Quantitative Assessment of Regularity and Synchronization of Intracardiac Recordings during Human Atrial Fibrillation

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Abstract

This study proposes the morphology-based evaluation of the regularity (R) and the synchronization (S) of intra-atrial electrograms acquired during atrial fibrillation (AF). R is defined as the degree of repetitiveness over time of the shapes of the activation waves detected in single atrial recordings. S accounts for the simultaneous presence of morphologically similar activation waves in two atrial electrograms, and for the dispersion of the propagation delays between the two sites. Both R and S resulted unitary for normal sinus rhythm and decreased significantly moving from atrial flutter (R=0.93, S=0.88) to AF of increasing complexity class (type I AF: R=0.75, S=0.66; type II AF: R=0.32, S=0.21; type III AF: R=0.19, S=0.01). During paroxysmal AF, the proposed indexes allowed to locate atrial regions with high degree of organization and other areas with more complex patterns of electrical activation.

1. Introduction

Even though atrial fibrillation (AF) has been classically described as a totally disorganized cardiac arrhythmia, in the last decade a large body of work has suggested that numerous factors such as anatomy, electrophysiological parameters, autonomic innervation, etc., should contribute to organize the electrical activity of the atria during AF. Since an unique definition of organization does not exist, several procedures attempting to quantify different aspects of the "organizational state" of AF have been provided [1-3]. The various methods have been recently categorized on the basis of the number of intra-atrial recordings involved into the analysis [4]. While single-site measures provide information on the local electrical activity of restricted atrial areas, the analysis of multiple recordings incorporates also the concept of spatial coordination among different sites.

The perpetuation of AF has been associated with the propagation throughout the atrial tissue of multiple activation wavefronts continuously changing in size and position [5]. As a consequence, the morphology of intra-atrial electrograms acquired during AF, reflecting the features of different spatial activation patterns such as wave collision or conduction blocks, is related to the degree of organization of the arrhythmia.

The present study proposes a morphology-based evaluation of the regularity of single electrograms and of the synchronization of pairs of electrograms simultaneously acquired during different atrial rhythms. This allows to investigate on both local and spatial aspects of arrhythmia organization by accounting for the similarity of the shapes of the atrial depolarizations detected in the analyzed signals.

2. Methods

2.1. Data collection

Intra-atrial electrograms were obtained from a multielectrode basket catheter in right atrium in five patients with paroxysmal AF. Thirty-two bipolar signals were simultaneously acquired for each patient. Conventional decapolar catheters placed in standard positions in the right atrium were exploited to acquire the reference normal sinus rhythm (NSR) signals prior to AF induction. The surface ECG (lead II) was also recorded. All signals were digitized at 1 KHz sampling rate and 12 bit precision. Finally, recordings of atrial flutter (FL) were taken from a data base previously collected [6].

AF signals were subdivided by an expert cardiologist in three classes of increasing complexity (AF1, AF2, and AF3) according to the Wells' criteria [7]. For each class of atrial rhythm, ten signals lasting five seconds were analyzed (NSR, FL, AF1, AF2, AF3).

2.2. Data pre-processing

First, ventricular electrical interference was removed by subtracting from each atrial recording an adaptive template obtained by averaging technique (see [8] for details). Atrial activation waves were recognized by a filtering procedure analogous to that proposed in [3]. To elicit the frequency components in the band of interest of AF activity, each atrial signal was band-pass filtered (40-

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Computers in Cardiology 2002;29:597–600.

