STUDIA UNIVERSITATIS BABEŞ-BOLYAI BIOLOGIA, LXII, 1, 2017 (p. 87-100)
doi:10.24193/subbbiol.2017.1.06

=== REVIEW ===

Heart rate variability: a practical review for the beginner

Ștefan-Claudiu Mirescu[1,2,✉], Andreea Loredana Ciocoiu[1], Leontin David[1] and Corneliu Tarba[1]

SUMMARY. Heart rate variability (HRV) refers to beat-to-beat interval changes on the electrocardiogram (ECG) and is considered a noninvasive measure of the autonomic balance. Although classical ECG is a well-known and standardized clinical method, HRV developed abruptly due to the evolution of computerized data acquisition systems in cardiology (digital electrocardiographs) and their software programs. HRV can be evaluated by visual methods (the beat-to-beat tachogram, the histogram and the Poincaré diagram) or by statistically computed parameters. Its applications include sympathovagal balance evaluation, monitoring of different neuropathies and contribution to survival prediction after cardiac acute events. Studies state that HRV can also be used as a method for rapid screening of some autonomic and cardiac diseases, along with other diagnostic procedures.

Keywords: autonomic nervous system, electrocardiogram, heart rate variability, sympathovagal balance.

Introduction

Heart rate variability (HRV) is a simple and noninvasive method that describes oscillations in the intervals between consecutive heart beats (Camm *et al*., 1996; Gardim *et al.*, 2014; Karim *et al*., 2006). On a standard electrocardiogram (ECG) trace, the maximum uphill deflection of a normal QRS complex is at the peak of the

[1] *Babeș-Bolyai University, Faculty of Biology and Geology, Department of Molecular Biology and Biotechnology, 5-7 Clinicilor Str., Cluj-Napoca, Romania*
[2] *Regional Institute of Gastroenterology and Hepatology „Octavian Fodor", Cluj-Napoca, Romania*
✉***Corresponding author: Ștefan-Claudiu Mirescu**, Babeș-Bolyai University, Faculty of Biology and Geology, Department of Molecular Biology and Biotechnology, 5-7 Clinicilor Str., Cluj-Napoca*
E-mail: claudiu.mirescu@ubbcluj.ro

R-wave. The interval between two consecutive R waves is called the R-R interval (Karim *et al*., 2006). Using computerized methods, R-R intervals can be extracted from a short-term (minimum 5 minutes) or long-term (24 hours or more) ECG trace and HRV parameters can be calculated.

On a more in-depth perspective, HRV is the variation of the period between consecutive heartbeats (Fig. 1), basically influenced by time and entirely dependent on the extrinsic regulation of the heart rate (HR), measuring the balance between the actions of the sympathetic mediators (epinephrine and norepinephrine) and the parasympathetic one (acetylcholine) released by nerve fibers, on both sinus and atrioventricular nodes, which leads to an increase or a decrease, respectively, in the heart rate as well as a secondary effect on the atrioventricular conduction (Karim *et al*., 2006).

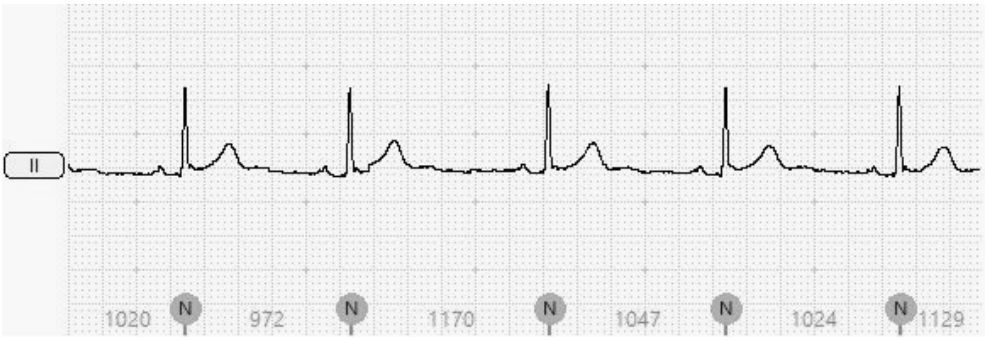


Figure 1. An ECG signal (DII lead) with R-R intervals in milliseconds. The letter "N" underneath every R wave designates that the corresponding beat is considered normal (it is not an ectopic beat)

Therefore, it can be said that HRV is a marker of the cardiovascular autonomic function (Camm *et al.*, 1996) and a powerful indicator of the relationship between psychological and physiological processes, also being an empirical and theoretical support for the emergence of HRV as an important marker for regulated emotional responding (Appelhans and Luecken, 2006).

