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ECG based prediction of Atrial Fibrillation using Support Vector Classifier

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Original scientific paper

In patients undergoing Coronary Artery Bypass Grafting (CABG) surgery postoperative atrial fibrillation (AF) occurs with prevalence of up to 40%. The highest incidence is between the second and third day after the operation. Following cardiac surgery AF causes various complications, hemodynamic instability, and can cause heart attack, cerebral and other thromboemolisms. AF increases morbidity, duration and expense of medical treatment. This study aims to identify patients at high risk of postoperative AF. An early prediction of AF would provide a timely prophylactic treatment and would reduce incidence of arrhythmia. Patients at low risk of postoperative AF could be excluded from the side effects of anti-arrhythmic drugs. The investigation included 50 patients in whom lead II electrocardiograms were continuously recorded for 48 hours following CABG. Univariate statistical analysis was used in the search of signal features that might predict AF. The most promising identified features were: P wave duration, RR interval duration and PQ segment level. On the basis of these a nonlinear multivariate prediction model was made deploying a Support Vector Machine (SVM) classifier. The prediction accuracy was found uprising over the time. At 48 hours following CABG; the measured best average sensitivity was 95.9% and specificity 93.4%. The positive and negative predictive accuracy were 88.9% and 98.8%, respectively and the overall accuracy was 94.6%. In regard to the prediction accuracy, the risk assessment and prediction of postoperative AF are optimal to be done in the period between 24 and 48 hours following CABG.

Key words: Post-operative atrial fibrillation, Coronary artery bypass grafting (CABG), Cubic spline baseline correction, PQ segment level

Predviđanje postoperacijske fibrilacije atrija korištenjem SVM klasifikatora. Postoperacijska fibrilacija atrija (AF) pojavljuje se u oko 40% pacijenata podvrgnutih operaciji aortokoronarnog premoštenja (CABG), s najvećom učestalosti pojavljivanja oko trećeg dana nakon operacije. Postoperacijska AF može stvoriti brojne komplikacije poput hemodinamske nestabilnosti, srčanog udara, cerebralnih i drugih tromboembolija; povećava morbiditet, trajanje i troškove liječenja. Studija ima za cilj rano otkrivanje pacijenta sa visokim rizikom razvoja postoperacijske AF, što bi osiguralo pravovremenu profilaktičku terapiju i smanjilo učestalost aritmije, dok bi pacijenti sa niskim rizikom razvoja postoperacijske AF bili pošteđeni nuspojava antiaritmičkih lijekova. Podatkovni skup uključuje 50 pacijenata, snimanih II standardnim odvodom elektrokardiografa, kontinuirano u razdoblju od 48 sati nakon operacije. Univarijatna statistička analiza korištena je za određivanje parametara signala koji bi mogli predvidjeti AF, te su kao najznačajniji određeni: trajanje P vala, trajanje RR intervala i razina PQ spojnice; na temelju kojih je izveden nelinearni multivarijatni predikcijski model zasnovan na SVM klasifikatoru. Ukupna predikcijska točnost modela povećava se s vremenom. U 48. satu nakon operacije najbolje prosječne značajke iznosile su: osjetljivost 95,9%, specifičnost 93,4%, pozitivna prediktivnost 88,9%, negativna prediktivnost 98,8% te ukupna točnost 94,6%. Prema rezultatima predikcijske točnosti, procjenu rizika i predikciju postoperacijske AF optimalno bilo bi načiniti u periodu između 24-tog i 48-og sata nakon operacije ugradnje aortokoronarnih premosnica.

Ključne riječi: postoperacijska fibrilacija atrija, operacija ugradnje koronarnih premosnica (CABG), korekcija nulte linije kubnom krivuljarnom (splajn) interpolacijom, depresija i elevacija razine PQ spojnice

1 INTRODUCTION

Postoperative atrial fibrillation (AF) is the most common supraventricular arrhythmia and postoperative complication occurring with the prevalence between 30 - 40 % after the coronary artery bypass grafting (CABG) surgery, with the highest rate of incidence on the third postoperative day. The undergoing patients specifically do not have prior preoperative AF history [1].

AF provokes many clinical complications, induces a hemodynamic instability, reduces a cardiac output 15 –

30 %, enlarges a risk of thromboembolic incidence like myocardial infraction, cerebrovascular accident and other organ damage due to systemic emboli [2], moreover AF increases mortality, but also the duration and expenses of hospitalization.