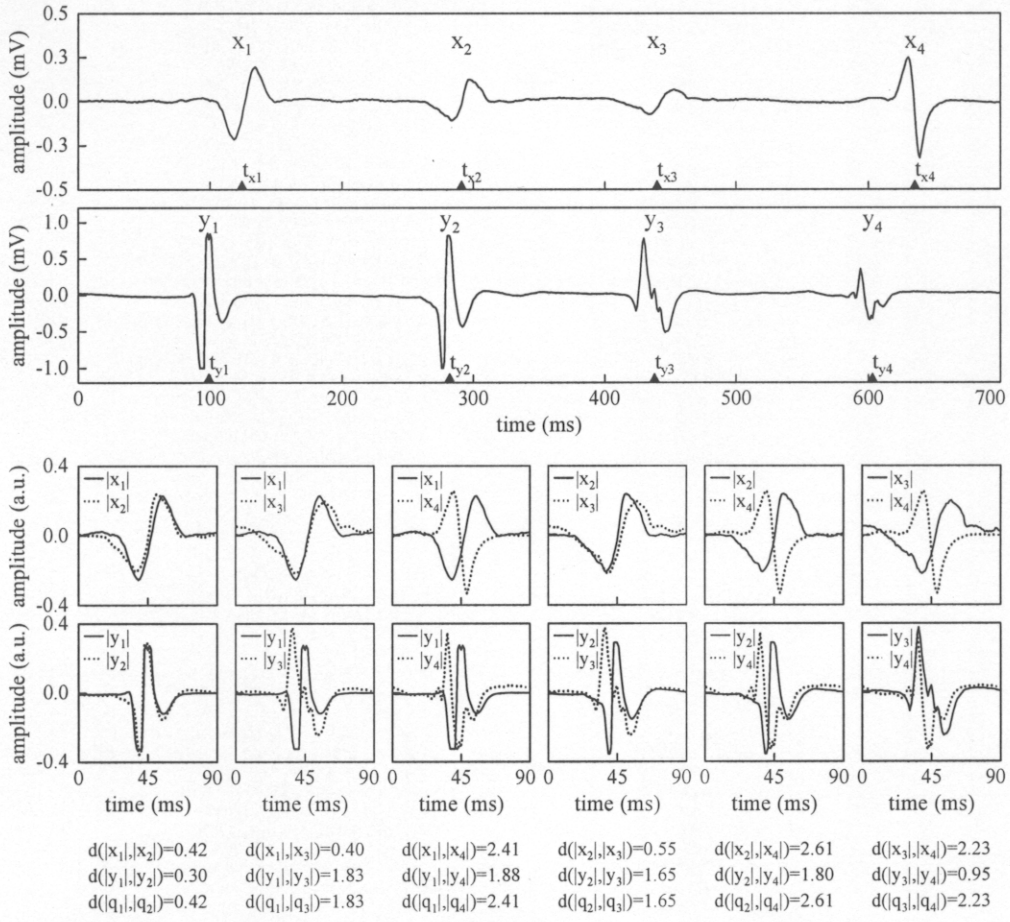

Figure 1. Description of the algorithm for regularity index and synchronization index calculation. From the two intra-atrial electrograms on the top, the APs $x_1,..x_4$ and $y_1,...y_4$ are derived as 90-ms windows centered in the activation times $t_{x1},...t_{x4}$ and $t_{y1},...,t_{y4}$. The morphological similarity between all pairs of normalized APs of each signal is then evaluated by distance calculation (lower panels). In the example, ρ_x=0.5; ρ_y=0.33; ρ_q=0.17 (with threshold ε=1.05 rad).

250 Hz), rectified, and further low-pass filtered (20 Hz). Atrial waveforms were then detected on the remainder electrogram by threshold crossing [8]. After activation waves recognition, the atrial activation times were detected by evaluating the local barycentre of the original electrograms [9]. Barycentre evaluation allowed to locate the fiducial points of each activation wave by accounting for its morphological features.

