Non-Invasive Assessment of Atrioventricular Conduction Properties and Their Effects on Ventricular Response in Atrial Fibrillation

AM Climent[1,2], D Husser[1], J Millet[2], VDA Corino[3], L Mainardi[3], HU Klein[1], A Bollmann[1]

[1]Otto-von-Guericke University Magdeburg, Germany
[2]Politecnic University of Valencia, Spain
[3]Politecnic University of Milan, Italy

Abstract

This study sought to determine the relation between mean RR intervals as well as its circadian rhythm and non-invasive markers of atrioventricular (AV) node refractoriness and concealed AV conduction obtained from Lorenz-plot (LP) analysis of 10-min and 24-h ECGs. In 29 patients with persistent atrial fibrillation (AF) the 1.0-s intercept of the lower envelope (LE1.0) of the plot and the degree of scatter (S) above the envelope were measured as markers for refractoriness and concealed conduction. Mean 24-h RR was independently associated with LE1.0 and S calculated from 10-min ECGs. In 48% patients, a significant circadian RR rhythm was present, which was independently associated with both S and LE1.0 amplitudes. AV conduction properties obtained from LP analysis of 10-min ECGs are useful for predicting mean 24-h heart rate in AF. The degree of variation in refractoriness and concealed conduction are determinants of significant circadian heart rate variation in AF.

1. Introduction

Atrial fibrillation (AF) is characterized by an unorganized electrical activity of the atria. This arrhythmia, the most common in clinical practice, is associated with irregular atrioventricular (AV) conduction leading to irregular ventricular responses (RR intervals) with typically shorter RR intervals than during normal sinus rhythm [1].

This irregularity sometimes presents like a completely random process but 24-hour Holter ECGs often show circadian variations in RR interval behaviour. Patients with AF have an increased risk of death, which is even attenuated by reduced circadian RR interval variation [2,3].

The role of AV nodal conduction properties in controlling and modulating the ventricular response during AF is not completely understood. In short, there are two main electrophysiologic factors that determine ventricular responses during AF [1]. Once atrial fibrillatory excitation waves have entered the AV node, many of the bombarding atrial impulses are blocked (annihilated) within the AV node due to its inherent refractory properties [2]. Several studies [3] have described that atrial impulses only partially penetrate the AV node, but still have an influence on the conduction of subsequent beat(s), which is referred to as concealed conduction. Even though these complex phenomena play a prominent role for achieving optimal ventricular rate control, they are not routinely evaluated in clinical practice; especially their possible influence on circadian RR interval variation is unknown.

Therefore, the purpose of this study was to determine the relation between mean RR intervals as measure of ventricular rate control as well as its circadian rhythm and non-invasive markers of AV node refractoriness and concealed AV conduction obtained from 10-minute and 24-hour ECG recordings in patients with persistent AF. This study was performed using a non-invasive technique based on Lorenz plot (LP) analysis of RR interval sequences.

2. Methods

Patients. In this study, 29 consecutive patients (20 men, 9 women, mean age 66±10 years, range 40 – 83) with persistent AF (AF duration 30±50 months, range 0.25 – 180). In every patient, ambulatory 24-hour Holter ECGs and 10-minute 12-lead resting ECGs were recorded.

ECG recordings. 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 a CardioMem CM 3000 recorder (Fa. Getemed, Teltow, Germany) with a sampling rate of 128 Hz. In addition, 12-lead ECGs were recorded under resting conditions after a 5 minute equilibration period using a CardioLink recorder (Fa. Getemed) with a sampling rate of 1024 Hz.

QRS complexes were detected and classified automatically by the CardioDay analysis platform (Fa. Getemed) for Holter recordings and by our own software for 10-minute recordings. Only normal beats were used for further analysis, while wide QRS complexes and artefacts were excluded. All results of automatic analysis were visually inspected and each error in the detection or labeling was corrected manually. The duration of each RR interval and the classification of all beats were exported for off-line analysis using Matlab 7 (The Mathworks, Inc., Natick, USA).

