Scale Specific and Scale Independent Measures of Heart Rate Variability as Risk Indicators

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(September 20, 1999)

We study the Heart Rate Variability (HRV) using scale specific variance and scaling exponents as measures of healthy and cardiac impaired individuals. Our results show that the variance and the scaling exponent are highly correlated. We find that the variance measure at certain scales are well suited to separate healthy subjects from heart patients. However, for cumulative survival probability the scaling exponents outperform the variance measure. Our risk study is based on a database containing recordings from 428 MI individuals (after myocardial infarct) and on database containing 105 healthy subjects and 11 heart patients. The results have been obtained by applying three recently developed methods (DFA - Detrended Fluctuation Analysis, WAV - Multiresolution Wavelet Analysis, and DTS - Detrended Time Series analysis) which are found to be highly correlated.

PACS numbers: 87.10.+e, 87.80.+s, 87.90+y

The study of heart rate variability (HRV) has been in use for the last two decades as part of clinical, prognostic work; international guidelines for evaluating conventional HRV-parameters do exist \cite{1}. The conventional parameters are power spectra \cite{2} and standard deviation \cite{3}. Recently three new methods of analyzing RR time-series have been developed, all of them showing signs of improved prognostic performance. The three methods are: Detrended Fluctuation Analysis (DFA) \cite{4–6}, Multiresolution Wavelet Analysis (WAV) \cite{7–9} and Detrended Time Series Analysis (DTS) \cite{12}. The question which method and which measure yield better separation between cardiac impaired and healthy subjects has been highly controversially discussed \cite{8,13}.

In this Letter we show that while for separating between healthy subjects and heart patients the scale specific measure, the variance, is well suited; for the MI (myocardial infarct) group the scale independent measure, i.e., the scaling exponent, serves as a better risk indicator. Moreover, we show that the three above mentioned methods for both variance and scaling exponent, are correlated and converge to similar results while the variance and the scaling exponent are highly uncorrelated.

In our study we use two groups, the MI group, containing 428 heart patients after MI and a control group, consisting 105 healthy individuals and 12 cardiac impaired patients. These groups are much larger than any of the groups used in the above cited studies. We applied the following methods.

The DFA Method. The detrended fluctuation analysis was proposed by Peng \textit{et al} \cite{4}. This method avoids spurious detection of correlations that are artifacts of nonstationarity. The interbeat interval time series is integrated and then divided into windows of equal length, $n$. In each window the data is fitted with a least square straight line which represents the local trend in that window. The integrated time series is detrended by subtracting the local trend in each window. The root mean square fluctuation, the variance $\sigma_{\text{dfa}}(n)$ of the integrated and detrended time series is calculated for different scales (window sizes); the variance can be characterized by a scaling exponent $\alpha_{\text{dfa}}$, defined as $\sigma(n) \sim n^{\alpha}$.

The WAV Method. In the WAV method \cite{7–9} one finds the wavelet coefficients $W_{m,j}$, where $m$ is a ‘scale parameter’ and $j$ is a ‘position’ parameter, by means of a wavelet transform. The standard deviation $\sigma_{\text{wav}}(m)$ of the wavelet coefficients $W_{m,j}$ across the parameter $j$ is used as a separation parameter. Further, in \cite{14} the procedure was slightly extended by introducing a filtering process consisting of calculating the inverse wavelet transform based on the wavelet coefficients, with the removal of irrelevant scale coefficients. The subsequent standard deviation of the inversely transformed time series, $\sigma_{\text{filter}}$, results in a considerable improvement in the separation of the group of healthy subjects from the group of patients. The corresponding scaling exponents are denoted by $\alpha_{\text{wav}}$ and $\alpha_{\text{filter}}$.

The DTS Method. The detrended time series method was suggested in \cite{12}. In this method one detrends the RR time series by subtracting the local average in a running window from the original time series, resulting in a locally detrended time series. The standard deviation
\( \sigma_{dts} \) is calculated for various window scales with a scaling exponent \( \alpha_{dts} \).

The first suggestion to use a scale independent measure of the HRV as a separation parameter was by Peng et al [4] who found that a critical value of the DFA scaling exponent could distinguish between healthy individuals and heart patients. Thurner et al [9] used, however, the scale specific WAV variance in order to successfully separate the two groups. This results was independently confirmed on different groups in Ref. [14]. Nevertheless, the controversy was maintained in two recent Letters [8,13], which claimed that one measure outperforms the other one.

