SPECTRAL ANALYSIS OF HEART RATE VARIABILITY: NEW EVALUATION METHOD

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Individual indices of spectral analysis (SA) of heart rate variability (HRV), which are used to diagnose the autonomic nervous system (ANS) activity, often give somewhat inconclusive and antagonistic results. Based on the results of age dependence (Šlachta et al., 2002), and dependence of exercise intensity (Stejskal et al., 2001) on the short-term SA HRV, the authors developed a new evaluation procedure. It consists of three complex indexes, which combine all age dependent parameters gained from the orthoclinostatic test: complex index of vagal activity, complex index of sympatho-vagal balance, and total score of SA HRV. The total score-to-age ratio was designated as the so-called functional age of ANS. The new evaluation method enables easier orientation in the comparison of standard parameters, simpler interpretation of the results, and clear identification of less perceptible changes in the power spectrum.

Keywords: spectral analysis of heart rate variability, age-dependent indices, complex indices of spectral analysis of heart rate variability.

INTRODUCTION

Spectral analysis (SA) of heart rate variability is a non-invasive method for the evaluation of the functional state of the autonomous nervous system (ANS). Although it is broadly used in research as well as in clinical practice (3205 MEDLINE references in past five years), there are some major discrepancies in the interpretation of individual parameters of spectral power (Saul et al., 1988; Sleight & Casadei, 1995). This leads the users of this method to a certain degree of caution, which causes a reduction in the use of parameters which yield a higher number of discrepancies (total spectral power, absolute and relative power of LF and HF component and their ratio LF/HF).

This approach often results in overlooking the VLF component (0.0033–0.04 Hz) and derived parameters during short-term examination. Despite of all the discrepancies VLF carries a lot of important information (Bigger et al., 1992; Francis et al., 2000; Musaeva et al., 2001; Tateishi et al., 2002), which can significantly extend the use of this method in clinical practice. In some cases it is probable that the spectral power in the very slow frequency zone can reflect more discreet changes than the fluctuation in the faster zones (Suda et al., 2001; Fleishman et al., 2001). According to Mamii et al. (2002) the VLF fluctuation closely communicates with the changes that occur in LF and HF zones ("cooperation spectrum") during 15 to 150 seconds, and thus is very important for their proper interpretation.

Regular exercise increases physical fitness and brings positive changes to ANS activity in patients (Pietila et al., 2002) as well as in healthy individuals (Levy et al., 1998; Stein et al., 1999). However, some authors, dealing with the effect of regular exercise on HRV, did not find the changes of individual parameters of SA HRV, though the indices of fitness, which are connected to the increase of vagal activity, were significantly improved (Boutcher & Stein, 1995; Davy et al., 1997; Duru et al., 2000). Such results are proving the low or insufficient sensitivity of the used SA HRV parameters.

The HRV spectral power is influenced by a variety of internal and external stimuli/conditions. The most significant is the influence of age (Ferrari, 2002; Okuda et al., 2002; Šlachta et al., 2002) and certain diseases that effect the ANS function ANS (Huikuri & Makikallio, 2001; Liao et al., 1998; Villareal et al., 2002; Ziegler et al., 2001; Doulalas et al., 2001; Quilliot et al., 2001; Hayano et al., 2001; Osaka et al., 1996; Kop et al., 2001; De Angelis, 2001); age and diseases influence the HRV spectral power in a similar way. Thus we can hypothesize that certain diseases and aging have a negative influence on ANS efficiency, and the parameters that decrease with disease and age can be identified as "positive" parameters, the opposite trend characterizes the "negative" parameters.

In practical use of laboratory methods we are trying to simplify the results to the point that their interpretation is unambiguous. It is common practice that the use of a larger number of parameters characterizing one phenomenon from different angles increases the value of the obtained information. Combining these parameters can lead to an increase in the sensitivity of the method.

