Development and Validation of a Model of Atrioventricular Conduction in Atrial Fibrillation Based on Junctional Intracardiac Electrograms

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Abstract

Ventricular activation in atrial fibrillation (AF) is irregular. Our aim was to develop and validate a new model of atrioventricular conduction (AVC) in AF.

Intracardiac electrograms (IEGM) were recorded in 4 dogs in AF near the AV junction. Four timing intervals with 8 parameters were used to create a model of AVC: absolute and relative refractory periods, slow and normal conduction times. 26406 RR intervals were used to calculate and 2142 intervals to validate the prediction accuracy.

Using the optimal combination of the parameters the RR interval prediction had an average error of 99±80 ms, validation showed a value of 99±77 ms.

In conclusion, prediction of RR intervals in AF is possible using IEGM near the AV junction.

1. Introduction

Chaotic atrial electrical activity and filtering effect of the atrioventricular (AV) node cause an irregular ventricular activation in atrial fibrillation. RR interval is the time between two consecutive ventricular activations, as seen on the electrocardiogram. Several experimental and clinical studies focusing on statistical analysis of RR intervals have been undertaken, with conflicting results regarding the randomness of ventricular response [1-4]. Models of AV conduction have been proposed, but the ability to predict RR intervals is still poor [5-7]. Our aim was to develop and validate a new model of AV conduction based on local electrophysiological properties of the AV junction.

2. Methods

2.1. Intracardiac electrogram recording

Recordings from 4 dogs used in our previous study were analyzed [8]. Bipolar epicardial electrodes were applied to the right and left atrial appendages after thoracotomy, atrial fibrillation was induced with 4.5 V direct current and 50 Hz high-frequency stimulation. A 10-polar electrophysiologic catheter was placed near the bundle of His via the superior vena cava; the distal part of the electrode was on the intraventricular septum. The atrial and ventricular signals were recorded simultaneously with the atrial and ventricular electrode pairs most proximal to the atrioventricular (AV) junction, using a Biotronik HBV20 electrophysiologic recording system (Biotronik GmbH & Co., Berlin, Germany) and Biocord software (Biotronik GmbH & Co., Berlin, Germany). The analysis of atrial and ventricular electrograms and the calculation of atrial and ventricular intervals were performed with a computer program developed by the authors (Figure 1). Intracardial AV delay was determined as the time interval between the corresponding atrial and ventricular signals in sinus rhythm.

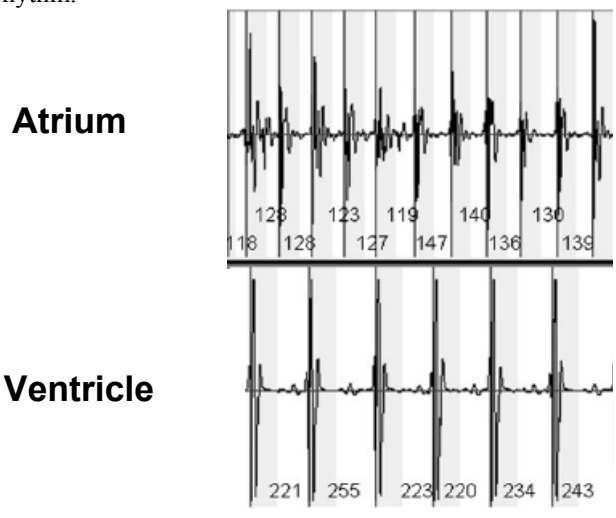


Figure 1. Atrial and ventricular electrical activity near the atrioventricular junction during atrial fibrillation. The amount of atrial impulses conducted to the ventricle is around 50% in this tracing, both the atrial and ventricular rates are irregular.

2.2. Model of AV conduction

The aim of our model was to predict ventricular activation based on atrial electrical activity. Each atrial impulse was analyzed and the assumption of conduction was made on its timing in comparison to the previously conducted atrial impulse. Four time intervals have been determined (Figure 2, Table 1).