As from an historical point of view, the Ancient Greeks were the first ones to acknowledge the importance of measuring HR, but it was not fully understood until 1733, when Rev. Stephen Hales managed to establish a connection between the variation of the pulse and the respiration, considering them directly proportional. Also, with the first record of the respiratory sinus arrhythmia (RSA) made by Carl Ludwig in 1847 and the measurement of the ECG (1855), followed by the apparition of the digital processing techniques, the HRV analysis has become more relevant, mainly, in the diagnosis of coronary heart diseases (Billman, 2011).

Recording of HRV

Basically, any method that records beat-to-beat intervals is suitable for HRV. Two classical methods for recording heart signals can be used for HRV purposes: photopletismography (PPG) and electrocardiography (ECG), each with its own conveniences and drawbacks.

PPG is a noninvasive optical technique used for measuring changes in blood circulation, mainly at skin level (Pilt *et al*., 2013). The PPG sensor consists of a light emitting diode (LED), which emits red or infrared radiation, and a photodetector (PD). The LED and the PD are placed on opposite sides of a finger (Pilt, 2013; Mirescu, 2015). The absorbance of the light emitted by the LED is proportional to the blood flow in the tissue between the LED and the PD (Singh, 2013). Thus, the amplitude of the signal captured by the PD is proportional to the volume of the blood that passes through the tissue, reciprocating the alternation between cardiac systole and diastole. Therefore, the PPG signal is composed of cyclic inflections and deflections, bearing a systolic peak that can be identified for HRV purposes (Fig. 2) (Elgendi *et al*., 2011; Mirescu and Harden, 2012; Elgendi, 2012).

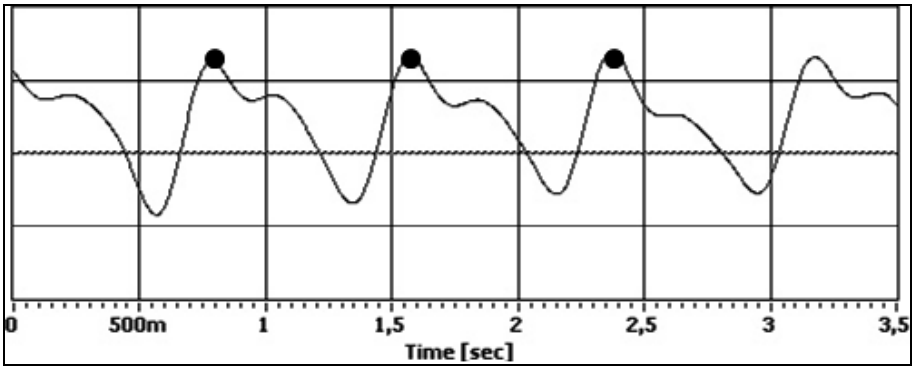


Figure 2. A finger PPG signal. The black dots mark the systolic peaks; the intervals between these peaks are further used for variability analysis

The circuit for a simple PPG device is easy to design: apart from the two optical diodes, it requires two voltage dividers (one for the LED and one for the PG), a voltage source (a low power battery) and an analog-to-digital converter, which can be a computer soundcard (Mirescu, 2015) or a microcontroller-based prototyping board. The signal is processed in order to extract beat-to-beat intervals used for HRV analysis.

This method is comfortable for the subject and convenient for the examiner. The only interface between the device and the subject is a clip on the finger. However, a significant disadvantage of PPG is the high sensitivity to artifacts, especially movement artifacts (Mirescu, 2014).

On the other hand, the ECG is a much more reliable method in detecting beat-to-beat intervals used for variability analysis, despite the more complex experimental setting and instruments. For ECG trace recording, a digital computer-connected electrocardiograph is needed, *e.g.* Neurosoft Poly-Spectrum-8®. This device functions as a classical 12-lead ECG device, but as a result of its software capabilities, it can be also used for extracting R-R intervals.

Because measurements of HRV require the detection of each heartbeat (Acharya, 2006), the software used must meet this requirement.

HRV parameters and plots are calculated from the R-R intervals. This can be accomplished by the ECG acquisition software or by a different one. One of the most used software equipment for this purpose is Kubios HRV Analysis, released by the Department of Physics from University of Kuopio, Finland. It is a very intuitive and easy to use freeware application program which requires a text file containing R-R intervals as input. The intervals can be measured in seconds or milliseconds.

Kubios HRV analysis is a powerful instrument which calculates time-domain parameters, frequency-domain parameters and nonlinear parameters, and also plots the tachogram, the histogram, the power-spectrum density and the Poincaré diagram. It also comes with a comprehensive instruction manual (Fig. 3) (Tarvainen, 2006).