This reasoning leads us to an attempt to use all the age-dependent parameters of SA HRV obtained from the orthoclinostatic maneuver and combine them into a minimum number of complex indexes. This study follows the research of the influence of age on individual parameters of SA HRV (Šlachta et al., 2002).

METHOD

To verify the proposed method we chose a group of healthy individuals (n = 216, age 12 – 70, $\bar{x}$ = 35.05 ± ± 14.30 years) who were the subject of our research on the influence of age on the SA HRV parameters (Šlachta et al., 2002). The entirely new method of evaluation of SA HRV was closely described in Šlachta's dissertation (1999). In this study we present the basic fundamental updates about the new relationships resulting from the changes of individual parameters during physical activity (Stejskal et al., 2001). The R-R intervals were monitored and the evaluation of the HRV data (minimum monitoring interval of 5 minutes and 300 R-R intervals) was carried out by the original diagnostic system VariaCardio TF4/TF3 (Salinger et al., 1995; Salinger et al., 1999). We used the orthoclinostatic stimulation (supine-standing-supine) procedure, which was described in previous study (Šlachta et al., 2002).

We modified the typically defined zone of 0.0033–0.04 Hz to 0.02–0.05 Hz. The reason for changing the lower zone limit was that we are unable to use the fluctuations slower than 0.02 Hz with the short-term examination. The reason for the shift of the upper zone limit to 0.05 Hz is to use the whole spectrum; there is no reason for omitting the 0.04–0.05 Hz range.

For the evaluation of SA HRV we used all the typically used parameters (spectral power, percentage share of individual components on the total spectral power, and ratios between individual components). In addition to these we used the coefficient of variation of individual components (CCV) (Hayano et al., 1991) to minimize the influence of different heart rate values on the SA HRV spectral field. Furthermore, the CCV has a closer correlation with the workload intensity than the component's power (Stejskal et al., 2001), and in factor analysis the CCV prove higher levels of communality (they present individual factors – TABLE 1).

The referential values were calculated for the age-dependent parameters. The age-dependent parameters were combined into five factors, as well as independently based on their relation to age (% HF in supine position, R-R, and LF/HF in standing) (TABLE 1) The regression equations were given 50 % and 95 % intervals of reliable accuracy in the age intervals in which the values of individual parameters were changing (e. g. the CCV HF in supine position in the age from 12 to 47 – Šlachta et al., 2002). For the interpretation of these values we assumed that in the 50 % interval are normal (physiological) values, between 50 % and 95 % are border values and values that are off the 95 % interval are abnormal.

TABLE 1
Parameters with similar course of age-dependence compound into five factors (underlined are the parameters with higher communality – "factor representative")

Factor	Parameters
F1	<u>*L CCVHF*</u>, $L\ P_T$, $L\ P_{HF}$
F2	<u>*S CCVLF*</u>, $S\ P_T$, $S\ P_{LF}$
F3	<u>*S CCVHF*</u>, $S\ P_{HF}$, *S % HF,*
F4	<u>*L LF/HF*</u>, *L % LF*
F5	<u>*L VLF/HF*</u>, *L VLF/LF, L % VLF*

L – supine position, *S* – standing position, *CCV* – coefficient of variation of a parameter, P_T – total spectral power, P_{HF} – HF power, P_{LF} – LF power

In the age intervals in which the values were not dependent on age (e. g. in CCV HF in supine position from the age of 47 and up – Šlachta et al., 2002) fractiles were calculated at 2.5 %, 25 %, 75 %, and 97.5 % of the normal distribution of data. For the interpretation of these values we assumed that between 25 % and 75 % fractiles are the normal (physiological) values, between 25 % and 2.5 % and between 75 % and 97.5 % fractiles are the border values and values above 97.5 % fractile are abnormal.

These obtained values were transformed into point values: physiological range was between –2.5 points and +2.5 points; the border values were between –4.75 and –2.5 points and between +2.5 points and +4.75 points; the abnormal values were smaller than –4.75 and bigger than +4.75 points.

