Role of the Atrial Rate in the Ventricular Response during Atrial Fibrillation

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Abstract

The ventricular response (VR) during atrial fibrillation (AF) presents particular characteristics which may play a relevant role in the selection of the most appropriate treatment. Preferential AV nodal conductions are visible when RR intervals Poincaré plots during AF are constructed.

The main objective of this work is the evaluation of the relationship between the position of more probable RR intervals and the atrial rate (AA).

Holter monitoring was used to demonstrate that in patients with one, two or even three clusters of RR intervals, these clusters track nth multiples of the atrial rate (i.e. 2•AA, 3•AA, etc.).

A possible classification of AF patients according to the ventricular response mechanism could help to improve the rate control treatments results.

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. The rate control strategy of AF deals with efforts to utilize and adjust the propagation properties of the atrio-ventricular (AV) node [1]. Nevertheless, atrioventricular conduction mechanisms during AF are not sufficiently understood, consequently treatment effects on the AV nodal conduction properties and VR are not easy to assess.

The ventricular response during AF presents particular characteristics which may play a relevant role in the selection of the most appropriate treatment [1-2]. Preferential AV nodal conductions are visible when RR interval histograms or Poincaré plots are constructed (i.e. bimodal distributions).

Recently, a novel method to analyze and characterize more probable RR intervals during AF has been presented: the Poincaré Surface Profile (PSP) [3]. This Poincaré plot based analysis uses the information of histographic Poincaré plots to filter part of the AV node memory effects (i.e. Wenckebach phenomenon). PSP technique allows a more accurate positioning of preferential RR interval and a short-term variation analysis.

These more probable RR interval populations have been suggested to be caused by the existence of AV node dual physiology [4]. Olsson's hypothesis suggested that conductions through the slow AV nodal pathway produce short RR intervals, while conductions thought the fast AV nodal pathway produce long RR intervals. Even a much stronger claim was done by presenting the possibility to analyse the AV node conduction properties of both, slow and the fast pathways, from measurements on short and long RR interval distributions [5].

The main objective of this work is the evaluation of the relationship between the position of more probable RR intervals and the atrial rate (AA). Our hypothesis is that positions of RR populations represent different AV conduction ratios of the atrial rate (i.e. 2•AA, 3•AA, etc.) and they are not necessarily determined by AV nodal anatomy. Similar atrioventricular conduction behaviour takes place in more organized atrial arrhythmias such as atrial flutter. Consequently, it should introduce a reasonable doubt about the hypothesis that different RR populations are caused by the conduction through different atrioventricular pathways with different conduction properties.

2. Methods

A. Analysis of RR clusters. The analysis of more probable RR intervals during AF was based in the PSP method [3]. Briefly, in a histographic Poincaré plot the value of each point is equal to the number of occurrences of RR interval pairs given by the (x,y) coordinates of the point (Fig 1.b). In order to reduce the variability of this scattergram a rotationally symmetric Gaussian lowpass

filter is used to construct a Poincaré Surface (Fig 1.c).

The Poincaré Surface Profile (PSP) is defined as the diagonal of the Poincaré Surface (Fig.1). This can be interpreted as filtering the RR interval histogram by considering only RR intervals that were preceded by beats with approximately the same RR interval and using bidimensional information of neighboring RR interval couples thanks to the previous smoothing process (Fig 1.d)

