Ability of Heart Rate Variability as Screening Tool for Heart Diseases in Men

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Abstract

The aim of this study was to analyze the ability of heart rate variability (HRV) indices to identify patients with heart diseases as a first diagnosis by the general practitioner (GP). In this study we applied linear and non-linear methods of short-term HRV analysis. 78 healthy male subjects (REF) and 378 male patients (PAT) with several heart diseases were investigated considering two age groups: younger men (YM) and elderly men (EM). The identification of patients with heart diseases was performed using a scoring system based on cut-off parameters calculated from REF. Comparing REF with PAT, in both age matched groups the specificity were selected to be 100%. Combining the best indices from all domains revealed sensitivities of 74.07% for YM and 77.44% for EM. In conclusion, short-term HRV analysis might offer a screening of heart diseases as a first diagnosis by the GP. Especially nonlinear parameters contribute to diagnosing heart diseases in men.

1.   Introduction

Heart diseases are the leading cause of mortality in the western world. Heart rate variability (HRV) analysis has become a relevant tool for identification cardiovascular risk in humans [1].

In the MONICA study, Ziegler et al. [2] determined whether the major cardiovascular risk factors are associated with diminished heart rate variability (HRV) and showed that diabetes the primary determined a reduced HRV.

Greiser et al. [3] showed that short-term HRV may be a marker for a cardiovascular disease.

The aim of this study was to analyze the ability of HRV indices to identify patients with heart diseases as a first diagnosis by the general practitioner (GP). For this analysis we developed a screening tool for the GP. This screening tool should allow a fast and simplified diagnosis and should avoid false referrals.

2.   Methods

2.1.   Methods and parameters

The time series of heart rate (tachograms) consisting of beat-to-beat intervals are extracted from 5 minute ECG recordings. Ectopic beats and artifacts within the tachograms were detected and corrected by an adaptive filter to generate the Normal-to-Normal (NN) heartbeat time series [4]. To analyze the ability of HRV indices we applied various linear and nonlinear methods:
- Linear methods:
    - time domain (TD)
    - frequency domain (FD)
- Methods from nonlinear dynamics (NLD):
    - detrended fluctuation analysis (DFA)
    - compression entropy (CE)
    - symbolic dynamics (SD)
    - short-term symbolic dynamics (STSD)
    - Poincaré plot analysis (PPA).

Linear HRV standard indices were calculated from time and frequency domain according to the Task Force [5].

The following indices from NLD were calculated and are described shortly in the following:

DFA based on a modified random walk analysis was introduced and applied to physiological time series by Peng et al. [6]. There are two parameters introduced, the short-term fractal exponent $\alpha 1$ over the range of $4 \leq n \leq 16$ heartbeats and a long-term scaling exponent $\alpha 2$ over a range $16 \leq n \leq 64$ heartbeats [6]. Reduced scaling exponents were found in patients with cardiovascular diseases.

CE is based on the Zip-algorithm developed by Ziv & Lempel [7] which is a universal algorithm for a lossless data compression, using string matching on a sliding window. Baumert et al. [8] introduced the CE method for the first time on NN interval time series. The index CE quantifies how much the data from a specific NN interval time series can be compressed. A significantly reduced

CE (that represents a reduced complexity) could be found in patients just before the onset of a ventricular tachyarrhythmia.
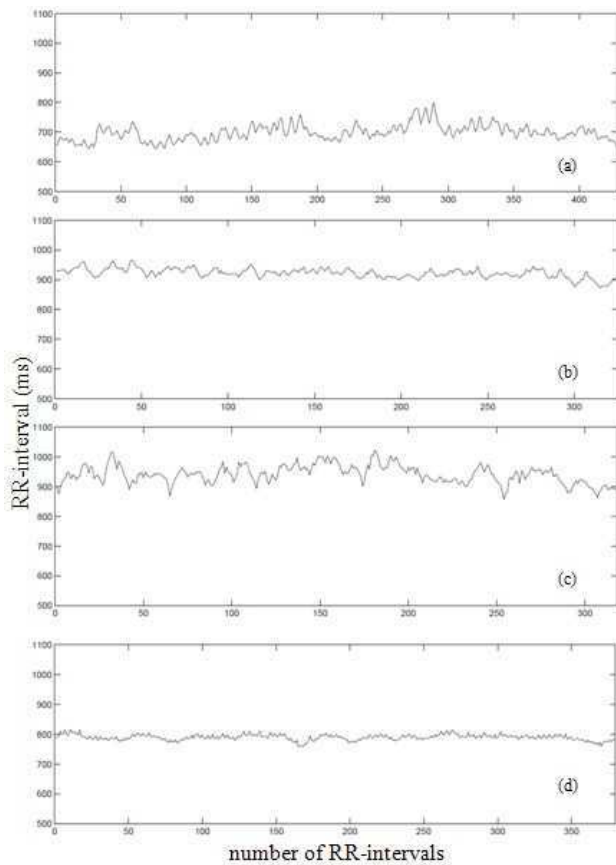

Figure 1. Tachograms of (a) a young healthy man, (b) a young man with HeF, (c) an elderly healthy man and (d) an elderly male patient with HeF.

