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CHALLENGES IN IMPLEMENTING HEART RATE VARIABILITY TESTING IN A FAMILY MEDICINE PRACTICE: STRENGTHS, PITFALLS AND CAVEATS

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SUMMARY. Heart rate variability (HRV) measures beat-to-beat changes in the duration of the RR intervals in the electrocardiogram (ECG). According to many studies, HRV-derived methods can contribute a certain amount of data to the screening for cardiovascular diseases, and also predict the outcome for cardiovascular patients. The study focuses on a trial of HRV measuring in a family general practitioner's office, in two different groups: healthy subjects and patients with a varied collection of organic diseases. Differences were found between the two groups, especially concerning nonlinear parameters of HRV and Poincaré diagram analysis. Although promising, screening by HRV in the general practitioner's office has many pitfalls and caveats, especially regarding technical problems and the approach of patients with multiple comorbidities.

Keywords: family medicine, heart rate variability, screening.

Introduction

The term "heart rate variability" (HRV) refers to a measure of the beat-to-beat changes in duration of the RR intervals (RRIs) in the electrocardiogram (ECG). The RRIs, or interbeat interval, is the distance between one R-spike and the next in the ECG recording (Lagos, 2008). From a pathophysiological point of view, HRV analysis is a collection of various mathematical and computational techniques that characterizes biologic time-series with respect to overall fluctuation, spectral composition, scale-free variation, and degree of irregularity or complexity (Ahmad, 2009).

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The methods for analyzing and quantifying HRV parameters are categorized as: time domain, spectral or frequency domain, and nonlinear dynamics methods (Poincaré plot derived parameters), respectively:

1. In time domain analysis, the intervals between adjacent R waves are measured over a period of recordings and a variety of statistical parameters can be calculated: average RR interval, standard deviation of the RR intervals, average heart rate, standard deviation of the heart rate (Thalange, 2010);
2. The heart rate frequency domain analysis is used to evaluate the contribution of the autonomic nervous system to HRV; it is a sensitive and non-invasive method for evaluating the cardiovascular control system (Buccelletti, 2009);
3. The Poincaré plot (return map) is a scattergram, which is constructed by plotting each RR interval against the previous one. The Poincaré plot may be analyzed quantitatively by fitting an ellipse to the plotted shape (Kitlas, 2005).

Although ECG is considered the most accurate method for data acquisition used in HRV analysis (Berntson, 1997), there are studies proclaiming that periphery photoplethismography (PPG) can be used as a surrogate method for recording signals used in variability analysis (Gil, 2010; Greve, 2012; Mirescu, 2012). PPG is based on calculating the amount of infrared light that travels through peripheral capillaries (from a finger or the earlobe), thus tracing peripheral blood flow curve, which is synchronous with the heartbeats. Although more prone to moving and light artifacts, PPG is more comfortable from the patient's point of view, because it does not need the application of cutaneous electrodes, necessary in ECG recordings.

Heart rate variability has been used in different clinical settings, including diabetes (Poanta, 2010), coronary artery disease (Kleiger, 1987; Mirescu, 2012), sudden cardiac death (Dougherty, 1992) and chronic renal failure (Lerma, 2003).

Family medicine contributes to the care of patients at all levels, throughout all stages of life. Family physicians focus on each individual in his or her given situation, integrating mental and physical health, within each individual's own social context. Family medicine is not only dedicated to patients, but also to healthy individuals that need medical advice or specific documents that attest their health state. Thus, a large number of individuals visiting the family medicine office are not under observation for any disease.

A large amount of the family medicine practitioner's time should be allocated to prevention and screening. According to the World Health Organization (WHO), screening is defined as the presumptive identification of unrecognized disease or defect by the application of tests, examinations, or other procedures which can be applied rapidly (Wilson, 1968). Modern methods include screening for cervical cancer or dysplasia (cervical smear test), prostate cancer (prostate specific antigen from serum) or breast cancer (palpation and mammography).

The purpose of this study is to assess the practical value of HRV in screening for cardiovascular disease in the family medicine office using a PPG device.

Materials and methods

The study investigated 50 volunteer visitors at the family doctor's office, both healthy and with various conditions (78% females, aged 19 – 70 years old). After the patient has rested for 10 minutes, the PPG measurement was started for another 10 minutes, in a seated position. The sensor was placed on the index finger of the right hand and it consisted of an infrared LED and an infrared receiver, both placed on opposite sides of the finger. The infrared receiver was connected to a computer via an Arduino board, using an analogical input pin. The Arduino board was programmed to output the interval between beats directly though its serial port. The intervals were recorded in a Microsoft Excel sheet.

