

Efficiency Evaluation of Autonomic Heart Control by Using the Principal Component Analysis of ECG P-Wave

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Keywords

Principal component analysis, autonomic heart control, ECG P-wave

Summary

Background: Cardiac output is controlled by the autonomic nervous system by changing the heart rate and/or the contractions of the heart muscle in response to the hemodynamic needs of the whole body. Malfunction of these mechanisms causes the postural orthostatic tachycardia syndrome and/or the chronic fatigue syndrome. Evaluation of functionality and efficiency of the control mechanisms could give valuable diagnostic information in the early stages of dysfunction of the heart control systems and help to monitor the healing process in rehabilitation period after interventions.

Objectives: In this study we demonstrate how P-wave changes evoked by an orthostatic test could be quantitatively evaluated by using the method based on the principal component analysis.

Methods: ECG signals were recorded during an orthostatic test performed according to the typical protocol in three groups of volunteer subjects representing healthy young and older persons, part of which had transient periods of supraventricular arrhythmias. Quantitative evaluation of P-wave morphology changes was performed by means of principal component analysis-based method.

Results: Principal component-based estimates showed certain variety of P-wave shape during orthostatic test, what revealed a possibility to evaluate the properties of parasympathetic heart control.

Conclusions: Quantitative evaluation of ECG P-wave changes evoked by an orthostatic test by using a newly developed method provides a quantitative estimate for functionality and efficiency of the heart rate control mechanisms. The method could be used in eHealth systems.

chronic fatigue syndrome [2]. Some systematic diseases can impact the autonomic heart control. Impairment of the autonomic heart control is observed in various stages of diabetic neuropathy [3, 4]. Defibrillating shocks delivered to the heart in an attempt to stop severe rhythm disorders inescapably impair the autonomic heart control [5, 6]. The same outcome may be expected after surgical interventions, catheter ablation procedures, etc. Evaluation of the functionality and efficiency of the control mechanisms can provide valuable diagnostic information in the early stages of dysfunction of the heart control systems and help to monitor the healing process or the rehabilitation period after interventions.

Different topology of sympathetic and parasympathetic nerve ganglia in the heart [7] as well as different mechanisms of action of the systems [8] cause different dynamic characteristics of the sympathetic and the parasympathetic heart rhythm control. These differences allow to identify the mechanisms and evaluate them separately by using heart rate variability criteria [8]. More detailed investigations are based on an ECG P-wave morphology analysis [9]. The P-wave shape reflects the spread of the electrical excitation front over the atria, which could be influenced by sophisticated heart rhythm control mechanisms. Electrical excitation of the heart starts in a group of cells with the highest spontaneous electrical activity called the true pacemaker that is normally situated in the sinoatrial node. There exist other groups of cells with spontaneous electrical activity that are situated either in the sinoatrial node or beyond it and are activated by electrical excitation coming from the true pacemaker. They are called latent pacemakers. Such

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1. Introduction

Cardiac output is controlled by the autonomic nervous system by changing the heart rate and/or contractions of the heart muscle in response to the hemodynamic needs of the whole body. Sympathetic influences accelerate the heart rate, increase the contractions of the heart muscle where-

as parasympathetic influences cause opposite effects. The heart rate is determined by the rate of spontaneous electrical activity of the cells usually located in the sinoatrial node. This rate is the result of permanent interplay between sympathetic and parasympathetic influences [1]. Malfunction of these mechanisms causes the postural orthostatic tachycardia syndrome and/or the