2.3. Regularity index

The regularity of an atrial signal is defined as the repetitiveness over time of the morphology of the detected activation waves [8]. First, the activation patterns (APs) are determined as signal windows of p samples centered in the detected activation times. In order to prevent the amplitude of bipolar electrograms from affecting the similarity measure, the APs are then normalized. The distance d between each pair of normalized APs is calculated by means of the standard metric of the p-dimensional unitary sphere and used to assess their morphological similarity. Specifically, two normalized APs are defined as similar if their distance is lower than a predefined threshold ε. Finally, the regularity is obtained as the fraction of similar APs found in the analyzed signal. For a signal x containing N APs $(x_1,...,x_N)$, the regularity index is:

$$\rho_x = \frac{2}{N(N-1)} \sum_{i=1}^{N} \sum_{j=i+1}^{N} \Theta\left(\varepsilon - d\left(\left|x_i\right|,\left|x_j\right|\right)\right) \qquad (1)$$

where Θ is the Heaviside function and $|\cdot|$ indicates normalization applied to the APs. The regularity index gives an estimate of the probability of finding similar APs in the signal under analysis.

The length of the APs was set at p=90 to cover the complete duration of each depolarization waveform and to avoid superposition between consecutive waveforms.

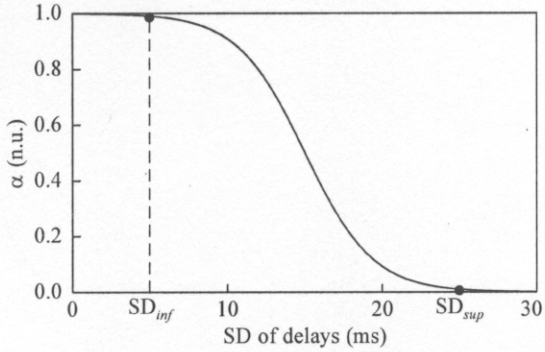

Figure 2. Corrective term to the synchronization index (α) derived from the standard deviation of the propagation delays of the activation waves.

The value of the threshold for distinguishing similar from dissimilar APs (ε=π/3 rad) was optimized to assure that all NSR signals exhibit maximum regularity. With this parameter setting, Figure 1 illustrates the calculation of the regularity index for two different signals.

2.4. Synchronization index

We propose a definition of synchronization based on the simultaneous presence of morphological similarity in the activation waves detected in the two atrial signals under analysis.

First, the APs of the signals x ($x_1,\ldots,x_N$) and y ($y_1,\ldots,y_M$) are aligned by pairing each AP of the signal with less atrial activations to the closest AP of the other signal. The ratio between $Q=min(N,M)$ and $max(N,M)$ is taken as corrective term for the synchronization analysis. After the alignment it is possible to define the joint AP as a two-dimensional vector formed by joining the paired activation patterns of the two signals:

$$q_i = \begin{bmatrix} x_i \\ y_i \end{bmatrix} \quad i = 1,\ldots,Q \tag{2}$$

Extending (1) to the joint APs, the probability of contemporarily finding similar APs in the two signals x and y can be estimated by:

$$\rho_q = \frac{2}{Q(Q-1)} \sum_{i=1}^{Q} \sum_{j=i+1}^{Q} \Theta\left(\varepsilon - d\left(|q_i|,|q_j|\right)\right) \tag{3}$$

where $d(|q_i|,|q_j|)=max\{d(|x_i|,|x_j|), d(|y_i|,|y_j|)\}$. An example of calculation of ρ_q is reported in Fig. 1. The synchronization between x and y is then evaluated by:

$$\hat{\sigma}_{xy} = \frac{2 \cdot \rho_q}{\rho_x + \rho_y} \tag{4}$$

By this definition, when morphological similarity in one signal always correspond to morphological similarity in the other signal (i.e., $\rho_x=\rho_y=\rho_q$), the synchronization between x and y is maximum. On the contrary, when for each pair of similar APs in one signal the corresponding APs of the other signal are not similar (i.e., $\rho_q=0$), the synchronization equals zero.

