The SRA

A summary

The SRA Procedure

Scientific base

Numerous scientific investigations during the last two decades have shown that the heart beat dynamics can provide much more information than just the heart rate. Conventional Heart Rate variability (HRV) is a very useful tool and extensively used, but it often fails in predicting clinical outcome. Including non linear methods in the analysis, the heart rate dynamics discloses much more information about the functional state of the heart and diseases. This is because non linear approaches are able to capture feedback mechanisms, which are numerously present in living organisms.

One of the frequently used methods its he time series analysis. Given any signal over a certain time, the time between distinct points from the signal are represented as a Lorenz plot or Poincaré plot. Each chose time distance is plotted against its previous one. The construction of a Lorenz plot from a continuous ECG recording is shown in figure 1.

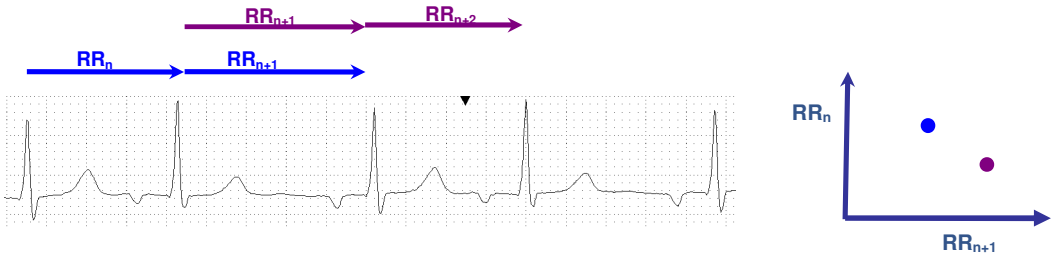

Fig. 1
Construction of s Lorenz plot.

The distinct points are the R peaks. The time between two R peaks is the RR interval. One RR interval is plotted against its previous one. The Lorenz plot for a one hour ECG is shown in figure 3. With this procedure, the ECG is transformed into a geometrical structure which is subjected to further mathematical treatment.

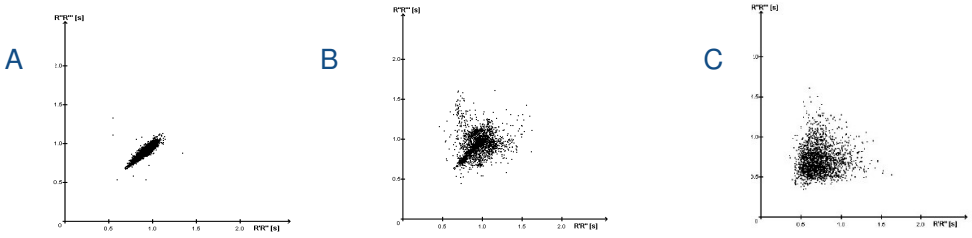

Fig. 2
Lorenz plots from one hour ECG recordings. A is from a healthy volunteer, B from a patient with paroxysmal atrial fibrillation and C from a patient with acute atrial fibrillation.

During fibrillation, the irregular ventricular Response is well known. This impaired heart rate dynamics has a certain expression in the Lorenz plot representation, as shown in figure 3 C.

Several recent publications have demonstrated an impaired ventricular response also outside of fibrillation episodes using different methods of non linear analysis.

This is the basic strategy used in the SRA procedure. With a combination of six different linear and non linear parameters, identification of patients with established paroxysmal atrial fibrillation outside of their fibrillation episodes was possible. With this approach, the sensitivity for the identification of patients with paroxysmal atrial fibrillation was significantly higher than finding them according to fibrillation episodes.

During the fully automated SRA procedure the ECG signal is first cleaned from artefacts. In parallel there is a beat type classification. This is necessary as only normal beats, which means beats that start in the atrium, are included in the calculation of the risk fore atrial fibrillation. Ventricular beats contain no information regarding the atrium. Those ventricular beats are stored and provided as an information about other cardiac disrhythmia besides atrial fibrillation. The corresponding points in the Poincaré plot will be marked in red (see also viewer function). The subsequent analysis combines then all the linear and non linear parameters into a decision matrix. This decision matrix is weighing the different parameters according to their relevance in predicting the risk for atrial fibrillation. The weighing factors were determined on patient data from different origin. An overview of the complete SRA procedure is given in the diagram in figure 3.