Based on the course of age-dependency of parameters we were able to divide the age-dependent parameters into four following groups (G1 – G4):

G1: supine position, descendent course (F1 + % HF)
G2: post orthoclinostatic stimulation, descendent course (F2 + F3)
G3: supine position, ascendant course (F4 + F5)
G4: post orthoclinostatic stimulation, ascendant course (R-R intervals, LF/HF)

The statistically significant dependence on age of the individual factors or parameters itself was highly variable (TABLE 2). We took notice of this in combining the parameters and based on the value of the coefficient of correlation of the factor or parameter with age (<u>r</u>) we gave individual factors or parameters distinct weight (TABLE 2). In the calculation of the weight of a parameter (V_i) we assigned the range of weight from 5 (smallest value of r) to 100 (highest value of r):

$$V_i = ((b_i - \underline{b} / \underline{a} - \underline{b}) . 95) + 5, \qquad \textit{equation 1}$$

where $\underline{b}$ – minimal absolute value of r; a – maximum value of r; b_i absolute value of r for the chosen parameter.

TABLE 2
Correlation coefficient (r) between the chosen SA HRV parameters (representing F1–F5 factors or independent parameters) and age and from them derived weight of the parameters

Parameter	r	α	weight
L CCV HF	–0.4994	$p < 0.001$	100
L VLF/HF	0.4934	$p < 0.001$	99
S CCV HF	–0.4466	$p < 0.001$	88
L % HF	–0.4017	$p < 0.001$	77
S CC-V LF	–0.3958	$p < 0.001$	76
L LF/HF	0.3616	$p < 0.001$	68
SRR	0.3272	$p < 0.001$	60
S LF/HF	0.2863	$p < 0.01$	5

α – level of statistical significance

By combining G1 with G2 and G3 with G4 we acquired two complex indexes, which associate factors and individual parameters with different courses of age dependence. The first complex index (CI1) combines the factors and parameters that decrease with age (F1, F2, F3, and % HF in supine position). The second complex index (CI2) combines the factors and parameters that increase with age (F4, F5, R-R in standing, and LF/HF in standing).

In the previous study, which described the changes of individual parameters during exercise (Stejskal et al., 2001), we found that some parameters change in close relation to the intensity of the exercise (based on the maximum heart rate reserve MHRR): values of % VLF, VLF/HF, and VLF/LF significantly increased with increasing exercise intensity, controversially the values of TS, power of individual components, and % HF decreased.

Significant changes in the values of individual components were already detected in the alteration of the exercise intensity of 10 % MHRR (Stejskal et al., 2001; Hrdličková, 2002). Due to the decrease of vagal activity with increasing exercise intensity, we may presume that the parameters with descending dependence on the exercise intensity are the indicators of vagal activity. This vagal activity decrease, which is up to certain level of exercise intensity joined with the increase of sympathetic activity, moves the sympatho-vagal balance towards sympathetic activity; thus the parameters increasing with exercise intensity can be interpreted as indicators of sympatho-vagal balance.

Parameters that show significant decrease with age and are combined in CI1 correspond with the parameters that decrease even with the increasing exercise intensity (P_T, power of individual components P_{VLF}, P_{LF}, P_{HF}, % HF). Thus we can call the CI1 the indicator of vagal activity (taking some exception since the exercise took place in seated position). Accordingly the CI2 could be called the indicator of sympatho-vagal balance.

