Poincaré Surface Profile. Novel Non-Invasive Method to Detect Preferential Ventricular Response during Atrial Fibrillation

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Abstract

The strategy of rate control during atrial fibrillation (AF) essentially deals with efforts to utilize and adjust the filtering properties of the atrioventricular (AV) node, allowing AF to continue and ensure that ventricular rate is controlled. In this work, a new tool based on the 3D Poincaré plots is developed for the characterization of the ventricular response (VR) and the clinical evaluation of rate control therapies.

Mechanisms underlying atrioventricular conduction during AF remain unclear. The role of the dual pathway AV nodal electrophysiology and the effects of the AV node modifications are still being an incognita. RR interval clusters exhibiting harmonic behaviour have been quantified suggestive of an underlying AV conduction ratio.

1. Introduction

Atrial fibrillation (AF) is characterized by an unorganized electrical activity of the atria. This is associated with irregular ventricular responses (VR) with typically shorter RR intervals than during normal sinus rhythm.

Current AF management guidelines suggest that there are fundamentally two ways to manage this rhythm disorder: to restore and maintain sinus rhythm or to allow AF to continue and ensure that ventricular rate is controlled. Given similar outcomes between rhythm and rate control strategies, rate control seems an attractive endpoint for the treatment of AF [1].

The strategy of rate control during AF essentially deals with efforts to utilize and adjust the filtering properties of the AV node [2]. However, atrioventricular conduction mechanisms remain unclear. Characteristics of AV conduction have been investigated in different species and with different techniques with the evaluation of the organization and predictability of the VR as objective [2]. The ventricular response during AF presents particular characteristics. By constructing histograms of RR intervals during AF, different RR populations can be found [2-4,7]. These multiple RR populations are not related with circadian variations of the heart rate [5]. Bimodal RR interval distributions have been suggested as an index of the presence of dual pathway AV nodal pathways [3]. Despite the attractiveness of this interpretation, the bimodal RR interval distribution does not provide full accuracy to detect dual AV node physiology. Unimodal histograms may still be associated with dual AV node pathways, and bimodal patterns of RR distributions can be present even after interruption of one pathway, i.e. by slow AV node pathway modification [4].

Many factors play a role in determining the VR and its irregularity in response to rapid atrial rates [6]. The conduction properties of the AV nodal cells and also the atrial rate have a complex relationship with the VR [3,7].

We hypothesized that different degrees of VR organization may be present during AF. In this work, a novel method for characterization of the VR during AF and for evaluation of VR control therapies is introduced. The Poincaré Surface Profile (PSP) was developed with the aim of improving the sensitivity for detecting different RR populations over existent techniques such as RR interval histogram analysis. The ability of this technique to monitor drug effects is illustrated.

2. Methods

Patients. 65 consecutive patients (52 male, 13 female, mean age 66±10 years) with persistent AF (AF duration 18±20 months) were included in this study. For every patient, an ambulatory 24-hour Holter ECGs was recorded. Holter recordings with a high degree of noise or with a percentage of extra beats > 80% were excluded (N=10). The digital ECG database for this study was established at the Otto-von-Guericke University Hospital

Magdeburg. Holter ECGs were acquired during usual daily activities using sampling rate of 128 Hz.

In two patients, Holter ECGs were recorded before and during rate control treatments with beta blockers or verapamil. These two patients were selected because both presented bimodal VR.

Poincaré Surface (PS). A new method based on Poincaré plots was developed. RR intervals are plotted against the corresponding preceding RR interval. By adding the number of occurrences (resolution of 1/128 ms) of RR-interval pairs, a three-dimensional Poincaré plot can be constructed [7].

$$PP(i,j) = \sum \delta(i - RR_{n-1}, j - RR_n) \quad (1)$$

A two-dimensional Gaussian low-pass filter was applied to the image in order to emphasize clusters and reduce the dispersion of occurrences around the peaks.

$$h_g(n_1,n_2) = e^{-(n_1^2+n_2^2)/2\sigma^2} \quad (2)$$

$$h(n_1,n_2) = \frac{h_g(n_1,n_2)}{\sum_{n_1}\sum_{n_2} h_g}$$

A 10x10 Gaussian convolution kernel (σ = 3) eliminates outliers while increasing the contrast.

$$PS(i,j) = \sum_{k_1=1}^{n}\sum_{k_2=1}^{n} h(k_1,k_2)PP(i-k_1, j-k_2) \quad (3)$$

The identity line of the Poincaré Surface was definided as the Poincaré Surface Profile (PSP). The PSP was used for the detection and evaluation of the presence of each RR distribution. The profile was defined as the diagonal of the normalized Poincaré Surface.

$$PSP = PS(RR_{n-1}, RR_n); \quad when \quad RR_{n-1} = RR_n \quad (4)$$

An algorithm to identify local maximum peaks was developed for the automatic detection of different RR populations on the PSP. In a first step, each point with a slope on the profile which changed from positive to negative was considered to be a peak. In a second step, an automatic threshold was computed as the 10% of the amplitude of the maximum peak. All peaks whose number of occurrences was lower than this threshold were considered noise. In a third step, if the distance between two peaks was lower than 50 ms, the peak with the lowest amplitude was considered interference. For each patient, peaks were labeled as 1, 2 or 3 according to the position of the RR distribution in ascending order.