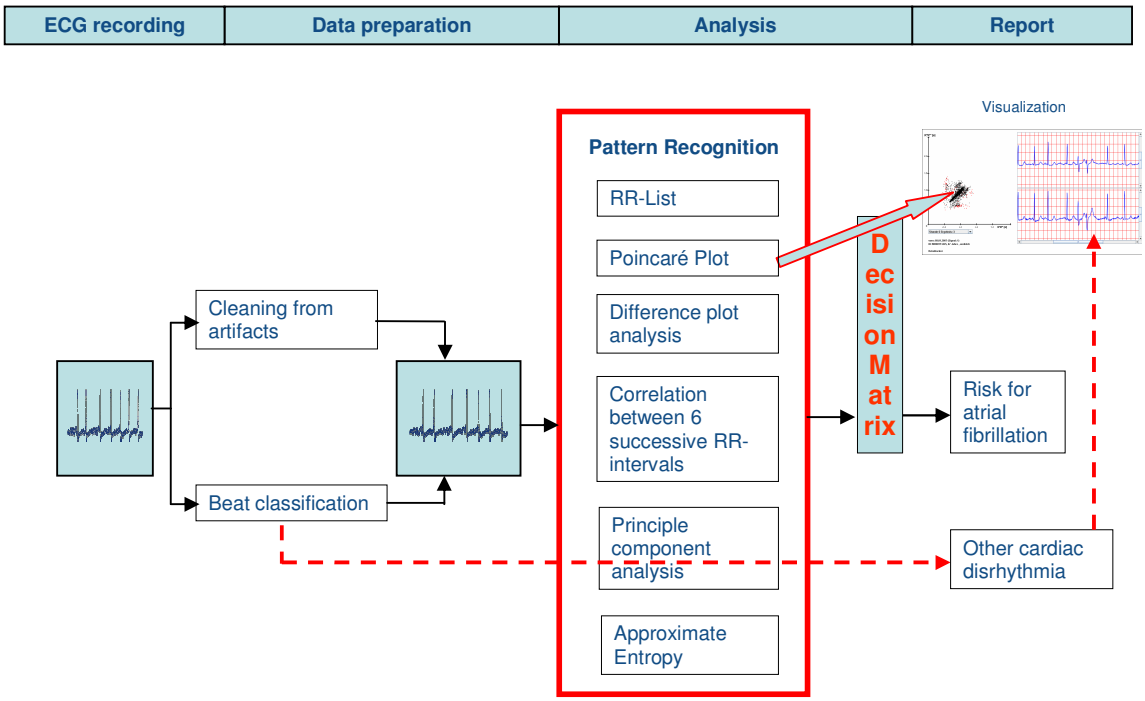

Figure 3
The SRA procedure

The SRA procedure has been retrospectively validated with a clinical trial. The results are summarized in an abstract in the appendix 1.

The SRA – Procedure in Practice

ECG recording and Report

Using the SRA procedure as a screening tool, just a one hour ECG recording is necessary. The ECG is digitally stored and transferred to the computer. With the help<of a small communication software tool, the ECG is transferred via internet to the analysis server of apoplex medical technologies, were the fully automated analysis is performed. The result is back within minutes at the doctors desk. An example report is included in appendix 3.

The Viewer - Function

To gain a fast overview over all cardiac disrhythmia in the ECG recording, the Viewer Function has been integrated into the SRA procedure. It allows fast assessment of all disrhythmia with the help of the Poincaré plot. To enter the viewer function, there is a link in the email with the report which allows access to the original ECG on the central analysis server. When the link is opened, the Poincaré plot of the corresponding ECG is visible (figure 4). As each point in the Poincaré plot is generated by two successive RR intervals, the corresponding RR intervals are shown by clicking one of the points in the Poincaré plot. Ventricular beats are now easily assessed just by clicking the red points (for example see figure 5) or even find existing fibrillation episodes when present (figure 6).

