The ECG T-Wave Duration as an Index of Dispersion of Ventricular Repolarization: Insights from Simulations

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Abstract

Dispersion of ventricular repolarization (DVR) is known to be an immediate precursor of potentially mortal arrhythmias. Recently, the duration of the ECG T-wave (TWD) has been proposed as an indicator of DVR. In this work, we have used computer simulations to quantify the relationship between the degree of DVR and the TWD. For this purpose, the Luo-Rudy dynamic (2000) model was used in combination with a monodomain model of the ventricular tissue to simulate the electrical activity of a ventricular strand.

The results of the simulations show that the duration of the T-wave increases almost linearly with dispersion of ventricular repolarization, independently of the cause of the increased DRV. Thus, the T-wave duration could indeed be a good indicator of the DRV, as suggested by other experimental works.

1. Introduction

A variety of experimental studies show that there are electrophysiological differences between the characteristics of cell membranes located on the ventricular surfaces (endocardium and epicardium) and those located on deeper layers of the ventricular wall [1].

Moreover, cells situated on the inner layers of the myocardium (M Cells) show an action potential with a spike-and-dome characteristic that is also typical of the morphology of cells from the epicardium [2,3,4]. The presence of a higher transient outward current (I_{to}) contributes to the appearance of a prominent notch on the early phase of action potentials of the epicardium and the midmyocardium, as can be observed in Figure 1[5]. On the other hand, both a lesser presence of the slow component of the delayed Potassium current (I_{Ks}) and a higher sodium current (I_{Na}) contribute to the appearance of higher action potentials in the cells of the midmyocardium.

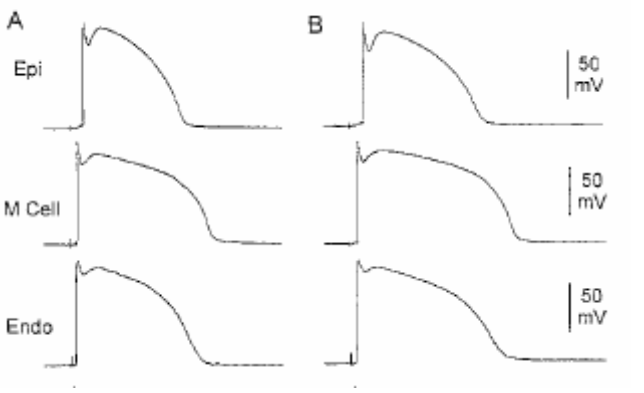

Figure 1. Epicardial, endocardial, and midmyocardial action potentials (taken from reference [5]).

These differences in the electric behaviour of cells along the walls of the ventricular myocardium are crucial when determining the shape of the T and U waves and even that of the QT segment of an electrocardiogram (ECG). They are also considered a factor that may be involved in the development of cardiac arrhythmias [2,3].

Even today, the interpretation of the shapes of electrocardiographic waves is basically empiric. Thus, it is important to establish a mechanics that relates cellular processes and the ECG, so that a specific diagnostic of electrophysiological disorders can be made. Using a detailed action potential (AP) model, which is physiologically based on the cardiac ventricular cell model that includes all the relevant ionic channels, pumps, and exchangers, and considering the dynamic changes in the concentration of Na^+, Ca^{2+}, and K^+ during the AP, it is possible to relate the different ECG waves with individual ionic currents in the membrane and the properties of the PA in a precise way [6].

Experimental studies show that there is a relationship between dispersion of ventricular repolarization (DVR) and severe ventricular arrhythmia [7]. Moreover, recent works hypothesize that the duration of the ECG T-wave (TWD) is a good indicator of DVR [8,9,10].

The aim of the present work is to verify, using simulation techniques, the hypothesis that a greater DVR

results in the widening of the T wave on the ECG. This would allow us to make use of the duration of the T wave as an indirect indicator of the risk of being prone to arrhythmias.

2. Methods

Following the Luo-Rudy dynamic cellular model [11,12,13], PA propagation has been reconstructed in a 1-dimensional fibre. This reconstruction shows a wave front that propagates from the endocardium towards the epicardium during the regular ventricular excitation. To take into account the heterogeneities of the ionic channels, a series of changes have been introduced in the formulation of the fibre. These changes are described below.