Lorenz plot analysis. Lorenz plots were generated for the RR interval sequence in each segment according to the previously reported method [5-7]; that is, each RR interval was plotted as the value on the vertical axis against the immediately preceding RR interval as the value on the horizontal axis (Fig. 1).

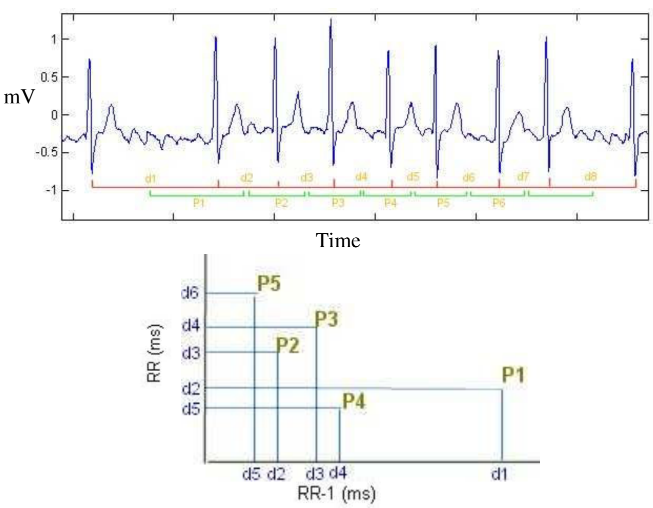

Fig 1. Schematic illustration of the principle for generating RR series (upper panel) used for Lorenz plot (lower panel). From the first two RR intervals (d1, d2) in the ECG, point P1 is obtained. Subsequent intervals (d2, d3) and (d3, d4) provide the location of points P2 and P3, respectively.

During AF, it is possible to non-invasively obtain several relevant electrophysiologic properties of the AV node. (1) The shortest RR interval for a given preceding RR interval reflects the functional refractory period of the AV node, while (2) the cycle-length dependency of AV nodal refractory is expressed by the slope of the lower envelope. (3) The scatter distribution of RR intervals above the lower envelope is as a measure of concealed conduction.

Several parameters were automatically obtained from Lorenz plots containing 512 successive RR intervals to quantify these properties (Fig. 2).

Lower envelope (LE). The axis of preceding RR intervals (horizontal axis) was divided into 16 regions; each section was formed for 32 points of the scatter. The minimal value in each 16 bins was identified and the sixteen points were used to calculate the regression line, from which its the 1.0-s intercept of the regression line on the lower envelope ($LE_{1.0}$) was determined.

Scatter index (S). The degree of scatter above the lower envelope was expressed as the root mean square difference between each RR interval couple and the regression line.

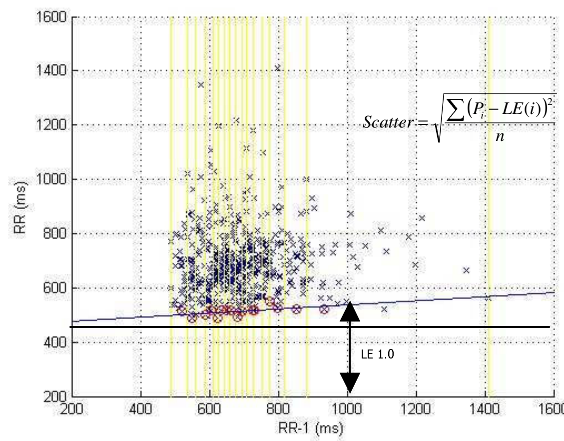

Fig 2. Lorenz plot of 512 successive RR intervals during atrial fibrillation. Vertical lines reflect the separations between sixteen sections, each one of that bin includes 32 points. Circled points are the minimal values of each section. The solid line is the calculated lower envelope by means of a regression line on the minimal values.

Analysis of circadian rhythms. We analyzed circadian variations of LP parameters (mean RR intervals, LE 1.0 and scatter index) from Holter recordings by assessing one LP with 512 RR intervals every five minutes (288 LP from overlapping sequential segments were generated).