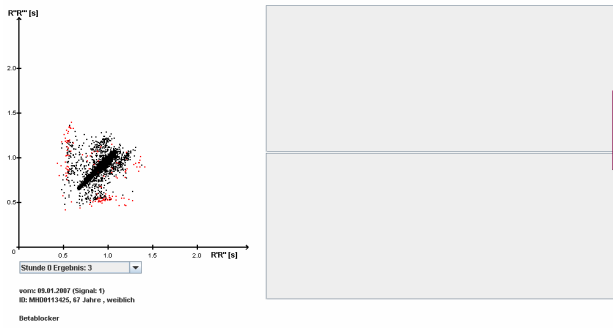

Figure 4
Start window of the Viewer Function

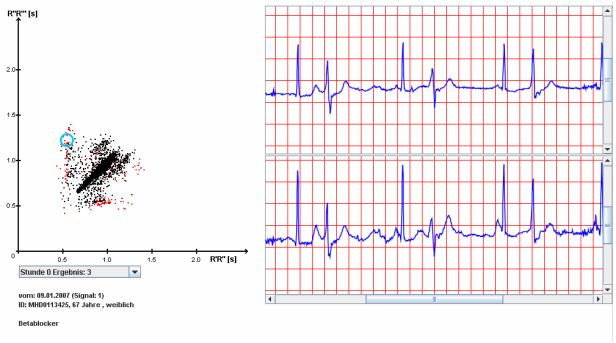

Figure 5
Clicking at a red point in the Poincaré Plot (blue circle) shows ventricular disrhythmia.

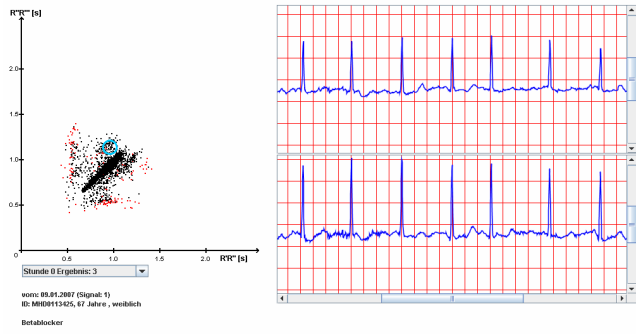

Figure 6
Clicking at a black point in the Poincaré Plot (blue circle) shows a fibrillation episode.

References

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G. Schmidt, G. E. Morfill
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M. Costa, A. L. Goldberger, C.-K. Peng
Multiscale entropy analysis of biological signals
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M. Marks, R. Reinhardt, T. Hepp, H. Heuer
Stroke prevention by an improved identification of paroxysmal atrial fibrillation with a new algorithm from a one hour ECG recording
European Journal of Cardiovascular Prevention and Rehabilitation (2006);13,Suppl.1,S68

T. Duning, M. Marks, H. Wersching, T. Hepp, R. Reinhardt, H. Heuer, S. Knecht
Improved identification of patients with paroxysmal atrial fibrillation by analysis of electrocardiographic R-R dynamics. A preliminary observational study
submitted

Appendix 1

Abstract


ANIM
ANIM 2007
24. Arbeitstagung für Neurologische Intensiv- und Notfallmedizin
18. bis 21. Januar 2007
Stadthalle Chemnitz
Deutsche Gesellschaft für Neurologische Intensiv- und Notfallmedizin in der Deutschen Gesellschaft für Neurologie e.V.
in Zusammenarbeit mit der Deutschen Schlaganfallgesellschaft und der Arbeitsgemeinschaft Autonomes Nervensystem

Improved identification of patients with paroxysmal atrial fibrillation: Analysis of electrocardiographic R-R-Interval Dynamics

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[3] Klinik für Innere Medizin I, Kardiologie, St. Johannes Hospital Dortmund

Introduction:
Atrial fibrillation (AF) is one of the most frequent reasons and the leading single risk factor for ischemic stroke (relative risk between 5 and 17, compared to hypertension (3 to 5) or smoking (1.5). Because oral anticoagulation is highly efficacious for both primary and secondary prevention of stroke in patients with AF, with a risk reduction of 61% (47% to 71%) versus placebo, detection of AF is essential.

As AF is often asymptomatic and intermittent, appropriate diagnosis – and thus treatment – is frequently missed. Even when suspected, more than 50% of cases of paroxysmal atrial fibrillation (PAF) may escape detection. Relative to standard ECG, 24 hour recording doubles the detection rate of PAF but still misses about one third of cases later identified by ambulatory 7-day ECG monitoring and up to 44% of cases detected by long-term event recorders. The diagnose of PAF is essential as the risk for ischemic stroke is not less than for chronic AF:

Since even short duration AF induces contractile and electrical atrial remodeling, previous episodes of PAF may increase the variability of the atrial electrical wavelength also in the absence of fibrillation. This phenomenon may manifest as increased R-R interval dynamics on ECG and, combined with an adequate analysis tool, it may increase the detection rates of PAF (fig. 1).

In this study we analyzed ECG data from patients with an increased risk for stroke because of established PAF to find out, whether analysis of R-R interval dynamics might lead to higher detection rates of PAF.

