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Usefulness of Signal-averaged ECG, Short-term Heart Rate Variability, QT Interval and T Loop Criteria in Predicting 2 Years Lethal Outcome after Myocardial Infarction

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Introduction

Over the last few decades a great interest was given to deriving prognosis of survival after myocardial infarction (MI). The aim of that study was to identify the variables correlated with prognosis and define patients at high risk of death [1-4]. Approximately haft of the deaths that occur following acute MI are attributable to recurrent ischemic events or to congestive heart failure related to left ventricular impairment. Various tests have been proposed as being useful for post–MI risk stratification of patients at risk of death: left ventricular function, signal–averaged electrocardiogram, Holter monitoring, baroreflex sensitivity, QT interval and dispersion, T wave alternans and T wave morphology [5]. Because no single diagnostic test has been found to have sufficient predictive ability, investigators have examined the ability of various combinations of the tests to predict arrhythmic events in the post MI population.

The aim of our study was: 1) to ascertain usefulness of signal–averaged ECG, short-term heart rate variability, QT interval and T loop parameters in predicting 2 years lethal outcome after myocardial infarction; 2) to make a logistic regression model and to evaluate the efficacy of this model using ROC curve.

Material and Methods

Between August 1998 and February 2002 a total of 180 consecutive patients with acute MI admitted to department of Cardiology of Kaunas Medical University clinic, were prospectively enrolled in the study. Inclusion criteria were: 1) presence of ischemic chest pain for more than 30 min; 2) ST segment elevation ≥1 mV in at least two of the surface ECG or abnormal Q waves with temporal ST segment and T wave changes. Exclusion criteria were: left and right bundle branch block, rhythm other than sinus, age>75 years, prior coronary artery bypass grafting. During hospitalization betaadrenoergic blocking agents and angiotensin-converting enzyme inhibitors were given according to practice guidelines. All patients were followed up to 2 years after MI. Follow up information with regard to clinical events was obtained by telephone from relatives and from the station of the first-aid. Sudden cardiac death was defined as death occurring within 1h after first symptom, which was unlikely to have other etiologies. For evaluation the parameters of T loop morphology we had to pick up the ECG records of patients to satisfy a specification of this methodology. Hereby the number of patients with all the estimated parameters decreased to 115.

A signal-averaged ECG was obtained 5 to 11 days after hospitalization. The patients were not receiving antiarrhythmic drugs, except the beta-blocking agents. The signal-averaged ECG was recoded with standard bipolar orthogonal X,Y and Z leads and calculated as $V=\sqrt{X^2+Y^2+Z^2}$, a noise level below 1.0 μV was required. The filter setting was between 40 and 250 Hz. Filtered QRS duration (QRSd), the root-mean-square voltage in the last 40 ms (RMS40) and duration of late potentials of ≤40 μV amplitude (LAS40) were recorded.

Heart rate variability (HRV) analysis was performed after adaptation period of 10–15 min in lying down position. HRV characteristics were assessed from rhythmograms, which were analyzed using computer system developed in the Institute of Cardiology Kaunas

Medical University. There were estimated following parameters of HRV: SDNN- standard deviation of all normal RR intervals, RRNN- mean interval of all normal RR intervals, coefficient of variation (CV) – SDNN/RRNN×100. Spectrum of HRV was divided into three frequencies: VLF – very low frequency component (from 0.003 to 0.04 Hz); LF – low frequency component (from 0.04 to 0.15 Hz) and HF – high frequency component (from 0.15 to 0.4 Hz).

QT interval variables were measured automatically employing appropriate computer software. 12 lead rest ECGs were recorded into a computer simultaneously. Noises from electrical network, muscles and breathing waves were eliminated by using low and high frequencies filters, and isoelectric line was restored. 12 lead ECG after dividing into 10 s intervals was averaged every 60 s and 10 s. QT and JT intervals were measured from standard (I, II, III, AVR, AVL, AVF) leads and from thoracic (V1-6) leads. QTd and JTd were calculated as follows: from the longest QT or JT interval subtract the shortest QT or JT intervals. QTc and JTc were calculated using Bazett formula.