Generally, in the clinical practice patients are only symptomatically treated. In the case of AF onset the first step in medical treatment is the decrease of high ventricular frequency and implementation of anticoagulant therapy for the prevention of thromboembolic risk, while the second step in the medical treatment is the preparation of patient for the potential pharmacological or electrical cardioversion.

The aim of this study is to develop a prediction model for an early detection and identification of patients prone to the onset and development of post-operational atrial fibrillation (AF group) that would provide well timed prophylactic therapy and reduce the incidence of postoperative AF. Meanwhile, the patients prone to maintain a sinus rhythm (SR group) would be excluded from the side effects of the antiarrhythmic drugs.

The etiology of AF is not completely understood, but it is assumed that is provoked by the postoperative trauma, inflammation and above all the atrial ischemia due to surgical injury of the myocardium [3-5]. The physiological mechanism that induces AF is primary an emergence of ectopic foci due to late depolarization that reaches the activation threshold or due to a higher depolarization frequency which effects a mechanism of higher automaticity. After the induction of AF the mechanisms that maintain AF are a re-entry in single or multiple reentrant circuits and electrical remodeling of physiological properties of atrial tissue. The physiological properties modified by the electrical remodeling are the shortening of action potential duration (thus the shortening of atrial refractory period) and the decrease of conduction velocity of atrial impulses [6].

Lausanne Heart Group has developed a bioelectrical (biophysical) model for computation and simulation of atrial activity during a normal sinus rhythm, atrial fibrillation and atrial flutter. For a successful induction and maintenance of AF the authors had a simulation protocol which included: 1) modification of electrophysiological properties of atrial tissue and 2) simulated short pacing of an appendage of the left atrium. The modified electrophysiological properties included: a) shortening and creating heterogeneity of the action potential duration (therefore an atrial refractory period as well) and b) decreasing of atrial conduction velocity [7].

The decreased atrial conduction velocity leads to prolongation of P wave duration [8], meanwhile our assumption is that the shortening of atrial action potential and the shortening of atrial refractory period cause premature atrial activation which leads to the change in elevation or depression of PQ segment level (Fig. 1).

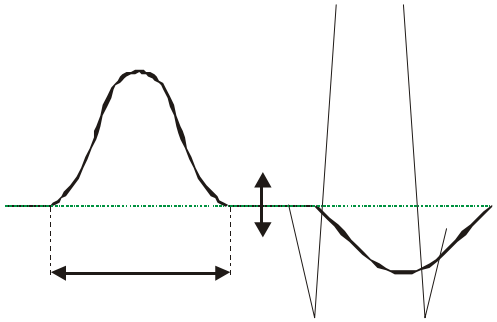

Fig. 1. Concept of prolongation of P wave duration and elevation / depression of PQ segment level. The first wave represents atrial depolarization (P wave), the second wave represents atrial repolarization (masked by QRS complex).

Some earlier studies have attempted to find risk factors and AF predictors at different demographic and clinical data acquired and monitored before, during or following the surgery, however none have showed a statistical significance to be clinically used as an independent AF predictor [1]. Meanwhile, other earlier studies based on standard ECG (lead II or V1) or signal averaged ECG (SAECG) have shown that it is possible to predict postoperative AF with some degree of accuracy [9]. All studies based on ECG were focused only on the P wave measuring, e.g. duration, variation of duration or spectral content of the P wave, neglecting PQ interval that covers some part of atrial repolarization and atrial late potentials.

2 METHODS

2.1 Dataset

The patients' electrocardiograms were recorded at the University Hospital Center Zagreb within the Department of Cardiac Surgery, with the approval of patients and the institution. Lead II signals of the standard 12-lead ECG were recorded, continuously, for 48 hours following CABG. Lead II was chosen since atrial activity is most clearly observable in this lead due to the highest ratio between P wave peak and R wave peak. ECG acquisition was made by means of the HP patient monitor 78330A and an ADC card (Measurement Computing CIO-DAS08 / JR). The sampling frequency was 1000 Hz, with the voltage resolution of 0.488 μV. The acquisition has required 7.2 MB / hour of data space for uncompressed ECG, which over 48 hours adds up to 360 MB / patients. In total, more than 2500 hours of the high time and amplitude resolution electrocardiograms were recorded.

