Assessment of the Infarct Size in High-Resolution Electrocardiograms

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Abstract

The present study was focused on high-resolution orthogonal electrocardiography (HR-OECG) analysis for assessment of the zone of necrosis after acute myocardial infarct (AMI). We examined HR-OECG recordings of 13 healthy controls, 9 patients with anterior AMI and 13 patients with inferior AMI. The AMI size was evaluated by the enzyme levels of creatine kinase-common (CPK) and its MB-fraction (CPK-MB). Multiple regression models were derived where the observed enzyme level was the dependent variable and the predictor variables were selected among the defined morphological descriptors of the QRS-T pattern. Since the measured amplitudes and durations of the QRS-T pattern for the three leads of the HR-OECG recordings depend on the AMI localization, we investigated the discriminating ability of these OECG descriptors for recognition of the two studied AMI types - anterior and inferior. The results showed that some of the OECG descriptors, which were selected in the best regression models of the enzyme fractions, were also included in the best discriminating sets. The results of this study indicate the need for further investigations of the HR-OECG potential as a fast and accurate method for assessment of the AMI size and localization.

1. Introduction

The early prognosis of the patents' outcome during the acute phase of myocardial infarction (MI) is directly related to the size of the functioning myocardium. In patients without indications for previous MI attacks, the prognosis depends on the size of the damaged myocardium supplied by the culprit coronary artery distal to the occlusion. Non-invasive methods for evaluation of the MI size applicable at the bedside of the patient and providing fast, easy, and accurate measurements are recently moved forward.

During the last years, the high-resolution electrocardiogram (ECG) has been widely introduced in the clinical practice [1]. This method is based on computerized amplification, digital filtering and signal averaging of specific ECG segments. Thus even the low amplitude signal components become eligible for reliable analysis. The most common application of the high-resolution ECG is in studies of the late potentials of myocardial depolarization (i.e. the atrial or ventricular late potentials) [2].

The technique for ECG signal averaging involves accumulation of periodic signals such as the consecutive heart cycles in time. By adding many consecutive heart cycles, the overall noise components of the signal sum that are unsynchronized with the physiological pattern will decrease while the stable signal components remain unchanged. The suppression of the uncorrelated noise components is proportional to the square root of the number of the averaged cycles. Thus, by diminution of the ECG signal inherent noise, a specific steady pattern of the heart cycle is derived for the ECG recording of one patient. The enhanced cardiac cycles for a group of cardiac patients form a set of standard patterns with improved resolution. This set becomes a basis for further classification study with quantitative diagnostic aim. We applied the method in high-resolution ECG for assessment of the myocardium status after MI, particularly for evaluation of the size of the necrotic zone during the acute infarction phase.

The orthogonal electrocardiography (OECG) is an informative method for MI diagnostics - estimation of the localization and size, especially in cases of abnormal Q-waves and several necrotic zones [3,4]. A lot of quantitative OECG descriptors have been studied, providing different accuracy levels, i.e. specificity and sensitivity concerning the nosology of heart and the assigned diagnostic indices. We should note that clear OECG criteria for assessment of the myocardial condition have not been defined yet, as well as the set of the most informative parameters for precise evaluation of the zone of acute MI necrosis remains unspecified [5]. Therefore, we studied the possibility for reliable evaluation of the infarction size using a set of OECG descriptors, which were derived by averaging the heart cycles in the three high-resolution orthogonal Frank leads. Moreover, we applied sensitive selection of the most reliable parameters for assessment of the MI size in dependence of the MI localization.

2. Materials and methods

2.1. ECG data

High-resolution ECG recordings of 22 patients (average age 67±10.5 years) were collected by 12-channel ECG data acquisition system [6] at the intensive coronary unit of the Department of Internal Medicine "Prof. St. Kirkovich", Medical University – Sofia. The patients were classified according to the MI localization in two groups, including 13 patients with inferior MI and 9 patients with anterior MI, all of them with clinical symptoms, ECG and laboratory data indicating AMI:

- Typical angina pain with duration ≥30 min;
- ST-elevation ≥1 mm in two or more neighboring peripheral leads, or ≥2 mm in two or more neighboring precordial leads;
- Enzyme levels of creatine kinase-common CPK > 180 U/L, and its MB-fraction CPK-MB > 20 U/L, CPK-MB > 10 % of the initial CPK value;
- Onset of the clinical symptoms up to 24 hours before admission to hospital.