pacemaker cell groups are most densely concentrated in the sinoatrial node [10]. The release of neuromediators from nerve terminals influences a spontaneous activity of the closest pacemaker cell groups. As has been reported [7], the topology of neural ganglionated subplexuses suggests that during a parasympathetic activity the neuromediators are released in the site of the true pacemaker, and the spontaneous activity of the true pacemaker is suppressed. Thus it is possible that a latent pacemaker, whose activity has been less impacted, would take over the role of the true pacemaker. Different sensitivity of the pacemaker cell groups to the parasympathetic activity in the sinoatrial node and other sites of the right atria as reported by Kodama et al. 1996 [11] supports the above idea of the existence of a mechanism of the true pacemaker shifting within the sinoatrial node or beyond it. This phenomenon has been studied previously [12, 13]. Shifting of the pacemaker site causes specific changes in the heart rate [11, 14–17]. The electrical excitation front spreads over the atria having originated from the true pacemaker site. If the location of the true pacemaker shifts, this will be reflected as changes in the electrical excitation front spread and ECG P-wave morphology [9]. The more distant are the true pacemaker shifts, the more pronounced are the changes in the P-wave morphology. However, only the first 1/3 part of the P-wave reflects the electrical excitation front spread in the right atria. The spread of excitation in the left atria is not always influenced by variation of excitation spread in the right atria. Thus the complexity of the overall changes in the P-wave morphology barely gives us a chance to develop an empirical criterion for its quantitative evaluation. The features describing the shape of each digitized P-wave of an electrogram are the samples of the vector representing it. Dimensionality of such representation is equal to the number of samples in the vectors (depending on the sampling rate, it could be a hundred or so). The method of principal component analysis (PCA) reduces the dimensionality of the data set and enables to retain the highest possible degree of variation present in it [18]. We propose to use this method for the extraction of representative features

describing the changes in P-wave morphology. The PCA transforms the original data set into a new set of vectors (the principal components) which are uncorrelated and involve information represented by several correlated variables in the original set. The calculated principal components are ordered so that the very first of them retain most of the variation present in all the original variables. Thus it is possible to perform a truncated expansion of P-wave vectors by using only the first several principal components. Every ordinary P-wave vector \mathbf{x}_i is then represented by using a linear combination of the principal components ϕ_k multiplied by coefficients $w_{i,k}$:

$$\mathbf{x}_i = \sum_{k=1}^p w_{i,k} \phi_k . \quad (1)$$

Variation of coefficients $w_{i,k}$ represents variation of the shape in the set of P-waves. Hence it is possible to construct the quantitative criterion that represents changes in the P-wave changes. In this study we demonstrated how P-wave changes evoked by an orthostatic test (which evokes sudden imbalance in the interplay between the sympathetic and the parasympathetic heart control) could be quantitatively evaluated by using the method based on the principal component analysis. This method could be used as a part of eHealth system extracting valuable diagnostic information about functionality and efficiency of the heart rate control mechanisms. Our preliminary results of the investigation were reported in [19].

2. Methods

ECG signals were recorded during an orthostatic test performed according to the typical protocol. The test was started with the patient lying in the supine position motionless for three minutes, then standing up and standing still for two minutes and then lying down again. The first (control) group of subjects consisted of 20 volunteer healthy students of either gender aging between 20 and 24. The second group of subjects consisted of 10 older healthy persons of either gender aging between 48 and 70. The third group consisted of 10 older persons of either gender aging be-

tween 48 and 70 who suffered transient periods of atrial fibrillation. Twelve-lead ECG signals were registered synchronically by using the system of ECG analysis called “Kaunas-Kruvis” [20] at 12-bit resolution and 500 Hz sampling rate. Only those recordings that were free of extrasystolic beats, fragments of atrial fibrillation or other rhythm disorders were selected for processing. The best-quality ECG recording from each of the 40 investigated persons was selected for processing. Totally, 40 recordings were processed.

The maximum point of R-wave was selected as a reference point for each cardiocycle. It was detected by the following procedure: the R-wave was provisionally detected where the first derivative of the ECG was exceeding 0.5 of its maximum value within three seconds sliding window in lead 2. To find a reference point of the cardiocycle, we used following function:

$$\mathbf{a}_i = \sum_{j=1}^{12} x_{i,j}^2 , \quad (2)$$

where $x_{i,j}$ is the i -th sample of the j -th ECG lead. The function is calculated by using a window of 80 samples that succeed the provisionally detected R-wave. The reference point of the cardiocycle was marked to be at function \mathbf{a} at its maximum. R-R intervals were calculated using the reference points. Seventy samples starting from the 80th sample before the reference point of the cardiocycle were extracted as a fragment representing P-wave. We decided not to concentrate on the detection of the start- and end-points of P-wave because it could be problematic in cases when P-wave morphology changed. On the other hand, we expected that the P-wave would remain within this interval during the possible P-Q interval changes and that such changes would be reflected simply as P-wave morphology changes.