In the earliest studies, ECG recordings over episodes lasted just a few minutes, while generally not specifying

the time of ECG acquisition with reference to the termination of CABG procedure [1,9]. In our approach high-resolution ECG monitoring was performed over an extended episode (up to 48 h) in the search for potential trends in the quality of prediction.

Simultaneously with our recording, experienced medical personnel monitored the patients in parallel and detected AF separately by the Philips CMS patient monitoring system. AF was defined as fibrillation or flutter lasting more than 1 hour. For the patients who developed AF during the recording episode, only a part of ECG during sinus rhythm, until the onset of AF, was included in the analysis.

Data were collected from 50 patients, of whom 14 patients (28%) developed AF during or after the recording, and 36 patients (72%) did not develop AF, neither during nor after the recording. The patient population consisted of 70% males and 30% females, of mean age 64.8 $\pm$ 6.3 (Table 1.). The group that developed AF post-operatively (AF group) consisted of 58% males, 42% females, of mean age 65.9 $\pm$ 3.5 (Table 1.). The patients that maintained sinus rhythm (SR group) consisted of 72% males, 28% females, of mean age 60.9 $\pm$ 6.4. The age difference between the groups was examined and was not found significantly different.

Table 1: Study patients.

Group	Male	Female	Age
AF group	58%	42%	65.9 ± 3.5
SR group	72%	28%	60.9 ± 6.4
Population	70%	30%	64.8 ± 6.3

2.2 Data processing

The electrocardiograms were processed using custom made P-QRS-T detector based on dyadic wavelet decomposition. The local maximums and minimums at the wavelet scales specify the points of fast and sharp changes in the ECG signal [10]. Dyadic wavelet decomposition of ECG allowed an excellent time localization of frequency components and featured robust detection, high accuracy and precision in determination of onset, peak and ending of respective waves. The P-QRT-T detector was designed and based on the template of Li, Zeng, Tai detector [11] with more additional custom made modifications (different time, frequency and amplitude thresholds, adaptive limits etc).

The most important segment of ECG for this study was the P wave. For P wave detection and segmentation, the P-QRT-T detection algorithm identifies five characteristic P wave markers: timing onset (Ponset), magnitude of apex (Peak), ending or offset (Poffset), maximal up-slope (Pslope1) and maximal down-slope (Pslope2) as showed in Fig. 2. These points were used for the subsequent measurement of different P wave features and their trends [9,12].

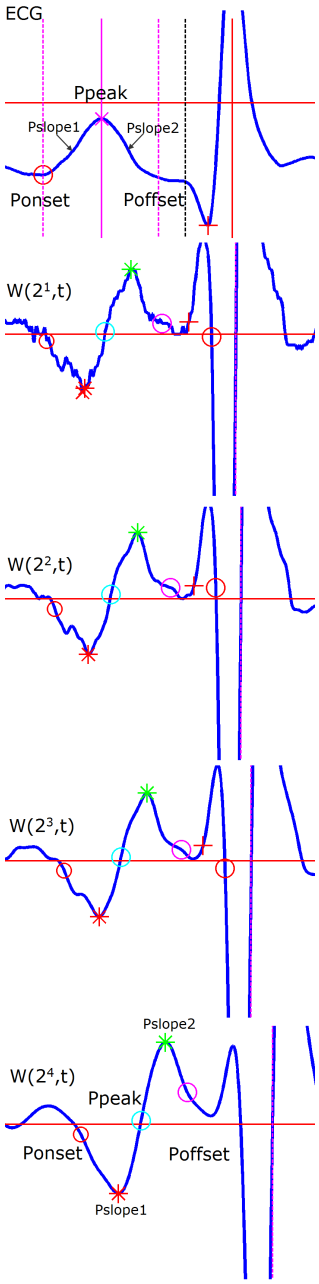

Fig. 2. P wave segment of ECG and related dyadic wavelet decomposition scales.