A control group of 13 healthy volunteers (average age 28±7.2 years) was also included in the study.

The ECG recording of each patient contains information about the 12-standard ECG leads (the peripheral leads I, II, III, aVR, aVL, aVF and the precordial leads V1-V6), sampled with frequency of 1kHz and resolution of 12-bit, with a total duration of about 5 min.

2.2. OECG leads and descriptors

The study was based on assessment of the high-resolution orthogonal Frank leads aiming to provide adequate information about the infarct size and location. Since the Frank lead system is optional for the conventional ECG equipment, thus being inaccessible in many clinical examinations of patients with MI, our study elaborated on the syntheses of the three OECG leads (X, Y, Z) from the 12-standard ECG leads by applying the transformations (1) [7]:

$$\begin{aligned} X &= 0.4*II - 0.8*(II + III)/3 + 0.2*V5 + 0.5*V6 + 0.1*V4 \\ Y &= 0.3*III + 0.8*II + 0.5*(II + III)/3 - 0.2*V5 - 0.3*V6 \\ Z &= -0.1*III - 0.2*II + 0.4*(II + III)/3 - 0.3*V1 - 0.1*V2 \\ &\quad -0.1*V3 - 0.2*V4 - 0.1*V5 + 0.4*V6 \end{aligned} \qquad (1)$$

A zone of 60^0 in the frontal plane, between lead I and lead II projection on the left ventricle, remains uncovered by any of the standard ECG leads [8]. In order to examine the possibility for improvement of the MI diagnostics we supplied additional information by inversion of the lead aVR (-150^0), so that lead *-aVR* traverses this zone at $+30^0$. We introduced the following abbreviations:

- X1, Y1, Z1 are the standard orthogonal Frank leads;
- X2, Y2, Z2 are the orthogonal Frank leads with inverted aVR, such as lead *III*=2*(*II*+*aVR*) is substituted in transformations (1) by *-aVR*.

A software system for ECG signal visualization and analysis was developed in Matlab 7.0. In order to derive the noise-free steady QRS-T pattern that is specific for one patient, we applied ECG processing procedures, including QRS detection and averaging of all heart cycles with synchronization by the R-peaks within the 5 min ECG recording. An experienced cardiologist marked specific points on the QRS-T pattern so that a set of morphological descriptors were measured, as follows:

Q_A – Q-wave amplitude; Q_D – Q-wave duration; R_A – R-wave amplitude; R_D – R-wave duration; S_A – S-wave amplitude; ST_A – ST-segment elevation amplitude; T_A – T-wave amplitude; QT_D – QT-segment duration;

The measurements of the CPK and CPK-MB serums for each patient were collected continuously during hospitalization. The maximal quantity of the cardiac markers CPK and CPK-MB is the measure for the MI size, as routinely used in clinical practice.

2.3. Statistical analysis

The measurements of the CPK and CPK-MB levels, as well as the defined above QRS-T pattern morphological descriptors for all synthesized OECG leads (X1, Y1, Z1, X2, Y2, Z2) and for all patients were involved into statistical analysis, using the data analysis software system Statistica 6.0 (StatSoft, Inc.).

The multiple regression analysis of the OECG descriptors was applied for verification of the possibility to predict the CPK and CPK-MB levels and therefore the infarct size. We used the multiple regression module, which performed least-squares multiple linear regression and computed detailed residual statistics. We applied forward stepwise selection of predictor variables, which were chosen among defined subsets of OECG descriptors. The forward stepwise method added or deleted the independent variables from the model at each step of the regression until the best regression model was obtained.