Equation (4) may not account for situations in which two signals are highly regular but not synchronized. Indeed, the situation $\rho_x=\rho_y=1$ always implies $\rho_q=1$ and thus the synchronization would be maximum even for uncoupled signals. For instance, this is the case of electrograms acquired on two independent stable re-entrant circuits. To overcome this limitation, a corrective term considering the temporal synchronism between the activation sequences of the two signals is introduced:

$$\sigma_{xy} = \alpha \cdot \hat{\sigma}_{xy} \tag{5}$$

The corrective term α is related to the dispersion of the propagation delays between the activation sequences of the two signals. The propagation delay δ_i is calculated as the difference between the activation times t_{xi} and t_{yi} (see Fig. 1), and the standard deviation of the delays is processed by a sigmoid function ranging between 0 and 1 to obtain the corrective term as shown in Fig. 2. The parameters of the sigmoid are adjusted in order to obtain the α-levels of 0.99 (high temporal synchronism) and 0.01 (low temporal synchronism) in correspondence to the input values SD_{inf} (low dispersion of delays) and SD_{max} (high dispersion of delays). The value SD_{inf} is set at 5 ms on the basis of experimental observations in conditions of correct propagation of the stimulus (NSR signals). The delay SD_{sup} is obtained, for each analyzed pair of signals, as the standard deviation of the delays between two independent surrogate activation sequences, which are derived by modeling the distribution of the atrial intervals by an Erlang-3 function preserving the original atrial rate (mean interval) and refractory period (minimum interval).

3. Results

Table 1 reports the calculation of regularity and synchronization values, expressed as mean ± SD, for the signals belonging to the five analyzed classes. Both indexes resulted maximum in condition of correct electrical propagation (NSR signals), and decreased significantly ($P<0.01$, t-test for unpaired data) moving from regular atrial arrhythmia (FL signals) to AF and increasing the complexity of AF as defined by Wells.

Table 1. Regularity and Synchronization indexes for different atrial rhythms.

Class	ρ	σ
NSR	1	1
FL	0.93 ± 0.08	0.88 ± 0.08
AF1	0.75 ± 0.28	0.66 ± 0.34
AF2	0.32 ± 0.14	0.21 ± 0.21
AF3	0.19 ± 0.09	0.01 ± 0.01

The proposed indexes were then calculated on signals acquired in different regions of the right atrium during episodes of paroxysmal AF. The atrium was subdivided in four regions, and two electrograms of five seconds per region were used. Results are shown in Table 2, where the values are expressed as mean ± SD over five patients. Both regularity and synchronization were high in the lateral and anterior walls, while decreased significantly ($P<0.01$) in the septal and posterior walls.

Table 2. Regularity and Synchronization indexes for different regions of the right atrium.

Wall	ρ	σ
Lateral	0.93 ± 0.08	0.89 ± 0.08
Posterior	0.52 ± 0.24	0.23 ± 0.14
Septal	0.31 ± 0.17	0.11 ± 0.13
Anterior	0.60 ± 0.19	0.40 ± 0.36

4. Conclusions

In this study, two measures quantifying the organization in the electrical activation of single atrial sites and the coupling between the activity of two atrial sites during AF were proposed. The regularity index provides a measure of the local organization of AF, while the synchronization index accounts for both temporal and morphological information to quantify the degree of spatial organization. With respect to previously proposed algorithms [1,3,4], the major distinctive feature of our indexes is the direct evaluation of the morphology of the atrial activation waves.

The sensitivity of regularity and synchronization values to changes in atrial rhythm and to variations in the complexity of AF demonstrated the suitability of morphology evaluation for quantifying the organization of atrial arrhythmias. Moreover, such measures were able to distinguish regions of the right atrium with low degree of organization from other areas with high organization during paroxysmal AF. Our results agree with a recent study demonstrating the presence of regular electrical activation in the anterior and lateral walls with respect to the posterior and septal ones [10].

Finally, the proposed indexes may be useful in the clinical treatment of AF. Indeed, by locating the areas of maximum arrhythmia complexity and determining the preferential directions of waveform propagation, such measures can be exploited to set the time of electrical cardioversion and overdrive pacing, or to guide the selective lesion of the atrial tissue during catheter ablation.

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