The theoretical fibre, with a length of 1.65 cm, is made up of 165 cells of the LRD model. These cells are linked through gap junctions. The transmural heterogeneity of the density of the ionic channels is introduced by distinguishing the three types of ventricular cells: endocardium, midmyocardium, and epicardium. The density of I_{Ks} varies, being lowest in M cells (Endocardium: G_{Ks}: G_{Kr} = 11:1, Midmyocardium: G_{Ks}: G_{Kr} = 5:1 and Epicardium: G_{Ks}: G_{Kr} = 17:1).

The unipolar extracellular potential (ϕ_o) generated by the fibre in a medium with conductivity σ_0 is computed from the transmembrane potential V_m using the following expression [14]:

$$\Phi_0(x',y',z') = \frac{a^2\sigma_i}{4\sigma_e}\int(-\nabla V_m)\left[\nabla\frac{1}{r}\right]dx \qquad (1)$$

$$r = \left[(x-x')^2+(y-y')^2+(z-z')^2\right]^{1/2}$$

Where ∇V_m is the spatial gradient of V_m, α is the radius of the fibre, σ_i is the intracellular conductivity, and r is the distance from a source point (x, y, z) to the point where the potential is being measured (x', y', z'). ϕ_o is calculated placing the electrode at point (x',y',z'), and constitutes the ECG under study in our work.

The duration of the T wave is determined by the intersection of the "base line" with the line that follows the steepest part of the T wave before and after its peak [6].

3. Results and discussion

Firstly, following the effect that d-Sotalol has on I_{Kr}, an increment of the DVR has been simulated by virtually administering this drug in different areas of the fibre. To do that, the conductance of the potassium channels has been changed, obtaining the results shown in Table 1.

		DVR	TWD
1	Control	13,7	58,98
2	G_{Kr} x 0,5 , cel[0-164]	16,6	76,92
3	G_{Kr} x 0,5 , cel[0-81]	19,24	75,29
4	G_{Kr} x 0,75 , cel[0-164]	15,01	67,13
5	G_{Kr} x 0,25 , cel[0-164]	18,52	88,88
6	G_{Kr} x 0,75 , cel[0-81]	16,3	69,31
7	G_{Kr} x 0,25 , cel[0-81]	22,52	81,27

Table 1. DVR and TWD in different simulations with d-Sotalol.

As can be seen, the duration of the T wave varies with the DVR, depending on $\overline{G}_{Kr}$ and the area where the variation is applied. The variation experimented by the T wave of the ECG as a consequence of changing the DVR is represented in Figure 2.

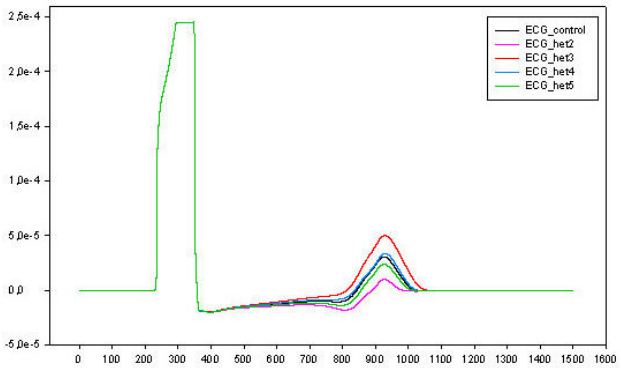

Figure 2. Effect of d-Sotalol on the ECG when administered in different areas of the fiber.

Secondly, a series of simulations have been performed in ischemic conditions in order to determine the effects of this pathology on the ECG and, more specifically, on the duration of the T wave. With this goal in mind, the value of all parameters relevant to this pathology has been modified in different parts of the fibre, as shown in Figure 3.

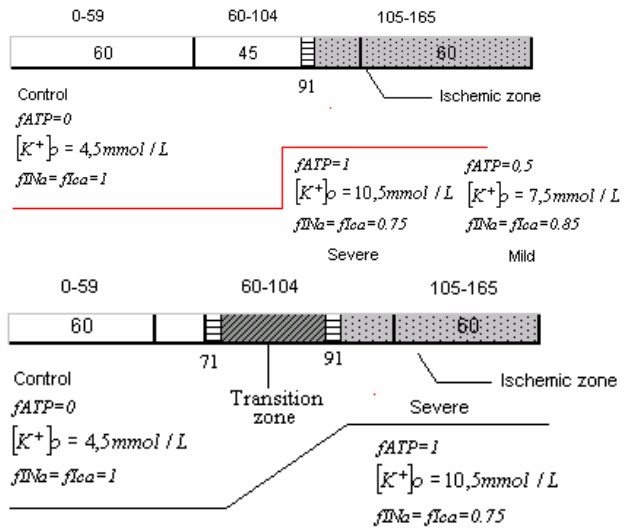

Figure 3. Upper panel: diagram of the fibre with acute and medium regional ischemia. Lower panel: Diagram of the fibre with acute regional ischemia.

