophysiological properties is stretching which, via mechanical feedback, gives rise to a change in transmembrane ionic currents in response to mechanical stimulation. Stretching fundamentally consists of a shortening of the duration of the action potential, refractoriness, and length of the activation wave. Changes in the ventricular fibrillatory pattern due to stretching can be present in different clinical situations, among them atrial or ventricular dilatation due to pressure or volume overload or regional contractility changes, and is associated with greater vulnerability to triggering and perpetuation of various rhythm disturbances, among them fibrillation. Changes in the ventricular fibrillatory pattern due to stretching have been described, and basically consist of a shortening of the duration of the action potential, refractoriness, and length of the activation wave./stretching fundamentally consists of a shortening of the duration of the action potential, refractoriness, and length of the activation wave. Changes in the ventricular fibrillatory pattern due to stretching can be present in different clinical situations, among them atrial or ventricular dilatation due to pressure or volume overload or regional contractility changes, and is associated with greater vulnerability to triggering and perpetuation of various rhythm disturbances, among them fibrillation.

METHODS

Experiment preparation

We studied 12 isolated perfused heart preparations from California rabbits (mean weight, 4.1 kg±0.4 kg). After anesthesia with ketamine (25 mg/kg i.v.) and heparinization, the heart was extracted and then submerged in cold Tyrode (4°C). Once the aorta was isolated, it was connected to a Langendorff system, with the aim of studying the changes in the ventricular fibrillation pattern obtained after altering the myocardial electrophysiological properties via ventricular dilatation, using frequency domain analysis techniques.

Data analysis

We analyzed the recordings corresponding to three 2 second intervals obtained at 5 minutes from the beginning of the arrhythmia (immediately before performing ventricular dilatation) to the end of the period of time during which the dilatation was maintained, and at 5 minutes after deflating the intraventricular balloon. We used Fourier rapid transform (Hanning window) to carry out spectral analysis of the 3 blocks of 2048 points selected (sample frequency 1 kHz), using the Welch method. We analyzed the signals recorded from each of the 121 contacts from the multiple-contact electrode and, after determining the dominant frequency (DFr) of each signal (Figure 1), we constructed
Data processing was performed using Matlab programming on a Hewlett-Packard 712/80 platform.

**Statistical calculations**

We calculated the basic statistical parameters of the quantitative variables analyzed: mean, standard deviation, the maximum and minimum values, and the difference between the two. Statistical significance of the differences was analyzed via the Student t test for paired samples, using the Bonferroni correction when multiple comparisons were made. We considered the level of statistical significance to be a $P < .05$.

**RESULTS**

In all the cases studied, the VF induced via over-stimulation persisted during the performance of the experimental protocol. In Figure 2 we show the mean maximum DFr values, the minimum values, and the difference between the two according to the isofrequency maps obtained before carrying out ventricular dilatation (control), after inflating the intraventricular balloon, and after stopping the dilatation. During the control period, the mean DFr obtained on the frequency maps was $14.3 \text{ Hz} \pm 1.7 \text{ Hz}$, the minimum DFr was $12.5 \text{ Hz} \pm 1.7 \text{ Hz}$, the maximum DFr was $16.2 \text{ Hz} \pm 1.4 \text{ Hz}$, and the average of the differences between the maximum and minimum values was $3.6 \text{ Hz} \pm 2.1 \text{ Hz}$. The difference between the maximum and minimum values was greater than 4 Hz in 4 cases, but in no case greater than 8 Hz. During ventricular dilatation there was a significant increase in the mean DFr ($21.1 \text{ Hz} \pm 6.1 \text{ Hz}; P < .0001$), the minimum DFr ($14 \text{ Hz} \pm 2.6 \text{ Hz}; P < .05$), and particularly in the maximum DFr ($26.6 \text{ Hz} \pm 7.7 \text{ Hz}; P < .0001$), so that the differences between the maximum and minimum values obtained on each frequency map were increased ($12.6 \text{ Hz} \pm 6.4 \text{ Hz}; P < .001$). During dilatation, the difference between the maximum and minimum values was greater than 4 Hz in all cases except one, and greater than 8 Hz in 9 cases. The maximum difference was 22.2 Hz, and the maximum DFr values were distributed heterogeneously on the isofrequency maps obtained during dilatation. Once the dilatation was stopped, the mean DFr ($13.6 \text{ Hz} \pm 1.6 \text{ Hz}$), maximum DFr ($14.9 \text{ Hz} \pm 1.7 \text{ Hz}$), minimum DFr ($12.2 \pm 1.1 \text{ Hz}$), and the differences between the maximum and minimum DFr values ($2.5 \text{ Hz} \pm 1.4 \text{ Hz}$) were similar to those obtained during the control period and without statistical significance. The differences between the maximum and minimum DFr was greater than 4 Hz in 2 cases but in no cases was greater than 8 Hz.

In the upper portion of Figure 3 the frequency spectrums corresponding to the recordings obtained from two electrodes in one of the experiments during the control period can be seen. We noted the minimum ($13.6 \text{ Hz}$) and maximum ($16.6 \text{ Hz}$) DFr values. During the same experiment, after ventricular dilatation (lower portion of the Figure), an increase in the minimum DFr value ($14.6 \text{ Hz}$) was produced and an even greater increase in the maximum DFr value ($22.5 \text{ Hz}$) occurred.

In Figure 4, we show the frequency maps corresponding to one of the experiments; during the control...
During dilatation, the minimum values were recorded in the mid superior side, as were the maximum values in the right upper side, the mid right side, and the central area. There is a high density of isofrequency lines due to the variations in DFr, and the frequency map is characterized by the heterogeneity of activation frequencies.