All vectors representing P-wave in each of the 12 ECG leads consisting of 70 samples were connected one by one into one vector consisting of 840 samples in total. The obtained vector represented P-wave of one ordinary cardiocycle. All 840 sample-long vectors representing P-waves in one ECG recording during an orthostatic test were joined into the following matrix:

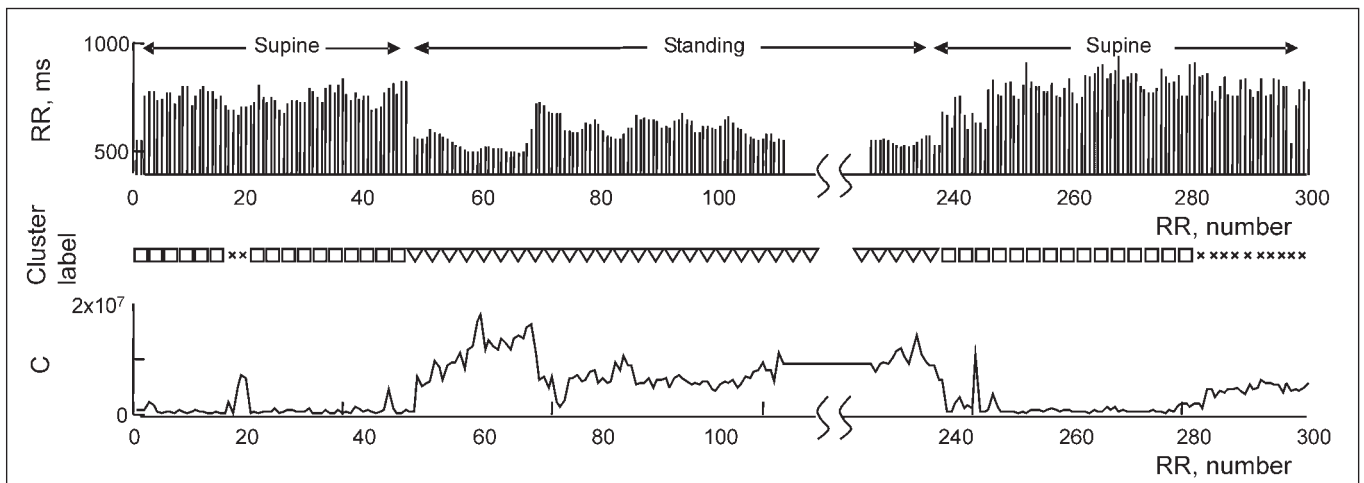


Fig. 1 Typical changes in the R-R interval during the orthostatic test (top graph), the labels of clusters to which estimates of P-wave belong (middle graph) and the values of the criterion C (Formula 7) of quantitative evaluation of the changes in the P-wave shape (bottom graph)

$$\mathbf{X} = \begin{matrix} x_{1,1} & x_{1,2} & \dots & x_{1,n} \\ x_{2,1} & x_{2,2} & \dots & x_{2,n} \\ \dots & \dots & x_{i,j} & \dots \\ x_{p,1} & x_{p,2} & \dots & x_{p,n} \end{matrix} \quad (3)$$

Here $x_{i,j}$ is the i -th sample of the j -th cardiocycle. p was always 840 whereas n varied from 120 to 150 depending on the number of cardiocycles registered during an orthostatic test. Hence, the shape of the P-wave during every cardiocycle was represented by 840 parameters (samples) whose values varied during an orthostatic test and thereby represented changes in the P-wave shape. The principle component analysis (PCA) was used to reduce dimensionality of this representation. The calculated principal components are ordered so that the first ones retain most of the variation present in all the original variables. A truncated expansion of every vector of samples of the P-wave x from one cardiocycle was performed by using only the first several principal components calculated by means of the PCA from the whole set of cardiocycles. This procedure is also known as Karhunen-Loeve transform [21]. We calculated the basis functions (principal components) as eigenvectors of covariation matrix R_x :

$$\mathbf{R}_x = \mathbf{E} \left[\mathbf{X} \cdot \mathbf{X}^T \right] \quad (4)$$

Calculation of the covariation matrix was performed by using MatLab™ function “COV” which gave mathematical expecta-

tion E after removing the mean from each column.

