

Prognostic Value of the Time Related Autonomic Balance Indicator for Risk Evaluation of Cardiovascular Events in Patients with Ischemic Heart Disease

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Abstract

The study comprised patients with unstable angina (UA), morning (MMI) and non-morning myocardial infarction (NMMI). The heart autonomic balance (HAB) circadian changes were assessed by Time Related Autonomic Balance Indicator – a non-parametric criterion for estimating the balance by HRV indices from ECG recordings in rest and by parasympathetic or sympathetic stimulation. The results indicated that: i) in patients with UA the sympathetic part in HAB is more time-dependent than in healthy subjects; the vagal circadian characteristic is normal and thus secures a favorable long-term prognosis; ii) in patients with MMI circadian characteristics of HAB consist of sympathetic hyper-activity and normal parasympathetic tone. The sympathetic dysfunction is the reason for the morning peak of CVE; iii) in patients with NMMI the circadian nature of the sympathetic activity is preserved, but the parasympathetic activity are almost absent.

1. Introduction

The ischemic heart disease (IHD) occupies a leading position among the causes for hospitalization and mortality in recent years. In spite of the development of pharmacological therapy, the methods of invasive cardiology and cardiosurgery, the mortality and the invalidization after IHD remain high. This requires more efforts for identifying the factors that trigger the appearance and development of IHD.

In our previous studies [1-3] we indicated that: i) the CVD (AH, CHF) have a different circadian profile of HAB, compared to the profile in healthy subjects; ii) the restoration of normal circadian characteristics of the HAB decreases the cardiac risk. In this study we analyze the specific abnormalities in HAB circadian changes in three groups of patients with IHD, and prognostic value of these circadian profiles for risk evaluation of

cardiovascular events (CVE).

More and more evidence is sought for the link between hypersympatheticotony and/or the lowered vagal tone and IHD progression [4]. However, the studies in coronary disease without previous MI are not unequivocal [5].

From the survey made it may be concluded that the research in field of circadian characteristic of the HAB in the acute coronary syndromes would improve the risk stratification of the patients with IHD.

2. Methods

The study comprised of: i). 26 patients with UA between 6 and 10 days after the beginning of the complaints (without CVE within the framework of one year – i.e. with good prognosis). Nine of the patients reported preceding hypertension. The therapy applied to the patients differed. It included nitrate drugs, calcium antagonists, ACE-inhibitors and antithrombotic agents. The patients subjected to preceding therapy with beta-blocker had at least 48 hours without administration of the blocker before the study of HRV. The exclusion criteria were diabetes, heart failure, previous myocardial infarction, renal failure and other general severe diseases. All patients are in sinus rhythm without conduction disorders. ii). 15 patients with MMI - for whom MI occurred in the morning between 6 and 11 a.m., and 19 patients with NMMI. There was no difference in the distributions of the localizations of the infarction in the two groups. The patients are without diabetes or other severe system diseases, conduction disorders, frequent arrhythmias and anti-arrhythmic therapy. The patients were subjected to outpatient follow-up examinations between the 3rd and the 5th month after the incident. There was no difference in the type of drugs administered to both groups of patients. The therapy with beta-blockers was discontinued at least 7 days prior to the study.

The HAB changes were assessed by HRV indices from ECG recordings in resting state (RS) and by

parasympathetic (Valsalva manoeuvre; VM), or sympathetic (handgrip test; HT) stimulation. In [6-7] we proposed the Time Related Autonomic Balance Indicator (TRABI) – a non-parametric criterion for estimating the circadian changes of HAB by comparing the values of the HRV indices in RS and by vegetative nervous system stimulation during two intervals – morning and afternoon. In this study, TRABI was used for evaluation of the specific changes in HAB in the three patient groups.

3. Results

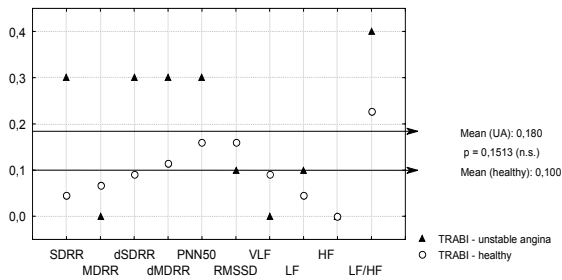


Figure 1. Values of TRABI for the HRV indices and respective mean values of TRABI in healthy individuals and in patients with UA with comparison between morning and afternoon measurements during RS and with HT.

