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The Informative Value of Changes in the ST Segment for the Prognostication of Lethal Outcome within 30 Days in Patients with Acute Myocardial Infarction

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Introduction

When deciding upon the treatment tactics, and making prognosis during the period of acute myocardial infarction (MI), it is very important to evaluate the risk for ischemic sequelae and lethal outcome (LO) [1,2,3]. MI prognosis can be established on the basis of the markers of separate clinical and electrophysiological studies, as well as the combinations of these markers. During the acute period of MI, the analysis of ECG changes performed within 24 hours is an informative marker for the determination of the risk for ischemic sequelae and LO within the first 30 days [4].

The informative value of clinical markers for the prognostication of LO within 30 days in patients with MI was analyzed in our previous study [5]. The findings showed that the most informative markers for the prognostication of LO were the following: acute heart failure (AHF) (Killip class III–IV) developed during the acute period of MI, age >65 years, sinusal tachycardia on hospitalization (pulse rate >90), non-fatal ventricular fibrillation (VF), paroxysmal atrial fibrillation (PAF), and LV ejection fraction (EF) ≤ 30%. They resulted in relative risk (RR) of LO that exceeded 5 and was reliably greater than 1. The following markers were less informative: the maximum elevation of the ST segment above the isoline by ≥ 5 mm, the maximum descent of the ST segment below the isoline by ≥ 3 mm, left ventricular hypertrophy (LVH), LV wall movement index (LV WMI) ≥ 1.5, Q-wave MI, diffuse MI, VASI ≥ 9, and proximal stenosis of the left coronary artery (CA) ≥ 70%. They resulted in RR of 3-5 and reliably greater than 1.

The aim of our study was: (1) to evaluate the complex informative value of the extent of the ST segment dislocations within the first 24 hours after MI for the prognostication of LO within 30 days with the help of the multidimensional logistic regression model; (2) to determine the risk groups for LO within 30 days.

Contingent and methods

The study included 462 patients (351 men and 111 women) who for the first time experienced MI with or without the ST segment elevation, and were treated at Kaunas University Department of Cardiology.

All patients underwent clinical examination, ECG, two-dimensional echocardiography (EchoCG) (86.5%), angiography of coronary arteries (74.1%), and cardioenzyme study.

Patient selection criteria: patients with MI and with or without the ST segment elevation. Exclusion criteria: intraventricular conduction disorders (Hiss bundle branch block), severe concomitant diseases, and the application of the intervention treatment prior to the onset of MI.

MI diagnosis was made according to the recommendations of the European Association of Cardiologists and the American College of Cardiologists (2002). MI was diagnosed in the presence of 2-3 criteria: angina pectoris syndrome, typical new ECG changes of the ischemic character, and the increase in cardioenzymes. Biochemical markers typical of MI were considered to be the increase in cardioenzymes (troponin I and creatinophosphokinase MB fraction) by ≥ 2 times over the reference level.

ECG changes typical of MI with the ST segment elevation were considered to be the ischemic-type elevation of the ST segment ≥ 0.2 mV above the isoline at point J, and the occurrence of the pathological Q-wave in two and more parallel derivations. Changes typical of MI without the ST segment depression were considered to be horizontal or declining descent of the ST segment below the isoline by ≥ 1 mm lasting for > 24 hours (the descent of other forms – by ≥ 2 mm), measured at the distance of 0.08 ms from the J point and/or changes in the T-wave, such as the negative T-wave (except for aVR and V_1). The dislocation of the ST segment was analyzed in ECG recorded on the first day of the onset. The dislocation of

the ST segment was evaluated in each derivation in 3 consecutive QRST complexes, the evaluation being followed by the calculation of the mean value. Changes in the ST segment were evaluated in 7 sites of the LV wall. The ST segment changes present in the V_{2-3} derivations were evaluated as reflecting the anteroseptal LV site, in the V_{3-4} derivations – the apical site, V_{5-6} – I-aVL – the lateral site, V^2_{2-3} – the antero-basal site, V^3_{4-6} – the lateral site, V_{7-9} – the postero-basal site, and II, III and aVF – inferior site. The data registry included the maximum extent of the ST segment dislocation in derivations reflecting each site of the LV wall. According to localization, MI was differentiated into the anterior non-diffuse (V_1 – V_4) or diffuse (V_1 – V_6 , I, aVL), and the inferior and posterior non-diffuse (II – III, aVF or V_{7-9}) and diffuse (II – III – aVF, V_{5-6}, I, aVL, V_{7-9}) ones. Changes in the ST segment in echocardiogram were evaluated according to the results of the computerized analysis, and subsequently manually verified by two physicians.

