Changes in T-peak-to-T-end Morphology Measured by Time-Warping Are Associated with Ischemia-Induced Ventricular Fibrillation in a Porcine Model

Neurys Gómez[1], Julia Ramírez[1,2], Alba Martín-Yebra[1,2], Pyotr Platonov[3], Juan Pablo Martínez[1,2], Pablo Laguna[1,2]

[1] Biomedical Signal Interpretation & Computacional Simulation (BSICoS)
Instituto de Investigación en Ingeniería de Aragón (I3A)
Universidad de Zaragoza, Mariano Esquillor s/n, 50018, Zaragoza, Spain.
Tel. +34-976762707, e-mail: ngomez@unizar.es
[2]Centro de Investigación Biomédica en Red – Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN)
[3]Department of Cardiology, Clinical Sciences, Lund University, Lund, Sweden

Abstract

In this work we assess, the association of a time-warping-based morphology variation index computed between the peak and the end of the T wave, d_w, with the occurrence of ventricular fibrillation (VF) episodes in ischemic conditions. Dynamic increases of the d_w index during ischaemia progression in pigs are associated with VF occurrence.

Introduction

The dispersion of ventricular repolarization reflected on the T_{pe} interval has shown potential in predicting arrhythmic risk [1], avoiding annotation errors on T wave onset determination as consequence of the ST elevation. The ability of the time-warping based index proposed by Ramírez et al. [2], restricted from the T-peak to T-end part of T wave, was evaluated during a human model of short time induced ischemia by percutaneous coronary intervention (PCI). In that study, the index capability in capturing ischemia induced T-peak to T-end waveform modification is reported. The present study aims to evaluate if this d_w index, restricted to T-peak to T-end, is associated with ventricular fibrillation risk in a porcine model of prolonged ischemia.

Materials and Methods

The study population included 26 pigs undergoing a closed-chest myocardial infarction model by PCI intervention [3]. Balloon inflation in the left descending artery (LAD) was performed in each pig to induce ischemia. 12-lead ECG recordings, digitized at a sampling rate of 1024 Hz and an amplitude resolution of 1.18 μV per bit, were used to monitor the pigs before the balloon inflation (Control stage) and throughout the 40-minute occlusion period (Occlusion stage). From the total study population, 16 pigs did not suffer from VF (non-VF group) and 10 pigs suffered from VF (VF group).

Quantification of T-peak to T-end wave morphology changes

Linear filtering, first with a low-pass 40-Hz cut-off frequency for electric and muscle noise removal, then with a high-pass 0.5-Hz cut-off frequency, for baseline wander attenuation, both bidirectional Butterworth of sixth-order was applied. ECG delineation was performed using a wavelet-transform-based single-lead method [4] to obtain the QRS fiducial points. Subsequently, a multi-lead selection rule strategy [5] was applied over the 8 single-lead sets of marks to obtain the multilead QRS fidutial points. Then, spatial Principal Component Analysis (PCA) transformation was performed over the 8 standard leads, and learned over the T wave, in order to emphasize T-wave content. Finally, the first principal component lead was again delineated, and each segmented T-wave further low-pass filtered at 20 Hz cut-off frequency, with a sixth order Butterworth filter, for subsequent analysis.

The T-peak to T-end wave morphology changes along time were quantified by the d_w index proposed by Ramírez in [2], and adapted in [6] to restrict it to the last part of the T wave. For each s-th 15 second moving signal window along the recording (with 10-s overlap between windows), T waves were extracted and a mean warped T-peak to T-end wave (MWTPE) was computed. The reference MWTPE was computed from the first 60 seconds at the beginning of the control stage so that d_w represents the T-peak to T-end wave morphological changes relative to the initial state. For each window, the marker $d_w(s)$ is estimated as the temporal reparametrization between

two waves, a MWTPE, $f^s = [f^s(t^s(1)), \dots, f^s(t^s(N_s))]^T$, where $t^s = [t^s(1), \dots, t^s(N_s)]^T$, together with a selected reference MWTPE, $f^r(t^r)$. d_w index is the mean amount of warping needed to minimise the time domain differences among these different MWTPE, the one under study $f^s(t^s)$, and the reference $f^r(t^r)$, resulting in a series $d_w^{PCA}(s)(s \in \{1, \dots, S\})$ sampled at each 5 seconds relative to the initial reference.