The significance of the circadian rhythm of these parameters was tested using the cosinor method. Details of the cosinor analysis method have been described elsewhere [8]. In brief, we determined a fitted cosinor curve with a 24-h rhythm for all measured parameters.

The cosinor fitting technique will tend to fit to the fundamental frequency rather than harmonics. The resulting fit approximates the fundamental component and DC offset like $y = M + A \cos (wt + Ø)$, where M is the midline estimating statistic of rhythm (mesor) or value about which the oscillation occurs, A is the amplitude in the maximum point of that oscillation, w is the pulsation: 2p/T, where T is the period. By using 288 measurement points in 24-hours, the period is 288. Ø is the acrophase or timing of the highest amplitude (Fig. 3). Within the framework of this study, we quantified the degree of circadian RR, LE1.0 and Scatter variation by their amplitudes (A).

The fit is achieved using a least mean squares (LMS) approach. This method does assume that the circadian variation in RR intervals can be modeled by a cosine. The limitations of cosinor method are well known. Among the most serious is its low efficacy when used with data series that do not follow a reasonably sinusoidal distribution. Via the zero-amplitude test, the simple cosinor method can confirm the existence of a circadian rhythm. The minimal level of significance accepted to consider a circadian rhythm present was $p < 0.05$.

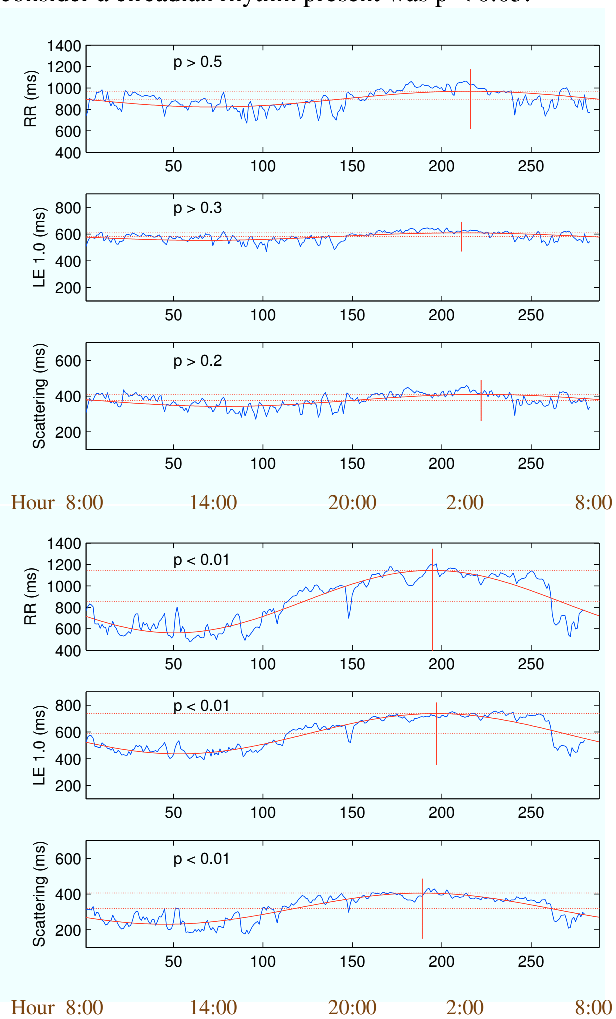

Fig 3. Circadian variations in variables obtained from Lorenz plot analysis with a time resolution of 5 minutes. Top: Patient without circadian rhythm in any parameter. Bottom: Patient with circadian rhythm in the RR, scattering index and 1.0s interception of the LP. Solid lines indicate the least square cosine curves. Solid vertical lines indicate acrophase.

3. Results

Parameters from 10-minute and 24-hour recordings are summarized in Table 1.