DISCUSSION

The analysis of the activation process during VF based on the construction of activation maps with the corresponding isochrones is complex and time-consuming, given that it is necessary to identify and verify the local activation times during a particular window of time for each of the contacts being studied. Analysis based on spectral techniques do not require the identification of local activation times and also allow rapid acquisition of the parameters related to ventricular activation apart from the frequency spectrums of fibrillatory signals. This type of analysis facilitates the acquisition of data concerning fibrillatory processes, both during prolonged periods of time and in broad areas of the ventricular myocardium. In the first scenario, information is obtained concerning the temporal evolution of the changes produced during ventricular activation, and in the second scenario information is obtained on the spatial distribution of activation frequencies in the area studied via the use of isofrequency maps that allow acquisition of the data of interest concerning the mechanisms that maintain VF. In this way, frequency gradients have been described during the ventricular activation process that support the hypothesis of some authors that the fibrillatory process is sustained due to the existence of fibrillatory conduction from areas of rapid activation, although the interpretation of the significance of the characteristics and variations of the frequency spectrums is subject to debate. The existence of localized areas of the ventricular myocardium...
Medium in which elevated dominant frequencies are observed may indicate the presence of fonts of periodic rapid activity caused by reentry mechanisms. Nevertheless, we cannot discount the importance of other phenomena, such as the presence of complex activation patterns in multiple block areas and the collision of activation fronts that, by creating double and multiple potentials, may cause transitory elevated dominant frequencies in these areas.

In our study, we observed that the construction of frequency maps during VF allowed us to document some limited variations in the DFr of signals recorded in the left ventricle lateral wall, and that during ventricular dilatation the patterns observed were characterized by their heterogeneity due to the marked increase in maximum values. Previous studies have found that myocardial stretching modifies the ventricular fibrillation pattern, giving rise to an acceleration of the process and also to an increase in the complexity of the activation, based on the analysis of epicardial activation maps. Burton and Cobbe observed that myocardial stretching caused shortening of the ventricular cycles during VF and an increase in the distribution of these intervals. The latter finding was attributed to an increase in the heterogeneity of the refractory periods as the modifying effect of stretching was not uniform. It has been postulated that stretching shortens the refractoriness and myocardial activation wavelength.
and also that it increases the slope of the initial phase of the electrical restitution curve. This curve is obtained by comparing the duration of the action potential (ordinate) to the preceding diastolic interval (abscissa) and, when its slope is equal to or greater than the unit, the phenomenon of alternance of the action potential duration appears, and destabilization of the re-entry activation fronts is favored. The initial phase of the curve corresponds to the short diastolic intervals; in other words, the more rapid activation frequencies. Changes in the electrical restitution curve have been related to variations in the regularity and stability of activation patterns during VF, so that the increase in the slope, when the alternance of the action potential duration increases, favors the interruption of the activation fronts and increases fibrillatory pattern complexity. Both the unequal distribution of the electrophysiological effects from stretching in the ventricular myocardium and the consequences of an increase in the slope of the electrical restitution curve could be implicated in the greater complexity of the VF and in the increase in heterogeneity of the frequency maps obtained during the arrhythmia. On the other hand, the parameters used to identify the effects of stretching have not shown significant differences.
with respect to baseline once ventricular dilatation has been overcome, indicating the reversibility of changes induced by the myocardial stretching in the experimental model used, as has been shown in previous studies. 18,19

**Limitations**

The stretching produced by the intraventricular balloon, by changing the tension of the ventricle wall, may produce changes in myocardial perfusion. In previous studies using similar methodology and a similar degree of dilatation, significant changes in coronary flow were not observed after the application of stretching during ventricular fibrillation. 19 Nevertheless, it must be taken into account that changes in the metabolic balance may cause additional changes in the electrophysiological properties of the myocardium. On the other hand, the triggering of ventricular fibrillation in vivo implicates the abolition of coronary perfusion, the appearance of ischemia, and the metabolic deterioration of the myocardium, which on their own change the characteristics of the myocardial activation pattern. 22,23,27 Maintenance of coronary perfusion during arrhythmia allows us to create stable reproducible experimental conditions that make it possible to analyze the effects of difference variables on the ventricular fibrillatory pattern without the interference of ischemia. For this reason, in different studies coronary perfusion is maintained during ventricular fibrillation in order to study phenomena related to arrhythmias; 18,25,26,31,32,39 this was also the methodology we used in our study.

**Clinical implications**

The analysis of the activation process during VF via the construction of frequency maps has allowed us to see the effect of stretching, which consists of an acceleration and an increase in the complexity of fibrillation. The analysis techniques applied allowed us to study the drugs or maneuvers that limit the consequences of stretching and its arrhythmogenic effects, as myocardial stretching favors the triggering and perpetuation of the fibrillatory processes. Analysis of the action of these drugs or maneuvers may provide useful information for the control of diverse clinical situations in which myocardial stretching is present, and in those cases where their arrhythmogenic effect has been postulated (dilatation, pressure or volume overload, or changes in segment motility). The effects of drugs that act on the channels activated by stretching, such as gadolinium, streptomycin, or beta-blockers, can be observed via the analysis of the changes observed in the ventricular fibrillatory pattern during ventricular dilatation. On the other hand, the reversibility of the effects observed means that, in situations of acute stretching, the suppression of same may re-establish electrophysiological conditions less favorable to the triggering of cardiac arrhythmias.

**CONCLUSIONS**

The construction of frequency maps during VF allows the observation of limited changes in the dominant frequency of signals recorded in the left ventricle lateral wall. During ventricular dilatation, the patterns observed are characterized by their heterogeneity, due fundamentally to the marked increase in the maximum frequencies. In the experimental model used, the effects of stretching remit once ventricular dilatation has been overcome.

**REFERENCES**