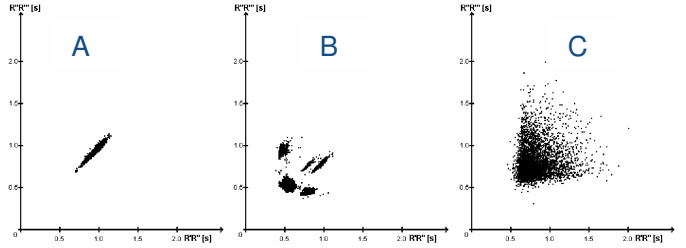


Fig. 1: Examples of time series analyses from R-R intervals. The plot from a healthy volunteer (A) shows the typical form of a baseball bat. The calculated risk level is 0. The disseminated cluster of a PAF patient (B) indicates an increased R-R interval dynamics (risk level 1). The plot of a patient with acute AF expresses the well known irregularity during fibrillation episodes (C). The calculated risk level is 2.

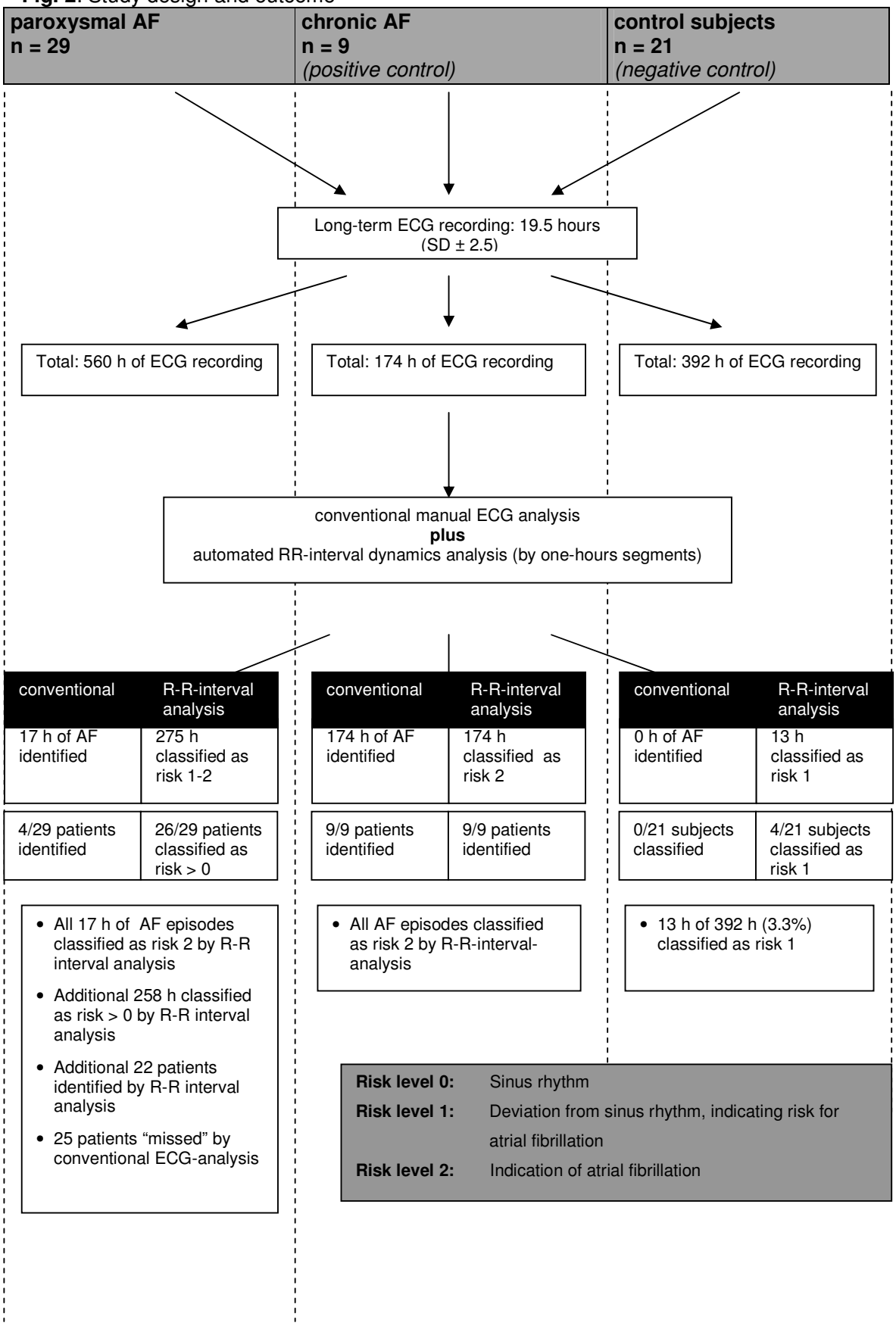
Methods:
29 patients with established diagnose of PAF underwent a conventional 24 hour ECG analysis. In addition the same ECG data have been subjected to a fully automated R-R interval analysis. 9 patients with chronic AF served as a positive control and 21 ambulatory patients with no diagnose of AF served as a negative control.

