TIME DOMAIN HRV ANALYSIS OF ISCHEMIA MANIFE-STATION AT ISOLATED RABBIT HEARTS

Oto Janoušek
Doctoral Degree Programme, FEEC BUT
E-mail: xjanou12@stud.feec.vutbr.cz

Supervised by: Jana Kolářová
E-mail: kolaraj@feec.vutbr.cz

ABSTRACT

The ischemia manifestation of seven New Zealand rabbit isolated hearts was analyzed using heart rate variability (HRV) parameters in time domain. The eight parameters commonly used in HRV analysis were computed by designed software for HRV analysis. Correlation between values of these parameters and phase of experiment was considered. Assessment of HRV was based on analysis of consecutive normal R-R intervals during 5 minutes interval in four section of measured ECG: control period and three ischemia periods.

1. INTRODUCTION

Cardiac disorders are one of the most frequent causes of death in the United States and Europe. In 2009, estimated 785,000 of Americans will have a new coronary attack, and about 470,000 will have a recurrent attack. About every 25 seconds, an American will have a coronary event, and about one every minute will die from it [1]. Electrocardiography allows predicting heart failure and sudden cardiac death in most cases. Although many methods for electrocardiogram analysis have been described and published, there is still a lot of space to introduce new algorithms and new parameters suitable for prevention of sudden heart attack. Because the heart disease plays an important role in sudden death all over the world, still it seems to be necessary to find new ways, how to predict ischemia.

Heart rate variability (HRV) analysis represents one way how to assess myocardial ischemia. HRV seems to be one of the most promising markers in recognition of significant relationship between the autonomic nervous system and cardiovascular mortality, including sudden cardiac death [2].

HRV is a noninvasive marker, which can be easily computed from common electrocardiogram. Heart rate variability describes the variations between consecutive heartbeats. HRV can be assessed from many parameters getting in numerous ways. The methods for obtaining of HRV parameters can be divided into two groups: time domain methods and frequency domain methods. Time domain methods comprehend common method, statistical method and geometrical method. Overview and definitions of most commonly used standardized HRV parameters can be found in [3].

2. METHODS

2.1. DATA ACQUISITION

The seven rabbit hearts were included in the study. Each heart was mounted on a Langendorf perfusion system, filled with Krebs-Henseleit (K-H) solution (1.25 mM Ca2+) and placed in a bath (37°C). The hearts were perfused at the constant pressure of 85 mmHg. The hearts were stabilized for 30 minutes – this period serves as control period. Afterward the oxygen supply was restricted for 15 minutes. This part of measured signal was used as the first ischemia period. Consecutive oxygen supply was again arranged for next 15 minutes. This part of measured signal was used as the first reperfusion. The same situation – restriction of perfusion and re-arranged of perfusion - was furthermore repeated twice.

The ECG signal was measured by three contactless Ag-AgCl disc electrodes in three orthogonal directions x, y, and z in water bath. ECG signals were recorded by data acquisition multifunction card PCI-6250 (National Instruments, USA) with sampling frequency fs = 2000Hz and acquired by designed application in LabView 7.1 software (Texas Instrument, 2008) The 16 bit analog to digital conversion was used. There were acquired three ECG signals with duration about two hour. Afterwards four period were extracted from measured signal: control period (5 minutes) and three ischemia periods (3 x 5 minutes)

R-peaks were marked via own designed R-wave detector. (No abstention or marker misplacing of R peaks were allowed in analyzed ECG). The detector was designed with aspect of frequencies, which can be found in QRS complex in rabbit heart.

2.2. TIME DOMAIN HRV PARAMETERS

In this study, time domain HRV parameters were used for ischemia consideration. Followed [3] eight of all contemporary known parameters for HRV analysis were used. There were analyzed 5 minutes periods of EGG signals in this study, therefore only short-time parameters were computed in proposal software. (Another parameters commonly used in HRV analysis are suitable for 24 hours measurement of ECG, but using long-time HRV parameters for short-time ECG studies can produce inaccurate results and scientist should avoid it.) Time domain HRV parameters computed by designed software are introduced in Table 1. Description of this parameter can be found in [3].