The derivation of optimal classification set of OECG parameters, in relation to the infarct localization, was obtained with linear discriminant analysis. We implemented the forward stepwise model of the linear discriminant analysis so that at each step the variable with the largest *F*-value (associated with the statistical significance of its contribution to the prediction) is chosen for inclusion in the model. The stepping terminates when no other variable has an *F*-value to enter that is greater than specified *F1*. Thus the method automatically selects the OECG descriptors that have statistical significance in the discrimination between the groups for MI localization.

3. Results

The measurements (Mean ± Standard deviation) of all defined QRS-T pattern descriptors from the OECG leads (X1, Y1, Z1, X2, Y2, Z2), are presented in Table 1,2,3 for the three groups of patients - healthy controls, anterior MI and inferior MI. Using the Student t-test for independent samples we identified the cases with significant statistical difference between the means of the different groups.

Table 1. Measurements for healthy controls (HC) (N=13); (p<0.05): * - HC vs. anterior MI; Ψ - HC vs. inferior MI.

	X1	Y1	Z1	X2	Y2	Z2
Q_A (mV)	0.041 ±0.018	0.054$^{\Psi}$ ±0.029	0.16* ±0.056	0.038$^{\Psi}$ ±0.027	0.11$^{\Psi}$ ±0.058	0.143* ±0.04
Q_D (ms)	24.95 ±5.59	24.41$^{\Psi}$ ±9.09	45.18* ±8.89	25.33 ±9.24	35.415 ±6.83	39.74$^{*\Psi}$ ±5.43
R_A (mV)	0.82* ±0.12	0.653$^{*\Psi}$ ±0.39	0.396 ±0.23	0.181 ±0.14	1.73$^{*\Psi}$ ±0.66	0.439 ±0.26
R_D (ms)	53.25 ±7.59	62.29$^{*\Psi}$ ±17.74	60.39* ±14.01	39.52$^{\Psi}$ ±8.82	66.58 ±15.4	63.26* ±8.75
S_A (mV)	-	-	-	-	-	-
ST_A (mV)	-	-	-0.06* ±0.04	-	-	-0.058* ±0.04
T_A (mV)	0.3$^{*\Psi}$ ±0.134	0.132$^{\Psi}$ ±0.1	-0.15* ±0.11	0.052* ±0.08	0.557$^{\Psi}$ ±0.2	-0.128* ±0.09
QT_D (ms)	416.4$^{*\Psi}$ ±35.1	415.8$^{\Psi}$ ±37.34	388.5$^{*\Psi}$ ±37.62	376.0$^{*\Psi}$ ±37.31	436.3$^{\Psi}$ ±38.82	399.3$^{*\Psi}$ ±46.19

Table 4 summarizes the subsets of OECG descriptors, which provide the best prediction of the CPK or CPK-MB serum levels after MI. For the anterior MI, the forward stepwise multiple regression combined the descriptors of only one lead, e.g. the leads X1 or Y1 showing very strong correlation (about 0.99). The significant prediction of CPK and CPK-MB for inferior MI, however, required regression using all OECG leads.

Table 5 represents the subsets of OECG descriptors, which were selected by the forward stepwise linear discriminant analysis to provide the best separation between the two MI localizations (anterior and inferior).

Table 2. Patients with anterior MI (N=9); * - p<0.05 - anterior MI vs. inferior MI.

	X1	Y1	Z1	X2	Y2	Z2
Q_A (mV)	0.036 ±0.02	0.052* ±0.04	0.04* ±0.03	0.044 ±0.04	0.092* ±0.056	0.035* ±0.04
Q_D (ms)	23.87 ±11.95	23.47 ±15.06	26.98* ±8.12	23.65 ±20.2	27.80* ±13.5	23.69* ±11.1
R_A (mV)	0.34 ±0.37	0.27 ±0.22	0.55* ±0.205	0.152 ±0.16	0.65 ±0.62	0.561* ±0.21
R_D (ms)	42.62 ±17.6	39.07 ±31.54	82.61* ±10.8	38.12* ±30.02	44.3 ±28.16	77.74* ±12.1
S_A (mV)	0.158* ±0.22	0.284* ±0.42	-	0.024 ±0.04	0.479* ±0.413	-
ST_A (mV)	0.044* ±0.07	0.013 ±0.05	-0.176* ±0.087	0.043* ±0.04	0.027 ±0.12	-0.185* ±0.1
T_A (mV)	-0.037 ±0.16	0.25* ±0.17	0.073* ±0.09	-0.108* ±0.113	0.389* ±0.36	0.082* ±0.09
QT_D (ms)	496.6 ±76.03	478.3 ±115	504.7 ±67.4	484.2 ±83	501.4 ±83.3	502.6 ±66.9