The first interval after a conducted atrial impulse is the absolute refractory period (ARP), where the next atrial impulse will not be conducted. The second interval is the relative refractory period (RRP), where an atrial impulse will be still blocked, but it will also increase the duration of the refractory period. The third interval is the slow conduction period (SCP), where the atrial impulse is conducted to the ventricle at a greater than normal delay. The fourth interval is the normal conduction period (NCP), where the conduction time is the baseline.

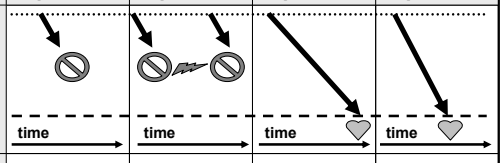
	ARP	RRP	SCP	NCP
	Absolute refractory period	Relative refractory period	Slow conduction period	Normal conduction period
Atrium AV junction Ventricle				
Parameters	t_{ARP}	t_{RRP} x_{RRP} y_{RRP}	t_{SCP} x_{SCP} y_{SCP}	t_{AVD}

Figure 2. Time intervals used in the model of atrioventricular conduction. Blocked signs indicate non-conducted atrial impulses. Heart icons represent an impulse conducted to the ventricle and ventricular activation. Lightning icon represents an increase in the RRP.

Parameter	Explanation
t_{ARP}	Length of absolute refractory period, ms
t_{RRP}	Length of relative refractory period, ms
x_{RRP}, y_{RRP}	Time parameters for relative refractory period extension $RRP_{ext} = x_{RRP} \times e^{\frac{-y_{RRP}}{t}}$ RRP_{ext}: extension of relative refractory period, ms t: time between start of RRP and atrial impulse, ms
t_{SCP}	Length of slow conduction period, ms
x_{SCP}, y_{SCP}	Time parameters for conduction delay in slow conduction period $t_{AVDslow} = t_{AVD} + x_{SCP} \times e^{\frac{-y_{SCP}}{t}}$ $t_{AVDslow}$: atrioventricular conduction time in the SCP, ms t: time between start of RRP and atrial impulse, ms
t_{AVD}	Conduction time in normal conduction period (in addition to what in sinus rhythm), ms

Table 1. Time intervals and parameters.

A sample of atrioventricular conduction using the model is shown on Figure 3.

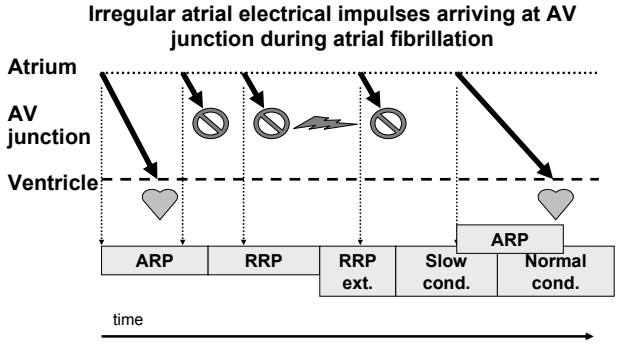


Figure 3. Atrioventricular conduction in atrial fibrillation using our model. The first atrial impulse is conducted to the ventricle with the baseline conduction time and starts the ARP. The second impulse is blocked in this interval. The third impulse comes within the RRP and prolongs it, causing the fourth impulse to be blocked. The fifth impulse comes within the SCP so it is conducted to the ventricle with a delay. This impulse restarts the cycle beginning with ARP.

Prediction accuracy was calculated using the 26406 RR intervals of the first three dogs. Optimal combination of the 8 parameters of 4 time intervals was determined by systematic search of the 8-dimensional parameter space. Average error (difference between the measured and predicted RR interval - time between ventricular activations due to conducted atrial impulses) and its standard deviation was calculated for each parameter set.

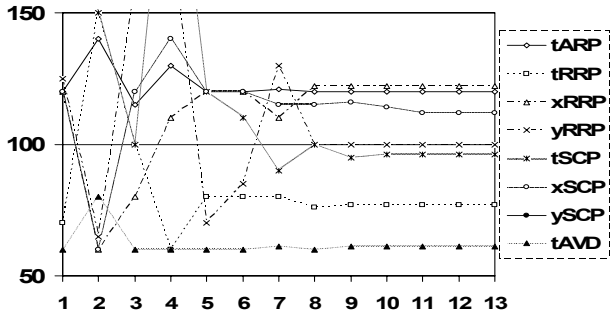
Results with the most precise parameters were validated with 2142 RR intervals of the last dog.