High resolution ECGs (5 min. duration, 2 kHz, 12 bit, 12-lead) were recorded at rest. Noise was reduced using 21 point triangle moving average filter. Vectorcardiographic X, Y, Z orthogonal Frank leads were synthesized using Dower matrix. Vectorcardiographic 3D T loop was projected onto a vertical plane, and the projection was inscribed into a square. The square was divided into 20x20 subsquares. From the shape of the filled subsquares two parameters of T loop morphology were evaluated: T loop area and T loop index (ratio of T loop area and T loop length) [6]. The third parameter - the angle between the mean QRS and T vectors in frontal plane (αQRS-T) was derived from the lead I and III leads, they were calculated using the formula:

$$y_i = \mathrm{arctg}\,(1{,}15\frac{\Delta y_i^{\mathrm{III}}}{\Delta y_i^{\mathrm{I}}} + 0{,}575), \qquad (1)$$

where $\Delta y_i^{\mathrm{III}}$ – is the sum of QRS, P and T wave amplitudes from lead III, Δy_i^{I} – the corresponding sum obtained from lead I. 1.15 and 0.575 coefficients are introduced in this formula because the leads I and III are not perpendicular to each other. The angles are measured not in the 0…360° interval, but 0…+180° and 0…-180° intervals, tgα value is negative in I and II quadrants and positive − in II and IV quadrants, therefore it was necessary to apply reduction formulae of these angles [7].

Echocardiographic report included the left ventricular ejection fraction (visually estimated).

To determine informative markers the logistic regression model was used:

$$P\ (\text{lethal outcome})=1/(1+\exp(b_o+b_1x_1+b_2x_2+...+b_nx_n)), \qquad (2)$$

where b_o, b_1, b_2, ... b_n are model parameters and x_1, x_2,...x_n – values of the markers. SPSS 10 was used for statistical analysis. ROC curves were computed to assess the sensitivity and specificity of logistic model for predicting deaths during follow-up.

Results and Discussion

Cardiac mortality during the first 24 months was observed in 18 patients; sudden death occurred in 9 patients (50%). The following clinical and ECG characteristics were included into logistic model: age, age groups, gender, previous myocardial infarction (MI), depth of MI, diabetes mellitus, hypertension, angina pectoris, left ventricular ejection fraction (LVEF), dispersion of corrected QT interval (OTcd), maximal QT interval (QTmax), T loop area (Tarea), T loop index (Tindex), angle between QRS and T vectors (αQRS-T), RRNN, CV, LF, LF/HF, VLF, QRSd, LAS40 and early percutaneous transluminal coronary angioplasty (PTCA) (table 1). Using logistic regression method we have estimated complex influence of informative parameters for probability of lethal outcome during 2 years after myocardial infarction. Optimal logistic model for probability of lethal outcome was compiled by inclusion method. Variables into logistic regression model have been included as long as p value has decreased. Into final model we included QRSd, αQRS-T, CV, LF, and LVEF.

$$p(\text{lethal outcome})=1/(1+\exp(-14.3+0.028\times\alpha QRST+0.114\times$$
$$\times QRSd-0.99\times CV+0.005\times LF-0.015\times LVEF)), \qquad (3)$$

$$\chi^2=36.34 \quad p=0{,}0001. \qquad (4)$$

This model helps to predict survival in 97.6 % and death probability in 61.5% during two years period after MI.

Sensitivity and specificity of logistic model to predict lethal outcome was evaluated using ROC curve. The accuracy of the test depends on how well the test separates the group. Accuracy is measured by the area under ROC curve. The ROC curve's position above the mean line demonstrates capability of the method to predict lethal outcome with some degree of precision. An area of 1 represents a perfect test. In our study area under ROC curve of this logistic model was 0.92±0.042 [0.837-1.003], p=0.0001.

Using the table of descriptives frequency we found cuf-off of infomative parameters (table 2) and applied these parameters to evaluate probability of lethal outcome 2 years after myocardial infarction using the created logistic regression model:

$$p(\text{lethal outcome})=1/(1+\exp(-10.3+3.4\times\alpha QRST>96+4.2\times$$
$$\times QRSd>109+4.6\times CV<3.1+1.99\times LF>111+1.16\times LVEF\leq40)), \qquad (5)$$

$$\chi^2=34.9 \quad p=0{,}0001. \qquad (6)$$

The area under ROC curve of the created logistic regression model was 0.919±0.039, p=0.0001 PI [0.843; 0.996] (Fig. 1).

According to our study more than a half deceased patients died suddenly. Because of small number of non-survived patients we did not divide mortality into cardiac and sudden death. A filtered QRS duration and an angle between QRS and T vectors are the most important variables and support the evidence that intraventricular conduction delay detected with averaging techniques is important in predicting sudden death and cardiac mortality after myocardial infarction [2; 4].