Additionally to the Poincaré Surface Profiles, **RR interval histograms** were computed with the same resolution than Poincaré plots (1/128 ms). Histograms were smoothed with a unidimensional Gaussian filter (3). The algorithm previously described in the previous section to identify RR populations was applied. Peaks were labelled as 1, 2 or 3 according to the closest peak found in the profile.

Statistical analyses were performed using the paired Student's t test. Associations between peaks were evaluated using Pearson correlation analysis. Chi-square test was used to compare methods. A p value <.05 was considered statistically significant.

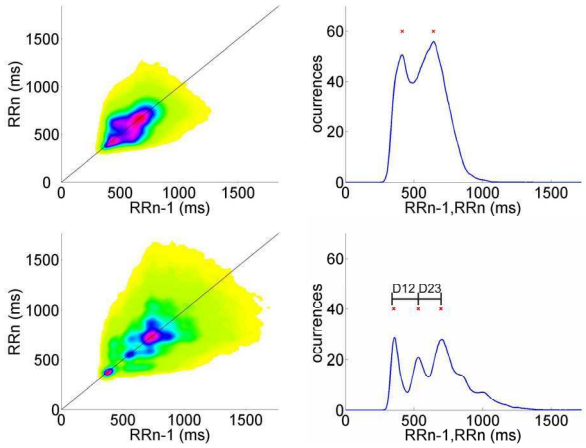

Figure 1. (Left) Poincaré Surface, colors scale represent the number of occurrence (yellow 0 – red 100) of consecutive RR intervals (RRn-1, RRn). (Right) Poincaré Surface Profile (blue), the position of detected peaks (red). D21 and D32 distances between peaks.

3. Results

Number of RR detected populations. By means RR histogram analysis, 25 patients (45%) presented two or more RR populations. In 3 of them (5.5 % of the total patients) 3 peaks were automatically detected.

Using PSP in 36 patients (65 %) at least two RR populations were automatically detected. In 11 patients (20 % of total patients) three or more peaks were automatically detected.

	3DPPP	Histogram
1 peak found	19	30
2 peaks found	25	22
3 peaks found	11	3

Table1. Distribution of patients according to the number of peaks detected by means PSP and Histogram method

All RR populations found in the whole histogram were detected by means of the PSP method. Location of peaks obtained with both methods were highly correlated (R=0.99, p<0.01) with a mean difference between peaks

of 20 ± 18 ms. Additionally, PSP detected 22 % more RR interval distributions.

Position of RR populations. When two or three peaks were found in the profile, the mean position of peaks 1, 2 and 3 was 459 ± 114 ms, 702 ± 147 ms and 946 ± 251 ms respectively. The three populations were highly correlated (R>0.90, p<0.01). Mean distance between peak 2 and 1 (D21: 246 ± 68 ms) was similar to the one between peak 3 and 2 (D32: 230 ± 78 ms, p=n.s.). In 11 patients in whom three peaks were detected, the difference between D32 and D21 was 15 ± 14 ms (R=0.97, p<0.01).

Concentration of RR populations. In 25 patients in whom two peaks were detected, the shorter RR interval was predominant in 10 cases (40%), while the number of occurrences in peak 2 was higher in 15 patients (60%) (p>0.4). In 11 patients in whom three peaks were detected, peak 1 was predominant in 6 cases, peak 2 in 2 cases and peak 3 in 3 patients (p>0.3).

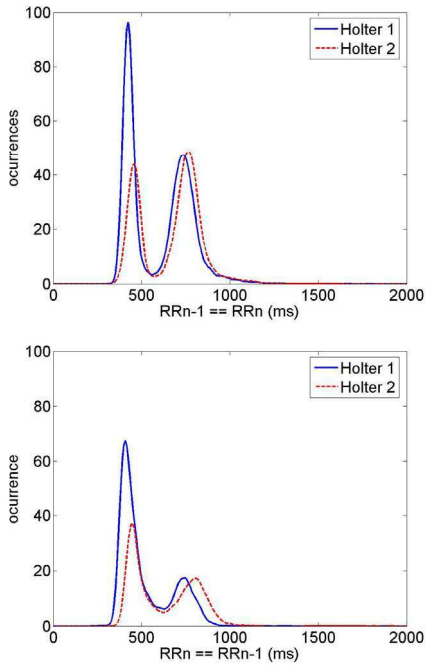

Figure 2. Profiles before (continuous line) and during (discontinuous line) Beta Bockers (Top) and Verapamil (Bottom) treatments.

Influence of VR control treatments.

Profiles before and during beta blocker (BB) and verapamil (VP) treatments are illustrated in figure 2. In both recordings two peaks were detected for both patients. Mean HR of 24 hours before and after treatment was 88 ± 21 bpm and 76 ± 30 bpm in the BB patient and 100 ± 34 bpm and 88 ± 31 bpm in the VP patient.