The important part of ECG processing was the estimation and correction of the baseline drift, which is a required condition for an accurate and precise measurement of the amplitudes of any ECG segment (e.g. PQ segment level, P wave amplitude, R wave amplitude, etc.). The estimation

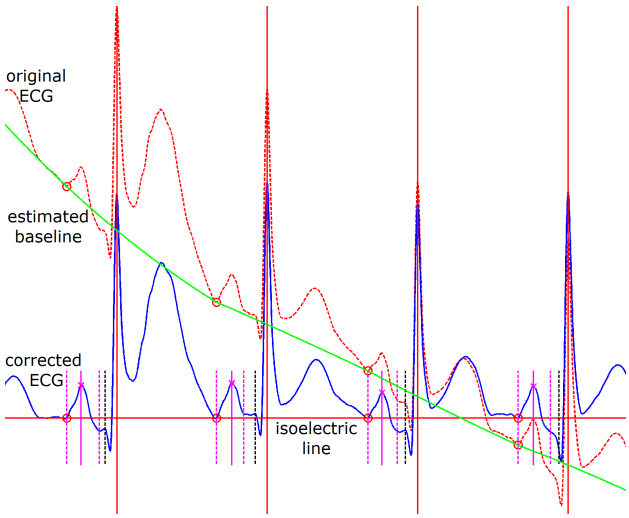

Fig. 3. Example of the baseline specification and its correction for drift. Original ECG (dash line), estimated baseline drift (descending solid line), P wave onset (circle), corrected ECG (solid line), isoelectric line (straight solid line).

of the baseline drift was made with a cubic spline interpolation through the onset points of successive P waves (Fig. 3). Afterwards, the estimated baseline was subtracted from the original ECG and the corrected ECG with the isoelectric line is obtained. The point of P wave onset was chosen for the cubic spline interpolation since it is the most quiet? and stable point in the whole electrocardiogram [13].

2.3 Measured features

For each individual P wave a vector consisting of 40 different measured features was determined (Table 2). Due to the huge dataset, every electrocardiogram was segmented into 15 minutes subsequent episodes and for each episode the mean value and the standard deviation of every single measured feature was calculated.

The measured features are subdivided into the subcategories as follows: absolute and normalized time features (Fig. 4), absolute and normalized amplitude features (Fig. 5), amplitude-time features and wavelet features.

Normalized time features Several timing features are correlated with the RR interval; therefore, all time features were normalized with the mean RR duration over the episode (PonPoff_RR, PonQon_RR, PpeakRpeak_RR).

Amplitude features The potential level of the PQ segment (PQlevel) was specified by the mean value of the signal in the interval between the ending of the P wave (Poffset) and the beginning of the Q wave (Qonset). It reflects the beginning of the atrial repolarization and it is not electrically silent as frequently stated [13].

Table 2: Measured features.

Feature	Description
Time features:	
PonPoff	P wave duration
PonPpeak	1st half of P wave duration
PpeakPoff	2nd half of P wave duration
PoffQon	PQ segment duration
PonQon	PQ interval duration
PpeakRpeak	PR interval duration
Pslope1Pslope2	Pslope1 - Pslope2 interval duration
RR, HR	RR interval duration and heart rate
Normalized time features:	
PonPoff_RR	P wave duration (normalized with RR)
PonQon_RR	PQ interval duration (normalized with RR)
PpeakRpeak_RR	PR interval duration (normalized with RR)
Amplitude features:	
PQlevel	Level of PQ segment
Pamp, Ramp	P wave and R wave amplitude
Qonamp	Level of Q wave onset (Qonset)
Poffamp	Level of P wave ending (Poffset)
Normalized amplitude features:	
relPQlevel_Pamp	Level of PQ segment (normalized with Pamp)
relPQlevel_Ramp	Level of PQ segment (normalized with Ramp)
relPamp_Ramp	Ratio between amplitude of P wave and R wave
Amplitude-time features:	
Pslope1	Maximal positive slope of P wave
Pslope2	Maximal negative slope of P wave
Aonoff	P wave surface area
relPslope1Pslope2	Ratio of maximal positive and negative slope
Wavelet features:	
Wenergy	P wave energy at 5 different wavelet scales
relWenergy	Relative P wave energy regarding to total
Wentropy	Entropy, measure of P wave energy dispersion

Normalized amplitude features The heart position relative to the electrode position influences the value of all measured amplitude features. In order to compensate this effect several amplitude features were normalized with respect to the P wave or R wave amplitude (relPQlevel_Pamp, relPQlevel_Ramp, relPamp_Ramp).

