HRV in Isolated Rabbit Hearts and In Vivo Rabbit Hearts

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Abstract

Heart rate variability of seven isolated and five in-vivo rabbit hearts was compared. Heart rate of isolated hearts is lower and RR-intervals longer than those of in-vivo hearts. Characteristic peaks in characteristic frequency bands are different and powers of these bands are almost twice higher in in-vivo hearts than in isolated ones. LF/HF ratio is more than five-times higher in isolated heart than in in-vivo hearts.

1.   Introduction

Heart rate variability (HRV) is a diagnostic tool based on evaluation of consecutive RR intervals. RR intervals are extracted from standard electrocardiogram; thus, HRV belongs to a group of non-invasive diagnostic methods. Despite decades of usage of HRV as experimental tool, it hasn't been clinically used until 1996, when Task Force society [1] standardized HRV parameters and their evaluation. HRV reflects behaviour of both parts of autonomous nervous system: sympathetic and parasympathetic [2]. Moreover humoral and metabolic mechanisms affect regulation of HRV [2]. Despite the fact that numerous articles with HRV studies have been published, only a few of them deal with isolated hearts. Isolated heart cannot be influenced by above mentioned mechanisms, however the heart responds (at the level of the intracardiac nervous system) to environmental changes [3]. Mechanisms leading to the presence of HRV despite cardiac denervation remain to be elucidated [4]. Comparison of HRV in isolated hearts and in-vivo hearts may help to understand mechanisms of HRV origin.

2.   Method

2.1.   Isolated hearts

All experiments followed the guidelines for animal treatment approved by local authorities and conformed to the EU law. Seven New Zealand rabbits were included in the study. Their isolated hearts were perfused according to Langendorff in the mode of constant perfusion pressure (85mmHg) [5]. In deep anaesthesia with xylasin and ketamin, the hearts were excised and fixed on perfusion apparatus filled with Kr   ebs-Henseleit (K-H) solution ($1.25mMCa^{2+}$, 37°C) and placed in a bath, where the hearts were stabilized for 30 minutes.

ECG signal was measured by touch-less method [7, 8]. Briefly, three Ag-AgCl disc electrodes in three orthogonal directions x, y, and z are placed in the walls of the bath which is a part of the perfusion system. Each isolated rabbit heart used in this study was positioned in the same way in the bath. ECG signals were recorded by data acquisition multifunction card PCI-6111E (National Instruments, USA) with sampling frequency fs=2000Hz. ECG signals were acquired by own application designed in LabView 7.1 software (Texas Instrument, 2008). The 12-bit analogue to digital conversion was used. The digital signal was stored on a hard disk for off-line processing.

Three ECG signals with duration approximately two hours were recorded. Five minutes long part was extracted in Matlab R2006a (MathWorks, 2006), beginning immediately after 30 minutes of heart stabilization. R-peaks were detected automatically by own R-wave detector designed in Matlab R2006a (MathWorks, 2006). The results of automatic analysis were reviewed and any errors in detection were corrected manually by human revision.

HRV parameters were computed from RR series interpolated with cubic spline method and resampled at fs=30Hz. Slow trends were removed by detrending procedure based on smoothness priors regularization with regularization parameter λ=3000. Signals were further analysed by Kubios HRV software [7].

2.2.   In-vivo hearts

ECG signals of five New Zealand rabbits were included in the study. The signals were recorded using a SEIVA recording system. Body surface wire electrodes were attached to the skin with miniature clips. These electrodes did not restrict free posturing. In order to get

stable signals in awake animals they were placed in plexiglas box. Box was sufficiently high for restriction of rabbit's lookout, which makes rabbits restless. ECG signals degraded by motion were extracted from further processing.

Five minutes long ECG signals were recorded. R-peaks were detected manually and RR intervals were processed by Kubios HRV software [7].

2.3. HRV parameters evaluation

Thirty-five standard HRV parameters [1] were evaluated by Kubios HRV software [7] both for isolated and in-vivo rabbit hearts. Means of each parameter were compared each to other. Change between isolated and in-vivo hearts were computed by following equation and expressed in percentages:

$$\text{Change} = \frac{\text{Mean value of isolated hearts}}{\text{Mean value of in} - \text{vivo hearts}} \times 100$$

3. Results

Parameters enumeration is summarized in Table 1 and Table 2, together with its results. Used parameters are standardized for clinical usage by Task Force society and its detail description can be freely found in [1]. Short description can be also found in Table 1 and Table 2.

Heart rate of isolated hearts is higher and has a narrower dispersion than in-vivo heart rate. This fact can be also seen in HRV triangular index (which represent integral of the RR interval histogram divided by the height of the histogram) and TINN (which shows width of the RR interval histogram).