Table 1. Clinical and electrocardiographic characteristics for probability of lethal outcome during 2 years after myocardial infarction applying univariate logistic regression method

Parameter	χ^2	p	β	Ex(β)	PI
Age	6.57	0.01	0.069	1.071	[1.01; 1.13]
Age group	6.94	0.008	0.466	1.593	[1.12; 2.27]
Gender	0.65	0.418	-0.606	0.545	[0.13; 2.24]
Previous MI	10.87	0.001	1.962	7.111	[2.27; 22.24]
Deep of MI	2.52	0.112	-0.549	0.578	[0.29; 1.16]
Diabetes mellitus	1.09	0.294	1.006	2.735	[0.46; 16.1]
Hypertension	2.01	0.157	0.715	2.045	[0.75; 5.54]
Angina pectoris	3.003	0.083	0.926	2.525	[0.84; 7.56]
LVEF	11.3	0.001	-0.096	0.908	[0.86; 0.96]
QTcd	2.08	0.153	-0.03	0.969	[0.93; 1.01]
QTmax	1.96	0.16	0.14	1.014	[0.99; 1.03]
T area	1.99	0.158	0.005	1.006	[0.99; 1.01]
T index	1.68	0.195	0.382	1.465	[0.82; 2.62]
αQRS-T	7.2	0.007	0.015	1.015	[1.0; 1.03]
RRNN	2.38	0.123	-0.003	0.98	[0.99; 1.0]
CV	5.97	0.015	-0.64	0.527	[0.29; 0.95]
LF	1.44	0.23	-0.003	0.997	[0.99; 1.0]
LF/HF	4.19	0.041	-0.377	0.686	[0.44; 1.07]
VLF	3.84	0.05	-0.002	0.998	[0.99; 1.0]
QRSd	18.6	0.0001	0.093	1.097	[1.05; 1.15]
LAS40	4.46	0.035	0.045	1.046	[1.0; 1.09]
PTCA	4.9	0.027	-1.833	0.16	[0.02; 1.26]

Table 2. Complex of informative parameters for probability of lethal outcome during 2 years after myocardial infarction applying multivariate logistic regression method

	β	S.E.	Wald	Sig.	Ex(β)
αQRS-T>96	3.410	1.258	7.348	0.007	30.256
QRSd>109, ms	4.209	1.356	9.630	0.002	67.278
CV<3.1	4.619	2.151	4.611	0.032	101.4
LF>111 ms^2	1.995	1.500	1.770	0.183	7.353
LVEF≤40%	1.161	0.990	1.376	0.241	3.192
Constant	-10.335				

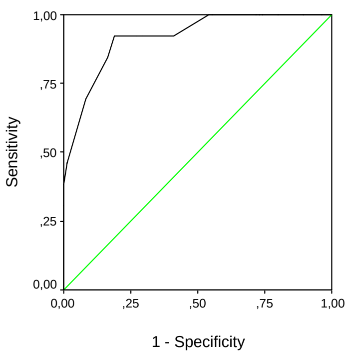

Fig. 1. ROC curve of the created model applying multivariate logistic regression method

Hereby we could define a “high risk” group of patients with αQRS-T>96, QRSd>109, CV<3.1, LF>111 ms^2, LVEF≤40%.

So the parameters αQRS-T>96 and QRSd>109 were included in our logistic regression model not incidentally. Reduced heart rate variability is another variable of risk for cardiac mortality [3; 4]. In our study CV<3.1 was related to lethal outcome. It is clear that the lower LVEF increases cardiac mortality [1; 4]. Our data showed that the cut-off of this variable was ≤40percent.

By applying multivariate logistic regression analysis we discovered a complex of informative parameters to determine lethal outcome in post –MI patients during 2 years.

Conclusions

Multivariate logistic regression analysis has revealed the combination of the informative indices: αQRS-T>96,QRSd>109 ms, CV<3.1, LF>111 ms^2, LVEF≤40%. The area under ROC curve of this created logistic regression model was 0.919±0.039, p=0.0001 PI [0.843; 0.996]. According to our data, it is useful to apply electrocardiographic characteristics for estimation the prognosis after myocardial infarction.

The proposed model is simple and could be applied in the clinical practice to evaluate the risk of death and to screen patients with unfavourable prognosis and to choose the best treatment for these patients.