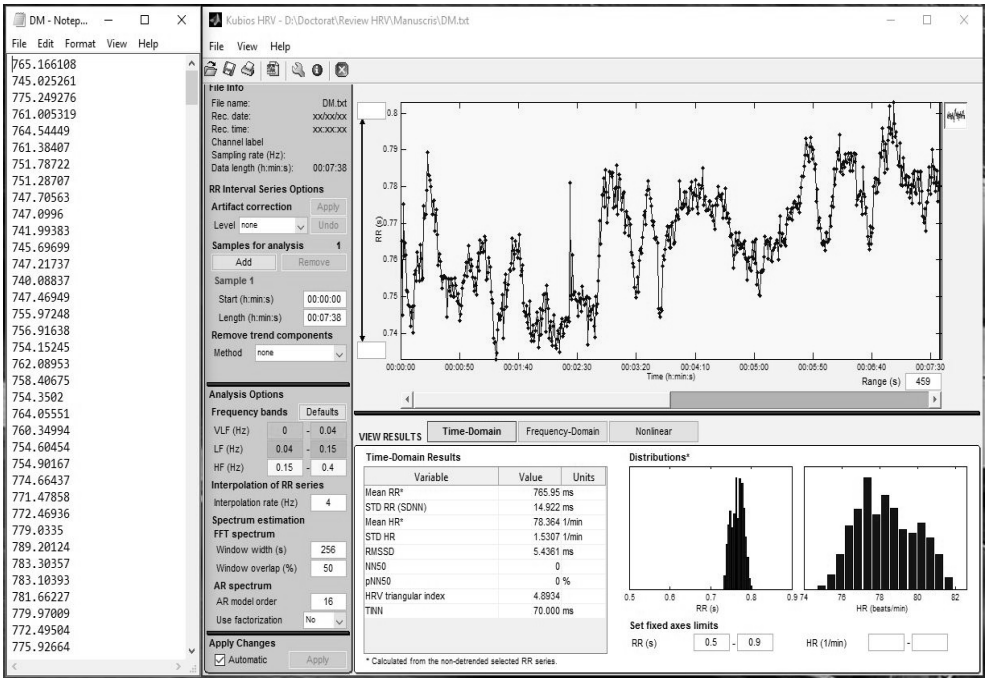


Figure 3. Left – A text file containing the R-R intervals in milliseconds; right – the main interface of *Kubios HRV Analysis*

The software supports beat-to-beat intervals and offers the users the possibility of converting the results within a HRV recording into a PDF report which can be used to have a more detailed examination. In addition, Kubios HRV allows the users to save the recording results as an ASCII file text, which can be opened by MS Excel, or some other file extensions, such as Matlab or MAT-file for ulterior editing (Tarvainen *et al*., 2006).

HRV visual descriptors

One of the fastest and most accessible approaches to HRV interpretations consists of the HRV visual descriptors. Usually, they include (1) the tachogram of R-R intervals; (2) the histogram of R-R intervals; (3) the Poincaré plot.

The tachogram of R-R intervals is an oscillatory curve produced when R-R intervals are plotted on a time scale (von Borell, 2007)(Carvajal, 2005). In a similar manner, momentary heart rates derived from R-R intervals can be plotted on a time scale, with the same scientific value. The tachogram of R-R intervals is a powerful visual aid in HRV interpretation, because it allows fast comparison between two subjects (usually a control subject and a patient with a certain disease). For example, Fig. 4 illustrates the difference between the tachogram of a normal healthy subject and a patient with advanced type II diabetes mellitus, both plotted on similar scales. It can be seen that the normal tachogram has frequent inflections and deflections, corresponding to a substantial HRV, while the diabetic tachogram is almost flat; hence, the diabetic patient has a lower HRV compared to the healthy subject. Historically, the tachogram is the first developed method for HRV analysis, not necessarily requiring a digital acquisition method for the ECG signal. Its simplicity still makes it one of the most reliable visual methods for HRV analysis.

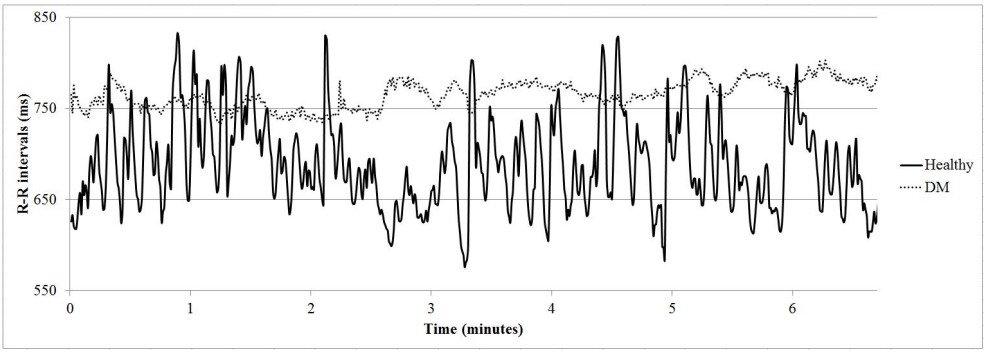


Figure 4. A comparison between a tachogram derived from a healthy subject (continous line) and one derived from a diabetic patient (dotted line).