Abbreviation	Name of parameter	Unit
RR mean	Mean of RR intervals	s
RR std	Standard deviation of RR intervals	s
HR	Heart rate	1/min
HR std	Standard deviation of heart rate	1/min
RMSSD	Root of the mean squared differences	s
NN50	The number of interval differences greater than 50ms	-
pNN50	NN50 divided by the total number of all NN intervals	%
max - min	The difference between the longest and shortest interval.	s

Table 1 Time domain HRV parameters

2.3. HRV ANALYSIS SOFTWARE

Designed HRV analysis software (HRV_time_domain_analysis) compute eight time domain HRV parameters described in **Table 1**. Software shows tachogram of measured period also. (Tachogram is defined as a set of RR-interval durations as a function of the interval number.) Software was designed in Matlab R2007b (Mathworks, 2007). Screen of designed software can be shown in Fig. 1.

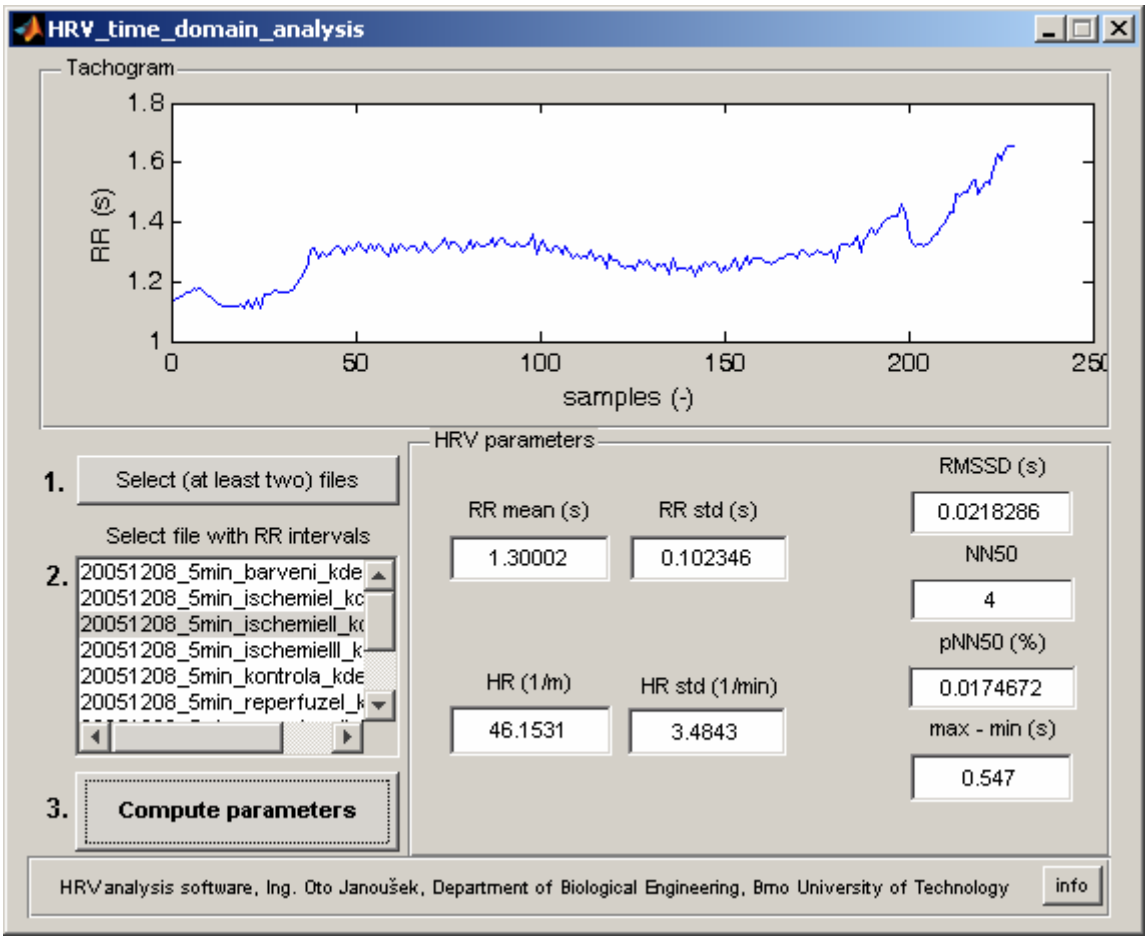

Fig. 1 HRV analysis software

3. RESULTS

The eight parameters were investigated with aim to distinguish ischemia ECG signal from normal ECG signal using HRV in time domain.