For determination of the minimal, yet sufficient, number of principal components (basis functions) for truncated expansion of P-wave samples array, we used the cross-validation criterion based on the parameter called PRESS (PREdiction Sum of Squares) [18]:

$$PRESS(m) = \sum_{i=1}^n \sum_{j=1}^p ({}_m\hat{x}_{ij} - x_{ij})^2, \quad (5)$$

where ${}_m\hat{x}_{ij}$ is the estimate of the original data set based not on all but the first m basis functions, x_{ij} – the original data set. Such procedure is computationally expensive for large data sets. Some authors [22] showed that for large data sets $PRESS(m)$ is almost equivalent to $\sum_{k=m+1}^p l_k$, where l_k is eigenvalue corresponding to the eigenvector (basis function) ϕ_k . As our data sets are comparatively large (more than 100 cardiocycles containing 840 samples and 840 principal components calculated), we used this simplified calculation. To decide on whether or not to include m -th eigenvector (the basis function), we used the ratio proposed by Wold, 1978 [23]:

$$PR(m) = \frac{PRESS(m)}{PRESS(m-1)}. \quad (6)$$

Unfortunately, a strict selection of the number of principal components to be included in truncated expansion remains problematic. As described previously [24],

the number was determined at which the specific non-smooth point was visually observed in the dependency of criterion PR (►Formula 6). The number of principal components corresponded to the number of weight coefficients w of the basis functions in graphs in which visual correlation with the changes in the heart rhythm evoked by the orthostatic test was observed. Changes in the coefficients of the basis functions quantitatively represented changes in the P-wave shape. As long as the basis functions (principal components) remained orthonormal, the sum of squares of differences between the initial values of the coefficients in the motionless supine position and the values during orthostasis or in the standing position quantitatively represented P-wave changes during the test. We calculated this criterion as following:

$$C_j = \sum_{i=1}^k (w_{i,j} - w_{i,init})^2, \quad (7)$$

where $w_{i,j}$ is the coefficient to the i -th basis function of the j -th cardiocycle, $w_{i,init}$ is the initial coefficient i -th basis function, determined as average of this coefficient during the first 20 cardiocycles. k is the minimal yet sufficient number of basis functions to be used for truncated expansion, determined by using criterion PR .

We performed a separate PCA procedure for the P-wave samples matrix of every recording during an orthostatic test.