The patients were followed up for 30 days from the onset of MI, including in-patient and post-inpatient period. 24 patients (5.2%) with MI died within the 30-day period.

Selection of the informative markers of the ST segment. The methods of the selection of informative markers for the prognostication of LO depend on the mathematical model used [6,7,8].

The quantitative marker of a patient is a random value with a certain distribution. This marker is informative for the prognostication of LO if the mean values of patients who survived and those who died within the 30-day period are significantly different. The comparison of mean values was performed using the t- and U- test. The work presents the p values of these test. A clinical marker is considered to be informative if $p<0.05$.

Let us presume that Y is a binary variable; $Y = 1$ if the patient died within the period of 30 days, and $Y = 0$ if the patient survived for 30 days. Thus, we presume that Y is a random value. Its distribution is fully defined by the probability $P\{Y = 1\}$ ($P\{Y = 0\} = 1 - P\{Y = 1\}$). $P\{Y = 1\}$ is dependent on the patient's condition, i.e. on the vector x of the markers characterizing the patient. For this reason, the determination of informative clinical markers is performed using $P\{Y = 1|x\} = p(x)$ regression models. One of the most common $p(x)$ models in medicine is the logistic regression model [7]:

$$P\{Y = 1|x\} = p(x) = \frac{\exp(b_0 + b_1 x)}{1 + \exp(b_0 + b_1 x)}, \qquad (1)$$

where b_0 and b_1 are model parameters, and x- the value of the clinical marker (factor). As in all regression models, here a presumption is made that the values of the factor are not accidental (i.e. determined). In the model, the factor can be both measured and categorized. Unknown parameters are evaluated using the maximum likelihood method, and the significance of the parameters is measured using the likelihood ratio test [7]. The informative value of a clinical marker for the prognostication of LO is determined according to p value of likelihood ratio statistic. The clinical marker is considered to be informative if $p<0.05$.

The search for the informative markers for the prognostication of LO within 30 days may be defined as the search for the informative markers for the classification of patients into classes. In addition to the aforementioned probability methods, we used only the assertion tree CARDS algorithm for this purpose [6]. For each clinical marker X with set of covariate pattern R all possible splits R_1 and R_2

$$R_1 = \{x \in R: x \le a\}, R_2 = \{x \in R: x > a\}, \qquad (2)$$

where a real value, are examined to find the largest improved in goodness of fit for prediction the lethal outcome. The three choices of goodness of fit measures are available: Gini, χ^2-square and G-square measure [8]. For determining the stop splitting were 3-fold cross validation used [6]. The clinical marker was considered to be informative if the cross-validation (CV) values were significantly different from the minimum CV values.

The complex influence of several markers on the probability of LO was evaluated using the multidimensional logistic regression model [7]. The significance of variables in the logistic model was evaluated using the likelihood ratio (G^2) and Wald statistics. Multidimensional logistic models were created applying the forward stepwise model building algorithm. When using the multidimensional logistic model coeffi-cients, we developed a risk score model for the evaluation of complex risk of ST markers. The prognostic value of the complex of markers is presented in a ROC curve.

In order to determine low-, medium-, and high-risk groups, we used the LO probability estimation in the multidimensional logistic model, or the logit function of the probability estimation log (p/(1 - p)).

Results

In the studied contingent of patients with MI, the elevation or depression of the ST segment from the isoline in ECG registered within the first 24 hours ranged from 0 to 9 mm. Not less than 65% of all values of the ST segment were equal to 0, and therefore we refuted the assumption about the normality of the distribution of the values of the ST segment (Fig. 1). Instead, the difference in the mean values of the ST segment markers between the survivors and the patients who died was evaluated using the U test, and the p value of t-test was presented only for comparison (Table 1).