d_w series estimation through warping functions. Let $\gamma(t^r)$ be the warping function that relates t^r and t^s such that the composition $[f^s \, o \, \gamma](t^r) = f^s(\gamma(t^r))$ denotes the re-parameterization, or time-warping, of the $f^s(t^s)$ using $\gamma(t^r)$. As in [2] the square-root slope function (SRSF) was used instead of the original signals, to find the optimal warping function so avoiding the so called "pinching effect". The optimal warping function, $\gamma^*(t^r)$, is the one that minimizes the amplitude difference between the SRSF of $f^r(t^r)$ and $f^s(\gamma(t^r))$. The level of warping represents the amount of time stretching needed to optimally fit the wave under study relative to the reference one. The d_w biomarker quantifies this level of warping required as the average of the absolute difference value between $\gamma(t^r)$ and t^r.

Results and discussion

During control recordings, d_w^{PCA} remained stationary with a median value [IQR] of 1.76 [1.80] ms. During artery occlusion, d_w^{PCA} followed a well-marked gradual increasing trend as ischemia progressed, with median of 15.47 [18.53] ms.

The average of d_w^{PCA} index measured in different 5 minutes intervals (last 5 minutes before the occlusion onset, at 1-5, 5-10, 10-15, 15-20, 20-25-minute intervals after occlusion onset and during 5 minutes prior to a VF episode), clustered for the two-pig group are presented in Fig. 1. These d_w^{PCA} averages were significantly higher for VF group than in the non-VF group with a median value of 0.82, 0.83, 6.25, 7.56, 8.02, 7.76, 7.81 and 7.65 vs 0.44, 2.35, 12.45, 18.78, 26.71, 23.96, 30.95 and 34.37, and p-value of 0.223, 0.011, 0.035, 0.001, 0.001, 0.007, 0.002 and 0.001, for each interval, respectively. As occlusion time progresses, significant inter-individual differences were found in the magnitude of d_w^{PCA} changes for VF group already from the first 5 minutes of occlusion, ranged from a negligible variation at the beginning of the occlusion to a pronounced magnitude as time elapses. The very significant increase in d_w^{PCA} for the VF group relative to the non-VF group as ischemia progress indicate that increases in d_w^{PCA} magnitude beyond some threshold are associated with the occurrence of VF episodes.

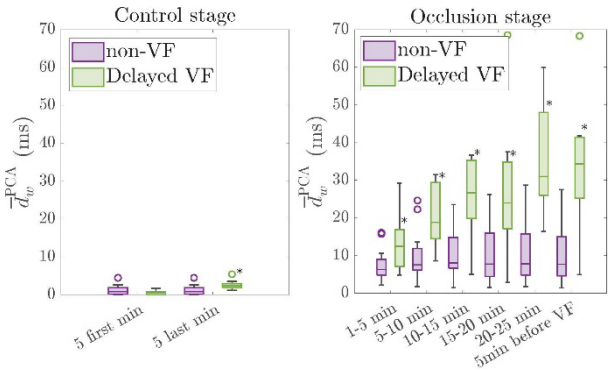

Figure 1. Comparison of d_w averages, for the VF subgroup and non-VF subgroup, measured in different 5 minutes segments. * indicates statistical significance between groups.

Conclusions

In a porcine myocardial infarction model, the time-warping-based marker, d_w, restricted to T-peak to T-end interval, allows to monitor ischemia-induced repolarization changes. Larger increase of d_w during ischaemia progression is associated with VF occurrence and suggest further evaluation in humans.

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