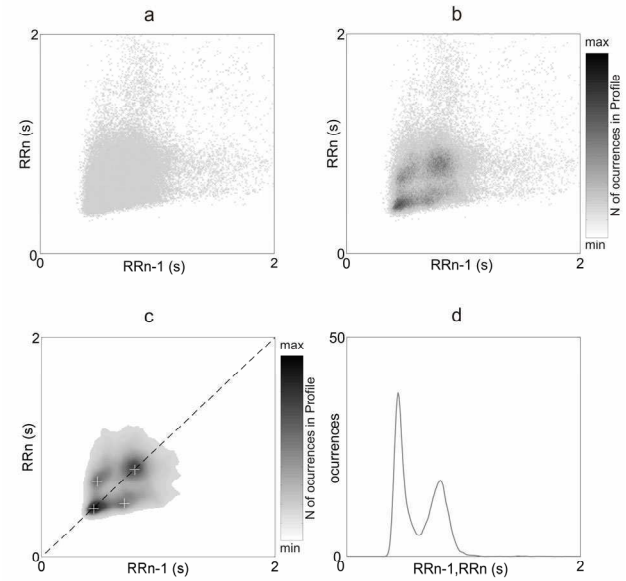

Figure 1. In Panel (a), a Poincaré plot with RR intervals obtained during 24 hours is depicted. In panel (b), the same Poincaré plot is shown, but the number of occurrences of RR pairs is color-coded. The darkest points represent the highest number of occurrences. In panel (c), the PS is illustrated. From the dashed line (Panel (c)) the PSP is constructed that is illustrated in panel (d).

An algorithm to identify preferential RR intervals on the PSP can automatically detect different RR populations on the PSP. A peak can be considered as significant if it fulfils two criteria: (1) be a local maximum and (2) have higher amplitude than a defined threshold. All peaks whose number of occurrences is lower than this threshold are considered noise. Finally, if two peaks are closer than a specific distance (ε) the peak with the lowest amplitude is also discarded.

Short-term variations in the ventricular response were analyzed by computing a 30-minute PSP every 15 minutes, with 50% overlapping (i.e. for a Holter recording of 24 hours, 95 PSP from overlapping sequential segments can be generated), so that the number and position of clusters along the day was monitored. For each 30 minute lag 1, 2 or 3 preferential RR intervals were detected.

In order to classify the patients according to the ventricular response pattern, the PSP of the 24 hour was computed. Patients were grouped according to their VR pattern into 3 groups:1) a narrow unimodal VR pattern (i.e. only one preferential RR interval is detected), 2) well defined multimodal VR pattern (i.e. two or more RR populations with valleys deeper than 20% of peak amplitudes) or 3) a wide unimodal VR pattern or with more than one peak but without well defined valleys between peaks.

B. Analysis of Atrial Rate. In order to obtain the dominant frequency, atrial fibrillatory signals were estimated from one surface Holter ECG lead by canceling the ventricular activity from the subtraction of a matching QRS-T template. This template was computed for each beat as a linear combination of the principal components previously obtained from the analysis of all beats in the ECG segment [6].

For every 10 seconds of ECG recording a Welch's periodogram was used to obtain the power spectral density of atrial signals (PAA) (hamming window of 2.5 seconds and 50% overlap). The dominant frequency (DF) was defined as the dominant peak in the power spectrum between 3 and 10 Hz. The atrial rate (AA) of each segment was defined as the inverse of the DF. The spectral concentration (SC) of the dominant frequency was used to indicate the quality of the AA estimation [6].

C. Comparison between RR clusters and Atrial Rate. For each 30 minute lag used to construct a PSP, 180 values of AA and SC were calculated (1 value of AA and SC every 10 seconds). For each 30 minute lag, if more than 70 % of 10 second lags presented a SC higher than 0.4, mean and standard deviation of the 180 AA values were measured. In case that the number of 10 second lags with SC higher than 0.4 was lower than 70% or in case that the standard deviation of the atrial rate was higher than 15 ms, the 30 minutes AA was marked as non-measurable.

A preferential RR interval was considered an nth multiple of the AA if RR-n•AA was lower than the standard deviation of AA in the segment (stdAA) (eq.1)

$$RR - n \cdot AA < n \cdot std_{AA}\,; \quad \text{n} = 2, 3, 4,\ldots \qquad (1).$$

D. Database. 55 consecutive patients (52 male, 13 female, mean age 66±10 years) with persistent AF (AF duration 18±20 months) and with a percentage of extrabeats < 20% were included in this study. For each patient, a clinically indicated ambulatory Holter ECGs of approximately 24 hours was recorded.

E. Statistical analysis. Student t-test was performed to evaluate if the difference of the means between the terms of eq. 1 were statistically significant in each case.