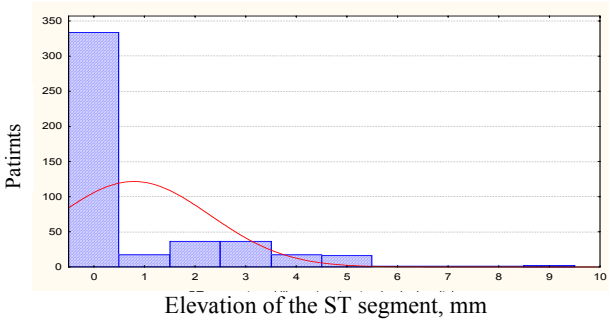

Fig. 1. Histogram of the elevation of the ST segment

Table 1. Comparison of the methods for the determination of the informative value of the ST segment dislocation for the prognostication of lethal outcome within 30 days

ST dislocation (mm)	p of t-test	p of U test	p of G^2 test	Cut value of CARDS
Maximum ST elevation	0.018	0.008	0.002	3
Maximum ST depression	0.098	0.11	0.02	3
Inferior ST↑	0.34	0.39	0.18	-
Antero-septal ST↑	0.22	0.22	0.13	-
Apical ST↑	0.048	0.32	0.007	4
Lateral ST↑	0.015	0.001	0.0002	2
Antero-basal ST↑	0.3	0.53	0.12	-
Latero-basal ST↑	0.15	0.19	0.012	-
Postero-basal ST↑	0.37	0.36	0.17	-
Inferior ST↓	0.32	0.9	0.049	-
Antero-septal ST↓	0.48	0.51	0.45	-
Apical ST↓	0.1	0.11	0.14	3
Lateral ST↓	0.16	0.14	0.052	-
Antero-basal ST↓	0.34	0.32	0.25	-
Latero-basal ST↓	0.33	0.36	0.23	-
Postero-basal ST↓	0.33	0.3	0.15	-

When analyzing the obtained results we determined that the logistic regression method for the determination of the informative value of the ST segment values is much more sensitive than the U test – the p values of the U statistic were higher than those of the G^2. CARDS and the logistic regression methods yielded different results. Instead of markers that did not have any influence on the probability of LO according to the logistic model but were informative according to CARDS, we used respective categorized markers.

The dependence between the ST segment elevation and descent changes was evaluated using Kendall's tau-b correlation coefficient. A strong relationship was found between the anteroseptal, apical, and antero-basal ST segment elevation (Kendall's tau-b ranged between 0.72 and 0.81 (Fig. 2), and a medium relationship – between the anteroseptal, apical, antero-basal, and lateral ST segment elevation (Kendall's tau-b ranged between 0.49 and 0.56). Also, a medium relationship was found between the anteroseptal, apical, antero-basal, lateral, and latero-basal ST segment elevation (Kendall's tau-b ranged between 0.4 and 0.53). The positive and negative correlation detected between other ST segment changes was weak.

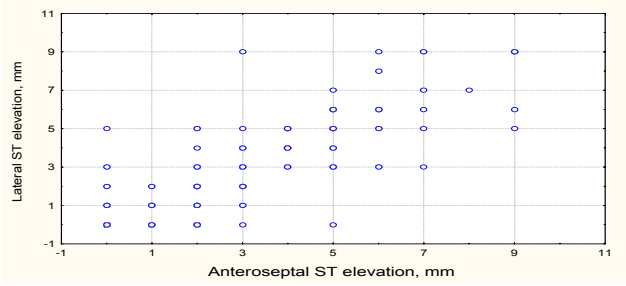

Fig. 2. Scatterplott between the anteroseptal and lateral ST segment elevation

The evaluation of the complex effect of the values of the ST segment elevation on the probability of LO within 30 days from the onset of MI was performed using the multidimensional logistic regression model. The model was developed using only those ST segment markers whose p values of the likelihood ratio statistic did not exceed 0.2.

The models were developed using the variable removal method, taking into consideration the strong correlation between some markers. The first-third model was developed without the inclusion of strongly correlated anteroseptal, apical, and antero-basal ST segment elevation. The coefficients and the p values of Wald statistic as well as the Yikelihood ratio statistic of the model (χ^2) are presented in Table 2.

As seen from Table 2, the 3rd model included only lateral elevation and descent of the ST segment. The difference between their coefficients was slight, and therefore both variables were joined into one – the change in the ST segment with respect to the isoline (elevation or descent) in the lateral site. This marker was used in developing logistic models 4 and 5 presented in Table 2.

The 1st - the 5th models did not include variables from the strongly correlated variable groups. The inclusion of any of such variables into models 1-5 resulted in the Wald statistics p value exceeding 0.2 and did not improve the model. No significant improvement of the model was achieved by including the maximum value of the ST segment elevation or descent (mm) into models 1-5.

