Relation between Atrial Rate and Preferential RR intervals during Atrial Fibrillation

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Abstract. During atrial fibrillation (AF), different populations of preferential RR (pRR) intervals can be found in RR interval histograms. These pRR intervals have been suggested to be multiples of the refractory period of the AV node or caused by the existence of a dual AV node physiology. In this study, the hypothesis that pRRs represent different conduction ratios of the dominant atrial cycle length (DACL) was tested. Bidimensional Histogram Profiles were generated from Holter ECGs for the identification of pRR in 55 patients with persistent AF. This method allows analyzing the dynamic behavior of the ventricular response (VR) during AF by means of bidimensional histograms (so-called Lorenz or Poincaré plots). The number and position of pRR intervals were detected and compared with the mean and standard deviation of the DACL. In all patients with more than one pRR interval (N=24) and in 47% with one pRR interval (N=9), clusters of RR intervals were related with multiples of the DACL. The relation between preferential AV nodal conduction during AF and multiples of DACL suggests that more probable RR intervals are caused by different conduction ratios of the atrial rate and not necessarily by conduction through different AV nodal pathways.

Keywords: Atrial fibrillation – Ventricular response – AV node conduction – Rate Control – RR Histogram

1. Introduction

The ventricular response (VR) during atrial fibrillation (AF) presents particular characteristics which may be related with the response to AV node modification or cardioversion [Bollmann 2006]. By constructing histograms of RR intervals or bidimensional histogram plots (so-called Lorenz plots or Poincaré plots) from Holter ECGs, different populations of preferential RR intervals (pRR) can be identified. While in some patients unimodal RR patterns are observed, in others bi- or multimodal patterns exist.

However, the mechanisms responsible for the occurrence of multimodal RR interval histograms are not fully understood. In one earlier study [Soderstrom 2005], it was postulated that pRR are multiples of the refractory period of the AV node. In more recent studies pRR have been suggested to be caused by the existence of dual AV node physiology [Olsson 1986]. It has been suggested that conduction through the slow AV nodal pathway (with a short refractory period) produce short RR intervals, whereas conductions through the fast AV nodal pathway (with a long refractory period) produce long RR intervals.

Usually, RR interval histograms have been used to analyze the VR during AF [Bollmann 2006]. Nevertheless, the position of pRRs in histograms is strongly influenced by the memory effects of the AV node (i.e. Wenckebach phenomenon). In order to reduce this blurring, preferential AV nodal conduction has been evaluated by means of the recently presented Bidimensional Histogram Profile (BHP) method [Climent 2009]. BHP reduces the dispersion of RR intervals, allowing robust and reproducible pRR detection.

The main objective of this study was the evaluation of the relationship between the positions of pRR intervals, evaluated by means of BHP, and the atrial rate (AA) during AF. We tested the hypothesis that the positions of pRR populations are caused by different conduction ratios of the atrial rate (i.e. 2•AA, 3•AA, etc.) and not necessarily by conduction through different AV nodal pathways.
2. Material and Methods

Study population and Holter ECG acquisition

In this study 65 consecutive patients with persistent AF were included. For each patient, a clinically indicated ambulatory Holter ECGs of approximately 24 hours was recorded. Holter recordings with a high degree of noise or with a percentage of ventricular ectopic beats and aberrant beats > 20% were excluded (N=10). The remaining 55 patients comprise the study population.

Holter ECGs were acquired during usual daily activities using a CardioMem CM 3000 recorder (Fa. Getemed, Teltow, Germany) with a sampling rate of 128 Hz. Duration of each RR interval and classification of all beats were exported for off-line analysis using Matlab 7 (The Mathworks, Inc., Natick, USA).

Analysis of RR clusters

The analysis of pRRs during AF was based on the Bidimensional Histogram Profile (BHP) method that has been presented in detail elsewhere [Climent 2009]. In brief, this methodology allows analyzing the dynamic behavior of the VR during AF. In a bidimensional histogram plot of RR intervals the value at each point is equal to the number of occurrences of RR interval pairs (RRn-1, RRn) (Figure 1.a). In order to reduce the variability of this scattergram a rotationally symmetric Gaussian lowpass filter is used to construct a bidimensional histogram surface (Figure 1.b).

The BHP is defined as the diagonal of the bidimensional histogram surface (Figure 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 due to the previous smoothing process (Figure 1.d). This procedure reduces the variability of the RR intervals introduced by variations in the AV nodal conduction time due to large variations between preceding RR intervals.