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For evaluation of prognostic power usefulness of parameters of signal averaged ECG, short-term heart rate variability (HRV), QT interval and T loop morphology 116 patients with myocardial infarction were enrolled to a follow up study. During follow up of 2 years 16 patients died. A signal-averaged ECG was obtained 5 to 7 days after hospitalization. QT interval variables were measured automatically by means of appropriate computer software. HRV characteristics were assessed from rhythmograms. Vectorcardiographic 3D T loop was projected onto a vertical plane and parameters of T loop morphology were evaluated. Using logistic regression there was established the complex of informative parameters for lethal outcome. Hereby we could define a "high risk" group of patients with αQRS-T>96, QRSd>109, CV<3.1, LF>111 ms^2, LVEF≤40%. The proposed model is simple and could be applied in the clinical practice to evaluate risk of death, to screen patients with unfavourable prognosis and to choose the best treatment for these patients. Ill.1, bibl. 7 (in English; summaries in English, Russian and Lithuanian).

Г. Урбонавичене, Л. Гаргасас, Р. Аржанаускене, З. Берташене, М. Тамошюнайте, И. Блужайте. Прогностическое значение критерий электрокардиографии высокого разрешения, вариабельности ритма сердца, оцененных за короткое время, QT интервала и T петли 2 года после инфаркта миокарда // Электроника и электротехника. – Каунас: Технология, 2006. – № 6(70). – С. 29–32.

В проспективное исследование были включены 116 больных после развития инфаркта миокарда. Электрокардиографии высокого разрешения, вариабельность ритма сердца (ВРС) и запись ЭКГ в 12 стандартных отведениях оценивалось в положении больного лежа на спине на 5–7-е сутки после начала заболевания. Параметры электрокардиографии высокого разрешения – амплитуда последних 40 мс комплекса QRS, длительности сигнала на уровне 40 мкВ после фильтрации в диапазоне 40–250 Гц и длительность фильтрованного комплекса QRS, QT интервала и T петли были определены. На 5-минутных участках ЭКГ оценивались средняя длительность интервалов R-R, стандартное отклонение интервалов R-R, коэффициент вариации и обычный набор спектральных характеристик ВРС. Длительность наблюдения составила два года. Умерли 16 пациентов от сердечных причин. Были проанализированы 22 показателей, включавших клинические данные, результаты эхокардиографического обследования, параметров ВРС, QT интервала и T петли. При анализе логической регрессии был найден комплекс наиболее информативных параметров для прогнозирования смерти :αQRS-T>96, QRSd>109, CV<3.1, LF>111 ms^2, LVEF≤40%. Таким образом, мы предлагаем простой алгоритм больным после развития инфаркта миокарда для выделения группы высокого риска Ил. 1, библ. 7 (на английском языке; рефераты на английском, русском и литовском яз.).

G. Urbonavičienė, L. Gargasas, R. Aržanauskiene, Z. Bertašiene, M. Tamošiūnaitė, I. Bližaitė. Suvidurkintos signalo EKG, širdies ritmo kintamumo, QT intervalo ir T kilpos parametrų įvertinimas, prognozuojant mirštamumą dviejų metų po miokardo infarkto laikotarpiu // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2006. – Nr. 6(70). – P. 29–32.

Ištirti 116 ligonių, persirgusių miokardo infarktu. 5–7 stacionarizavimo parą registruota suvidurkinto signalo elektrokardiograma (EKG), 5 min ritmograma, standartinė 12 derivacijų automatinė elektrokardiograma. Buvo įvertinti suvidurkinto signalo EKG (laikinės charakteristikos), širdies dažnio variabilumo (laikinės ir spektrinės charakteristikos), QT intervalo (QTd, QTcd, QTmax, QTc) ir T kilpos morfologijos (T plotas, T indeksas, αQRS-T kampas tarp QRS ir T vektorių) parametrai. 16 ligonių per dvejus metus po miokardo infarkto mirė nuo išeminės širdies ligos. Logistinės regresijos metodu surastas informatyvių parametrų kompleksas letaliai baigčiai prognozuoti: αQRS-T>96, QRSd>109, CV<3.1, LF>111 ms^2, LVEF≤40%. Logistinės regresijos modelis, pasiūlytas mūsų straipsnyje, yra nesudėtingas ir galėtų būti pritaikytas klinikinėje kardiologijos praktikoje stratifikuojant riziką bei parenkant atitinkamą ligonių, persirgusių miokardo infarktu, gydymą. Il. 1, bibl. 7 (anglų kalba; santraukos anglų, rusų ir lietuvių k.).