The histogram of the R-R intervals is a statistically derived HRV plot. Essentially, the histogram is a bar graph representation of the number of beats contained in a certain interval (Acharya, 2006; Cam *et al.*, 1996; von Borell, 2007). As for interpretation, a high HRV is translated into a larger distribution of the R-R intervals on the histogram, describing a normal (Gaussian) distribution (Fig. 5).

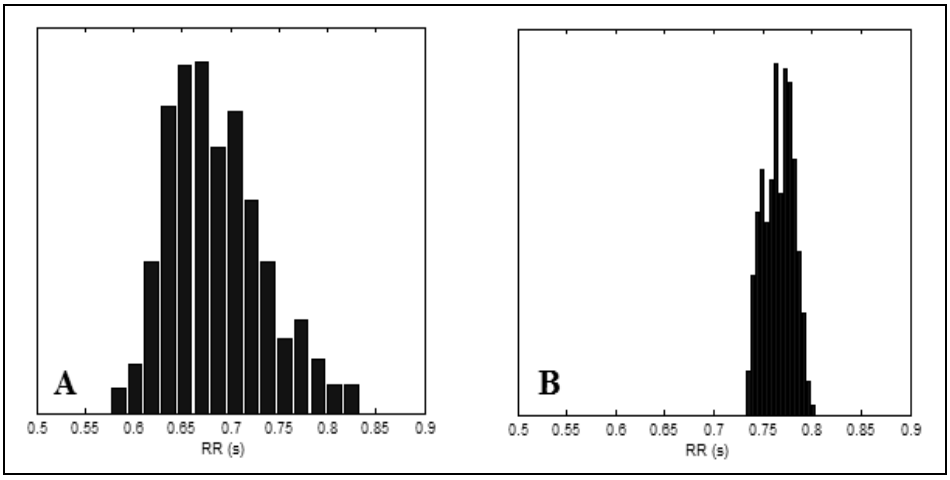


Figure 5. Histogram of R-R intervals in a healthy subject (A) vs. histogram of R-R intervals in a diabetic patient (B).

The Poincaré plot is considered the most powerful visual descriptor of HRV, being a quantitative-visual method extracted from non-linear dynamics. A Poincaré plot is a scattergram representing every $R\text{-}R_{i+1}$ interval as a function of RR_i. The result is a comet-shaped scattergram (Fig. 6). An increased variability is depicted by a large area of the distribution of the points, and vice versa.

Despite its value as a visual descriptor, the indexes extracted from it have been proven not to provide additional information to that obtained by other methods (Milagro, 2016; Brennan, 2001). It is also one of the few HRV methods that have been tested in clinical settings, allowing the detection of patterns resulting from non-linear processes, otherwise not observable (Corbi, 2013).

The Poincaré plot is also useful in real-time detection and classification of cardiac ectopic beats (Thalange, 2010).

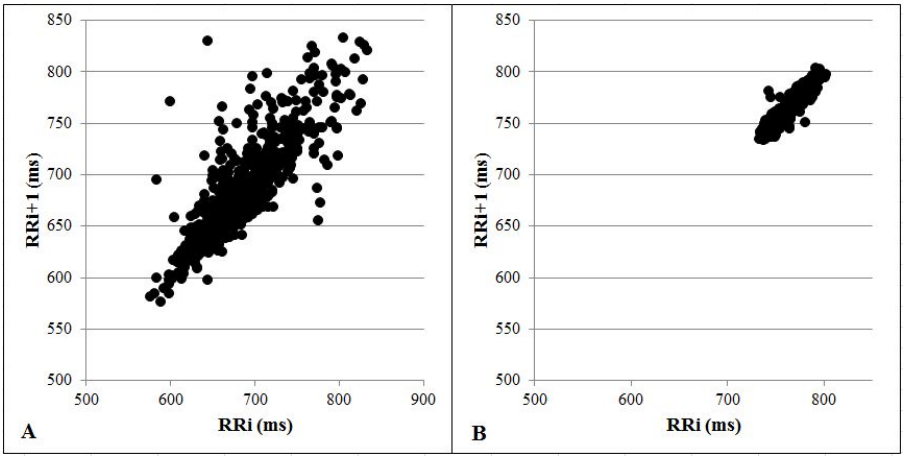


Figure 6. The Poincaré plot of a healthy subject (A) vs. the Poincaré plot of a diabetic patient (B).

HRV parameters

Although helpful, the visual descriptors of HRV are not enough to characterize the behavior of the variability of cardiac rhythm. Complex mathematical and statistical models were developed in order to extract HRV parameters from R-R intervals arrays. These parameters fall into three categories: time-domain parameters, frequency-domain parameters and nonlinear dynamics parameters. The most commonly used parameters in HRV studies and their significance are summarized in Table I.