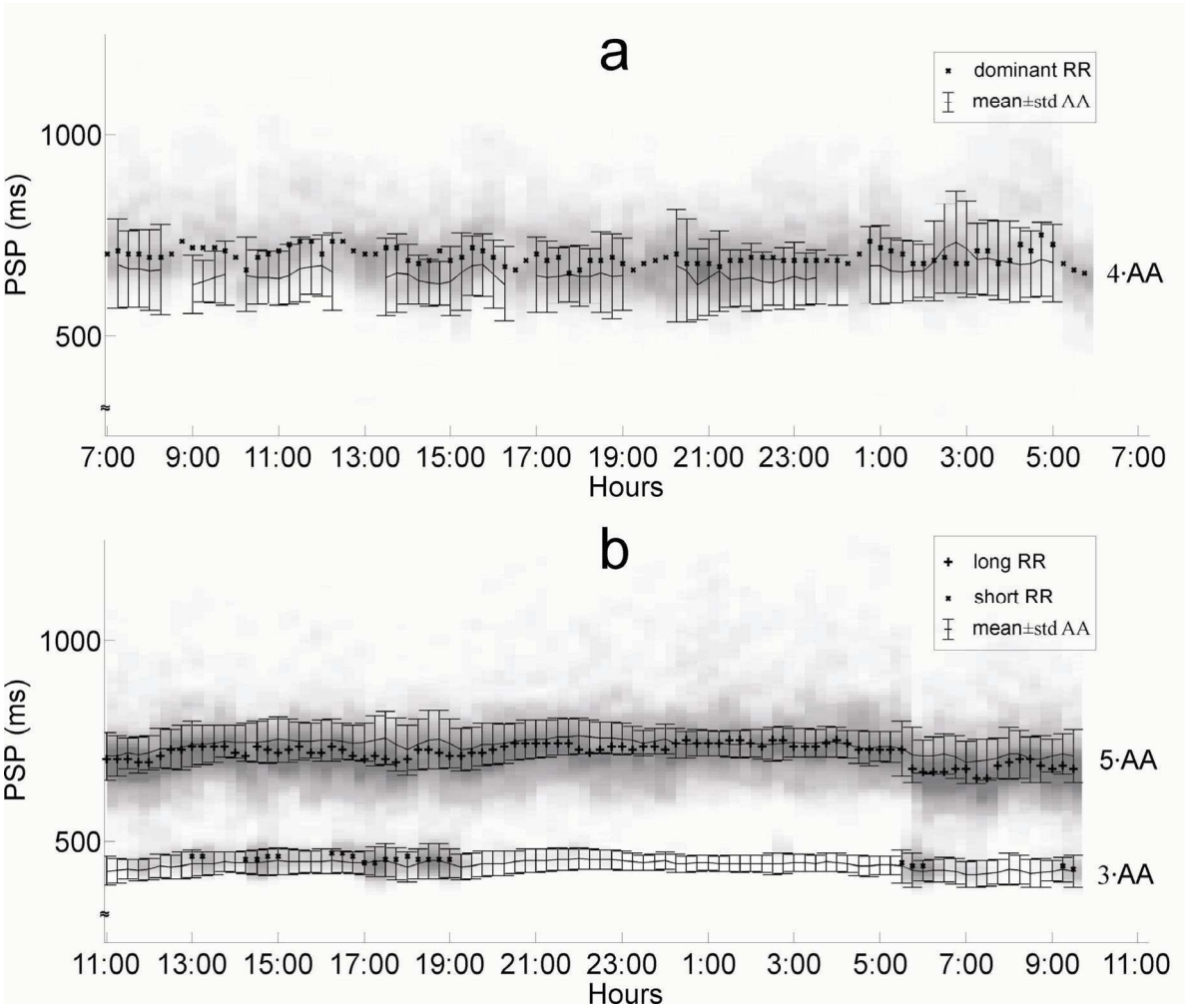

Figure 2. Short time variations of the PSP during the day are represented according to a colour scale (from white to dark grey). Crosses represent the local maximum of each PSP lag automatically detected. Atrial rate multiples are represented as the mean and standard deviation of each 30 minutes lag. In panel a, a patient from group 1 is depicted. A unimodal PSP was detected during the whole day. The fourth multiple of the atrial rate is shown. In panel b, a group two patient is depicted. Bimodal PSP was detected during several lags of the day, third and fifth multiples of the atrial rate are shown.

3. Results

By means of the analysis of PSPs of 24 hours: 14 patients were classified as group 1, 18 patients as group 2 (10 with two preferential RR intervals, 8 with 3 preferential RR intervals) and 23 patients as group 3. If more than 50% of lags were excluded for any of the reasons described in section 2.B the patient was considered as no measurable (e.g. 4 patients in group 1, 4 in group 2 and 18 in group 3).