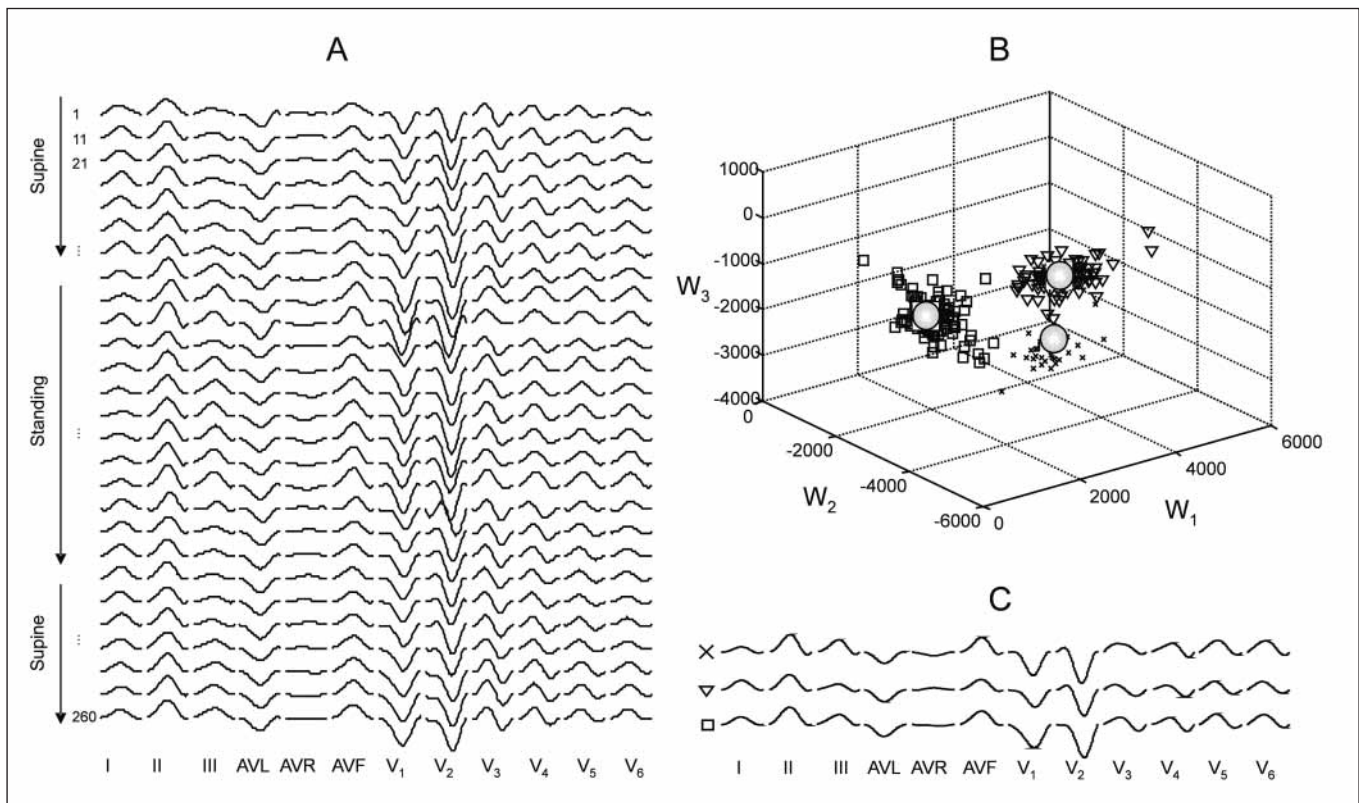


Fig. 2 The variety of the P-wave shape of all 12 ECG leads during typical recording (every 10th cardiocycle is presented on A), three-dimensional representation of P-wave shape using calculated coefficients of the first three principal components (B), P-wave shapes calculated using coordinates of the weight centers of coefficient clusters (C)

3. Results

In the recordings of all patients we observed specific R-R interval changes of different magnitude that were related to the orthostatic test. Changes in the P-wave shape could be visually detected during the orthostatic test. The top graph in ▶Figure 1 illustrates typical changes in the R-R interval during the test. The variety of the P-wave shape of all 12 ECG leads is shown in ▶Figure 2A. For a greater clarity, only the P-waves of every 10th cardiocycle are presented in the figure. The time scale of the protocol of the test is shown on the left-hand margin. Visually, only a small variation in the shape of P-wave can be observed in the stable supine and the stable standing positions. Substantial differences in the P-wave shape are noted when the shapes of cardiocycles in the supine position versus those in the standing position are compared.

The values of criterion PR (▶Formula 6) for selection of minimal yet suffi-

cient number of principal components demonstrated a similar dependency in all recordings with specific non-smooth point at seventh principal component. Therefore we selected first seven principal components for truncated expansion of all recordings.

The values of the criterion C (▶Formula 7) of quantitative evaluation of the changes in the P-wave shape are shown in ▶Figure 1 below the RR intervals. Marked changes in the values of this criterion visually correlated with the changes in the bodily position during the orthostatic test which enabled the detection and evaluation of changes in the P-wave (by using this criterion).

The calculated coefficients of the principal components quantitatively describe the shape of every P-wave in the recording as a point in n -dimensional space, where n is the number of principal components used for truncated expansion. ▶Figure 2B is an appropriate illustration. Yet only the first three, and not seven coefficients used for

this recording, are presented due to plotting possibilities. Visually we can determine at least three clusters of these points. The hierarchical clustering method according to Euclidean distance (MatLab function *clusterdata*) showed three clusters. We used testing of statistical hypothesis of uniformity [25] to identify the clusters. Points belonging to them are marked as crosses, triangles and squares. Labels of clusters to which estimates of P-wave belong are shown on graph of ▶Figure 1, below RR intervals. As we can see, most of the shape estimates of P-waves registered in the supine position belong to the cluster marked with squares. Shape estimates of P-waves registered in the standing position mainly belong to the cluster marked with triangles. Some shape estimates of P-waves registered in the supine position at the end of recording belong to the cluster marked with crosses. All small fluctuations of P-wave shape around three major positions form some n -dimensional body (cloud) covering all points belonging to each cluster. Competi-