For that purpose the 24 hour ECGs were divided in one hour ECG recordings. For each hour the risk for having PAF was calculated.

Risk level 0: Sinus rhythm
Risk level 1: deviations from the pattern of sinus rhythm, significant hint for PAF
Risk level 2: acute AF

Results:
Conventional ECG analysis identified 4 of the 29 (14%) patients with PAF, the R-R interval analysis 26 patients (90%). In 17 hours out of 560 hours (3%) there were fibrillation episodes and hence were identified by both methods. A further 258 (46%) hours without fibrillation events were identified as risk for PAF by the analysis of the R-R interval dynamics (fig. 2).

Fig. 2: Study design and outcome



Conclusion:
The part of identified patients with established diagnose of PAF was 6 times higher with the R-R interval analysis than with conventional 24 hour analysis. The fully automated algorithm and the easy handling of the hardware allows the use of the R-R interval analysis for an effective screening of stroke patients in stroke units. Patients with a risk for PAF but with no fibrillation episodes are then subjected to further diagnose e.g. 7 day ECG monitoring. Analysis of the R-R interval dynamics could result in a more efficient use of diagnostic resources (fig. 3).

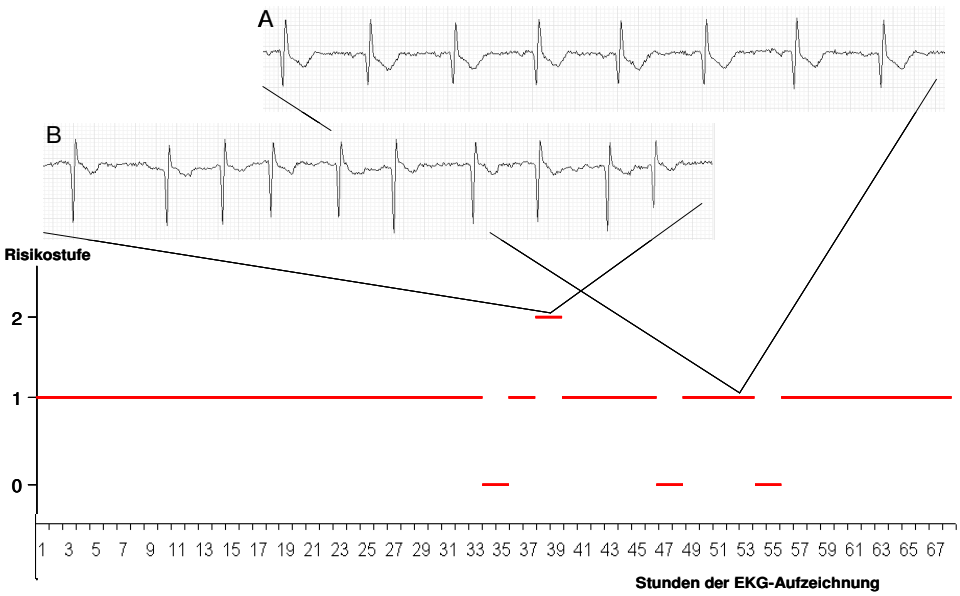


Fig. 3: Example of a 68 hour long term ECG analysis from a stroke patient with unclear stroke aetiology. Fibrillation episodes were only present in two hours. Classification with conventional ECG analysis would have rated 66 hours from 68 hours as false negative whereas the R-R interval analysis classified 62 hours as risk level 1 (risk for PAF) and the two hours with fibrillation episodes as risk level 2 (acute fibrillation)

Appendix 2

Further Reading

Further reading

Basics

How to describe the complex system „Heart“ has been addressed by the paper of Schmidt and Morfill.
Georg Schmidt, Gregor Morfill
Complexity Diagnostics in Cardiology: Fundamental Considerations
Pacing and Clinical Electrophysiology, (1994)17, 6, 1174-1177

A special edition of „Cardiovascular Research“ published many contributions concerning non linear dynamics in the cardiovascular system
Cardovascular Research 31 (1996) 331-433
www.elsevier.com

Atrial fibrillation and non linear dynamics:

Vikman et al. find a reduction in the complexity of the R-R dynamics and a change in fractal properties before the onset of atrial fibrillation.