Table 1: Frequency domain HRV parameters

Parameter HRV**	Description	Unit	Mean - isolated	Mean - in-vivo	Change*
FFT VLF peak	Band peak in frequency range 0Hz – 0.04Hz	Hz	0.021	0.027	22%
FFT LF peak	Band peak in frequency range 0.04Hz – 0.15Hz	Hz	0.051	0.052	2%
FFT HF peak	Band peak in frequency range 0.15Hz – 0.4Hz	Hz	0.237	0.173	-37%
FFT VLF power	Absolute power of 0Hz – 0.04Hz band	ms2	5.10^{-6}	5.10^{-5}	89%
FFT VLF power prc	Relative power of 0Hz – 0.04Hz band	%	56.79	34.45	-65%
FFT LF power	Absolute power of 0.04Hz – 0.15Hz band	ms2	2.10^{-6}	6.10^{-5}	97%
FFT LF power prc	Relative power of 0.04Hz – 0.15Hz band	%	21.2	44.69	53%
FFT LF power nu	Powers of 0.04Hz – 0.15Hz band in normalized units	n.u.	67.6	68.6	1%
FFT HF power	Absolute power of 0.15Hz – 0.4Hz band	ms2	2.10^{-6}	3.10^{-5}	93%
FFT HF power prc	Relative power of 0.15Hz – 0.4Hz band	%	22	20.86	-6%
FFT HF power nu	Powers of 0.15Hz – 0.4Hz band in normalized units	n.u.	32.4	31.4	-3%
FFT LF/HF power	Ratio between LF and HF band powers	ms2	18.55	3.005	-517%
AR VLF peak	Band peak in frequency range 0Hz – 0.04Hz	Hz	0.015	0.018	19%
AR LF peak	Band peak in frequency range 0.04Hz – 15Hz	Hz	0.043	0.049	13%
AR HF peak	Band peak in frequency range 0.15Hz – 0.4Hz	Hz	0.272	0.152	-78%
AR VLF power	Absolute power of 0Hz – 0.04Hz band	ms2	4.10^{-6}	5.10^{-5}	91%
AR VLF power prc	Relative power of 0Hz – 0.04Hz band	%	51.38	30.58	-68%
AR LF power	Absolute power of 0.04Hz – 0.15Hz band	ms2	2.10^{-6}	7.10^{-5}	97%
AR LF power prc	Relative power of 0.04Hz – 0.15Hz band	%	23.9	47.6	50%
AR LF power nu	Powers of 0.04Hz – 0.15Hz band in normalized units	n.u.	66.33	68.4	3%
AR HF power	Absolute power of 0.15Hz – 0.4Hz band	ms2	3.10^{-6}	3.10^{-5}	92%
AR HF power prc	Relative power of 0.15Hz – 0.4Hz band	%	24.72	21.82	-13%
AR HF power nu	Powers of 0.15Hz – 0.4Hz band in normalized units	n.u.	33.67	31.6	-7%
AR LF/HF power	Ratio between LF and HF band powers	ms2	16.95	2.487	-581%