3. Results

The set of parameters providing the best RR interval prediction (least average error) was determined after the 13th iteration of systematic search, each looking for values of parameters in a narrower range than the previous one, centered around the optimal value for each parameter of the previous iteration (figure 4, table 3).

The average error of RR interval prediction using the best set of parameters was 99±80 ms. Using the same set with the RR intervals of the 4th dog (which were not used to determine the best values), the validated prediction accuracy was 99±77 ms.

The optimal t_{AVD} was 61 ms (AV conduction delay 61 ms longer in the normal conduction period than in sinus rhythm).



100	112	108	106	100	99	99	99	99	99	99	99	99	Avg. err.
84	67	76	79	80	79	81	81	80	80	81	81	80	SD

Figure 4. Optimal parameters, average error and standard deviation of RR interval prediction for each pass. The graph is zoomed, ySCP if off-scale high.

Parameter	Range	Best value
t_{ARP}	0 – 180	120
t_{RRP}	0 – 210	77
x_{RRP}	0 – 180	122
y_{RRP}	5 – 190	100
t_{SCP}	0 – 300	96
x_{SCP}	0 – 190	112
y_{SCP}	5 – 1500	1461
t_{AVD}	-60 – 120	61

Table 2. Range of parameter search (all iterations combined for each parameter) and best values after 13th pass.

4. Discussion and conclusions

Ventricular rhythm is controlled by the AV node during AF: it functions as a barrier, which limits the conduction of high atrial frequency to the ventricles. The complex pattern of impulse propagation within the AV node is due to dependence of refractoriness on the atrial impulse rate, concealed conduction, and annihilation or summation of wave fronts. AF is most frequently described as a microreentry of several activation wavelets, with very small or no excitable gap. The atrial cycle length and refractory period changes continuously, which makes the activation of the AV node even more complex [9]. Ventricular activation is also affected by exercise [10], changes in vegetative tone [11], retrograde conduction [12], drugs [10, 13], age and gender [14].

Our model was based upon the basic electrophysiological phenomenon of the impulse generation and propagation in the excitable tissue: the action potential. During an action potential a rapid depolarization of the cell membrane occurs, no further depolarization is possible in the absolute refractory period for duration depending on the cell type, usually few hundred milliseconds in the myocardium. After a sustained depolarized state repolarization occurs, during which there is a relative refractory period where only a supranormal stimulus can initiate a new action potential. After the completion of repolarization the ion channel functions are restored and normal excitability is regained.

Our model was based on the AV node simplified as a singe unit with a simulated behavior of an excitable cell. To simplify calculations the atrial intracardiac electrogram was recorded in one place. Atrial electrical activity is not homogenous during atrial fibrillation and the direction from where the impulse enters the AV node may affect the response [15]. We tried to eliminate this effect by recording the atrial activity as close as possible to the atrioventricular junction.

The parameters of time periods providing the most optimal RR interval prediction are close to their physiological counterparts observed in single myocardial cells. The systematic search of all parameters and checking time interval durations of 0 ms for each one provided the opportunity to eliminate a parameter from the model if it would not increase the prediction accuracy. However, all of them had a value different from 0 in the final set, indicating their role in the model. The conduction delay in the normal conduction period was longer than in sinus rhythm, which indicates a possible effect not included in this model. A plausible explanation would be the electrotonic modulation of the atrioventricular node, what we could not quantify in our study as only the atrial spikes (impulses above a threshold) were analyzed. An other option is the effect of retrograde activation and consecutive anterograde block in the atrioventricular node due to premature activation of ventricles or the atrioventricular node [16]. The average error of RR interval prediction is large, which suggest that factors not included in the model play a significant factor in atrioventricular conduction during AF.

The average error of validation was identical to the one found in the data set used for calculation, which means that the optimal parameters for the model may be uniform, at least in the studied animals.

In conclusion, prediction of RR intervals in atrial fibrillation is possible using intracardiac atrial recordings near the atrioventricular junction and our model of conduction.

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