Saila Vikman, et al.
Altered complexity and correlation properties of R-R interval dynamics before the spontaneous onset of paroxysmal atrial fibrillation
Circulation, 1999; 100:2079-2084

Altered Complexity and Correlation Properties of R-R Interval Dynamics Before the Spontaneous Onset of Paroxysmal Atrial Fibrillation

Saila Vikman, MD; Timo H. Mäkikallio, MD; Sinikka Yli-Mäyry, MD; Sirkku Pikkujämsä, MD;
Anna-Maija Koivisto, BSc; Pekka Reinikainen, MD;
K.E. Juhani Airaksinen, MD; Heikki V. Huikuri, MD

Background—Trigger mechanisms for the onset of paroxysmal atrial fibrillation (AF) in patients without structural heart disease are not well established. New analysis methods of heart rate (HR) variability based on nonlinear system theory may reveal features and abnormalities in R-R interval behavior that are not detectable by traditional analysis methods. The purpose of this study was to reveal possible alterations in the dynamics of R-R intervals before the spontaneous onset of paroxysmal AF.

Methods and Results—Traditional time and frequency domain HR variability indices, along with the short-term scaling exponent α_1 and approximate entropy (ApEn), were analyzed in 20-minute intervals before 92 episodes of spontaneous, paroxysmal AF in 22 patients without structural heart disease. Traditional HR variability measures showed no significant changes before the onset of AF. A progressive decrease occurred both in ApEn (1.09 ± 0.26 120 to 100 minutes before AF; 0.88 ± 0.24 20 to 0 minutes before AF; $P<0.001$) and in α_1 (1.01 ± 0.28 120 to 100 minutes before AF, 0.89 ± 0.28 20 to 0 minutes before AF; $P<0.05$) before the AF episodes. Both ApEn (0.89 ± 0.27 versus 1.02 ± 0.30; $P<0.05$) and α_1 (0.91 ± 0.28 versus 1.27 ± 0.21; $P<0.001$) were also lower before the onset of AF compared with values obtained from matched healthy control subjects.

Conclusions—A decrease in the complexity of R-R intervals and altered fractal properties in short-term R-R interval dynamics precede the spontaneous onset of AF in patients with no structural heart disease. Further studies are needed to determine the physiological correlates of these new, nonlinear HR variability measures. **(*Circulation*. 1999;100:2079-2084.)**

Changes in the ECG before the onset of atrial fibrillation have been found by Hnatkova et al. Katerina Hnatkova, et al.
Analysis of the cardiac rhythm preceding episodes of paroxysmal atrial fibrillation
Am Heart J 1998;135:1010-9

Analysis of the cardiac rhythm preceding episodes of paroxysmal atrial fibrillation

Katerina Hnatkova, PhD, Johan E.P. Waktare, MD, Francis D. Murgatroyd, MD, Xiaohua Guo, MD, Xie Baiyan, PhD, A. John Camm, MD, and Marek Malik, PhD *London, United Kingdom*

Aims This study seeks to elucidate whether there was a common mode of initiation of paroxysmal atrial fibrillation (PAF) episodes that might suggest new therapies.

Methods A library of 177 digitized and analyzed 24-hour Holter recordings from PAF pharmacotherapy trials was studied. All noise-free PAF episodes ≥0.5 minutes were identified. PAF episodes and the preceding 2 minutes of sinus rhythm were printed as tachograms and visually inspected. Heart rate and ectopic beat behavior were used to characterize modes of PAF onset by comparing half-minute segments of the final 2 minutes of sinus rhythm.

Results Thirty-four recordings (from 19 patients, aged 61.7 ± 11.5 years) provided 231 PAF episodes suitable for analysis. No patients had a consistent mode of PAF onset. This was confirmed by systematic analysis of the five patients with the most episodes. Overall, a highly significant increase in ectopic beats, from 1.34 to 6.52 min^{-1} ($p < 0.001$) was found, but heart rate did not significantly change (mean heart rate at onset = 64 beats/min). PAF was initiated by a solitary ectopic beat in more than half of the cases. No consistent evidence for short-long-short sequences, seen in ventricular arrhythmias, was found.