The volunteers were asked not to talk during recordings, in order to avoid the influence of forced respiration on HRV. Medical data (diagnostic and medication) were collected from the patients medical records.

Calculation of the HRV parameters was performed using Kubios HRV software. Table 1 summarizes the analyzed parameters.

After the recording, ectopic beats (due to arrhythmias, atrial and/or ventricular premature contractions) were removed.

Table 1.

HRV parameters that were analyzed in the study

Parameter	Unit	Description
Time domain parameters		
Average RR interval	ms	Average of the interval between two adjacent beats
RR standard deviation	ms	Standard deviation of the intervals between adjacent beats
Average heart rate	beats/minute	Average of heart beats
Heart rate standard deviation	beats/minute	Standard deviation of heart beats
Frequency domain parameters		
HF/LF	-	Ratio between high frequency spectral power and low frequency spectral power; it represents a measure of autonomic balance
Nonlinear parameters		
SD1	ms	Standard deviation 1 of the Poincaré plot (short axis)
SD2	ms	Standard deviation 2 of the Poincaré plot (long axis)

Results and discussion

One of the major problems we initially encountered was severe artifactuation in some of the recordings. Artifacts were mainly due to patient moving or shaking. In one instance, the recording was influenced by ambiental (sun) light, which was too intense and fell directly on the recording device. In this situation, the finger with the sensor mounted on it had to be covered. Fig. 1 depicts such an artifactuated recording, which could not be used for further interpretation.

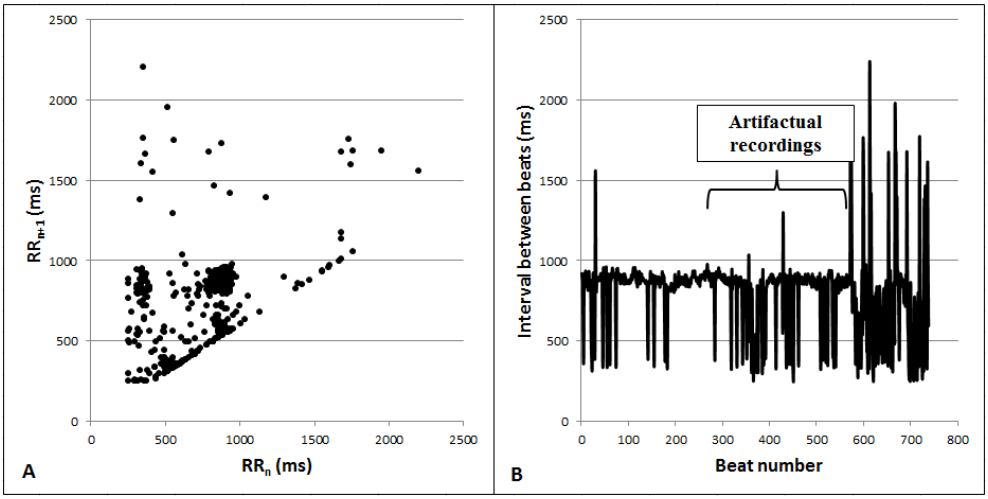

Figure 1. A strongly artifactual recording (A – the Poincaré scattergram shows very dispersed points, typical for an artifactual recording; B – a tachogram of the same subject with artifactual alterations).

One of the major pitfalls was confusing artifactual recording with a form of arrhythmia. Sometimes, the differentiation between the two requires interpretation by a cardiologist, who is familiar with the electrocardiographic aspect of arrhythmias. The method was not feasible in the patients whose hand trembled during measurement.

Mainly, tachograms containing many values that drop down to the baseline can be considered artifactual. If there are few basal values present in the trace, they can be manually removed. This operation has to be done carefully, in order not to delete any value that is correctly recorded, thus useful in variability analysis. Following this manual cleanup, the trace can be uploaded to Kubios HRV for parameter calculation.

A typical recording of a healthy patient, as reported by Kubios HRV software, is showed in Figs. 2 and 3.