For further combination of the complex indexes into SA HRV total score (TS) we have to submit to a hypothesis that the ANS changes occurring during aging are negative. Thus we have to subtract the value of CI2, which combines parameters of age ascending course (complex index of sympatho-vagal balance – negative interpretation), from the value of CI1, which combines parameters descending with age (complex index of vagal activity – positive interpretation). E. g. the acquired value of CI2 = –4.8 points (it means significantly lowered values of % VLF and % LF in supine position and R-R a LF/HF in standing) will be transformed as stated above to +4.8 points and interpreted as positive (similarly to the positive interpretation of positive CI1 values).

$$TS = CI1 - CI2 \qquad \textit{equation 2}$$

TS value, which reflects all of the combined age-dependent parameters, can be also described by the age that would correspond with its value. With some circumspection we could call the altered TS the functional age of ANS (FA). The computation of FA is based on the overall valuation of the age-dependent parameters expressed in TS, on the age spectrum of the whole group of tested individuals, and on the calendar age of each of the tested individuals. The computation of FA is as follows:

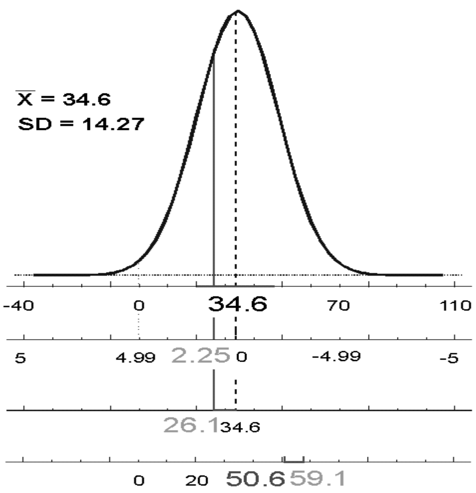
First we convert the TS point value onto $\underline{p}$ value according to the equation $\underline{p} = 1 - (5 - TS)/10$ (conversion from the –5 to +5 scale to 0 to 1 scale). Then we assign the $100\underline{p}$ % fractile x_p normal distribution of the age values of the monitored group N (μ, σ), where μ = 34.6 years and σ = 14.27 years (Šlachta et al., 2002). FA is calculated from the following equation:

$$FA = \text{calendar age} + (\mu - x_p) \qquad \textit{equation 3}$$

E. g. TS = 2.25 corresponds with the age 8.5 years lower than the mean age value. Thus if the calendar age of an individual is 59.1 years, the FA would be 50.6 years (Fig. 1).

Statistical analyses were done via the computer programs STATGRAPHICS version 5.0 and MS Excel 97.

Fig. 1
Graphic representation of transfer of the total score point values to the functional age of ANS



DISCUSSION

Based on our experience from the longitudinal monitoring of the differences among the SA HRV results it seems that the complex indexes are significantly more sensitive than the usually used SA HRV parameters. To prove this statement we summon the changes of the SA HRV parameters that were monitored in an age-homogenous group of 30 non-smoking men (55–62 years, 57.83 ± 1.80 years), who had a qualified risk for developing ischaemic heart disease. The results from before and after short-term complex intervention were compared. The 2 months intervention was based on laboratory testing and included physical activity, diet, food supplements and cognitive-behavioral treatment. The risk was quantified on a 7 points scale (–3 to +3 points), based on blood lipid levels, blood pressure, physical activity, and diet. The risk score was expressed not only as an absolute value of the risk parameter, but also by its dynamics during the intervention.

Significant decrease of the risk was noticeable after the intervention (entrance values –2.63 ± 3.21 points; after the intervention 1.73 ± 4.53 points; difference 4.37 ± 4.72 points, $p < 0.001$). As TABLE 3 shows, it is evident that, except for the total power, all other normally used parameters demonstrated significant changes: the values of CCV VLF, CCV LF, %VLF, % LF and LF/HF decreased, values of CCV HF and % HF increased. Theses changes prove that although the HRV changes were not significant (the intervention interval might have been too short), the spectral power has moved to the area with the fastest fluctuations, which indicates the increase of vagal activity. From the point of the statistical significance of the data before and after the intervention it is evident that the complex parameters reflect these changes significantly.

Correlating the changes of the risk point values and the SA HRV parameters, we found that the relation of the complex indexes to the risk changes is much closer in comparing the typically used parameters (TABLE 3). The very close relationship which was found, for example, between the risk and the TS ($r = 0.9018$) brings hope that its use may reveal even discreet changes and enable the discovery of statistically significant relations with even smaller amounts of compared data.