Amplitude-time features The maximal positive slope (Pslope1) and the maximal negative slope (Pslope2) of the P wave were determined by using the wavelet transform. The wavelet coefficients of Pslope1 and Pslope2 are linearly proportional to the values of the ECG slopes expressed in mV/ms units [12]. The P wave slopes depend on the propagation velocity of atrial impulses, the premature onset of atrial repolarization and the P wave amplitude.

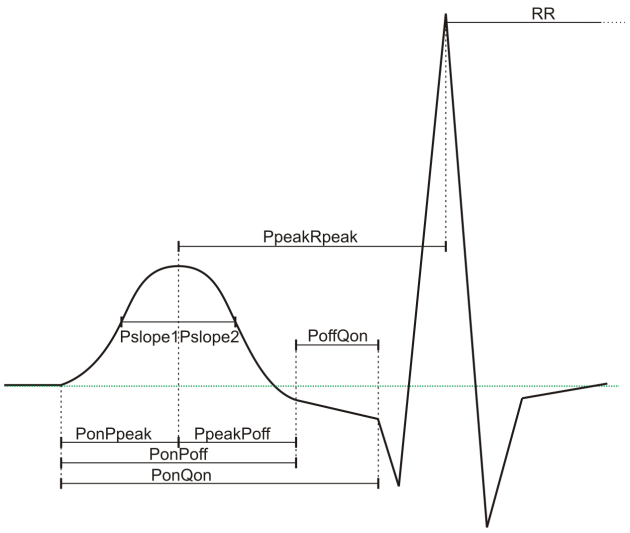

Fig. 4. Time features.

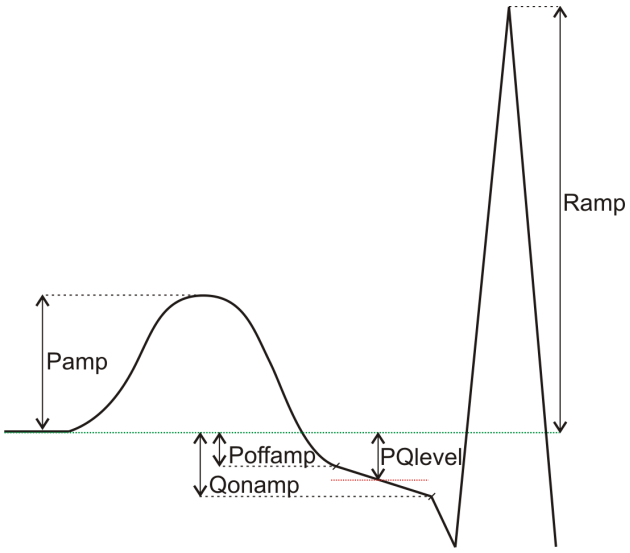

Fig. 5. Amplitude features.

Wavelet features Wavelet decomposition of the ECG can be viewed as a filtering of the signal with the filter bank consisting of bandpass filters (wavelet scales) [14]. Different parts of the spectrum contain different parts of the P wave. Because of this, P wave energy was measured at different wavelet scales (Wenergy), as was the ratio of the energy at each wavelet scale and the total P wave energy (relWenergy). Entropy is a measure of P wave energy dispersion at different parts of spectrum.

2.4 New feature - PQ segment level

The level of PQ segment (Fig. 6) has not been fully clinically explored. The PQ level elevation or depression is a characteristic very similar to a well accepted measure of ST segment level. The level of PQ segment is often associated with an acute pericarditis, as was described by Spodick and the authors in the pioneering works [15]. The same authors concluded that the change in the level of PQ segment indicates an irregular atrial repolarization probably caused by defects in subepicardium part of the atrium due to inflammation caused by pericarditis.

The activity of atrial repolarization for the time of PQ segment can be indentified only if the baseline (zero line) drift is properly estimated and corrected (Fig. 3). Usually, the PQ interval is not long enough to cover the end of atrial repolarization, due to the onset of ventricular depolarization. Therefore, the part of PQ segment is masked and is not completely visible, but the visible part of PQ segment indicates the direction and convergence towards isoelectric line, indicating the completion of atrial repolarization [13]. This observation is supported by the recent studies of atrial repolarization based on a biophysical model which implies that the duration of action potentials in the atrium is shorter than those that are commonly taken as a reference [7].