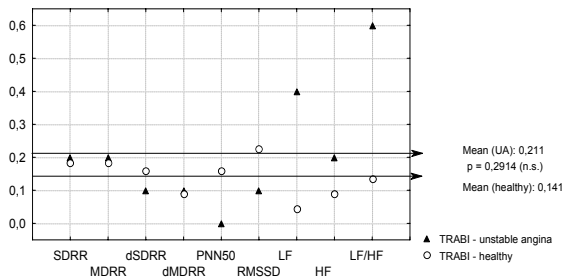


Figure 2. Values of TRABI for the HRV indices and respective mean values of TRABI in healthy individuals and in patients with UA with comparison between morning and afternoon measurements during RS and with VM.

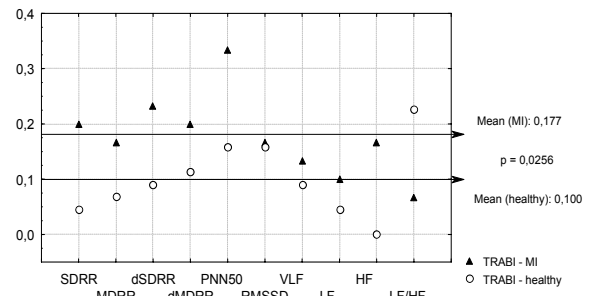


Figure 3. Values of TRABI for the HRV indices and respective mean values of TRABI in healthy individuals and in patients with MMI with comparison between morning and afternoon measurements during RS and with HT.

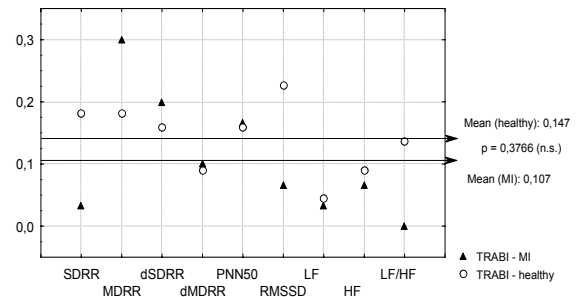


Figure 4. Values of TRABI for the HRV indices and respective mean values of TRABI in healthy individuals and in patients with MMI with comparison between morning and afternoon measurements during RS and with VM.

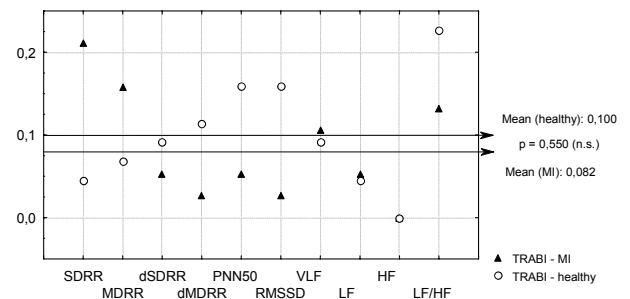


Figure 5. Values of TRABI for the HRV indices and respective mean values of TRABI in healthy individuals and in patients with NMI with comparison between morning and afternoon measurements during RS and with HT.

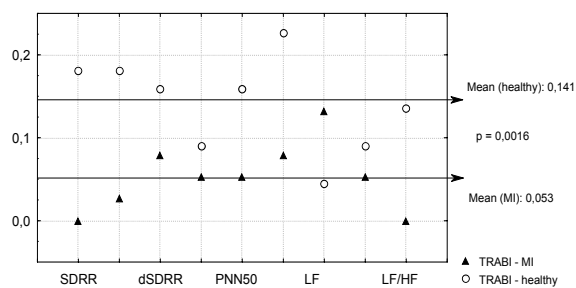


Figure 6. Values of TRABI for the HRV indices and respective mean values of TRABI in healthy individuals and in patients with NMMI with comparison between morning and afternoon measurements during RS and with VM.