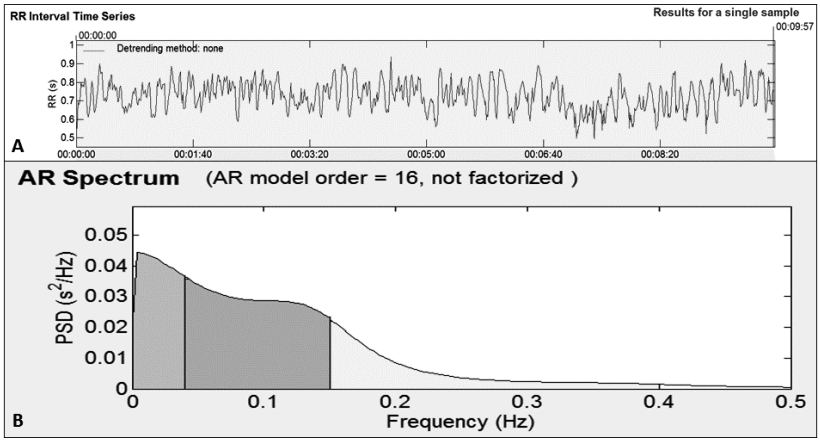

Figure 2. A. Typical tachogram of beat-to-beat intervals of a healthy subject; B. Power spectral density plot of the same subject.

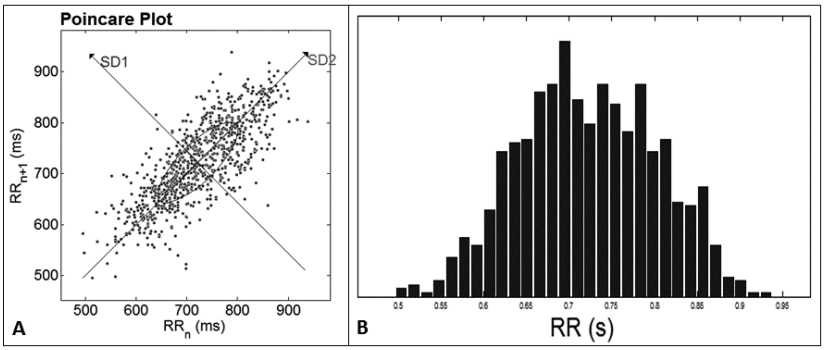

Figure 3. A. Typical Poincaré scattergram of a healthy subject; B. Histogram of RR intervals of the same individual.

Healthy vs. cardiac subject. According to the majority of the authors (Yukishita, 2010), increased HRV parameters are associated with a state of health of the individual, as compared to patients with cardiac diseases. This was also a finding of our study. Fig. 4A expresses a typical beat-to-beat interval plot (tachogram) of a healthy individual, while Fig. 4B represents the plot for a patient with a history of treated myocardial infarction (the plots use the same scale on both axes). The Poincaré scattergram also confirms this finding (Fig. 5).

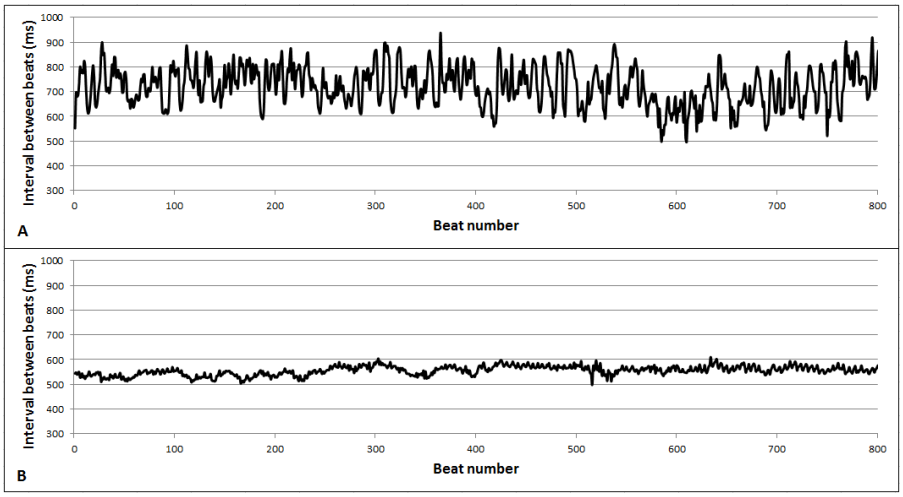

Figure 4. A. Typical Poincaré tachogram of a healthy subject; B. Tachogram of RR intervals of the same individual.