TABLE 3
Individual and complex SA HRV parameters and R-R intervals before (BI) and after complex intervention (AI)

Parameter		BI	AI	D	α	r
P_T (ms^2)	x	1495	1481	–14	NS	0.4474
	SD	735	648	423		p < 0.05
CCV VLF	x	1.445	1.176	–0.269	p < 0.05	–0.4002
	SD	0.757	0.478	0.681		p < 0.05
CCV LF	x	1.549	1.355	–0.193	p < 0.05	–0.1458
	SD	0.387	0.373	0.421		NS
CCV HF	x	2.099	2.371	0.272	p < 0.05	0.6333
	SD	0.396	0.538	0.617		p < 0.001
VLF (%)	x	22.78	16.10	–6.68	p < 0.05	–0.4885
	SD	15.10	10.11	16.76		p < 0.01
LF (%)	x	27.56	21.24	–6.32	p < 0.05	–0.3422
	SD	11.25	9.93	15.20		NS
HF (%)	x	48.66	62.67	14.01	p < 0.01	0.4914
	SD	15.92	14.40	20.10		p < 0.01
LF/HF	x	0.6378	0.3891	–0.2487	p < 0.01	–0.4098
	SD	0.3649	0.2769	0.4508		p < 0.05
CI1 (bod)	x	0.766	1.492	0.726	p < 0.01	0.8440
	SD	0.767	1.034	1.109		p < 0.001
CI2 (bod)	x	1.937	3.101	1.164	p < 0.001	0.7999
	SD	1.486	1.031	1.641		p < 0.001
TS (bod)	x	1.198	2.017	0.818	p < 0.001	0.9018
	SD	0.880	0.850	1.186		p < 0.001
RR (min^{-1})	x	1.086	1.092	0.007	NS	0.2142
	SD	0.104	0.131	0.089		NS

CI1 – complex index of vagal activity, *CI2* – complex index of sympatho-vagal balance, *TS* – total score of SA HRV, x – mean, SD – standard deviation, D – difference between AI and BI, a – statistical significance level D, NS – insignificant, r – correlation coefficient D of a parameter with a point value of a quantified risk

CONCLUSION

The new evaluation method enables easier orientation and simpler interpretation of the SA HRV results. In the case of a longitudinal study it enables unambiguous identification of less vivid changes of the power spectrum, which may not be pronounced while using the standard procedures. For further specification and verification of the accuracy and utilization of this method it is necessary to enlarge the group of tested individuals not only within the age area (12–70 years), but also above and below this limit.

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NOVÁ METODA HODNOCENÍ SPEKTRÁLNÍ ANALÝZY VARIABILITY SRDEČNÍ FREKVENCE

(Souhrn anglického textu)

Jednotlivé ukazatele spektrální analýzy (SA) variability srdeční frekvence (HRV), používané k diagnostice aktivity autonomního nervového systému (ANS), vykazují často málo průkazné a někdy i protichůdné výsledky. Na základě výsledků sledování vlivu věku (Šlachta et al., 2002) a intenzity zatížení (Stejskal et al., 2001) na krátkodobý záznam SA HRV navrhli autoři nový postup hodnocení pomocí tří indexů sdružujících všechny věkově závislé ukazatele získané při ortoklinostatickém vyšetření: komplexní index vagové aktivity, komplexní index sympatovagové rovnováhy a celkové skóre SA HRV. Vztažení celkového skóre k věku probanda nazvali autoři funkční věk ANS. Nová metodika hodnocení umožňuje při srovnání se standardními ukazateli snadnější orientaci, jednodušší interpretaci výsledků a jednoznačnou identifikaci méně výrazných změn výkonového spektra.

Klíčová slova: spektrální analýza variability srdeční frekvence, ukazatele závislé na věku, komplexní ukazatele spektrální analýzy variability srdeční frekvence.