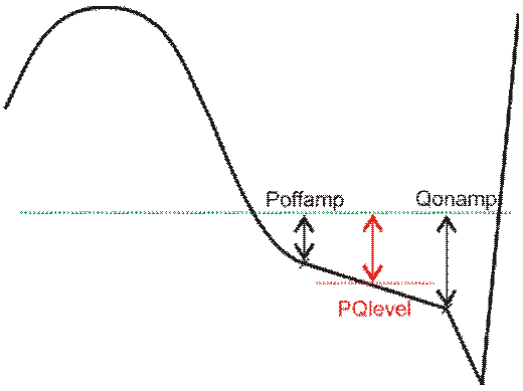

Fig. 6. PQ segment level.

2.5 Statistical analysis and modeling

The complete data set comprised the data of 50 patients. For each patient, the 48 h ECG was divided into 15 min episodes, yielding a total of 192 episodes. For each episode, segment by segment, we conducted two sample t-tests ($p < 0.05$) for normally distributed data and the non-parametric Wilcoxon rank sum test (Mann–Whitney U-test, $p < 0.05$) for non-normally distributed data. This test was used to test univariate group differences between the mean or median values over the individual episodes of the 40 measured variates.

For each of the features listed in Table 2, over each of the 192 successive episodes the results of the statistical tests (independent two sample t-tests and Wilcoxon rank sum test) were scored as 1 if significance was observed,

else as 0. For each feature the cumulative score over the 192 episodes was inspected. The parameter that had the highest sum of rejected null hypotheses was considered the most significant. In this way, the RR interval and P wave duration were identified as the most promising univariate predictors of AF. [9].

In the standard statistical tests the PQ segment level did not show a significant difference in the mean or median values between groups. However, the inspection of estimated density distributions of both groups suggested clear differences based on a bimodal distribution observed in the AF group, compared to a unimodal distribution in the SR group (Fig. 7.). The AF group showed two subgroups of patients (AF1 and AF2): one with higher depression of PQ segment level (-52±18 μV) and the other with a higher elevation of the PQ segment level (-7±9 μV), relative to the level in the SR group (-29±30 μV) [9]. To resolve the controversy the patients of the bimodal AF group were divided into the two unimodal subgroups: the AF1 subgroup with the average level of the PQ segment lower than -27 μV and the AF2 subgroup with the average level higher than -27 μV.

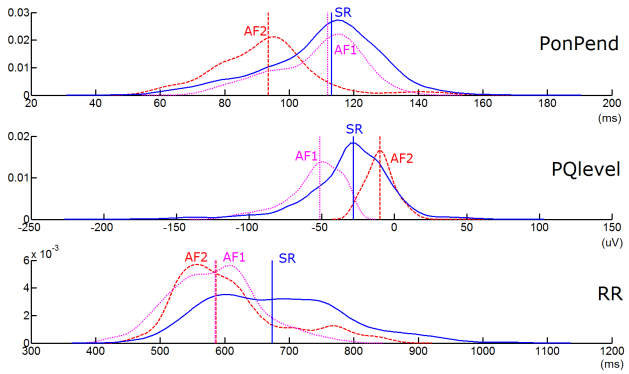

Fig. 7. Probability density functions for three dominant predictors: P wave duration (PonPoff), level of PQ segment (PQ level) and heart rate (RR), for: SR group (solid line), AF1 subgroup (dotted line), and AF2 subgroup (dashed line). Vertical lines mark the median values for each group and subgroup.

Theoretical and experimental results from the domain of pattern recognition suggest that the ratio of patients (sample size) per class M versus the number of features or predictors of n (dimensionality) to be in the range $M/n \geq 3 \div 5$or higher [16]. So, if we have smaller AF class with sizes M = 14 patients, the largest number of features (predictors) used in the prediction should be in the range of up to $n \leq 3 \div 5$ predictors, otherwise the result will be too perfect separation of classes, and the classification model will be overlearned, overfitted or overparameterized.

Here, we decided to test the application of linear models based on Fisher linear discriminant analysis (FDA) and nonlinear models based on Support Vector Machine (SVM) classifier. FDA and SVM models had 7 different configurations: 3 univariate (having one predictor), 3 bivariate (having combinations of two predictors) and 1 trivariate model (having all three predictors: RR interval, level of PQ segment and P wave duration) (Fig. 8).

For a comparison of prediction models in the analysis we included two models that do not implement any prediction – if all patients are classified prone to AF (NOMODEL AF) or if all patients are classified prone to hold SR rhythm (NOMODEL SR) (Fig. 8).

