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SPECTRAL ANALYSIS OF HEART RATE VARIABILITY FOR ASSESSMENT OF AUTONOMIC NERVOUS SYSTEM ACTIVITY DURING HEAD-UP TILT TABLE TESTING

Polona Likar[1], Neža Starič[2], Mojca Škafar[2], Matjaž Klemenc[1]

[1] Splošna bolnišnica "Dr. Franca Derganca" Nova Gorica, Ulica padlih borcev 13a, 5290 Šempeter pri Gorici
[2] University of Ljubljana, Faculty of Medicine, Vrazov trg 2, 1104 Ljubljana

Abstract — Spectral analysis of heart rate variability was used to assess changes in activity of autonomic nervous system (ANS) in 84 patients with history of recurrent syncope and 21 normal controls. The analysis was done in different phases of tilt table testing procedure to attempt to relate such changes to specific types of response to a trigger such as decrease of arterial blood pressure when standing up. Frequency domain measurements of the high (HF), low (LF) frequency bands and the ratio LF/HF were derived from ECG recordings and computed by Fast Fourier transform (FFT) for a sequential 5 min intervals of the whole 55 min tilt testing procedure. A statistically significant increase of the LF component and decrease of the HF component of the HRV spectrum were observed during the transition from the supine position to head-up tilt (HUT) in subjects with a history of syncope. However, there were no differences in the ANS activity in comparable testing intervals between subjects who experienced syncope, to those who did not. There were also no differences in the ANS activity in subjects with tilt-induced syncope compared to healthy control subjects. We therefore suggest that HRV is a suitable method for investigating the activity of ANS during the head-up tilt table testing, however with existing methodology is not possible to predict the outcome of the head-up tilt table test in its early stages.

Index Terms — TRANS2CARE, vasovagal syncope, tilt- table testing, Heart rate variability

1 BACKGROUND

Syncope is a transient loss of consciousness due to transient global cerebral hypo-perfusion. Reflex syncope is its most common form, and it is caused by an inappropriate response of the autonomic nervous system (ANS) to orthostatic stress. A decrease in the arterial blood pressure leads to a diminished baroreceptor outflow which results in an increased sympathetic activity and a decreased vagal nerve activity. In the course of reflex syncope, however, there is a sudden decrease of the sympathetic activity and an accompanying paradoxical stimulation of the vagal nerve. Head-up tilt table (HUT) testing is the most widely used technique to provoke ANS instability this neurogenic instability, where the syncope may be induced in the susceptible individuals .

Spectral analysis of heart rate variability (HRV) is a non-invasive technique for the quantitative assessment of autonomic nervous system (ANS) function. Spectral analysis of HRV provides information on the power of RR- interval variations in the very low frequency (VLF), low-frequency (LF) and high-frequency bands (HF), which are related to modulation of sympathetic and vagal activity at the level of sino-atrial node. During different phases of the head-up tilt testing the ANS activity changes, and thus the HRV change as well. The low-frequency (LF) component of the HRV spectrum is used as a reflection of the sympathetic activity, while the high-frequency (HF) component reflects the parasympathetic activity. Different studies have used such approach to explore the changes in the ANS activity during tilt testing. However there have been published a conflicting answers on questions whether it is possible to predict the result of the test; namely, the onset of syncope, based on the analysis of HRV parameters during the initial phases of the test. In the frame of our research, we studied subjects with a history of reflex syncope (H) and healthy control subjects (C).

2 OBJECTIVES

The aim of this study was to investigate the parameters of heart rate variability (HRV) in patients with neurally mediated reflex syncope in comparison with healthy subjects. The main goal is to develop a new approach in vasovagal syncope diagnosis related with development of new software based on HRV, which would permit assessment of probability of positive or negative tilt test result in the very beginning of the test. This will results in more comfortable, shorter and no-provoking syncope testing procedure for patients and less time consuming diagnostics procedure which will reduce healthcare costs.

3 APPROACH & METHODS

General approach

To assess the utility of HRV parameters for assessing the autonomic nervous system activity during the testing with HUT and to predict the result of the test, namely the onset of syncope based on the analysis of HRV values during the initial phases of the test.

Methods

Subjects

We studied 84 patients with diagnosed syncope referred for tilting (retrospective study) and 21 healthy control subjects (prospective study). All subjects were instrumented for ECG telemetry and applanation tonometry for continuous blood pressure monitoring. The participants gave thier written consent and the study was approved by the Ethics Committee of the Republic of Slovenia.

Protocol

We followed the modified Italian protocol as the protocol of choice for the tilt-table test (Bartoletti et al., 2000). Briefly, following the rest period of 5 minutes in the supine position, each subject was tilted to 65 °for 45 minutes, after 30 minutes a 400 µg of nitoglicerin spray was given sublingually. If typical symptoms of pre-/syncope occured during HUT, the patient was immediately returned to the supine position. A positive response was defined by syncope (transient loss of consciousness associated with loss of postural tone) or near-syncope (pallor, nausea, lightheadedness, diaphoresis, blurred vision) associated with the following hemodynamic changes: a decrease in systolic blood pressure 60% from baseline values or an absolute value 80 mm Hg (vasodepressor response) and/or a decrease in HR 30% from the baseline value or an absolute value 40 beats/min (cardioinhibitory response).