Table 3. Patients with inferior MI (N=13)

	X1	Y1	Z1	X2	Y2	Z2
Q_A (mV)	0.098 ±0.19	0.273 ±0.3	0.23 ±0.16	0.018 ±0.02	0.22 ±0.1	0.208 ±0.16
Q_D (ms)	33.14 ±23.7	41.46 ±22.8	48.45 ±11.8	17.22 ±18.4	38.71 ±5.13	47.22 ±10.6
R_A (mV)	0.84 ±0.67	0.188 ±0.158	0.29 ±0.26	0.417 ±0.43	0.784 ±0.38	0.33 ±0.27
R_D (ms)	55.72 ±21.3	39.73 ±23.1	59.01 ±17.9	58.76 ±16.8	56.92 ±21.4	58.24 ±18.4
S_A (mV)	0.016 ±0.06	0.02 ±0.05	0.006 ±0.02	0.105 ±0.19	0.084 ±0.14	0.0075 ±0.027
ST_A (mV)	-0.056 ±0.1	0.173 ±0.30	-0.045 ±0.06	-0.06 ±0.08	0.118 ±0.14	-0.047 ±0.06
T_A (mV)	0.101 ±0.196	-0.142 ±0.21	-0.178 ±0.13	0.066 ±0.151	-0.128 ±0.432	-0.168 ±0.127
QT_D (ms)	508.1 ±83.8	523.1 ±83.7	521.1 ±97.8	511.1 ±69.79	514.2 ±86.96	510.9 ±96.01

Table 4. Results from multiple regression analysis: Selected subsets of morphological descriptors that most accurately predict the enzyme levels CPK and CPK-MB in the acute phase of anterior and inferior MI.
* - OECG descriptor with statistical significance ($p<0.05$) in the regression; *SEE* – Standard error of estimate.

MI	Enzyme	Lead	OECG descriptors	Regression Summary
ANTERIOR	**CPK**	X1	$X1(Q_A)^*$, $X1(T_A)^*$, $X1(S_A)$, $X1(Q_D)$, $X1(R_D)$, $X1(QT_D)$	Adj.R^2=0.9882; F=99.0; p<0.08; SEE=109.35
	CPK-MB	X1	$X1(Q_A)^*$,$X1(T_A)^*$, $X1(S_A)^*$, $X1(R_A)$, $X1(R_D)$, $X1(QT_D)$	Adj.R^2=0.9981; F=624.5; p<,031; SEE=4.275
	CPK-MB	Y1	$Y1(Q_A)^*$, $Y1(R_A)^*$, $Y1(S_A)^*$, $Y1(R_D)^*$, $Y1(Q_D)^*$	Adj.R^2=0.9992; F=1389; p<0.0007; SEE=3.14
INFERIOR	**CPK**	X1,Y1,Z1	$X1(Q_A)^*$,$X1(ST_A)^*$,$X1(R_D)^*$,$X1(QT_D)^*$,$Y1(T_A)^*$,$Y1(R_D)^*$, $Y1(QT_D)^*$, $Z1(R_A)^*$, $Z1(ST_A)^*$, $Z1(R_D)^*$, $Z1(Q_D)^*$	Adj.R^2=0.9999; F=302e2; p<0.001; SEE=2.04
	CPK-MB	X1,Y1,Z1	$X1(R_A)^*$, $X1(T_A)^*$, $X1(R_D)^*$, $X1(QT_D)$, $Y1(T_A)^*$, $Y1(R_D)^*$, $Z1(R_D)^*$, $Z1(QT_D)^*$, $Z1(Q_D)^*$	Adj.R^2=0.9999; F=74950; p<0.003; SEE=0.47
	CPK-MB	X2,Y2,Z2	$X2(R_D)^*$, $X2(QT_D)^*$, $Y2(R_A)^*$, $Y2(ST_A)^*$, $Y2(QT_D)^*$, $Y2(R_D)^*$, $Z2(R_A)^*$, $Z2(ST_A)^*$, $Z2(QT_D)^*$	Adj.R^2=0.9999; F=1556e3; p<0.0006; SEE=0.1