![Figure 1](image_url)

An algorithm to identify pRRs on the BHP was used in order to automatically detect different RR populations. A peak in the BHP is considered as significant pRR if it fulfills two criteria: (1) be a local maximum and (2) have higher amplitude than a defined threshold (10% of the maximum peak). All peaks whose number of occurrences is lower than this threshold are considered noise. Finally, if two peaks are closer than 50 ms, the peak with the lowest amplitude is also discarded.

Short-term variations in the VR were analyzed by computing a 30-minute BHP every 15 minutes, with 50% overlapping (i.e. for a Holter recording of 24 hours, 95 BHP from overlapping sequential segments can be generated), so that the number and position of pRRs during the recording was monitored. For each 30 minute segment, 1, 2 or 3 preferential RR intervals were detected. Patients were grouped according to their VR pattern into 2 groups: 1) a unimodal VR pattern (i.e. only one pRR is detected in > 90% of BHPs) or 2) a multimodal VR pattern (i.e. two or more pRRs were detected in >10% of BHPs).

Analysis of atrial rate

In order to estimate the mean atrial fibrillatory rate, the dominant frequency (DF) of atrial fibrillatory signals was estimated from the surface Holter ECG lead. Ventricular activity was reduced...
by subtracting 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 [Castells 2005].

For every 10 seconds of ECG recording, a Welch’s periodogram was used to obtain the power spectral density of atrial signals (hamming window of 2.5 seconds and 50% overlap). The 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) around the DF (±0.5Hz) was used to indicate the quality of the AA estimation [Castells 2005].

For each 30 minute segment used to construct a BHP, 180 values of AA and SC were calculated (1 value of AA and SC every 10 seconds). If more than 70% of the 10 second segments presented a SC higher than 0.4, mean and standard deviation of AA (stdAA) values of these specific segments were measured. Also in order to avoid overlapping of multiples of the stdAA around multiples of AA, segments that presented an stdAA higher than 15 ms were rejected.

Comparison between atrial rate and preferential AV nodal conduction

A pRR was considered to be an nth multiple of AA if it was inside a window of ±n•stdAA centered at n•AA, where n is each one of the possible multiples of the atrial rate. For instance, if during 30 minutes the measured atrial rate was 150±5 ms, a pRR was considered a second multiple if its duration was between 290 and 310 ms, a third multiple if its duration was between 345 and 465 ms, etc.

**Statistical analysis**

One tailed t-test was performed in order to evaluate the hypothesis that pRR-n•AA was lower than n•stdAA for each patient. A p value <0.05 was considered statistically significant.

3. Results

**Atrial rate and preferential AV nodal conduction**

By analyzing short time variations of BHPs over 24 hours, 21 patients presented a unimodal VR pattern and 34 patients a multimodal VR pattern (23 with 2 pRR intervals and 11 with 3 pRR intervals). There was no difference in clinical characteristics between patient groups (Table 1). Of those, 2 patients with unimodal VR patterns and 10 patients with multimodal VR patterns were excluded from further analysis due to QRS canceling artifacts and estimation of atrial rate in < 50%.

For all patients with a multimodal VR pattern (N=24) and for 47% of the patients with a unimodal VR pattern (N=9) it was statistically demonstrated that pRR intervals were harmonics of the atrial rate. In 10 patients with a unimodal VR pattern it was not possible to demonstrate the relation between pRR intervals and the atrial rate. In these 10 patients, the standard deviation of the position of the pRR interval was 90±50 ms, significantly higher than in the other 9 patients with a unimodal pattern (50±23 ms, p<0.05).

In figure 2, short-term variations of BHP and multiples of AA of three patients are depicted. From the recording in panel a, one peak was detected in the BHP during the whole day (697±20 ms). Atrial rate was measurable in 72 of the 93 segments (177±9.7 ms). The detected pRR was inside the window of the 4th multiple of the AA in 100% of the 93 segments (p<0.01).

The recording in panel b was classified as multimodal due to the existence of two pRR intervals in 23 (25%) BHP segments. The analysis of short-term BHP (Figure 2.a.) detected one pRR at 720±23 ms present during the whole day and a shorter pRR present at 452±10 ms during 23 segments of the day. In this patient, the AA was measurable during the whole day (156±13 ms) and 3rd and 5th multiples of AA are depicted. The long pRR was inside the window of the 5th multiple of the AA in 100% of the 93 segments (p<0.01). Similarly, the short pRR interval was inside the window of the 3rd multiple of the AA in 100% of the 23 segments (p<0.01).