Heart rate variability

To assess the autonomic nervous system function during HUT, power spectral analysis of HRV was performed. Spectral indices were computed by Fast Fourier transform (FFT) for 11 intervals each 5 minutes long. All intervals were visually checked for missing or premature beats. The power spectrum was calculated as high frequency (HF: 0.15-0.40 Hz), low frequency (LF: 0.05-0.15 Hz), and the ratio of LF to HF power (LF/HF). Measurements were done in normalized units [n.u.].

4 RESULTS

A significant increase of the LF component and a significant decrease of the HF component of the HRV spectrum were observed during the transition of patients from the supine position to tilt at the beginning of the passive phase of the test in subjects with a history of syncope (two–tailed Student t test for paired samples, $p < 0.05$) (Figure 1). This showed an increased sympathetic and reduced vasovagal activity when patient is tilted to the semi-standing position.

However, the comparison of HRV parameters (HF, LF and ration LF/HF) of two groups of patients with a history of syncope (patients with tilt-induced syncope versus patients without tilt-induced syncope) showed no significant differences in comparable intervals of the head-up tilt table test (two–tailed Student t test for independent samples, $p > 0.05$). Furthermore, the comparison of HRV parameters between patients with a history of syncope versus healthy controls shows no differences in comparable intervals (two–tailed Student t test for independent samples, $p > 0.05$). The results therefore suggest that there are no differences in ANS activity between subjects, with history of reflex syncope, to which we provoked syncope compared to those in which we did not. There are also no differences in the ANS activity in subjects with tilt-induced syncope, including those with a history of reflex syncope compared to healthy control subjects (Figure 1). Thus, we conclude that with method of spectral analysis of heart rate variability it is not possible to predict the onset of syncope in the early stages of a tilt test.

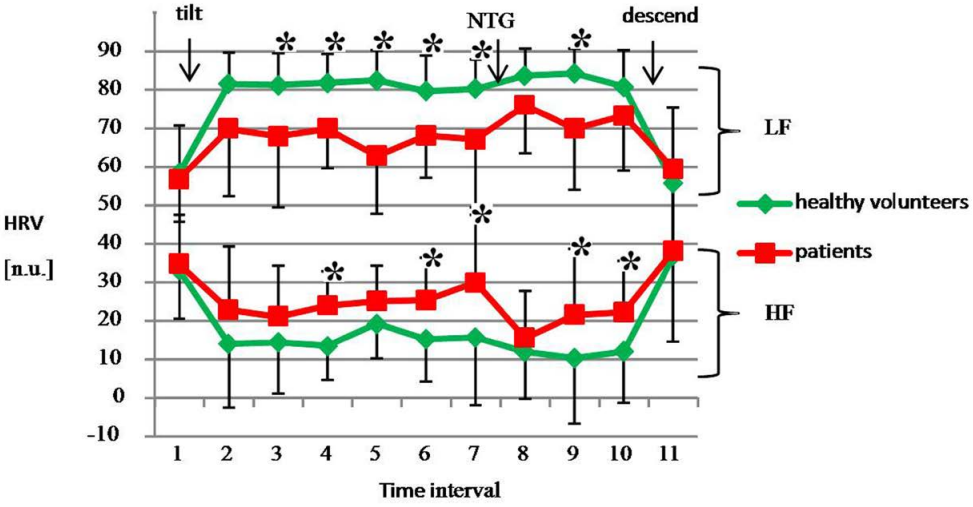

Figure 1: The average values with standard deviation of LF and HF parameters of five-minute intervals in patients and healthy volunteers aged up to and including 35 years in which we did not provoke syncope. The * indicates the interval with a statistically significant difference ($p < 0.05$) between the values of LF and HF in patients and healthy subjects. NTG - nitroglycerin, n.u. - normalized units.

5 POTENTIAL NEW PRODUCTS & SERVICES

Product: New software or/and point-of care device for a physicians that would serve for assessment the function of autonomic nervous system in vasovagal syncope diagnosis.

Service: New, shorter and improved approach in vasovagal syncope diagnosis.

6 CURRENT COLLABORATIONS

6.1 With other researchers

In the field of methodology of Heart Rate variability we have established a valuable and permanent collaboration with assistant professor Petra Golja from Biotechnical faculty at University of Ljubljana and prof. Tanja Princi from Department of Life Sciences at University of Trieste.

7 CONTACT OR COLLABORATIONS NEEDED

Connection with research groups specialized in mathematical, statistical or informatics studies should be established to develop a new approaches in analysis of Heart Rate Variability. Furthermore, a connection with industry should be established with main goal develop a new software for assessing Heart Rate Variability and other technical support.

8 COMMUNICATION TOOLS

The expertise in the field Heart Rate Variability and its applicability in different medical conditions is disseminated through the high quality scientific publications.

9 FUNDS NEEDED

9.1 For basic research (investigation of biological mechanisms): 50.000 €

9.2 For applied research (solutions for real-world problems): 50.000 €

9.3 For pilot & demonstrator activities (to develop a prototype): 50 - 100.000 €

10 CONCLUSION

Our method opens new frontiers in clinical and pre-clinical investigations of activity of autonomic nervous system (ANS). In this study we demonstrated that HRV is a suitable technique for monitoring the function of autonomic nervous system during the tilt table testing as have been already reported in published studies. This non-invasive methodology provides a physician additional information about the ANS activity at the level of sinoatrial node during HUT. However, with an existing linear analysis of HRV it is not possible to predict the outcome of the test at its very beginning. To overcome these barriers we suppose to develop a new, non-linear methods for analysing of HRV, with whose we believe it could be possible to achieve this challenge.

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