Time-domain parameters are the simplest to quantify and are based on the instantaneous heart rate (Camm *et al., 1996)*. They include statistical parameters like the mean R-R interval, the standard deviation of the R-R intervals, the mean heart rate and the standard deviation of the mean heart rates (Camm *et al.*, 1996; Karim *et al*., 2006; Tsai *et al*., 2014; Gardim *et al.*, 2014).

Another independent descriptor of HRV is NN50, which represents the number of consecutive R-R intervals that differ by more than 50 milliseconds. A derivative of NN50 is pNN50, which is the percent NN50 from the total number of intervals. out of the total R-R intervals (Camm *et al.*, 1996; Karim *et al*., 2006; Medeiros, 2010; Henry *et al*., 2010).

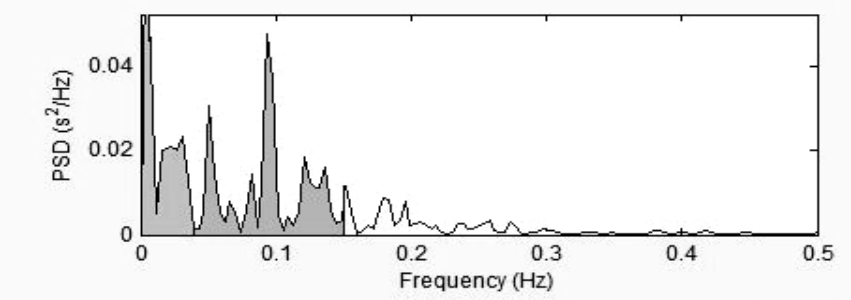
Baseline width of the minimum square difference triangular interpolation of the highest peak of the histogram of all R-R intervals is the TINN Index (ms), which is also an independent marker of HRV (von Borell, 2007; Acharya, 2006).

Frequency-domain methods are spectral methods for the analysis of HRV and imply the use of complex mathematical algorithms (the fast-Fourier transform – FFT). Power spectral density analysis provides information on how power distributes as a function of frequency (Camm *et al.*, 1996).

Power spectral density analysis usually separates the cyclic modifications of HRV into three components, whose interpretation is controversial (ChuDuc *et al*., 2013):

- High frequency (HF) component, from 0.15 Hz to 0.04 Hz;
- Low frequency (LF) component, from 0.04 Hz to 0.15 Hz;
- Very low frequency (VLF), from 0.003 Hz to 0.04 Hz (Fig. 7).

Until recently, most authors accepted that HF reflects the activity of the parasympathetic nervous system (vagal tonus) and LF is a reflection of the sympathetic activity (ChuDuc *et al*., 2013; Jaiswal *et al*., 2013). However, there are studies that contradict this hypothesis, revealing that LF/HF ratio does not accurately measure cardiac sympathovagal balance (Billman, 2013).



Frequency Band	Peak (Hz)	Power (ms^2)	Power (%)	Power (n.u.)
VLF (0-0.04 Hz)	0.0039	909	36.7	
LF (0.04-0.15 Hz)	0.0938	1137	45.9	72.6
HF (0.15-0.4 Hz)	0.1523	428	17.3	27.4
Total		2475		
LF/HF		2.654		

Figure 7. Power-spectrum density of HRV components according to the mentioned frequency intervals

For accurate frequency-domain measurements, certain recommendations must be taken into account. According to most authors, it is suggested that the duration of the recording should be at least two-times the wavelength of the lowest frequency component (Aubert *et al*., 2003). Thus, the minimum duration for the assessment of

the HF component (0.15 Hz) should be at least 13.3 seconds and for the LF – at least 50 seconds. However, many authors that focused their research on short-term HRV recommend a minimum duration of 5 minutes (Aubert *et al*., 2003; Paritala, 2009; Nunan *et al*., 2010).

Nonlinear dynamics methods of HRV analysis mainly refer to the Poincaré plot parameters and to entropy parameters. They have proven their prognostic value in clinical setting, but their physiological origin is not very well established (Camm *et al*., 1996; Weippert, 2014).

The standard descriptors of the Poincaré plot are SD1, which represents the fast R-R variability, and SD2, which describes the longer-term variability. Studies showed that SD1 reflects mainly parasympathetic activity, while SD2 reflects both sympathetic and parasympathetic contributions to the heart rate (Fig. 8) (Makivić, 2013; Melillo, 2011).

Among the entropy parameters, Sample Entropy (SampEn) is the most popular, due to its high correlation with traditional HRV indices (Weippert, 2014). SampEn quantifies the probability that sequences of patterns in a data set that are initially closely related remain close in the next incremental comparison, within a specified tolerance (Henry, 2010).