Table 5. Results from linear discriminant analysis: Selected morphological descriptors, computed for each OECG lead (X1, Y1, Z1, X2, Y2, Z2), that showed statistical significance in the discrimination between the two studied groups of acute MI - anterior and inferior MI.

	Lead	OECG descriptors	True Anterior	False Anterior	True Inferior	False Inferior	Common mean
aVR	X1	$X1(Q_A)$, $X1(T_A)$, $X1(S_A)$, $X1(ST_A)$, $X1(Q_D)$	100 %	0 %	84.6 %	15.4 %	90.9 %
	Y1	$Y1(R_A)$, $Y1(T_A)$, $Y1(S_A)$, $Y1(Q_D)$, $Y1(QT_D)$	88.9 %	11.1 %	92.3 %	7.7 %	90.91 %
	Z1	$Z1(R_A)$, $Z1(T_A)$, $Z1(ST_A)$, $Z1(Q_D)$, $Z1(R_D)$, $Z1(QT_D)$	100 %	0 %	100 %	0 %	100 %
-aVR	X2	$X2(Q_A)$, $X2(ST_A)$, $X2(R_D)$	77.8 %	22.2 %	92.3 %	7.7 %	86.37 %
	Y2	$Y2(Q_A)$, $Y2(R_A)$, $Y2(S_A)$, $Y2(ST_A)$, $Y2(Q_D)$, $Y2(R_D)$	77.8 %	22.2 %	100 %	0 %	90.92 %
	Z2	$Z2(T_A)$, $Z2(Q_D)$, $Z2(QT_D)$	100 %	0 %	100 %	0 %	100 %

4. Discussion and conclusions

The aim of this paper was to investigate the potential of the high-resolution OECG signals for fast assessment of the MI size and localization during the acute phase.

This is a preliminary study based on analysis of real ECG data from a scanty number of patients but the results give promising expectations about the general OECG applicability for accurate MI size/localization evaluation. This complex problem was studied here by several signal processing techniques and statistical methods for assessment of a defined set of QRS-T pattern features. An important preprocessing technique involved the signal averaging, which provided noise-free and stable QRS-T pattern. The Student t-tests proved that many of the OECG descriptors had significant differences when considering the damaged infarct area – its presence and location (see the marked cells in Table 1,2,3). Some of these parameters were selected by the linear discriminant analysis to achieve the highest sensitivity/specificity discriminant models of the MI location (see Table 5). They provide more than about 90% total accuracy (estimated by the common mean). An interesting result is that most of the descriptors included in the discriminant models were also being steady elected by the multiple regression for accurate prediction of the CPK and CPK-MB levels (regression coefficient about 0.99, see Table 4), and therefore they are sensitive to both the infarct localization and size. We have doubts about the advisability of the OECG leads with inversion of the lead *aVR*, since they did not present improvement in the MI evaluation. An exception is the traditional difficulty in assessment of inferior MI size, where the two leads -(*aVR*) and (*–aVR*) presented almost equivalent performance. The promising results from this study are the basis for planning a more extensive investigation of MI by using the synthesized high-resolution OECG leads and the respective QRS-T pattern descriptors. The unexplored resources of the orthogonal vectorcardiographic loops present also a future challenge.

Acknowledgments

This work was supported in part by the Science Fund 'Young scientist' Grant, No7-D-Medical University-Sofia.

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