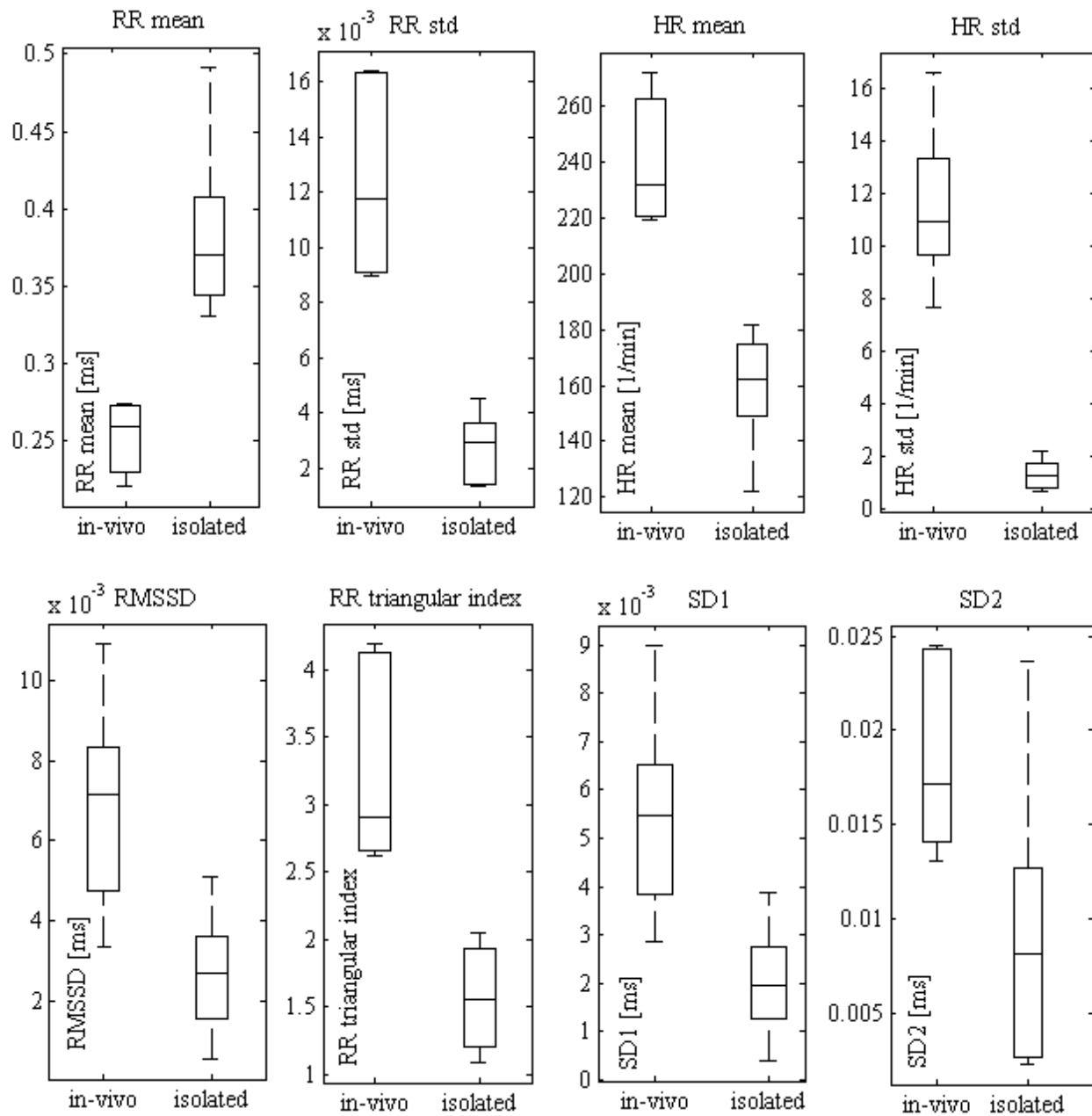*Change from isolated to in-vivo mean. **FFT –Fast Fourier Tranformation, AR – autoregressive.

Figure 1: Representative HRV parameters in in-vivo and isolated rabbit hearts. Detail description of presented parameters can be found at [1].

Parameter VLF peak in HRV spectrum of isolated hearts is located in the area close to the right part of VLF band, whereas HF peak is situated more to the s left part of HF band vice versa. LF peaks in both isolated and in-vivo spectra are situated almost at same frequencies.

Power of each band – VLF, LF and HF – is almost twice higher in in-vivo spectra than in isolated ones. Nevertheless the percentage distribution of these powers in individual bands is significantly different in isolated and in-vivo hearts. Smaller (–98%) VLF band and higher (+50%) LF band is present in in-vivo hearts in comparison with isolated hearts; HF bands for in-vivo and isolated hearts remain almost equal. LF/HF ratio is more than five-times higher in isolated heart than in in-vivo hearts.

Table 2: Time domain and geometrical HRV parameters

Parameter HRV	Description	Unit	Mean - isolated	Mean - in-vivo	Change*
RR mean	The mean of RR intervals	ms	0.366	0.252	-45%
RR std	Standard deviation of RR intervals	ms	0.005	0.013	59%
HR mean	The mean heart rate	1/min	167.6	240.7	30%
HR std	Standard deviation of intravenous heart rate	1/min	3.051	11.57	74%
RMSSD	Square root of the mean squared differences between successive RR intervals	ms	0.007	0.007	-8%
NN50	Number of successive RR interval pairs that differ more than 50 ms	count	6.571	1.2	-448%
pNN50	NN50 divided by the total number of RR intervals	%	0.743	0.102	-627%
HRV triangular index	The integral of the RR interval histogram divided by the height of the histogram		1.733	3.297	47%
TINN	Baseline width of the RR interval histogram	ms	0.028	0.098	72%
Poincare SD1	The standard deviation of the Poincaré plot perpendicular to the line-of-identity	ms	0.006	0.005	-10%
Poincare SD2	The standard deviation of the Poincaré plot along the line-of-identity	ms	0.01	0.019	45%

*Change from isolated to in-vivo mean.

4.   Conclusions

Behaviour of HRV of in-vivo hearts and isolated hearts is different. Parameters of HRV in Langendorff-perfused isolated heart significantly differ from those typical of in-vivo hearts in time domain, spectral domain and geometrical domain. HRV persist even in isolated heart, indicating that heart has its own controlling mechanism(s) for controlling the heart rate.

Acknowledgements

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