Interestingly, no significant change in peak position, but change in ratio of preferential conduction as mode of rate slowing are appreciable in the figure 2.

4. Discussion and conclusions

Performance of Profile Method.

In this work, we present a novel method for detecting RR populations and characterizing VR during AF. RR interval histograms and heart-rate stratified histograms (HRSH) have been previously used with similar objectives [3]. However, the HRSH technique was developed for the indirect characterization of multiple intranodal pathways of the AV node, rather than characterizing VR. It was oriented to emphasize the presence of only two RR distributions, excluding the effect of more RR populations and the possible relation of the atrial fibrillatory rate. These hypotheses have been disputed by Mazgalev and co-workers [2, 4]

RR intervals histograms were compared to the Profile of the 3D Poincaré plot method. *PSP* detected all RR populations present in complete RR interval histograms; in addition 22% more RR populations were detected by the *Poincaré Surface Profile method*. The convenience of using the *PSP method* for detecting RR interval distributions in the VR during AF has been proved.

In order to characterize VR during AF, a better understanding of mechanisms underlying atrioventricular conduction during AF is needed. Currently, there are no full explanations about the meaning of different clusters of RR intervals. The RR interval distributions have been suggested as resulting from conductions via fast pathway (FP) and slow pathway (SP) respectively, on the assumption that dual pathways exist in the AV node.

This theory has been supported by several studies where bimodal VR predicted better success rates of SP ablation [2]. However, not all patients with bimodal RR distributions were confirmed to have dual AV pathways

More recently, a novel index of dual pathway electrophysiology (i.e. “His electrogram (HE) alternans”) has been introduced by Zhang et al. [2] In experiments using rabbit hearts it was shown that this index could be used to determine on a beat-by-beat basis the origin of the ventricular activation (i.e., through FP or SP) during AF. Since the HE alternans existed in all examined preparations, it provides strong evidence that dual AV node physiology is the normal feature of the AV conduction. In particular, the index of HE alternans detected SP and FP propagation even when RR histograms exhibited only a single peak [4]. In this study, 6 rabbits showed a bimodal RR interval pattern after SP ablation, even though only FP conduction was left.

Besides, the hypothesis suggested by Olsson does not explain the appearance of a third or even more peaks. In our results, the location of the third peak is too short (946

± 251 ms) to be interpreted as AV nodal escape rhythm. Also, the high degree of correlation between peaks discards this possibility. Nevertheless, the highly significant similarity between D21 and D31 suggests that the different RR distributions are multiples of a single time intervals, rather than conduction through different pathways.

A plausible interpretation of this finding is that RR populations are harmonics of the atrial rate (2:1, 3:1, 4:1 AV node conductions). In previous studies performed on rabbits, it was demonstrated that VR during AF is not only determined by the refractory period of the AV node but also by the rate and degree of irregularity of the fibrillatory wave [6]. We have not found previous clinical reports relating the VR during AF with the number and rate of atrial waves in humans. On the assumption than if different RR interval distributions are harmonics of the atrial waves; rate and variability of atrial fibrillatory waves should be evaluated in future studies.

Rate control treatment. Beta blockers and verapamil are used for rate control treatment because they may slow VR by prolonging the AV node effective refractory period (ERP), slowing AV node conduction, but not affecting the atrial rate significantly. After drug administration, mean HR decreased in both patients. The amplitude of the short RR distribution of the PSP was lower in both cases. However, there were no noticeable variations on the amplitude of the second peak. Interestingly, the position of all peaks was weakly increased and the distance between the two peaks (D21) was almost constant. This is consistent with the hypothesis that both RR populations are harmonics of atrial rate (2:1 and 4:1). Reduction of the ERP of the AV node reduces the probability of the shortest RR intervals (2:1 conduction), but as atrial fibrillatory rate is not significantly modified, the position of the peaks and the distance between them is almost constant.

In summary, many factors play a role in determining the VR during AF which cannot be neglected [5]. VR can be interpreted as the output of a non deterministic system in which most probable cases (2:1, 3:1, 4:1, etc. AV node conduction) are reflected in RR interval clusters. If dual AV node pathways exist, they could be interpreted as two similar inputs. Intermittent blockages between conductions through FP and SP may enhance shorter His-to-His activations [2]. In addition, irregular small changes in the atrial rate might cause a sudden change in the postion of AV node where the waves are blocked (concealed conduction) making the output even less predictable. Future studies relating the atrial rate and the position of the RR distributions in the VR should shed some light on this complex electrical conduction system.

Conclusions. A new method for evaluating different treatments has been presented. The PSP technique presents an improvement over currently available methods such as RR interval histograms as detection of clusters of preferential AV conduction is enhanced.

Mechanisms underlying atrioventricular conduction during AF remain unclear. RR interval clusters exhibiting harmonic behaviour have been quantified suggestive of an underlying AV conduction ratio.

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