SD is suitable to describe the global short- and long-term dynamics of beat-to-beat variability (Kurths et al. [9], Voss et al. [10]). At the beginning of the analysis the time series is transformed into a symbol sequence consisting of four symbols of the alphabet A = {0, 1, 2, 3} to classify the dynamic changes within that time series. Then words of three successive symbols are constructed from this symbol sequence, leading to 64 different possible word types. The histogram of the 64 word types contains the probability distribution of each single word type occurrence. From this word type distribution the Shannon and Renyi entropy are calculated.

Another type of symbolic dynamics is the short-term symbolic dynamics (STSD) introduced by Porta et al. [11]. With this method short-term tachograms of only 300 NN intervals are analyzed. The full range of sequence is uniformly spread into six levels (0-5) and

patterns of length L=3 are constructed. All patterns are grouped, without any loss, into four families. The rate of occurrence of these pattern families are indicated in %. In this study we enhanced this method splitting the pattern families and grouping them without any loss into some new and more detailed pattern families.

The last applied NLD method is the Poincaré plot analysis which is a quantitative technique of phase space characterization, whereby the shape of the plot is categorized into functional classes as suggested by Kamen et al. [12]. PPA provides special and detailed beat-to-beat information on the dynamical behavior of the heartbeat sequence. For a two-dimensional graph, the NN_n is plotted against NN_{n+1}. Three indices are calculated from the plot: The standard deviation of the short-term NN interval variability (minor axis of the cloud, SD1), the standard deviation of the long-term NN interval variability (major axis of the cloud, SD2) and the axes ratio (SD1/SD2). However, we have to consider the high correlation of these indices with linear ones.

Altogether 20 indices were calculated which were grouped into the following method families: TD (6), FD (2), SD (5), STSD (3), CE (1), DFA (1) and PPA (2).

2.2. Statistics

In this study we analyzed short-term ECG segments of five minutes durations from healthy male subjects (REF) and male patients with several heart diseases (PAT):

- myocardial infarction (MI)
- heart failure with peripheral arterial disease (PAD)
- heart failure without peripheral arterial disease (HeF)

Considering the known age and gender effects on HRV (Voss et al. [13], Zhang et al. [14]) we separated both groups into two matched groups of 30-50 and 51-70 years.

Table 1 gives an overview of the different groups with the number of included subjects.

Table 1. Healthy subjects (REF) and heart disease patients (PAT) with the number of subjects in every subgroup; in brackets: mean age for every subgroup.

	young males (30-50 years)	elderly males (51-70 years)
healthy (REF)	52 (40.00 years)	26 (58.77 years)
patients (PAT)	81 (45.01 years)	278 (60.73 years)

2.3. Scoring system

To investigate the ability of HRV indices to identify patients with heart diseases a scoring system was introduced. In both healthy subgroups, for each index the maximum and minimum value was calculated that defines the upper and lower cut-off value. Then each index from every patient of both age groups was tested whether it was lying outside the cut-off values. In this case the respective patient got one point. The points were summed up for each patient. A maximum of 20 points could be reached. If a patient got one or more points, he was classified as a patient with a heart disease.

The scoring system was developed in such a way that a specificity of 100% was reached in every analyzed subgroup.

Further on, we applied the scoring system for the combination of different methods. For each combination we calculated the specific sensitivity (table 2).

3. Results

Figure 1 illustrates examples of different short-term tachograms (5 minutes) of each subgroup. In general, healthy subjects show, as expected, a pronounced variability of heart rate compared to patients.

Considering all methods with the scoring system, the sensitivity was in the group of young men (YM) 74.07% and in the group of elderly men (EM) 77.44%.

Having regard to only time domain parameters the estimated sensitivity was 39.51% in the group of YM and 9.43% in the group of EM. Applying only frequency domain parameters the estimated sensitivity was 9.88% in YM and 18.18% in EM. In contrast, the sensitivities increased applying only nonlinear dynamics indices to 64.20% (YM) and 72.39% (EM).