	Min	Max	Mean	Std.
Mean RR in 10-min (ms)	559	1147	778	155
LE1.0 in 10-min	336	881	527	140
Scatter in 10-min	193	446	296	59
Mean RR in 24-h (ms)	462	1154	763	165
RR amplitude in 24-h	14	454	136	86
LE1.0 amplitude in 24-h	16	151	61	36
Scatter amplitue in 24-h	7	115	45	24

Table 1. Parameters obtained from 10-minutes and 24-hour recordings.

Mean 24-hour RR measured 763 ± 165 ms (range 462 – 1154 ms) and was independently associated with LE1.0 (B=0.883, p<.001) and S (B=0.847, p<.001) obtained from 10-minute ECGs.

In 14 patients (48 %), a significant circadian RR rhythm was present (zero amplitude test). Parameters are compared between patients with and patients without RR interval variability (Fig 4). Patients with significant circadian RR rhythm exhibited higher LE1.0 and S amplitudes than their counterparts without RR rhythm variation.

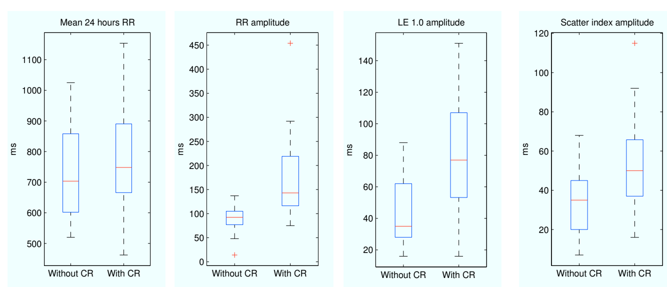

Fig 4. Comparison of parameters from Holter recordings in patients with and patients without circadian RR interval variation.

LE1.0 amplitude (B=.061 p=.03) and S amplitude (B=.077, p=.002) were independently associated with significant circadian RR rhythm.

4. Discussion and conclusions

Several experimental investigations have presented the relation between shorter RR intervals and the functional refractory period of the AV node. The high frequency of atrial fibrillatory impulses that bombard the AV node (concealed conduction) have also an important influence on sequential RR intervals.

On the contrary, systematic non-invasive clinical studies on this issue are rare, which at least in part can be attributed to a lack of proper methods to study this complex phenomenon. We examined properties of AV conduction during AF by a non-invasive technique of sequential Lorenz plot analysis of RR intervals in Holter signals. Comparable parameters were also evaluated in 10-minute resting ECGs.

Interestingly, electrophysiologic properties quantified from 10-minute recordings predicted mean heart rate over 24-hours. Since the latter is the most commonly used parameter to clinically evaluate adequate rate control, shorter recordings may be sufficient for this purpose. If confirmed in future studies, this approach may prove beneficial for the patients and reduce health care resource consumption.

Significant circadian rhythms have been observed in around fifty percent of our patients with persistent AF. Circadian heart rate rhythms are associated with better prognosis of AF patients [2,3]. As suggested in previous studies [7], we have also observed that the AV node refractoriness and the degree of concealed conduction can show a circadian rhythm during AF. Of special note is the observation, that these two properties are independent contributors to the observed circadian variations of the RR intervals.

Conclusions. This study suggests that AV nodal conduction properties obtained from Lorenz plot analysis of 10-minute ECG recordings are useful for predicting mean 24-hour heart rate in AF patients, until now the most useful parameter to define effective rate control. The variation degree of AV node refractoriness (LE1.0 amplitude) and concealed AV conduction (scatter index amplitude) are the main determinants of significant circadian heart rate rhythm in AF. Further studies are, however, needed to clarify the role of atrial fibrillatory inputs and the modulatory role of the autonomic nervous system as well as clinical implications of those findings for improved rate control management.

Acknowledgements

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Address for correspondence:

AM Climent
Department of Cardiology, Medizinische Fakultät
Otto-von-Guericke-Universität Magdeburg
39120 Magdeburg, Germany

Department of Electronic Engineer, ETSIT,
Polytechnic University of Valencia,
46022 Valencia, Spain

bamarcli@gmail.com