The variation in APD along the fibre is represented in figure 4. As can be seen, the APD is reduced considerably in the area of the fibre where ischemia was simulated, which translates into a widening of the T wave (Figure 5).

When simulating mild regional ischemia, we obtained DRV=45ms and TWD=100ms, and when ischemia was severe the results were DRV=63ms and TWD=129ms.

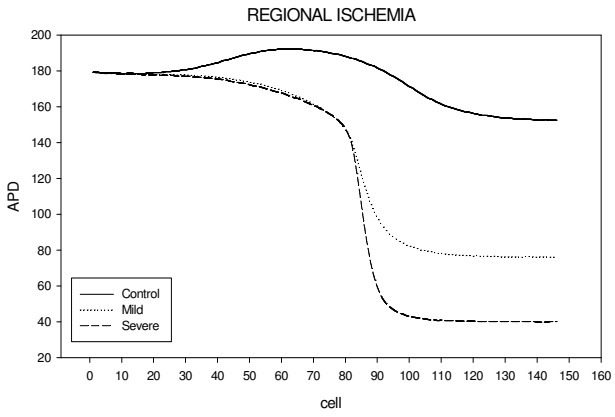

Figure 4. APD along a fiber with mild and severe ischemia.

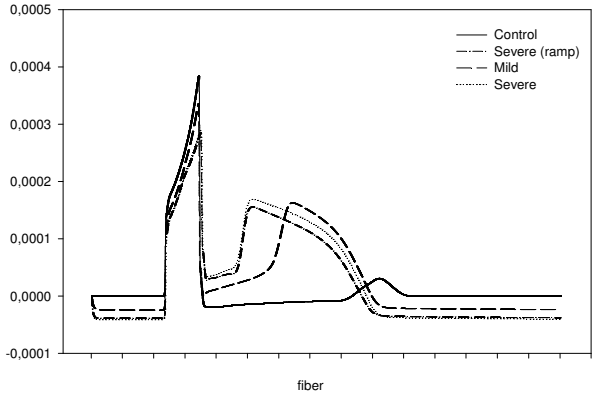

Figure 5. Effect of regional ischemia on the ECG.

Experimental studies show that there is a relationship between dispersion in ventricular repolarization (DVR) and acute ventricular arrhythmia [7,15]. They also show that there is a significant level of correlation between the duration of the QT and the dispersion of APD, as well as with the dispersion of the recovery time.

One of the most recent experimental studies produced results that corroborate the hypothesis that an increment of the dispersion in ventricular repolarization along the myocardium entails an increment in the duration of the T wave, when DVR increases along the myocardium [9,10].

According to our simulation results, if we plot the duration of the T wave and the dispersion of the APD along the fibre (Figure 6), it can be observed that, as dispersion increases, so does the duration of the T wave, being the correlation coefficient between the two of them 0.89.

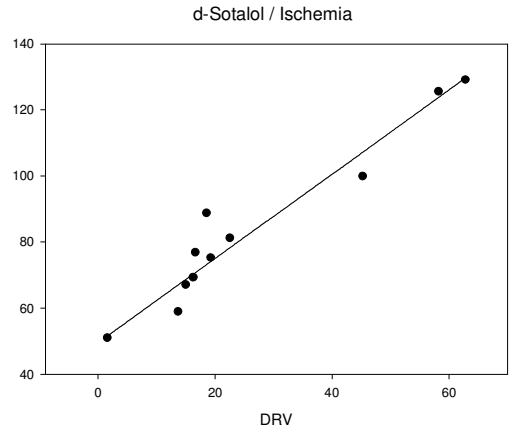

Figure 6. T wave duration (TWD) vs. APD dispersion (DVR).

4. Conclusions

From the aforementioned arguments, we can conclude that a greater dispersion in the duration of the action potential (APD), independently of whatever the origin of the dispersion may be, results in the widening of the T wave on the electrocardiogram.

Since the dispersion in the APD is related to the appearance of arrhythmias, this study theoretically support the hypothesis according to which the TWD is a good indirect indicator of the risk of propensity to arrhythmia.

Acknowledgements

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