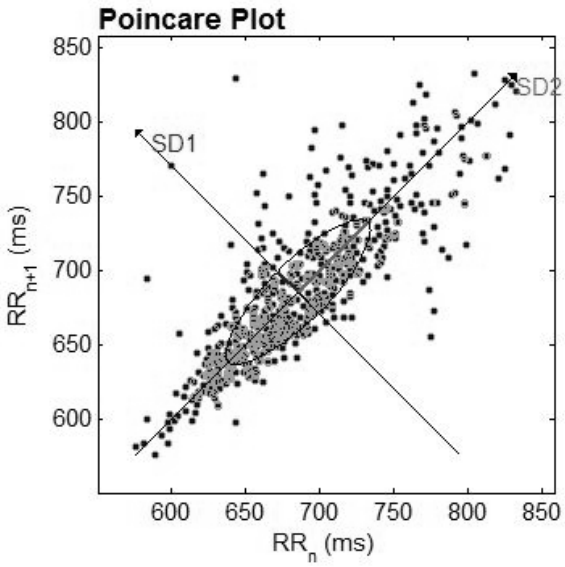


Figure 8. A typical Poincaré plot with the short and long axis standard deviations (SD1 and SD2, respectively)

Clinical significance of HRV measurements

Many studies have attested the role of HRV measurements in health and disease. Most of them have been performed on conditions that influence the autonomic balance. A significant number of studies assessed HRV in different autonomic nervous system (ANS) dysfunctions.

HRV and myocardial infarction. One of the first applications of HRV in clinical practice was the use of HRV parameters as risk predictor after acute myocardial infarction (MI). In MI survivor patients, an increase in the sympathetic tone has been demonstrated, which is transient and ceases after a few weeks. Given the fact that the increase in the sympathetic tonus (thus, a decreased HRV) predisposes to malignant ventricular arrhythmias, it has been concluded that a prolonged decreased HRV is an independent risk factor for death after MI (Stys *et al*., 1998; Niakan *et al*., 1986; Balcıoğlu *et al.*, 2015).

HRV and diabetes. Many studies associated global decreased HRV with diabetes mellitus (DM) and its complications. In a study performed on DM type I young patients, Jaiswal *et al*. (2013) discovered that SDRR, an independent descriptor of HRV, was 10 ms lower among patients, compared to non-DM subjects ($p = 0.003$) (Jaiswal *et al.*, 2013). Similar results were obtained by Gardim *et al*. (2014) on DM type I children (Gardim *et al.*, 2014). According to many authors, decreased HRV in diabetic patients (both type I and type II) is not only associated with poor prognosis, but also precedes autonomic neuropathy (Camm *et al.*, 1996). In another study, Orlov *et al*. (2012) concluded that HRV is a measure of both small and large autonomic nerve fibers functionality and, therefore decreased HRV is present in both early and late phenotypes of diabetic neuropathy (Orlov *et al*., 2012).

Table 1.

Commonly used HRV parameters (Camm *et al.,*, 1996; von Borell, 2007)

Parameter	Unit	Significance
Time-domain parameters		
Mean RR	ms	Average of consecutive beats intervals
STD RR	ms	Standard deviation of consecutive beats intervals
Mean HR	beats/min	Average heart rate
SD HR	beats/min	Standard deviation of heart rate averages
NN50	#	Number of consecutive heartbeats with a difference of at least 50 ms
pNN50	%	Percent of consecutive heartbeats with a difference of at least 50 ms
TINN	ms	The baseline of the intervals histogram

Parameter	Unit	Significance
Frequency-domain parameters		
LF/HF	-	Ratio between low frequency spectral power and high frequency spectral power
Nonlinear dynamics parameters		
SD1	ms	Standard deviations according to the Poincaré plot of the intervals between heartbeats
SD2	ms	
ApEn	-	Approximate entropy of the stationary signal
SampEn	-	The likelihood that runs of patterns that are close to each other will remain close in the next incremental comparisons
Correlation dimension	-	Entropy parameters
DFA α1	-	
DFA α2	-	

HRV and depression. Many clinical trials associated depression with imbalances of the ANS, which are quantified by HRV measurements. Depression is correlated with an increase in the sympathetic tone, which may lead to other cardiac diseases (ChuDuc *et al.*, 2013). These findings were as well correlated to depression in childhood (Sharma *et al.*, 2011). Changes in the respiratory sinus arrhythmia, also measurable by HRV, are likewise linked to depressive disorders (Sinatra *et al.*, 2011; Bylsma *et al*., 2014; Assad *et al*., 2012).

Cardiac arrhythmias, although not a direct expression of the autonomic nervous system activity, can be investigated by HRV, especially by nonlinear dynamics methods (entropy methods and the Poincaré diagram) (Qu and Weiss, 2006; Thalange and Mergu, 2010).