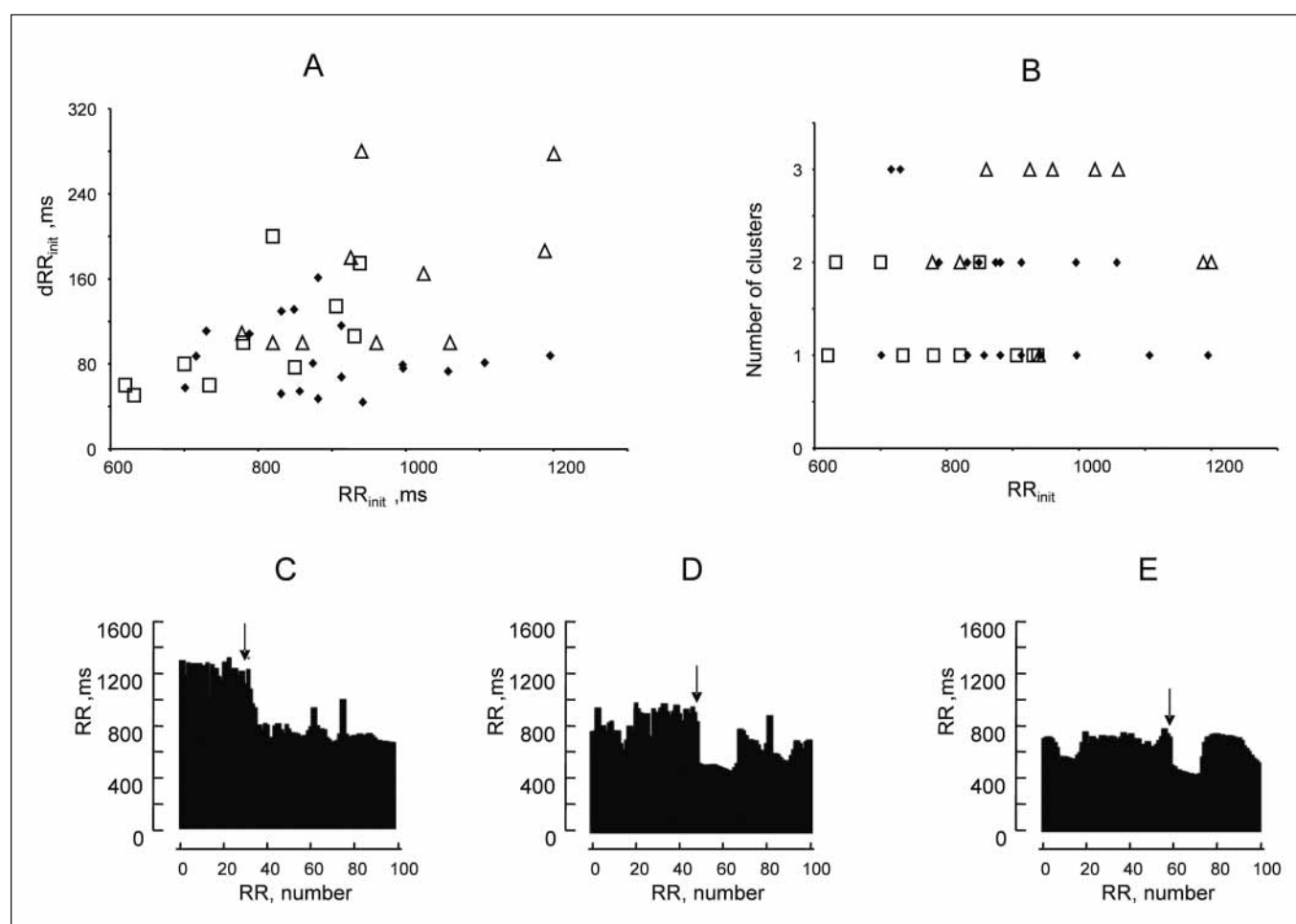


Fig. 3 The dependency of acceleration of heart rhythm (RR shortening) as compared to the initial heart rate (A); number of clusters of P-wave shape representations in all the recordings plotted against the initial value of RR intervals (B); three fragments of RR intervals from three recordings: from most noticeable acceleration (C), through (D) till least noticeable acceleration (E). All the three graphs only cover the moment of orthostasis pointed by the arrow, but do not cover the moment of lying down again.

tive Neural Network realized in MatLabTM was used to determine values corresponding to the centers of such n -dimensional body. Coordinates of these weight centers taken as values of coefficients of basis functions could represent average P-wave shape representing each cluster (presented in ► Fig. 2C).