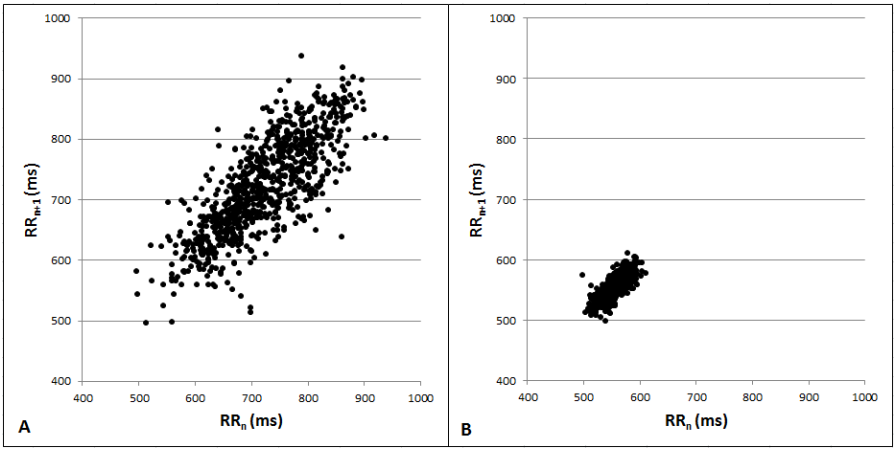

Figure 5. A Poincaré scattergram of a healthy individual (A), compared with the Poincaré plot of a patient with a history of treated acute myocardial infarction (B). Agglomeration of points can be observed in the second graph, due to decreased HRV parameters.

The mean values and standard deviation of HRV parameters of healthy subjects are summarized in Table 2.

Table 2.

Mean and stadard values of HRV parameters in healthy subjects

Parameter	**Unit**	**Mean and standard deviation**
Time domain parameters		
Average RR interval	ms	740 ± 91
RR standard deviation	ms	54 ± 27
Average heart rate	beats/minute	82 ± 5
Heart rate standard deviation	beats/minute	5 ± 2
Frequency domain parameters		
HF/LF	-	3 ± 1,6
Nonlinear parameters		
SD1	ms	25 ± 13
SD2	ms	72 ± 36

A case of a patient with advanced diabetic neuropathy worth special mentioning, because of the resulted Poincaré diagram (Fig. 6A). The classical (two-dimensional) Poincaré diagram exhibits a four-arm distribution of points, prior unseen by the authors in other cases. Because of this particular aspect, we tried a three dimensional (3D) modelling of the points, using a Microsoft Excel plugin for 3D scattergrams. The result is showed in Fig. 6B, where one can observe that the four arms of the Poincaré plot are not located in the same plane, but in three different plans, converging to a central point. Further studies will investigate whether this 3D aspect is characteristic or pathognomonic for advanced diabetic neuropathy.

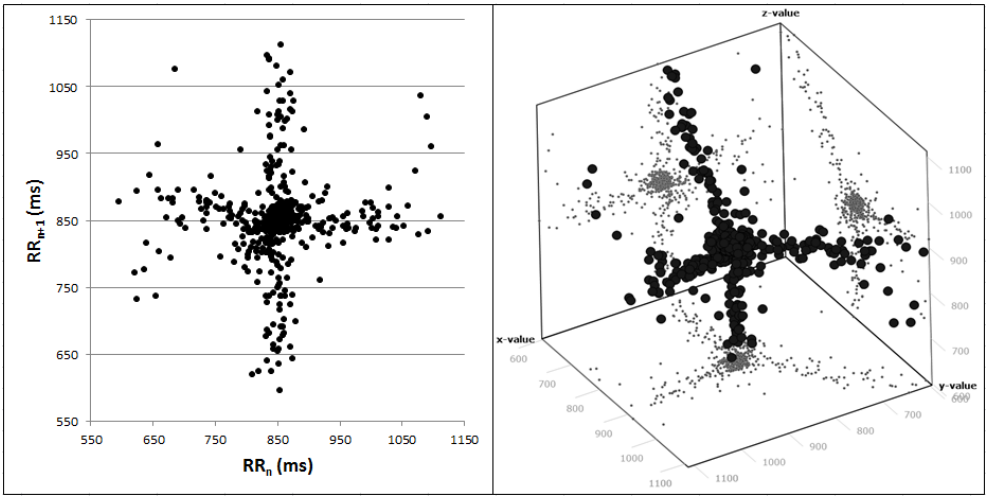

Figure 6. Two-dimensional Poincaré scattergram of a subject with advanced diabetic neuropathy (A). Three-dimensional Poincaré scattergram of the same patient (B).

Conclusions

The major outline of this pilot study is that HRV parameters are unique for each individual, and further studies will be performed to highlight patterns of connection with pathology. However, great caution must be taken in interpreting the results, because HRV parameters can be influenced by various conditions, even in healthy subjects: smoking or running prior to the measurements, anxiety or other emotions.