Most ectopic beats can be noticed on the Poincaré diagram. Mainly any deviation from the cloud appearance of the points distribution (regardless of the area of the cloud) reflects ectopic beats (atrial or ventricular premature contractions). Atrial fibrillation appears as a multi-cloud Poincaré plot. Special care has to be taken to subjects showing a prominent respiratory sinus arrhythmia, which is characterized by an asymmetrical appearance of the Poincaré plot cloud (Brennan *et al*., 2001). However, when analyzing time-domain and frequency-domain parameters, ectopic beats have to be eliminated, in order to obtain relevant values of the parameters (Mirescu and Harden, 2012; Mirescu, 2015).

Conclusions

HRV proved to be a valuable instrument in clinical studies, as well as for research purposes. As a result of the rapid development of computerized ECG acquisition systems and software, HRV brings about an accessible and easy-to-use set of parameters in evaluating the autonomous nervous system balance. Albeit many studies have been performed, the intimate mechanisms of HRV origin are not completely understood and some applications are yet to be investigated.

REFERENCES

Appelhans, M., Luecken, L. (2006) Heart Rate Variability as an Index of Regulated Emotional Responding, *Rev. Gen. Psychol.* **10**(3):229–40

Assad, S, Ding, F., Fu, N, Xu Y. (2012) *Correlating Heart Rate Variability with Mental Fatigue*, Worchester Polytechnic Institute, Massachusetts

Aubert, A., Seps, B., Beckers, F. (2003) Heart Rate Variability in Athletes *Sports Medicine* **33**(12):889–919

Balcıoğlu, A., Müderrisoğlu, H. (2015) Diabetes and Cardiac Autonomic Neuropathy: Clinical Manifestations, Cardiovascular Consequences, Diagnosis and Treatment, *World J. Diabetes* **6**(1):80–91

Billman, G. (2011) Heart rate variability - a historical perspective, *Front. Physiol*. doi: 10.3389/fphys.2011.00086

Billman, G. (2013) The LF/HF Ratio Does Not Accurately Measure Cardiac Sympatho-Vagal Balance, *Front. Physiol.*, **4**:1–5

Brennan, M., Palaniswami, M., Kamen, P. (2001). Do Existing Measures of Poincaré Plot Geometry Reflect Nonlinear Features of Heart Rate Variability?, *IEEE Rev Biomed Eng*., **48**(11):1342–47

Bylsma, L., Salomon, K., Taylor-Clift, A., Morris, B., Rottenberg, J. (2014) Respiratory Sinus Arrhythmia Reactivity in Current and Remitted Major Depressive Disorder *Psychosom. Med.* **76**(1):66–73

Carvajal, R., Wessel, N., Vallverdú, M., Caminal, P., Voss., A. (2005) Correlation Dimension Analysis of Heart Rate Variability in Patients with Dilated Cardiomyopathy, *Comput. Methods Programs Biomed.* **78**(2):133–40

Chevalier, G., Sinatra, S. (2011) Emotional Stress, Heart Rate Variability, Grounding, and Improved Autonomic Tone: Clinical Applications, *Integr. Med. Clin. J.,* **10**(3):16–22

ChuDuc, H., NguyenPhan, K., NguyenViet, D. (2013) A Review of Heart Rate Variability and Its Applications, *APCBEE Procedia* **7**:80–85

Corbi, G., D'Addio, G., Russo, G., Rengo., G., Pinna, G., Maestri, R., Rengo, F., Ferrara, N. (2013) A Non-Linear Analysis of Heart Rate Variability in Stroke Patients, *Mathematics and Computerns in Contemporary Science,* 117–22

Elgendi, M., Jonkman, M., De Boer, F. (2010) Heart Rate Variability Measurement Using the Second Derivative Photoplethysmogram, Proceedings of the Third International Conference on Bio-Inspired Systems and Signal Processing

Elgendi, M., Jonkman, M., DeBoer, F. (2011) Heart Rate Variability and the Acceleration Plethysmogram Signals Measured at Rest *CCIS* **127**:266–77

Gardim, C., de Oliveira, B., Bernardo A, Gomes, R., Pacagnelli, F., Lorençoni, R., Vanderlei, L. (2014) Heart Rate Variability in Children with Type 1 Diabetes Mellitus, *Revista Paulista de Pediatria* **32**(2):279–85

Henry, B., Minassian, A., Paulus, M., Geyer, M., Perry, W. (2010) Heart Rate Variability in Bipolar Mania and Schizophrenia, *J. Psychiatr. Res.* **44**(3):168–76

Jaiswal, M., Urbina, E. M., Wadwa, R. P., Talton, J. W., D'Agostino, R. B., Hamman, R. F., Fingerlin, T. E., Daniels, S., Marcovina, S. M., Dolan, L. M., Dabelea, D. (2013) Reduced Heart Rate Variability among Youth with Type 1 Diabetes: The SEARCH CVD Study, *Diabetes Care* **36**(1):157–62