Conclusion The mode of onset of atrial fibrillation is inconsistent, both across a population with PAF and within individuals. This has implications for understanding the mechanisms of atrial fibrillation onset in human beings and for the treatment of the disorder. (Am Heart J 1998;135:1010-9.)

Changes in the RR dynamics in connection with atrial fibrillation are also found by Krstacic et al. More can be found on their web page: www.irb.hr.
G. Krstacic et al.
Some important R-R interval based paroxysmal atrial fibrillation predictors
In press and personal communications

Abstract

Atrial fibrillation is the most common sustained cardiac arrhythmia. The result of series of machine learning experiments is detection of some promising paroxysmal atrial fibrillation predictors. Based on ratio of short and long R-R intervals there is a possibility to generate rules for PAF screening and predicting. For PAF screening the calculated ratio were 2.00 for successive R-R intervals. The problem of imminent PAF prediction is much more difficult and the concept of normalisation had to be implemented. The optimal seems to be ratio between the shortest and the longest R-R interval, which was at least 1.75 times larger than ratio during the normalisation time for the same patient. Also it was detected that maximal distance of the longest and the shortest R-R intervals should be up to six R-R intervals.

The question about changes in the RR dynamics before the onset of fibrillation in patients with paroxysmal atrial fibrillation has also been addressed by Moody et al. The best prediction was achieved by a combination of premature atrial activity and P-wave variability.
GB Moody et al.
Predicting the onset of paroxysmal atrial fibrillation:

The computers in cardiology Challenge 2001, Computers in Cardiology 2001;28:113116

Abstract

The advent of pacing techniques for preventing the onset of atrial arrhythmias motivates the development of accurate predictors of these arrhythmias, and of paroxysmal atrial fibrillation (PAF) in particular. The goals of the second annual Computers in Cardiology Challenge were to determine if segments of ECG that do not include PAF contain information sufficient (1) to distinguish subjects at risk of PAF from others not at risk, and (2) to predict imminent PAF in at-risk subjects. Via PhysioNet, 18 teams of participants studied training and test databases containing two half-hour ECG recordings from each of 100 subjects (of whom 53 experienced PAF immediately following one of the two recordings). Results indicate that roughly 80% of the subjects can be correctly classified (as at-risk or not), and that imminent PAF can be predicted in roughly 80% of subjects at risk. The most successful approaches were based on analysis of the incidence of premature atrial complexes (PACs) and P-wave variability.

In the following paper the authors are able to predict cardiac abnormalities with a certainty of 80% just from RR dynamics. Among them are atrial fibrillation, left bundle branch block and dilative cardiomyopathy.

R. Acharya U et al.
Classification of cardiac abnormalities using heart rate signals
Med. Biol. Eng. Comp., 2004,42,288-293

Classification of cardiac abnormalities using heart rate signals

R. Acharya U[1] A. Kumar[1] P. S. Bhat[2] C. M. Lim[1] S. S. Iyengar[3] N. Kannathal[1] S. M. Krishnan[4]

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[2]Department of ECE, National Institute of Technology Karnataka, Surathkal, India
[3]Department of Computer Science, Louisiana State University, Baton Rouge, USA
[4]Biomedical Engineering Reseach Centre, Nanyang Technological University, Singapore

Abstract—*The heart rate is a non-stationary signal, and its variation can contain indicators of current disease or warnings about impending cardiac diseases. The indicators can be present at all times or can occur at random, during certain intervals of the day. However, to study and pinpoint abnormalities in large quantities of data collected over several hours is strenuous and time consuming. Hence, heart rate variation measurement (instantaneous heart rate against time) has become a popular, non-invasive tool for assessing the autonomic nervous system. Computer-based analytical tools for the in-depth study and classification of data over day-long intervals can be very useful in diagnostics. The paper deals with the classification of cardiac rhythms using an artificial neural network and fuzzy relationships. The results indicate a high level of efficacy of the tools used, with an accuracy level of 80–85%*

Keywords—*Neural networks, Heart rate variability, Lyapunov exponent, Correlation function, Fuzzy equivalence relationship*

Med. Biol. Eng. Comput., 2004, **42**, 288–293

Vascular factors that contribute to the development of Dementia have been described by Knecht and Berger in Deutsches Ärzteblatt Jg. 101 Heft 31-32 am 02.08.2004.