Changes in the heart rate were noted in all of the recordings. However, not all of the recordings revealed a typical acceleration reported by many authors. A high amplitude of acceleration was found in the recordings with slow initial heart rate. Three fragments of RR intervals from three recordings presented in ► Figure 3 (C–E) illustrate that. In the left-hand graph (C) we can see acceleration from RR of about 1300 ms to below 800 ms, while in the

right-hand graph (E) we can see about 750 ms initial RR in supine position followed by a short-term acceleration to about 420 ms. All the three graphs only cover the moment of orthostasis pointed by the arrow, but do not cover the moment of lying down again. Decelerations in the medium and the right-hand graphs do not correspond with the patient's lying down. Such dependency was only observed in the recordings taken from older patients (groups 2 and 3). The dependency of acceleration as compared to the initial heart rate is presented in ► Figure 3A. The highest amplitude of acceleration was observed in the patients with transient periods of atrial fibrillation (group 3, marked by triangles). Not all representations of the P-wave shapes in 7-dimensional space of

coefficients of principal components formed several clusters as in the given example. In some recordings they formed one cluster only. In ► Figure 3B the number of clusters in all the recordings is plotted against the initial value of RR intervals. We expected that slower heart rate in the supine position would be a result of a higher parasympathetic tonus and more pronounced changes in the heart rate would be present during the orthostatic test. This would possibly involve more pronounced changes in the shape of P-wave and a bigger number of clusters of P-wave shape representations, or at least a clearer distinction between the clusters. However, we observed just a visual negative correlation between the heart rate in the supine position and the number of clusters in the recordings of the control

group (marked by diamonds). The representations of P-wave shapes in older patients with transient periods of atrial fibrillation formed two or three clusters (marked by triangles) whereas only one or two clusters were observed in the recordings of healthy older people (group 2, marked by squares).

4. Discussion

The suggested method based on the principle component analysis gives a possibility of quantitative evaluation of P-wave shape changes correlating with the changes in the heart rate during an orthostatic test. Digitized samples of P-waves from all 12 leads joined into one single vector give an abundant but comprehensive representation of excitation spread in the atria during each cardiocycle. The principal components calculated from the ensemble of such vectors concentrate all variation present in the whole recording. Therefore, the proposed criterion C (►Formula 7) is a representative estimate of P-wave changes reflecting all possible variations in all of the 12 leads. Representation of the P-wave shapes by values of coefficients of principal components as a point in multidimensional space revealed new possibilities for a more detailed analysis of P-wave morphology and interpretation of the results. It is possible that clusters of points represent particular positions of the true pacemaker in the right atria. Dimensions of the cluster or the ‘cloud’ of points in the multidimensional space could be determined by many factors: signal noises, heart axis movements during respiration, etc. However, at the moment we have no strong evidence supporting any of mentioned factors. Difference in number of clusters found in our recordings could be explained by varying efficiency of the autonomic heart rate control. We have a big range of one to three clusters in young healthy persons (group 1) and only 1 or 2 clusters in healthy adult persons (group 2). It complies with the data on age-related decrease in the efficiency of the autonomic heart rate control [26]. Two or three clusters in group 3 recordings show an increased vagal activity that could be associ-

ated with atrial fibrillation [27]. We did not attempt at constructing universal basis functions (principal components) by pooling all P-wave ensembles from all recordings as this would require calibration in terms of determination of anatomical and physical locations of the true pacemaker during registration. Irrespective of the fact that the registering devices were well calibrated, differences in the amplitude of signals in different recordings also appeared due to physical differences in the bodies of the investigated persons. It has a crucial influence and makes a further ‘universal’ analysis impossible. The calibration of the method could be done by using direct electrical stimulation of particular atrial zones, possibly by using a catheter navigation system, such as CARTO® or similar. Afterwards, the tracking of the exact location of the true pacemaker could be done non-invasively and “on line”.

5. Conclusions

The quantitative evaluation of changes in the ECG P-wave evoked by an orthostatic test by using the method of principal component analysis yields some valuable diagnostic information on the functionality and the efficiency of the autonomic heart control.

A detailed analysis of the quantitative estimates of the ECG P-wave shape could reveal the potential mechanisms of the heart rhythm control.

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