As seen in Table 2, the linear combination of the ST segment dislocation above and below the isoline values was informative for the risk of LO within the period of 30 days.

0.477*(lateral ST↑) + 0.413* (postero-basal ST↑) + 0.264* (inferior ST↓) + 0.542*(lateral ST↓).

Instead of the aforementioned linear combination we introduced the ST informative score (STS), which is more attractive for physicians and is more convenient for usage due to integer values of coefficients:

STS = 6*(lateral ST↑) + 5* (postero-basal ST↑) + 3* (inferior ST↓) + 7*(lateral ST↓).

When using the ST score, the patients were differentiated into ST score risk groups. Low ST risk was attributed to patients whose STS was ≤ 11, medium – to those whose STS ranged between 12 and 25, and high – to those whose STS was > 25.

Table 2. Coefficients of the multidimensional logistic regression models (β), p value of Wald test, the likelihood ratio statistic of the model (χ^2) and its p value

No.	ST changes, mm	β	p	χ^2	p
1	lateral ST↑ postero-basal ST↑ inferior ST↓ lateral ST↓ intercept	0.477 0.413 0.264 0.542 -3.890	0.001 0.140 0.140 0.002	24.8	0.000055
2	lateral ST↑ inferior ST↓ lateral ST↓ intercept	0.483 0.243 0.541 -3.78	0.001 0.165 0.002	22.9	0.000042
3	lateral ST↑ lateral ST↓ intercept	0.517 0.530 -3.70	0.001 0.002	21.2	0.000025
4	ST change in the lateral site intercept	0.521 -3.69	0.001	21.2	0.000004
5	ST change in the lateral site inferior ST↓ intercept	0.497 0.222 -3.69	0.001 0.178	22.8	0.000011

Table 3. Risk of lethal outcome at different ST scores

ST score	ST risk degree	Patients	Deceased		χ^2	p
		n	n	%		
≤ 11	0	308	6	1.9	46.1	< 0.0001
12- 25	1	121	9	7.4		
>25	2	29	9	31.0		

* - χ^2 statistic was used to evaluate the dependence between the degree of risk and the frequency of LO

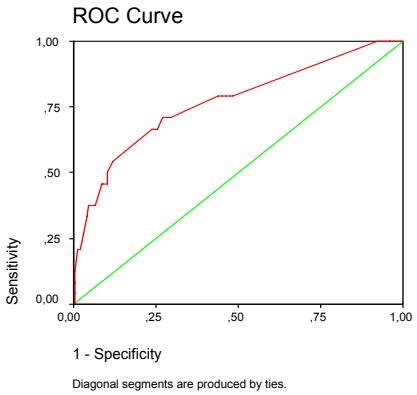

Fig. 3. ROC curve of the ST score

The influence of the STS value on LO is presented in table 3. The ROC curve illustrates the prognostic value of the ST total score (Fig. 3).

Thus, the calculation of ST score risk during the acute period of MI allows for the identification of patients with high, medium, and low risk of LO within 30 days, requiring different tactics of follow-up and treatment. During the acute period of MI, the identification of patients who have high risk of LO within 30 days and who require urgent myocardial revascularization improves the short-range and long-range prognosis of their survival [9,10].

Conclusions

1. The distributions of the ST segment dislocation markers are not normal values, and therefore the determination of the informative values of these markers for the prognostication of LO or any other event may not be performing with the help of only one statistical method, not to speak about the t criterion.

2. The extent of the dislocation of the ST segment from the isoelectric line in resting ECG recorded within the first 24 hours after the onset of MI is a significant marker for the prognostication of the risk for LO within 30 days.

3. ST score is an independent marker for the risk prognostication of the risk for LO within 30 days in the presence of MI: in the high-risk group (ST score > 25) LO occurred in 31% of patients, in the low risk group (ST score ≤ 11) LO occurred in 1.9% of cases (p<0.0001).

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M.R. Babarskienė, D. Lukšienė, B. Šlapikienė, I. Milvidaitė, J. Venclovienė. ST segmento pokyčių informatyvumas sergančių ūmiu miokardo infarktu letalios baigties rizikai 30 parų laikotarpiu numatyti // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2004. – Nr. 6(55). – P. 20-24.