Einfluss vaskulärer Faktoren auf die Entwicklung einer Demenz

Stefan Knecht[1], Klaus Berger[2]

Zusammenfassung

Erkrankungen, die höhere, integrative Leistungen des Gehirns beeinträchtigen, können zu einer Demenz führen. Die Ursachen sind unterschiedlich (degenerativ, vaskulär, entzündlich) und wirken additiv. So können vaskuläre Erkrankungen nicht nur die primäre Ursache einer Demenz sein, sondern auch demenzielle Entwicklungen anderer Genese beschleunigen. Dabei sind akute vaskuläre Erkrankungen wie Schlaganfälle nur die Spitze eines Eisberges. Fünfmal häufiger sind unbemerkte ischämische Hirnläsionen, die als radiologischer Zufallsbefund oder in Bevölkerungsstudien auffallen und die Wahrscheinlichkeit, eine Demenz zu entwickeln, verdoppeln. Da Demenzen vor allem zum Lebensende hin auftreten, könnte eine Erkrankungsverzögerung von zwei Jahren die Gesamtzahl von einer Million Betroffenen in Deutschland um ein Viertel verringern. Die Identifikation und Behandlung vaskulärer Risikofaktoren dürfte wegen des vaskulären Beitrags zur Desintegration neuronaler Funktion derzeit noch einer der effektivsten Wege sein, die Entwicklung einer Demenz zu verlangsamen und damit die Prävalenz von Demenz zu senken.

Schlüsselwörter: Demenz, Morbus Alzheimer, Schlaganfall, Risikostratifizierung, Geriatrie

Summary

Vascular Factors Contributing to the Development of Dementia

Dementia can be conceptualized as the final common pathway of diseases that disintegrate information processing in the brain. The underlying causes differ (e. g. degenerative, vascular, and inflammatory processes) and act cumulatively. Thus, cerebrovascular disease may be a primary cause of dementia or contribute to dementing processes based on other pathologies. Symptomatic brain infarcts are only the tip of the iceberg. Silent brain infarcts are five times more prevalent than symptomatic strokes. Such clinically unrecognized infarcts are usually diagnosed by coincidence or in radiological cohort studies and double the risk for dementia. Since dementia primarily affects the elderly, a delay in onset of two years would considerably reduce the total number of patients. Because cerebrovascular disease accelerates brain disintegration, prevention of symptomatic and silent brain infarcts by identification and treatment of cerebrovascular risk factors seems one of the most promising ways to lower the prevalence of dementia in the general population.

Key words: dementia, Alzheimer's disease, stroke, risk assessment, geriatrics

Appendix 3

Example Report

SRA - Analysereport

Screening auf Vorhofflimmern und andere Herzrhythmusstörungen

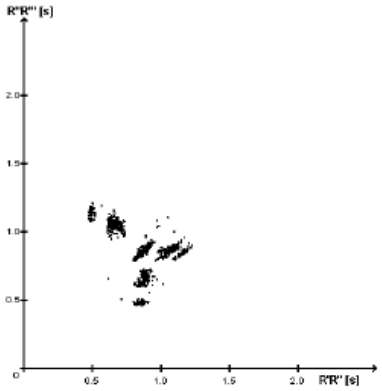
Internistische Gemeinschaftspraxis
Dres. Musterfrau und Mustermann
Hauptstraße 4
12345 Musterstadt
www.internisten_in_musterstadt.de

Report erstellt am: 10.10.2006 um 11:04
Untersuchungsdatum: 10.10.2006

Patientenname:	
Patientennummer:	1234
Geburtsdatum / Alter:	51 Jahre
Geschlecht:	männlich
Kommentar:	mein Kommentar

SRA - Analyseergebnis:		Sinusrhythmus
		Atriale Herzrhythmusstörungen Überprüfung auf paroxysmales Vorhofflimmern erforderlich.
		Andere Herzrhythmusstörungen
	x	Signifikante Anzeichen für paroxysmales Vorhofflimmern
		Signifikante Anzeichen für akutes Vorhofflimmern

Lorenzplot:
(graphische Darstellung der Herzrhythmusdynamik)



■ Atrialer Ursprung ■ Anderer Ursprung

Signal: 1

Created by apoplex medical technologies GmbH, 1.2.826.0.1.3680043.2.1101.1.1.1586472353.437394475.32767.5.1, 1.2.826.0.1.3680043.2.1101.1.1.1586472353.437394475.32767.2.1, 1586472353.4373453.35666.8.0, 10:57