4. Discussion and conclusions

The mean value of TRABI for the HRV indices from the comparative study of the response to the HT with respect to RS in the morning and in the afternoon in the patients with UA is higher, although insignificantly, than the respective value in healthy individuals. For certain indices the values of the index in the patients considerably exceeded the values in the healthy individuals. Such are the assessments for SDRR, dSDRR, dMDRR, PNN50 and the LF/HF ratio (Figure 1). **These results indicate that in patients with UA the sympathetic component in AB is more time-dependent than in healthy individuals.** The comparison between the values of the HRV indices during rest and with the Valsalva manoeuvre in the morning demonstrates considerable response compared to the parasympathetic sample. In the morning the vagal tone is low and permits stimulation. The response in the afternoon hours is weaker, because the parasympathetic has attained a relative stability. There is a pronounced circadian nature of the parasympathetic part in the HAB in the patients with UA.

The mean value of TRABI for the HRV indices from the comparative study of the response to the Valsalva manoeuvre and rest in the morning and in the afternoon in the patients with UA does not differ significantly from the value in healthy individuals (Figure 2). For most time-domain indices the values of TRABI in patients with UA and in healthy individuals are close. **This result is in support of the conclusion that the circadian characteristic of the parasympathetic tone in persons with UA is analogous to the normal one.** However, the values of the indicator for the indices LF and LF/HF are higher in patients with UA than in healthy individuals, being 0.4 for LF and reaching 0.6 for LF/HF. Probably in the sample in which there is a sympathetic component as well, the stimulation of the sympathetic is suppressed due to its blocking described above. As a result, the

frequency indices respond in a range in which there was no saturation of the values, and the time changes in the autonomic control can be reflected.

The results from the study in patients with UA indicate the existence of autonomic dysfunction with blocked sympathetic activity. The evaluations of the HRV indices with TRABI show a slightly more pronounced circadian nature of sympathicotony than in healthy individuals. However, the parasympatheticotony in the patients with UA has a considerably pronounced circadian nature, similar to the circadian nature in healthy controls. During stress (blocking the sympathetic), the parasympathetic performs a protective role and thus secures a favorable long-term prognosis for the patients with UA in the population studied.

The mean value of TRABI for the HRV indices from the comparative study in the morning and in the afternoon of the response to the HT compared to RS for the patients with MMI is significantly higher than for healthy individuals (Figure 3). **It can be claimed that the patients with MMI have a marked circadian characteristic of the sympathetic.** For all indices, with the exception of LF/HF, the values of TRABI are higher in the patients with MI. The lower value of the index for LF/HF is explained with hypersympatheticotony and blocked response to stress, on the one hand, and decreased circadian nature of the parasympathetic – on the other, which does not allow this indice to reflect the time changes in HAB.

The mean value of TRABI for the HRV indices from the comparative study in the morning and in the afternoon of the response to VM compared to RS in the patients with MMI does not differ significantly from the value in healthy individuals (Figure 4). The patients preserve the normal circadian nature of the parasympathetic component in HAB. The evaluations of TRABI for the indices SDRR, RMSSD and LF/HF are lower in patients with MMI. The result can be explained with the relatively decreased circadian nature of the parasympathetic part of the autonomic balance compared to the marked circadian nature of the sympathetic part in this group of patients.

The mean value of TRABI in healthy individuals is 0.100 in the comparative study between HRV during RS and with the HT, and 0.141 in the study during RS and VM. The result shows that the circadian characteristic of the parasympathetic in healthy individuals is more pronounced. The results in the patients with MMI are very different. In the first study, TRABI had a mean value of 0.177, in the second – 0.107. Consequently, abnormal circadian nature of the HAB is observed in the patients with MMI. The circadian nature in these patients is more pronounced for the sympathetic part of the balance, unlike the circadian nature in healthy

individuals.