In Fig. 2, short-term variations of PSP and multiples of atrial rate of two representative patients of group 1 and 2 are depicted. In patient from panel a, one peak was detected in the PSP during the whole day (697±20ms). The atrial rate was measurable in 72 of the 93 lags (177±9.7ms). The fourth multiple of AA is depicted in the figure as the standard deviation above and below the curve that represents the mean AA of each lag. The difference between the 4th multiple of AA and the detected cluster of the PSP was lower than the standard deviation of AA in 90% (66 of 72) of lag ($p<0.01$).

Patient from panel b was classified into the group 2 due to the existence of two well defined peaks in the 24-hours PSP. The analysis of short-term PSP (Fig.2.a.) detected one RR cluster at 720±23ms present during the whole day (long RR in the figure '+') and a shorter RR cluster present at 452±10 ms during 23 lags of the day (short RR in the figure '×'). In this patient the AA was measurable during the whole day (156±13ms). The 3rd and 5th multiples of AA are depicted. The difference

between the 5th multiple of AA and the long RR cluster was lower than the standard deviation of AA in 100% of the 93 lags ($p<0.01$). Similarly, the difference between the 3th multiple of AA and the short RR cluster was lower than the standard deviation of AA in 100% of the 23 lags ($p<0.01$).

Summarizing, in group 1 patients (N=10), 83±10 lags were measured, in 86±7% of them RR-n•AA was lower than n•stdAA ($p<0.05$). 55% of the lags corresponded to 4•AA and 45% to 5•AA. In group 2 patients (N=14), 104±25 lags were measured, in 93±8% of them RR-n•AA was lower than n•stdAA ($p<0.01$). 38 % of them correspond to 4•AA and 29% to 5•AA, rest of lags were 2nd, 3rd, 6th, 7th, 8th and 9th multiples of AA. In group 3 patients (N=5), 56±26 lags were measured, in 53±35% of them RR-n•AA was lower than n•stdAA (p=n.s.).

4. Discussion and conclusions

In this work, for the first time, a reasonable relation between the atrial rate and the ventricular response during AF has been demonstrated. Preferential RR intervals have been evaluated by means of the recently presented Poincaré Surface Profile [3], this method allowed a more accurate location of RR populations. Position of these dominant RR intervals has been demonstrated to be correlated with multiples of AA in all analyzable patients from groups 1 and 2. The presented relations are measured from mean values of the atrial rate and mean values of preferential AV node conductions. Consequently they should be analyzed as a probabilistic phenomenon rather than a deterministic relation between the atrial rate and the more probable RR intervals.

Several limitations to this work can not be underestimated: the process to measure the AA is far from being perfect [6]. In added it is necessary remark than the AA measured in a superficial ECG electrode is only an estimation of the rate of the atrial wave bombarding into the AV node. Even when a dominant frequency is measurable, small errors in the positioning of the dominant frequency can produce big dispersions when a nth multiple of it is calculated (i.e. 10 ms of error in the measurement of the AA are translated to 50 ms of error for the 5^{th} multiple of AA). Besides, the precision in the measurement of dominant RR intervals for a sample rate of 128 Hz was of 8 ms [3].

These technical limitations make reasonable to consider a RR interval multiple of AA even if the RR interval is not a perfect multiple of AA, but differs from the mean AA in less than the standard deviation of AA.

In this paper, 30 minute lags have been used due to the necessity of sufficient RR intervals for the evaluation of preferential AV nodal conductions. Variations in AA during these lags could produce big dispersion of the preferential RR intervals. This could explain the high number of lags without measurable AA in patients with wide and non-uniform VR pattern (group 3).

A possible classification of AF patients according to the ventricular response mechanism could help to improve rate control treatments results.

Our theory about the atrioventricular mechanism during atrial fibrillation is the first one that gives an explanation to the existence of more than 2 RR intervals clusters. Short and long RR distributions do not necessarily imply conductions though slow and fast AV nodal pathways respectively [1]. Multiple clusters of RR intervals can be explained as being multiples of the AA and are not necessary caused by a dual AV nodal physiology, although the existence of two pathways could make small multiples of the AA more probable.

Acknowledgements

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