Clinical Characterization by Principal Component Analysis of Stress Test ECG

Giovanni Bortolan[1], Ivaylo Christov[2], Iana Simova[3], Nikolay Dimitrov[4], Irena Jekova[2], Vessela Krasteva[2]

[1]Institute of Biomedical Engineering ISIB-CNR, Padova, Italy
[2]Institute of Biophysics and Biomedical Engineering, Bulg. Acad. of Sci, Sofia, Bulgaria
[3]Department of Noninvasive Cardiovascular Imaging and Functional Diagnostics, National Cardiology Hospital, Sofia, Bulgaria
[4]University Hospital "St Ekaterina", Sofia, Bulgaria

Abstract

The aim of the study is to investigate whether and how QRS-complex and T-wave heterogeneity is influenced by different cardiac risk factors and clinical data.

Digital ECG during stress test was acquired in 106 patients (age 63±10 years, 45 males). Two indices obtained by Principal Component Analysis (PCA): complexity (PCA_1) and non-linear components (PCA_2) were used for the analysis of the heterogeneity of the different clinical groups. Mean, max, and standard deviation values were examined in the study.

Significant difference ($p<0.01 \div 0.05$) between PCA1 of QRS (PCA_1_QRS) was found between subgroups of patients defined according to the presence or absence of angina pectoris, diabetes mellitus, stroke and smokers. Significant difference for PCA_2_QRS was obtained in the presence of angiographically significant coronary artery disease, diabetes mellitus, positive stress test and triglycerides. For the T wave significant difference was found respectively for PCA_1_T in: myocardial infarction, angiographically significant coronary artery disease and gender and for PCA_2_T in: angiographically significant coronary artery disease, percutaneous coronary intervention and gender.

1. Introduction

The principal component analysis (PCA) is a technique that aims to represent a large number of signals by means of a limited number of fundamental values [1]. When applied to digital ECG tracings, the method determines the "principal components" which represent most of the ECG information. The first three eigenvalues of the PCA provide nearly the total energy of the ECG. Since the mathematical procedure calculates fundamental orthogonal components, PCA analysis of the ECG signal is a modern approach, which can substitute in a certain degree the vectocardiography based on the orthogonal X, Y, and Z leads [1].

The study of the heterogeneity of the ventricular repolarization has been implicated by long in the analysis of the genesis of ventricular arrhythmias [2]. Theoretical and experimental studies suggest that ventricular repolarization occurs in a nonlinear and inhomogeneous fashion. Measures of repolarization that take into account the T-wave complexity using PCA should be a useful surface ECG marker of heterogeneity of repolarization.

Whilst the diagnostic [3-5] and prognostic [2,6] value of PCA of the T wave has been demonstrated, the effect of physiological factors on the QRS and T wave complexity is unknown. The T wave shape or polarity can be influenced by age, sex, heart rate, body position, autonomic activity, respiration, temperature, electrolyte concentration, food and mental activity [7-11]. It is possible that these factors can also affect T wave complexity. PCA has been used for the investigation of the effect of heart rate and body position on QRS and T wave complexity [12] and also for the analysis of the post-extrasystolic changes of the T-wave and QRS complex [13].

The aim of the study is to investigate whether and how QRS-complex and T-wave heterogeneity is influenced by different cardiac risk factors and clinical data.

2. Methods and material

2.1. ECG database

We studied 106 patients: age 63±10 years, 45 males, 39 with diabetes mellitus (DM), 85 with AP, 34 with positive stress test, 18 with a history of myocardial infarction (MI), 48 with angiographically significant coronary artery disease (AS-CAD). Controllable risk

Table 1. Distribution of the cardiac risk factors and clinical variables for the whole group of patients. SD – standard deviation; BMI – body mass index; DM – diabetes mellitus; AH – arterial hypertension; MI – myocardial infarction; AS-CAD - angiographically significant coronary artery disease; PCI – percutaneous coronary intervention; n – number.

Clinical variable	Distribution n = 106
Age – mean ± SD	62.8 ± 10.3
Male – n (%)	45 (42%)
BMI – mean ± SD	28.0 ± 4.3
AH – n (%)	96 (90%)
DM – n (%)	39 (36%)
Dyslipidemia – n (%)	87 (81%)
Total cholesterol (mmol/l) – mean ± SD	5.09 ± 1.1
Triglycerides (mmol/l) – mean ± SD	2 ± 1.8
Family history of CAD – n (%)	11 (10%)
Smokers (present or ex) – n (%)	41 (39%)
Angina pectoris – n (%)	85 (80%)
History of MI – n (%)	18 (17%)
Positive stress ECG test – n (%)	34 (32%)
AS-CAD – n (%)	48 (45%)
PCI – n (%)	40 (37%)
Coronary artery bypass grafting – n (%)	10 (9%)
Stroke	6 (6%)

factors (smoke, high blood pressure, high blood cholesterol, and obesity), not controllable risk factors (gender, age and heredity) and other clinical data for this group of patients are presented in Table 1. Ex smokers are considered individuals who quitted from at least 6 months.