An optimum result (including as less as possible methods to reduce computational time, 17 indices) in discriminating healthy subjects from heart disease patients was achieved combining indices from time domain, frequency domain, compression entropy, symbolic dynamics and short-term symbolic dynamics (70.37% in YM and 76.09% in EM).

4. Discussion and conclusions

In this study we analyzed the ability of HRV indices to identify patients with heart diseases as a first diagnosis by the general practitioner. We calculated 20 HRV indices from different domains (time and frequency domain as well as nonlinear dynamics).

Altogether, we compared 78 healthy men and 378 patients with different heart diseases.

Table 2. Sensitivities in both age groups for different method combinations applying the scoring system

method combination	sensitivities in %	
	young men (YM)	elderly men (EM)
all methods	74.07	77.44
without DFA &PPA	70.37	76.09
without TD & FD	64.20	72.39
only TD	39.51	9.43
only FD	9.88	18.18

A scoring system was applied to differentiate between patients with heart diseases and healthy subjects. The combination of HRV parameters from TD, FD, SD, STSD and CE achieved a sensitivity of 70.37% for the group of young men and of 76.09% for the group of elderly male with a specificity in both age groups of 100%.

Some limitations of this pilot study are the relatively low number of healthy subjects in every subgroup especially in the elderly group and the restricted number of different heart diseases. We further did not yet differentiate between treatments and co-morbidities.

In conclusion, short-term HRV analysis might offer a screening of heart diseases as a first diagnosis by the general practitioner. In contrast to linear indices, especially nonlinear parameters contribute to discriminating heart diseases in men. Upcoming is a further study including women as well as a considerable enlargement of the enrolled patients and healthy subjects to overcome some of the limitations of this pilot study.

Acknowledgements

References

[1] Stein PK, Kleiger RE. Insights from the study of heart rate variability. Annu Rev Med 1999; 50: 249-261.

[2] Ziegler D, Zentai C, Perz S, Rathmann W, Haastert B, Meisinger C and Lowel H. Selective contribution of diabetes and other cardiovascular risk factors to cardiac autonomic dysfunction in the general population. Exp Clin Endocrinol Diabetes 2006 114: 153-159.

[3] Greiser KH, Kluttig A, Schumann B, Swenne CA, Kors JA, Kuss O, Haerting J, Schmidt H, Thiery J and Werdan K. Cardiovascular diseases, risk factors and short-term heart rate variability in an elderly general population: the CARLA study 2002-2006. Eur J Epidemiol 2009 24: 123-142.

[4] Wessel N, Voss A, Malberg H, Ziehmann C, Voss HU, Schirdewan A, Meyerfeldt U, Kurths J. Nonlinear analysis

of complex phenomena in cardiological data. Herzschrittmachertherapie und Elektrophysiologie 2000; 11: 159-173.

[5] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation 1996; 93: 1043-1065.

[6] Peng CK, Havlin S, Stanley HE and Goldberger AL. Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. Chaos 1995; 5: 82-87.

[7] Ziv J, Lempel A. Universal algorithm for sequential data compression. IEEE Trans Inf Ther 1977; 23: 337-343.

[8] Baumert M, Baier V, Haueisen J, Wessel N, Meyerfeldt U, Schirdewan A, Voss A. Forecasting of life threatening arrhythmias using the compression entropy of heart rate. Methods Inf Med 2004; 43: 202-206.

[9] Kurths J, Voss A, Saparin P, Witt A, Kleiner HJ, Wessel N. Quantitative analysis of heart rate variability. Chaos 1995; 5: 88-94.

[10] Voss A, Kurths J, Kleiner HJ, Witt A, Wessel N, Saparin P, Osterziel KJ, Schurath R and Dietz R. The application of methods of non-linear dynamics for the improved and predictive recognition of patients threatened by sudden cardiac death. Cardiovasc Res 1996 31: 419-433.

[11] Porta A, Guzzetti S, Montano N, Furlan R, Pagani M, Malliani A and Cerutti S. Entropy, entropy rate, and pattern classification as tools to typify complexity in short heart period variability series. IEEE Trans Biomed Eng 2001; 48: 1282-1291.

[12] Kamen PW, Krum H, Tonkin AM. Poincare plot of heart rate variability allows quantitative display of parasympathetic nervous activity in humans. Clin Sci (Lond) 1996; 91: 201-208.

[13] Voss A, Schulz S, Schroeder R, Baumert M, Caminal P. Methods derived from nonlinear dynamics for analysing heart rate variability. Philos Transact A Math Phys Eng Sci 2009; 367: 277-296

[14] Zhang J. Effect of age and sex on heart rate variability in healthy subjects. J Manipulative Physiol Ther 2007; 30: 374-379.

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