All prediction models, linear and nonlinear in this study were first trained on a randomly selected training (learning) sample, which consisted of 10% of all data. After the learning (training) of the model the remaining 90% of the data from the beginning to the end of the recording was used as a testing sample for a cross-validation. With this approach, the results presented here do not represent a post hoc analysis because all models are evaluated on the testing sample, which differs from training or learning sample.

In the classification Fisher linear discriminant analysis (FDA) models use a discriminant function, which is actually the separation hyperplane that separates the AF and SR groups according to the values of predictors. Discriminant function has the form $f(x) = \langle w \cdot x \rangle + b \geq 0$ for AF group, and $f(x) = \langle w \cdot x \rangle + b < 0$ for SR group where **w** is the separation hyperplane, **b** is a shift of hyperplanes and **x** is a vector with the values of predictors.

Traditionally neural networks approach has a generalization problem, producing models that can overfit the data. Support Vector Machines (SVM) approach embodies structural risk minimization principle, which has shown to be superior to traditional empirical risk minimization principle employed by conventional neural networks. SVM have greater ability to generalize, which is the goal in statistical learning and empirical data modeling.

Support vector machine classifier maps the input data into a higher dimensional feature space by a suitable choice of kernel function$K(x, y) = \Phi(x) \cdot \Phi(y)$ that can be e.g. linear, polynomial, radial basis function etc. The goal is to find the optimal separating hyperplane in a higher dimensional feature space that separates without error and with the maximal distance between the closest vectors known as support vectors.

The optimal separating hyperplane can be obtained as follows:$y = f(x) = sign\left(\sum_i \alpha_i y_i K(x_i \cdot x) + b\right)$, where x represents new data for classification and $D = \{(x_i, y_i), x \in \mathbb{R}^n, y \in \{-1, 1\}\}$ represents training vectors and α_i is Lagrange multiplier from the constrained optimization problem of the support vector classification problem [17].

3 RESULTS

When applied to the subsequent recorded episodes, the nonlinear SVM model revealed a rising trend in the quality of the prediction (Fig, 9,10). Around the second day after CABG when the AF incidences are the most frequent, the prediction model becomes more and more accurate.

The best trivariate (SVM3) prediction the model reaches 48 hours after CABG. At that time, the model has the highest average sensitivity of 95.9 %, specificity of 93.4 %, positive predictive value of 88.9 %, negative predictive value of 98.8% and overall accuracy of 94.6 % (Fig. 9).

The ratio of the average sensitivity (true positive rate) and 1 – specificity (false positive rate) is shown in Figure 10. The curve shows a trend of uprising prediction

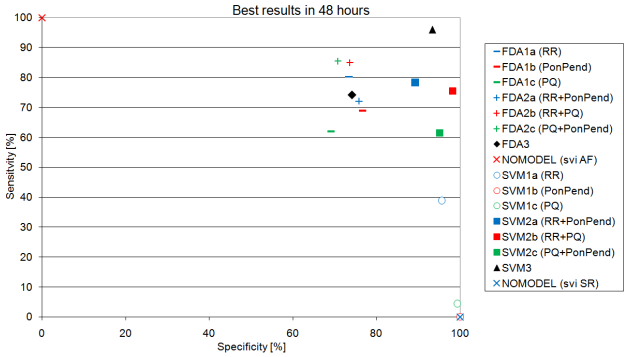

Fig. 8. Specificity vs. Sensitivity of univariate (FDA1), bivariate (FDA2) and trivariate (FDA3) linear models based on Fisher linear discriminant analysis and univariate (SVM1), bivariate (SVM2) and trivariate (SVM3) nonlinear models based on Support Vector Machine classifier.