Straipsnyje logistinės regresijos metodu įvertinta daugiamačio kintamojo – ST segmento dislokacijos nuo izoelektrinės linijos informatyvumas mirtinai baigčiai (MB) numatyti 30 parų laikotarpiu ir nustatytos MB rizikos grupės. Ištirti ir įvertinti 462 ligonių, kurie pirmą kartą patyrė miokardo infarktą, klinikiniai, elektrofiziologiniai, angiografiniai duomenys. Tirtame kontingente per pirmąsias 24 val. registruotose EKG ST segmento nusileidimas ir pakilimas nuo izolinijos svyravo nuo 0 iki 9 mm. Modeliui sudaryti naudojome tik tuos ST segmento rodiklius, kurių tikėtinumo santykio kriterijaus vienmačiame logistiniame modelyje p vertės neviršijo 0,2. Modelius sudarėme kintamųjų pašalinimo metodu, atsižvelgdami į stiprią kai kurių rodiklių koreliaciją. Straipsnyje praktiniam klinikiniam darbui pasiūlyta ST informatyvumo balas (STB). Remiantis ST balo vertėmis ligoniai suskirstyti į 3 rizikos grupes: didelės rizikos grupėje (ST balas > 25) MB ištiko 31 proc. ligonių, mažos rizikos grupėje (ST balas ≤ 11) – 1,9 proc. ($p < 0,0001$). Il. 3, bibl.10 (anglų kalba; santraukos lietuvių, anglų ir rusų k.).

M.R. Babarskienė, D. Lukšienė, B. Šlapikienė, I. Milvidaitė, J. Venclovienė. The Informative Value of Changes in the ST Segment for the Prognostication of Lethal Outcome within 30 Days in Patients with Acute Myocardial Infarction // Electronics and Electrical Engineering. – Kaunas: Technologija, 2004. – No. 6(55). – P. 20-24.

In this paper was analyzed the informative value of the multidimensional variable – the dislocation of the ST segment from the isoelectric line for the prognostication of lethal outcome (LO) within 30 days with the help of multivariate logistic regression and determined the risk groups for LO within 30 days. The study included 462 patients who for the first time experienced acute myocardial infarction (MI).The patients were followed up for 30 days from the onset of MI, including hospital period. In our patients the elevation or depression of the ST segment from isoline in ECG registered within the first hours ranged from 0 to 9 mm. The multivariate model was developed using only those ST segment markers whose p values of likelihood ratio statistic in multidimensional logistic regression model did not exceed 0,2. The models were developed using the variable removal method, taking into consideration the strong correlation between some markers. In this study for clinical practice was introduced the ST informative score (STS). When using ST score, the patients were differentiated into ST score 3 risk groups: low, medium and high. In the high risk group (ST score > 25) lethal outcome occurred in 31 % of patients, in the low risk group (ST score ≤ 11) lethal outcome occurred in 1.9 % of cases ($p < 0.0001$). Ill. 3, bibl. 10 (in English; summaries in Lithuanian, English and Russian).

М.Р. Бабарскиене, Д. Лукшиене, Б. Шлапикиене, И. Милвидайте, Й. Венцловиене. Информативность смещения сегмента ST в остром периоде ИМ при выявлении риска летального исхода в течение 30 суток // Электроника и электротехника. – Каунас: Технология, 2004. – № 6(55). – С. 20-24.

В статье для определения риска смерти в течение первого месяца при инфаркте миокарда (ИМ) анализируется информативность смещения сегмента ST от изоэлектрической линии методом логической регрессии. В исследование были включены 462 больные, заболевшие первым инфарктом миокарда (ИМ). Оценивались клинические, ангиографические, эхокардиографические и ЭКГ данные. На ЭКГ, зарегистрированной в течение первых 24 часов заболевания ИМ, смещение сегмента ST вниз или вверх от изоэлектрической линии составляло 0-9 мм. При составлении многомерной логической модели использованы только те показатели смещения сегмента ST, у которых p значение критерия соотношения вероятности в логической модели было меньше чем 0,2. Модель составлялась на основании исключения переменных в соответствии с сильной корреляцией между показателями. В настоящей работе представляется оценка риска смерти по информативности числа балов смещения сегмента ST (БST). При выявлении БST > 25 умерло 31 проц. больных – группа большого риска смерти; при БST ≤ 11 – 1,9 проц. ($p < 0,0001$) – группа малого риска смерти. Ил. 3, библ. 10 (на английском языке; рефераты на английском, литовском и русском яз.).

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