Further studies are needed in order to determine how HRV parameters vary in healthy subjects and how they can predict outcome or contribute to diagnostic in patients with certain pathologies. Also, in order to test the screening capacity of HRV parameter determination, double-blinded studies are needed.

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R E F E R E N C E S

Ahmad, S., Tejuja, A., Newman, K., Zarychanski, R., Seely, A. (2009) Clinical review: a review and analysis of heart rate variability and the diagnosis and prognosis of infection, *Critical Care* **13**, available online at http://ccforum.com/content/13/6/232

Berntson, G., Tommas Bigger JR, J., Eckberg, D., Grossman, P., Kaufmann, P., Malik, M., Nagaraja, H., Porges, S., Philip Saul, J., Stone, P., Van Der Molen., M. (1997) Heart rate variability: origins, methods and interpretive caveats, *Psychophysiology* **34**, 623-648

Buccelletti, F., Gilardi, E., Scaini, E., Galiuto, L., Persiani, R., Biondi, A., Basile, F., Gentiloni Silveri, N. (2009) Heart rate variability and myocardial infarction: systematic literature review and metanalysis, *Eur. Rev. Med. Pharmacol. Sci.* **13**, 299-307

Dougherty, C., Burr, R. (1992) Comparison of heart rate variability in survivors and nonsurvivors of sudden cardiac arrest, *Am. J. Cardiol.* **70**, 610-615

Gil, E., Vergara, J., Laguna, P. (2010) Pulse time transit variability versus heart rate variability during decreases in the amplitude fluctuations of photoplethysmography signal, *Int. J. of Bioelectromagn.* **12**, 95-101

Greve, M., Kviesis-Kipge, E., Rubenis, O., Rubins, U., Mecnika, V., Grabovskis, A., Marcinkevics, Z. (2012) Comparison of pulse rate variability derived from digital photopletismography over the temporal artery with the heart rate variability derived from a polar heart rate monitor, *Proceedings of the 7th ESGCO 2012*, 22-25

Kitlas, A., Oczeretko, E., Kowalewski, M., Borowska, M., Urban, M (2005) Nonlinear dynamics methods in the analysis of heart rate variability, *Rokz. Akad. Med. Bialymst* **50**, 46-47

Kleiger, E., Miller, P., Bigger, T., Moss, A. (1987) Decreased heart rate variability and its association with increased mortality after acute myocardial infarction, *Am. J. Cardiol.* **59**, 256–262

Lagos, L., Vaschillo, E., Vaschillo, B., Lehrer, P., Bates, M., Pandina, R. (2008) Heart rate variability biofeedback as a strategy for dealing with competitive anxiety: a case study, *Biofeedback* **36**, 109-115

Lerma, C., Infante, O., Perez-Grovas, H., Jose, M. (2003) Poincaré plot indexes of heart rate variability capture dynamic adaptations after haemodialysis in chronic renal failure patients, *Clin. Physiol. Funct. Imaging* **23**, 72-80

Mirescu, C., Harden S. (2012) Photopletismography as a potential alternative to electrocardiography for recording heart rate intervals used in variability analysis, *Journal of Medicine and Life* **5 (special issue)**, 123-128

Mirescu, C., Harden, S. (2012) Nonlinear dynamics methods for assessing heart rate variability in patients with recent myocardial infarction, *Rom. J. of Biophys.* **22**, 117-124

Poantă, L., Damian, I., Albu, A. (2010) Variabilitatea frecvenței cardiace și toleranța la efort la pacienții cu diabet zaharat tip II, *Palestrica Mileniului III – Civilizație și Sport* **3**, 198-201

Thalange, A., Mergu, R. (2010) HRV analysis of arrhythmias using linear – nonlinear parameters, *Int. J. Comput. Appl.* **12**, 71-77

Wilson, J., Jungner, G. (1968) Principles and practice of screening for disease, *Public Health Papers* **34**, 11-12

Yukishita, T., Lee, K., Kim, S., Yumoto, Y., Kobayashi, A., Shirasawa, T., Kobayashi, H. (2010) Age and sex-dependant alterations in heart rate variability: profiling the charasteristics of men and women in their 30s, *J. Anti Aging Med.* 7, 94-99

*** (2013) The Family Medicine Milestone Project, a joint initiative of The Accreditation Council for Graduate Medical Education and The American Board of Family Medicine