Both in this group of patients and in the patients with UA we found sympathetic autonomic dysfunction with hypersympatheticotony and blocked response to stress. Unlike the unstable angina, here the preventive function of the vagus is lacking. ***The abnormal circadian characteristic of the HAB and the sympathetic autonomic dysfunction during stress are probably the reason for the peak in the frequency of CVE in the morning.***

The mean value of TRABI for the HRV indices from the comparative study in the morning and in the afternoon of the response to HT compared to RS in the patients with NMMI almost coincided with the value in healthy individuals (Figure 5). This result means that ***in the patients with NMMI there was no substantial impairment in the circadian nature of the sympathetic part of the balance.*** Only for the indices SDRR and MDRR the values of the indicator are higher in patients with NMMI compared to the evaluations in healthy individuals. Obviously, the circadian nature of the vagus is impaired and hence also partial manifestation of the circadian nature of the sympathetic part of the balance is possible.

The values of TRABI for the HRV indices from the comparative study in the morning and in the afternoon of the response to VM and to RS in the patients with NMMI suggest that the parasympathetic sample leads to identical response in both time intervals (Figure 6). The mean value of the indicator is significantly lower than that in healthy individuals. ***This result shows almost totally lost circadian nature of the vagal tone.*** Only for the indice LF the value for TRABI is higher in the patients with NMMI compared to healthy individuals. The result supports the hypothesis that the strongly decreased circadian nature of the vagus allows the manifestation of the circadian nature of the sympatheticus.

Summarizing the results in patients with NMMI, we can assume that the circadian nature of the sympathetic part of the autonomic balance is preserved, with a ***strongly decreased circadian nature of the parasympathetic part of the balance.***

It was already stressed that in healthy individuals the circadian nature of the parasympathicus prevails over that of the sympatheticus. For the MMI the mean value of TRABI is much higher in the comparative study between RS and with the HT than the mean value in the comparative study during RS and with the VM. It would be justifiable to conclude that the circadian nature of the sympatheticus is more strongly pronounced. With the NMMI it is interesting to note that TRABI has very low mean values both in the first (0.082) and in the second study (0.053). This result shows strongly decreased circadian nature of the HAB. The mean value of TRABI

in the comparative study between RS and with the HT remains higher than the mean value in the comparative study between RS and with the VM, which shows that in the case of NMMI, too, there is abnormal circadian nature of the HAB. For the sake of comparison, we shall recall that in the patients with UA the circadian characteristic of the HAB remains normal. The mean value of TRABI in the comparative study between RS and with the VM in the patients with UA remains higher than the mean value of TRABI in the comparative study between RS and with the HT. ***From these results we can conclude that the sympathetic dysfunction is the trigger for the appearance and poor prognosis of cardiovascular incidents, whereas the vagal activity has a protective role.***

References

- [1] Matveev M, Prokopova R, Nachev Ch. Time-related heart autonomic balance characteristics in healthy subjects. *Physiol. Meas.* 2003;24:727-43.
- [2] Prokopova R, Matveev M. Heart autonomic balance changes in mildly hypertensive subjects. Method of assessment, characteristics, treatment. *Journ of Hypertens* 2004;22:S209-10.
- [3] Prokopova R, Matveev M, Nachev CH. Correlating changes in heart autonomic balance and ventricular arrhythmias reflecting the positive effect of treating heart failure with Carvedilol. *Europ J of Heart Failure Suppl* 2005;4/1:37-8.
- [4] Bigger JT, Fleiss JL, Steiman RC, Rolnitzki LM, Shneider WJ, Stein PK. RR Variability in Healthy , Middle-Aged Persons Compared With Patients With Chronic Coronary Heart Disease or Recent Acute Myocardial Infarction. *Circulation* 1995;91:1936-43.
- [5] Wennerblom B, Lurje L, Tygesen H, Vahisalo R, Hjalmarson A. Patients with uncomplicated coronary artery disease have reduced heart rate variability mainly affecting vagal tone. *Heart* 2000; 83:290-4.
- [6] Matveev M, Prokopova R, Nachev Ch. Time-Related Heart Vegetative Balance Characteristics. *Computers in Cardiology* 2003;30:457-60.
- [7] Matveev M, Prokopova R. Normal and abnormal circadian profiles of heart autonomic balance, evaluated by time-ralted common indicator of heart rate variability. *The Anatolian J Cardiol* 2007;7/S1:125-9.

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