Ethics: Signing an inform consent was a prerequisite for inclusion in the study. The study protocol was approved by the local ethical committee and complied with the Declaration of Helsinki.

Patients were included regardless of their sex or age. Exclusion criteria were left ventricular systolic dysfunction with ejection fraction < 40%, haemo-dynamically significant valvular heart disease, history of ventricular tachycardia, patient unable to perform the stress ECG test or unwilling to sign the inform consent.

Digital 12-lead electrocardiograms (ECG) were acquired during stress ECG test using veloergometer (GE Marquette Stress PC ECG Application) – 2-min stages 25W incremental workload.

The test was considered positive in the setting of ≥ 1 mm horizontal or downward-sloping ST depression 80 msec after J-point.

2.2. Principal component analysis

QRS detection algorithm [14] and automatic delineation of the QRS and T wave onsets and offsets [15] were performed to bound the segments for the PCA estimation.

Two indices by PCA analysis have been used for this analysis: 1) complexity index, the ratio between the second and the first eigenvalues:

PCA_1: λ_2/λ_1,

and 2) non linear components (or relative residuum) , the ratio between the sum of all the eigenvalues excluding the first three and the sum of all:

PCA_2: $(\lambda_4+\lambda_5+\ldots+\lambda_n)/sum_{i=1:n}(\lambda_i)$.

PCA_1 and PCA_2 are applied to the QRS complex and to the T wave. Mean values, max values and standard deviation are the parameters examined in the study.

The parameters based on mean and standard deviation of PCA_1 values are defined by:

$mean\_PCA_1\_QRS = mean_i (PCA_1\_QRS_i)$

$mean\_PCA_1\_T = mean_i (PCA_1\_T_i)$

$std\_PCA_1\_QRS = std_i (PCA_1\_QRS_i)$

$std\_PCA_1\_T = std_i (PCA_1\_T_i)$

In addition in order to capture short term dynamics, the max value of the mean values of 3 consecutive beats are considered:

$max\_3\_PCA_1\_QRS = max_i (mean_{i-1:i+1} (PCA_1\_QRS_i))$

$max\_3\_PCA_1\_T = max_i (mean_{i-1:i+1} (PCA_1\_T_i))$

The PCA_2 parameters are calculated in the same way.

2.3. Statistical analysis

We tested the distribution of different parameters using the Kolmogorov Smirnov test. This analysis showed that the majority of the considered parameters did not present a normal distribution. Consequently, we compared the results of different groups with the non parametric Mann-Whitney U test.

3. Results

Results of PCA_1 and PCA_2 for the QRS complex, reported in Table 2, are showing statistical differences between the CAD/noCAD groups only in $std\_PCA_2\_QRS$ ($p=0.02$) and $max\_3\_PCA_2\_QRS$ ($p=0.04$).

Table 3 reports the results of the same parameters for T wave. It appears that all parameters of the "non linear

Table 2. Results for coronary artery disease CAD/noCAD for the QRS complex.

	CAD	noCAD	p
$mean\_PCA_1\_QRS$	3.06±2.1	3.14±1.9	-
$std\_PCA_1\_QRS$	0.63±0.45	0.74±0.41	-
$max\_3\_PCA_1\_QRS$	4.73±2.53	5.00±2.33	-
$mean\_PCA_2\_QRS$	0.78±0.95	0.86±0.80	-
$std\_PCA_2\_QRS$	0.78±1.1	1.03±0.83	0.02
$max\_3\_PCA_2\_QRS$	4.29±4.9	6.1±6.6	0.04

Table 3. Results for coronary artery disease CAD/noCAD for T wave.

	CAD	noCAD	p
mean_PCA_1_ T	1.81±0.96	1.95±0.92	-
std_PCA_1_ T	1.19±0.49	1.41±0.49	0.013
max_3_PCA_1_ T	5.12±1.78	5.64±1.62	-
mean_PCA_2_ T	4.60±3.9	6.75±5.6	0.022
std_PCA_2_ T	4.61±3.9	6.49±5.2	0.039
max_3_PCA_2_ T	21.9±17.5	31.2±22.1	0.017

Table 4. Results in the angina pectoris AP/noAP comparison: PCA_1 for QRS and PCA_2 for T wave.