3.1. APPROPRIATENESS OF PARAMETERS RR MEAN AND HR FOR ISCHEMIA ANALYSIS STUDY

As can be seen in Fig. 2, parameter mean increased in all three ischemia period (ratio between control period and increased value varies from 1,42x to 2,65x). Increase is statistically significant (α=0.01). Parameter HR decreased in all three ischemia period (ratio between control period and ischemia periods varies from 0,74x to 0,37x). Decrease is statistically significant (α=0.01). This parameter is inversed mean parameters; therefore this result doesn't bring new information for ischemia analysis studies which use mean parameter.

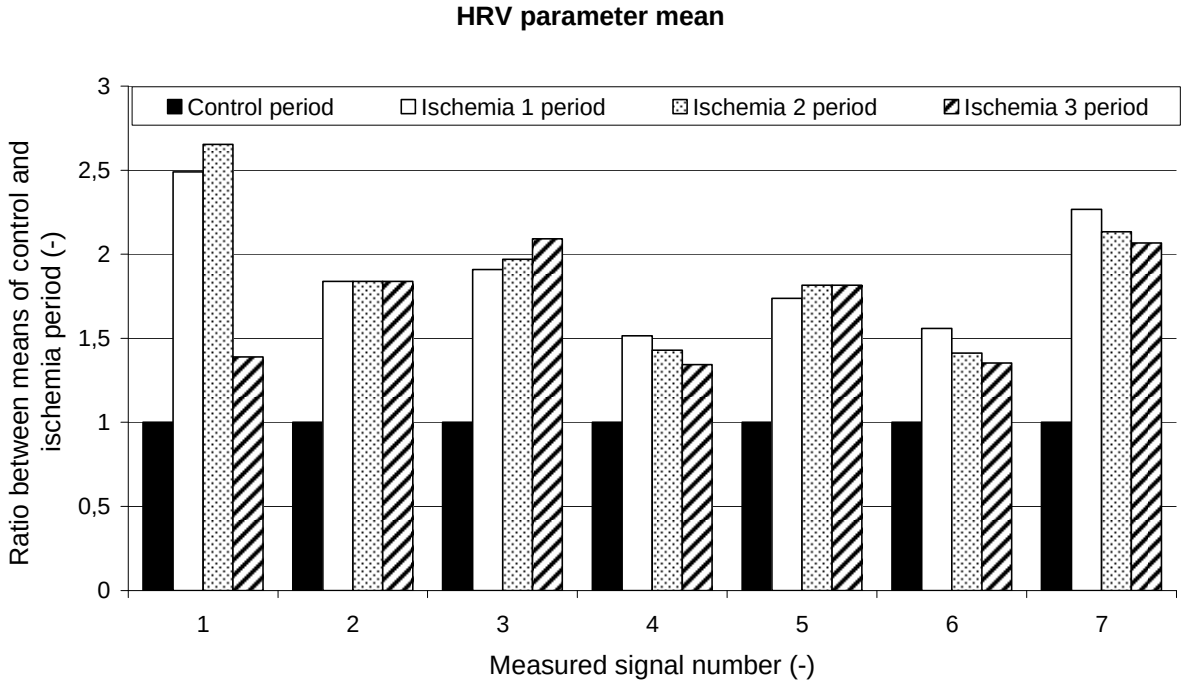

Fig. 2 Ischemia manifestation in HRV parameter mean

3.2. APPROPRIATENESS OF PARAMETER RR STD, HR STD, RMSSD AND MAX-MIN FOR ISCHEMIA ANALYSIS STUDY

Standard deviation of RR intervals, standard deviation of HR, RMSSD and MAX-MIN parameters randomly varies in studied periods; therefore these parameters are not appropriate for ischemia analysis.