Karim, N., Hasan, J., Ali S. (2016) Heart Rate Variability – A Review, *Medi. Biol. Eng. Comput.* **44**(12):1031–51

Makivić, B., Nikić, D., Willis, S. (2013) Heart Rate Variability (HRV) as a Tool for Diagnostic and Monitoring Performance in Sport and Physical Activities, *J. Exerc. Physiol. Online* **16**(3):103–31

Mandeep, S., Nagpal, S. (2013) Features Extraction in Second Derivative of Finger PPG Signal: A Review, *IJCSC* **4**(2):1–5

Camm, A. J., Malik, M., Bigger, J. T., Breithardt, G., Cerutti, S., Cohen, R. J., Coumel, P., Fallen, E. L., Kennedy, H. L., Kleiger, R. E., Lombardi, F. (1996) Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *Eur. Heart J.*, **17**(3):354-381

Medeiros, J. (2010) Development of a Heart Rate Variability Analysis Tool, Plux, Engenharia de Biosensores

Melillo, P., Bracale, M., Pecchia, L. (2011) Nonlinear Heart Rate Variability Features for Real-Life Stress Detection. Case Study: Students under Stress due to University Examination, *Biomed. Eng. Online* **10**(1):96

Milagro, F. (2016) Poincaré Plot Analysis And Graphical User Interface Development For The Study Of Heart, Master of Science Thesis, Faculty of Computing and Electrical Engineering

Mirescu, C. (2015) Computer Sound Card Used as Analog-to-Digital Converter in a Teaching Physiology Laboratory, *Studia UBB Biologia*, **60**(2):85-88

Mirescu, C., Harden, S. (2012) Photopletismography as a Potential Alternative to Electrocardiography for Recording Heart Rate Intervals Used in Variability Analysis, *J. Med. 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, *Romanian J. Biophys.* **22**(2):117–24

Mirescu, C., Petrescu, M., Petrescu, F., Mirescu, N., David, L. (2014) Challenges in implementing heart rate variability testing in a family medicine practice: strengths, pitfalls and caveats, *Studia UBB Biologia*, **59**(2):105-113

Niakan, E., Harati, Y., Comstock, J. (1986) Diabetic Autonomic Neuropathy, *Metabolism* **35**(3):224–234

Nunan, D., Sandercock, G., Brodie., A. (2010) A Quantitative Systematic Review of Normal Values for Short-Term Heart Rate Variability in Healthy Adults *PACE - Pacing and Clinical Electrophysiology* **33**(11):1407–17

Orlov, S., Bril, V., Orszag, A., Perkins, B. (2012) Heart Rate Variability and Sensorimotor Polyneuropathy in Type 1 Diabetes, *Diabetes Care* **35**(4):809–16

Paritala, S. (2009) *Effects of Physical and Mental Tasks on Heart Rate Variability*,Thesis for Master of Science, Kakatiya University, India

Pilt, K., Ferenets, R., Meigas, K., Lindberg, L., Temitski, K., Viigimaa, M. (2013) New Photoplethysmographic Signal Analysis Algorithm for Arterial Stiffness Estimation, *Scientific World J.* 2013:1–10

Qu, Z., Weiss, J. (2006) Dynamics and Cardiac Arrhythmias, *J. Cardiovasc. Electrophysiol.* **17**(9):1042–49

Sharma, R., Balhara, Y., Sagar, R., Deepak, K., Mehta, M. (2011) Heart Rate Variability Study of Childhood Anxiety Disorders, *J. Cardiovasc. Dis. Res.* **2**(2):115–22

Stys, A., Stus, T. (1998) Current Clinical Applications of Heart Rate Variability, *Clin. Cardiol.* **21**:719–24

Tarvainen, M., Niskanen, J. (2006) *Kubios HRV Analysis, version 2.0 beta, User's Guide*, University of Kuopio, Finland

Thalange, A., Mergu, R. (2010) HRV Analysis of Arrhythmias Using Linear - Nonlinear Parameters, *Int. J. Comput. Appl.* **1**(12):75–80

Tsai, J., WenChun, C., Jou, S., Lin, C. (2014) Heart Rate Variability and Meditation with Breath Suspension, *Biomed. Res. India* **25**(1):6–10

Von Borell, E., Langbein, J., Després, G., Hansen, S., Leterrier, C., Marchant-Forde, J., Marchant-Forde, R., Minero, M., Mohr, E., Prunier, A., Valance, D., Veissier, I. (2007) Heart Rate Variability as a Measure of Autonomic Regulation of Cardiac Activity for Assessing Stress and Welfare in Farm Animals - A Review, *Physiol. Behav.* **92**(3):293–316

Weippert, M., Behrens, M., Rieger, A., Behrens, K. (2014) Sample Entropy and Traditional Measures of Heart Rate Dynamics Reveal Different Modes of Cardiovascular Control during Low Intensity Exercise, *Entropy* **16**(11):5698–5711