	AP	noAP	p
mean_PCA_1_ QRS	3.3±1.9	2.1±1.9	0.006
std_PCA_1_ QRS	0.71±0.40	0.59±0.51	-
max_3_PCA_1_ QRS	5.1±2.3	3.8±2.5	0.024
mean_PCA_2_ T	5.4±4.3	7.4±7.3	-
std_PCA_2_ T	5.2±4.0	7.3±7.0	-
max_3_PCA_2_ T	25.0±17.2	35.3±30.0	-

components" PCA_2 present a statistical difference between the CAD/noCAD groups, while for the "complexity index" PCA_1 only the standard deviation is presenting a statistical difference (p=0.013).

Table 4 shows the results for PCA_1 for QRS complex and PCA_2 for T wave comparing patients with and without AP.

The coronary artery bypass grafting, total cholesterol, dyslipidemia, arterial hypertension, body mass index, age and family history of CAD among the groups of demographic characteristics and risk factor distribution (presented in Table 1) did not show statistical difference for QRS and T wave.

Table 5 reports a summary of all the comparisons with statistically significant difference. Significant difference between the PCA of the QRS was found between subgroups of patients defined according to the presence or absence of AP ($p<0.01$ for PCA_1), AS-CAD ($p<0.05$ for PCA_2), DM ($p<0.05$ for both PCA_1 and PCA_2), positive stress test ($p<0.05$ for PCA_2), stroke ($p<0.01$ for PCA1), triglycerides > 1.7 ($p<0.01$ for PCA_2), and present or ex smokers ($p<0.01$ for PCA_1). The only clinical parameters that are not providing statistically significant difference in the QRS complex analysis are: MI, PCI and gender.

Significant difference between the PCA of the T-waves was present between subject with or without a history of MI ($p<0.05$ for PCA_1), presence or absence of AS-CAD ($p<0.05$ for PCA_1 and PCA_2), gender ($p<0.01$ for PCA_1 and PCA_2), and PCI ($p<0.05$ for PCA_2). The clinical parameters that are not providing statistically significant difference in the T wave analysis are: AP, CAD, DM, positive stress test, stroke, triglycerides and smokers.

Table 5. Summary of the results for PCA_1 and PCA_2 for QRS and T wave. The most significant differences among mean, std and max_3 are illustrated.

	QRS complex		T wave	
Presence vs absence	PCA_1	PCA_2	PCA_1	PCA_2
MI	-	-	p<0.05	-
AP	p<0.01	-	-	-
AS-CAD	-	p<0.05	p<0.05	p<0.05
DM	p<0.05	p<0.05	-	-
Pos. Stress Test	-	p<0.05	-	-
Stroke	p<0.01	-	-	-
Gender M	-	-	p<0.01	p<0.01
Triglycerides >1.7	-	p<0.01	-	-
Smokers	p<0.01	-	-	-
PCI	-	-	-	p<0.05

Decreased PCA values were found in the groups of: MI, AS-CAD, DM, positive stress test, triglycerides, smokers and PCI. Increased PCA values were found in: AP and stroke. In addition, females show higher PCA values than males.

4. Discussion

Different cardiac risk factors and clinical parameters have a distinct influence on the two indices based on the Principal Component Analysis applied on the QRS complexes and T-waves during stress ECG Test.

From clinical perspective it is important to predict which patients are at risk for ventricular arrhythmias and sudden cardiac death in order to adopt primary prophylactic measures. History of MI is a well known risk factor for future ventricular arrhythmias and in the present analysis PCA of the T wave showed a significant difference between groups of patients with or without MI, supporting previous knowledge [16]. The population with a history of MI, however, is not a homogeneous one and maybe PCA has the possibility to distinguish those subjects, who are at a particularly increased risk. This will be evaluated in a further study with prospective follow-up of the selected cohort.

Few comparable studies concerning the influence of demographic and clinical variables on QRS or T wave PCA are present in literature [17-19]. Higher values for PCA of the T wave in patients with CAD has been reported [17]. There is some initial work done on QRS complex PCA in the setting of previous MI [18]. Some authors are analyzing the T wave PCA in the course of acute transmural ischemia, induced by prolonged balloon occlusion during PCI [20].

5. Conclusions

The general conclusion of our study is that the cardiac risk factors and clinical data influence the homogeneity of the QRS-complex and T-wave. The indices of the QRS complex based on PCA analysis showed a higher number of significant differences and proved to be more sensitive to the different clinical conditions.

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Address for correspondence.

Giovanni Bortolan
Institute of Biomedical Engineering, ISIB -CNR
Corso Stati Uniti, 4
35127 Padova
Italy
Giovanni.Bortolan@isib.cnr.it