The recording in panel c was classified as unimodal, as one peak was detected in the BHP during the whole day at 706±63 ms. In this recording, AA was measurable in 81 segments, with a mean value of 137±15 ms. The pRR interval was inside the window of the 5th multiple of the AA in 63 segments (p=n.s.). In this recording it was not possible to statistically demonstrate that pRR intervals were multiples of the atrial rate.
Figure 2. Short-time variation of the BHP during the day is represented according to a color scale (from white to dark gray). Crosses represent local maxima of each BHP segment automatically detected. Atrial rate multiples are represented as the mean and standard deviation of each measurable 30-minute segment. In panel (a) a unimodal VR is depicted in which a single pRR was found during the whole day together with the 4th multiple of AA which was statistically related with the pRR. In panel (b), a multimodal patient is depicted in which a bimodal BHP was detected during several segments of the day, the 3rd and 5th multiples of the atrial rate were statistically related with pRR intervals. In panel (c), a unimodal patient in which the pRR interval was not statistically related with the multiple of the atrial rate is depicted.

4. Discussion

In this study, a relation between the atrial rate and the ventricular response during AF has been demonstrated. For the first time, the position of preferential RR intervals has been shown to be correlated with multiples of the atrial rate during AF.

The VR during AF is usually assumed to be random phenomenon. However, the existence of a certain relationship between each RR interval and the preceding RR series has been demonstrated by means of bidimensional histograms (so-called Poincaré plots) and autocorrelation functions [Bollmann 2006] where different populations of more probable RR intervals (pRR) can be found.

In 1950, Söderström postulated that pRR conductions should be multiples of the refractory period of the AV node [Söderström 1950]. Although it was a reasonable hypothesis, it does not explain satisfactorily the variations of pRRs during day and night. Since AV nodal refractory period is modified by the vagal tone, position of pRR should gradually change between day and night, following the vagal tone. Rather than this, as visible in panel b of figure 2., the reduction of the mean RR during the night was caused by a modification in the number of occurrences of each RR interval cluster, whereas the position of clusters did not change.

In 1956, Moe et al. presented evidence of the existence of a AV node dual physiology [Moe 1956]. It was demonstrated that the so-called slow-pathway has a shorter refractory period but higher conduction velocity than the so-called fast-pathway. The concept of two pathways with separated conduction properties was used later by Olsson et al. [Olsson 1986] for suggesting that pRR intervals during AF are caused by conduction through different AV node pathways. However, even when the slow pathway presents a slightly shorter refractory period than the fast pathway, both refractory periods range from 250 to 350 ms, differences that do not exceed 100 ms, far from the positions of the pRR intervals observed in our results and previous studies [Olsson 1986].
In our study, in 100% of patients with a multimodal VR pattern and in 47% patients with a unimodal VR pattern, pRR intervals were multiples of the atrial rate. In the rest of unimodal patients, it was not possible to demonstrate a relation between the position of pRR intervals and the AA. In these patients, VR patterns were wide and without a well defined peak. One example is given in figure 2.c. in which a certain relation between the RR intervals and the atrial rate can be discerned, although we were unable to statistically demonstrate this relation.

Different approaches have been developed in animal models in order to clarify the role of the atrial rate in the VR during AF. By pacing from different sites of the atria in rabbit experiments, Chorro et al. [Chorro 1990] concluded that the ventricular rate during AF was not only determined by the properties of the AV node but also by the rate and irregularity of the fibrillatory process. This reaffirms the idea presented by Kirsh et al. [Kirsh 1988], who suggested that the irregularity of the VR to AF is primarily a consequence of the irregularity inherent in the atrial activity and the role of the AV node is predominantly confined to that of scaling the atrial activity. Our findings relating pRR and the mean atrial rate in Holter ECG recordings from humans are consistent with this finding.

Limitations

This study included a heterogeneous patient group with respect to underlying heart disease and cardiac medication. Whether or not a certain VR pattern is dependent on these variables is not known.

The signal processing techniques used to measure the AA did not allow to measure AA from all recordings due to QRS cancellation residuals [Castells 2005]. In addition, the AA measured in a surface ECG is a global estimation of the atrial rate of the atrial wave bombarding into the AV node and does not reflect localized phenomena which would require invasive mapping studies. These technical limitations may have influenced our inability for demonstrating a relation between AA and VR in some patients.

5. Conclusions

The relation between preferential AV nodal conduction during AF and the multiples of the atrial rate suggests that more probable RR intervals are caused by different conduction ratios of the atrial rate and not necessarily by conduction through different AV nodal pathways. This finding represents a novel hypothesis and may contribute to a better understanding of the role of the AV node during AF.

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References