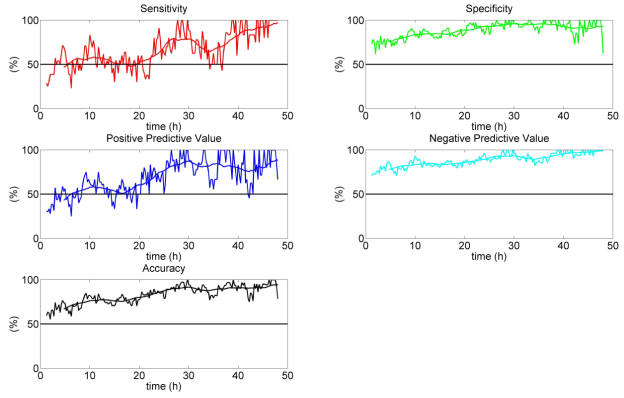

Fig. 9. Prediction quality of the nonlinear method based on a trivariate SVM classifier over time, specified by sensitivity, specificity, positive predictive value, negative predictive value and accuracy (thin lines). The thick lines represent the trends smoothed by a moving average window (involving 16 points) as a more correct trend measure.

quality of postoperative AF in time. The sensitivity and specificity of the model is improved in time. In the period 0-24 hours after the surgery prediction can be described as "fairly good" because the curve is located between the ROC curve areas 0.80-0.60. In the period 24-48 hours after the surgery the prediction becomes "excellent" since the curve is located between the curve surface 1.00-0.90.

Generally, the risk assessment and prediction of postoperative AF should be done in the period 24-48 hours after the surgery of coronary artery bypass grafting. It is assumed that in the period 0-24 hours after surgery, the mechanisms that lead to postoperative AF are not yet sufficiently developed, and it is not possible to predict AF with satisfactory accuracy. Also, the prediction of AF in the period of 24-48 hours after the operation meets the criteria of early detection of AF risk, thus leaving enough time for a good prophylactic treatment.

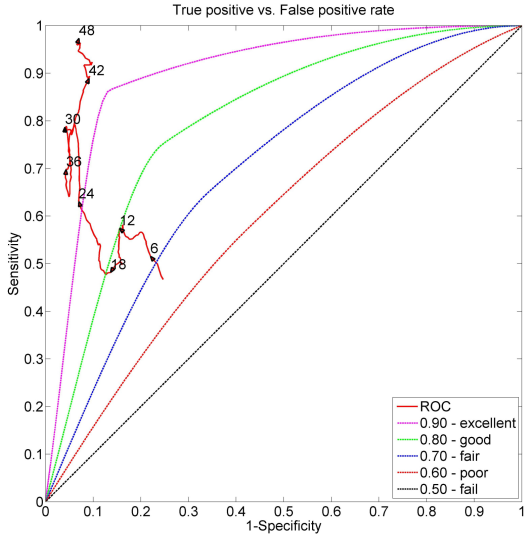

Fig. 10. True positive versus false positive rate of the nonlinear prediction model based on the trivariate SVM classifier. The solid line shows an uprising trend in AF prediction quality with time. Arrows show the trend direction with time. The numbers next to the arrows represent the time in hours with reference to the termination of CABG.

4 CONCLUSION

RR interval (heart rate), P wave duration and PQ segment level are defined in this paper as the three ECG features that are important for assessing the risk of postoperative atrial fibrillation.

The same features could be applied generally to assess the risk of atrial fibrillation in the general population. It is expected that the sensitivity and specificity of the same

prediction model could be higher than presented in this paper. The reason lies in the fact that it is easier to classify and discriminate patients prone to develop AF from the healthy populations. In previous studies, greater efficiency and AF prediction quality was reported by a group of authors who had compared the normal healthy population with a population of patients prone to develop AF [18-19]. Another group of authors, who deal with the prediction of postoperative AF in a population where both AF and SR group of patients underwent the coronary artery bypass grafting surgery, reported much lower prediction quality [8,20-26].

It was observed that the morphology of P wave is very unstable and variable over time, especially in the AF group. In some patients in AF group abnormal P wave was observed at the beginning of the recording and the abnormal morphology stayed consistent throughout the remaining part of the recording. In other patients in AF group abnormal P wave was more sporadic in the beginning of the recording and became increasingly frequent in the later episodes.

Since the process of emergence of postoperative AF process is unsteady, variable by nature, continuous monitoring reveals its temporal dynamics.

A different lead system to record ECG signal e.g. optimized atriocardiogram (OACG) would optimally describe the electrical activity of atrium before and during AF since it contains more independent lead information than standard leads system [27].

The features of the electrocardiogram in assessing the risk of postoperative AF are defined. The model for predicting postoperative AF based on the analysis of electrocardiograms is developed and is statistically evaluated. The developed prediction algorithm allows prediction of postoperative AF in real time and an appropriate time interval for the prediction of postoperative AF is estimated and recommended.

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