In Fig. 1 we compare the conventional measures for HRV for the control group: the variance for the DTS and WAV method (\( \sigma_{dts} \) and \( \sigma_{wav} \)) and the scaling exponent for the DFA method (\( \alpha_{dfa} \)). One notes that the scale dependent \( \sigma \)-measure yields a nearly perfect separation of cardiac impaired subjects (denoted by □) from healthy subjects (denoted by ○), whereas this is definitely not the case for the scale-independent measure \( \alpha_{dfa} \) [15].

This outcome is reversed when we applied the measures on the MI group. Since we have no diagnostics on this group, but rather do know the follow-up history for 328 individuals, we investigated the survival probability of this group as expressed in the so-called survival curve. In these curves one divides the entire group by means of a specific value of the \( \sigma \) or \( \alpha \) measure, called the critical value \( \sigma_c \) or \( \alpha_c \). For each subgroup we calculate the cumulative survival probability given by

\[
P(t + \Delta t) = P(t) \left[1 - \frac{\Delta N}{N(t)} \right],
\]

where \( P(t) \) is the probability to survive up to \( t \) days after the ECG recording, \( N(t) \) denotes the number of individuals alive at \( t \) days after the examination and \( \Delta N \) denotes the number of individuals who died during the time interval \( \Delta t \). Fig. 2 shows a comparison of survival curves where the separating measure in figures (a) and (c) is the critical variance \( \sigma_c \) and in figures (b) and (d) the critical scaling exponent \( \alpha_c \). Individuals with \( \sigma > \sigma_c \) (or \( \alpha > \alpha_c \)) belong to the subgroup with the higher survival probability; the upper panel extracts the subgroup with a high survival probability, whereas the lower panel extracts the subgroup with a low survival probability. From this comparison it is obvious that the scaling exponent serves as a better prognostic predictor.

In Fig. 2 we used the measures of the WAV method; but as we shall show below all above discussed methods are well correlated and no significant difference is noticeable in the survival curves when using DFA and DTS measures.
The 328 subjects are sorted according to the value of $\sigma_{\text{wav}}$ or $\alpha_{\text{wav}}$, respectively. The entire group was divided into overlapping subgroups of 100 subjects. The probability to die is plotted versus the average value of $\sigma$ and $\alpha$ for each subgroup. The vertical solid lines indicate the critical values $\sigma_c$ used in Fig. 2 (a) and (c) while the vertical dashed lines indicate the critical values $\alpha_c$ used in Fig. 2 (b) and (d).

The inferiority of the variance is also confirmed by Fig. 3, which shows the total number of deaths normalized by the total population. The greater sensitivity of the $\alpha$ dependent curve is expressed by the larger negative slope.

In order to investigate how the various methods are correlated we applied them to the larger MI group. The top panel of Fig. 4 shows that the variances of the three methods are well correlated, which is also true for the scaling exponents (middle panel). These comparisons indicate that indeed the various methods yield the same results in terms of variance and scaling exponents. On the other hand, the lower panel of Fig. 4 shows that the scale specific variance and the scale independent scaling exponent measures are uncorrelated for the DTS and DFA and are only faintly correlated for the WAV method. From this we conclude that the $\alpha$ and $\sigma$ measures characterize the interbeat interval series in different ways; the variance is a measure in the time domain (and thus is almost invariant to shuffling [9]), while the scaling exponent depends on the order of events and thus is a measure in the frequency domain (e.g., $\alpha_{\text{dfa}} = \frac{1}{2}$ for white noise and equals 1 for $1/f$ noise).

From this we conjecture that the variance reflects changes in either the sympathetic or the parasympathetic activities which are affected by changes in the cardiac inotropic state; thus the variance may hint on the instant condition of the physical properties of the heart. From the above we also conjecture that the scaling exponent depends on the interplay of the two contradicting parts of the autonomic nervous system and is thus an expression of the underlying mechanism of heart regulation (which influences the conventional power spectrum [2]) [16].

Acknowledgements. We wish to thank Nachemsohn’s Foundation for financial support.


[15] From a clinical point of view the top diabetics are considered as cardically healthy.

[16] An increase/decrease in one of the activities is usually compensated by a decrease/increase in the other activity. In cardiac failure the regulation between the two activities breaks down.