3.3. APPROPRIATENESS OF PARAMETER NN50 AND PNN50 FOR ISCHEMIA ANALYSIS STUDY

Parameter NN50 count the number of interval differences of successive NN intervals greater than 50ms. Parameter pNN50 is derived from NN50. These parameters are standardized for using in human ECG signals, and many studies uses these parameters, so result from different studies can be compared. However, human heart rate is approximately 70-75bpm in comparison with rabbit heart rate which is 130 – 325bpm [5]. In this study the heart rate of isolated rabbit heart was approximately 160bpm for control period and approximately 100bmp for ischemia period. For this reason, the parameters NN50 and pNN50 may be inappropriate for rabbit heart ischemia analysis. Moreover parameter NN50 and pNN50 varies in considered period, and can not be used for ischemia detection also.

4. CONCLUSION

HRV analysis software was designed in Matlab for computation of most common standardized time domain HRV parameters. Eight HRV parameters were computed by designed software with aim to explore relation between these parameters and ischemia manifestation in isolated New Zealand rabbit hearts.

Six parameters – RR std, HR std, RMSSD, max-min, NN50 and pNN50 randomly varies in analyzed signals. For this reason these parameters are not appropriate for ischemia detection.

Two parameters – RR mean and HR – can be used as ischemia indicator. Parameter RR mean increased in all three ischemia period in comparison with control period. Ratio between RR mean of ischemia period (for each of three measured periods) and RR mean of control period was used as criterion of increase. Ratio varies from 1,34 to 2,65. Sign test was used for consideration of statistical significance of this increase. According to result of sign test increase of RR mean in ischemia period is statistically significant with significance level $\alpha=0.01$. Parameter HR decreased in all three ischemia period. Ratio between HR of ischemia period and HR of control period varies from 0,74 to 0,37. Decrease is also statistically significant ($\alpha=0.01$).

Because HR is inversed value of RR mean, only one of these parameters suffice for reliable ischemia detection.

ACKNOWLEDGMENT

The research was supported by the grants 102/07/P521, 102/07/1473 and 102/09/H083 from Grant agency of Czech Republic and partially supported by the grant MSM0021622402 and by grant MSM 0021630513, both grants sponsored by the Ministry of Education of the Czech Republic.

REFERENCES

[1] Lloyd-Jones D, Adams R, Carnethon M, DeSimone G, Ferguson TB, Flegal K, Ford E, Furie K, Go A, Greenlund K, Haase N, Hailpern S, Ho M, Howard V, Kissela B, Kittner S, Lackland D, Lisabeth L, Marelli A, McDermott M, Meigs J, Mozaffarian D, Nichol G, O'Donnell C, Roger V, Rosamond W, Sacco R, Sorlie P, Stafford R, Steinberger J, Hong Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics–2009 Update. A Report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2008 Dec 15.

[2] G.G. Berntson, J.T. Bigger Jr., D.L. Eckberg, P. Grossman, P.G. Kaufmann, M. Malik, H.N. Nagaraja, S.W. Porges, J.P. Saul, P.H. Stone, and M.W. Van Der Molen. Heart rate variability: Origins, methods, and interpretive caveats. Psychophysiol, 34:623–648, 1997.

[3] Task force of the European society of cardiology and the North American society of Laciny and electrophysiology. Heart rate variability – standards of measurement, physiological interpretation, and clinical use. European Heart Journal 17, p. 354-381, 1996

[4] Kyoung B., Jin-Young M., Domyung P., Sung-I Ch. and Mia S., International Heart Journal, Is 5-Minute Heart Rate Variability a Useful Measure for Monitoring the Autonomic Nervous System of Workers?, Vol. 49 (2008) , No. 2 pp.175-181, online ISSN: 1349-3299, print ISSN: 1349-2365

[5] Biology of the Rabbit, Lousiana Veterinary Medical Association, online at <http://lvma.org/rabbit.html>, February 2009.