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Evaluation of the Prognostication of Cardiovascular Events within one year in Patients with Ischemic Syndromes

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Introduction

Ischemic heart disease (IHD) is the major cause of death in Europe among males over 45 years of age and among females aged over 65 years. In order to decrease mortality from IHD and to increase life expectancy in the affected population, studies have been undertaken to identify factors and mechanisms that cause IHD and promote its progression, and to clarify the relationships of these factors with the clinical course of the disease, the treatment and prognosis.

The principal aim of most scientific clinical studies evaluating patients' survival and prognosis was the assessment of the complex risk of an unfavorable health event (e.g. death or myocardial infarction) within a certain time interval on the basis of the indicators of patients' condition. For this reason, a risk score model has been created, where the probability of an unfavorable event within a certain time interval (Y=1) was modeled using multivariate logistic function. The values of variables included into this multivariate regression model are multiplied by weights – integers proportional to values $e^{\beta i}$, where β_i is a regression coefficient by i-th factor. The sum of the resulting products – the risk value – shows the complex risk of an unfavorable event. However, the presence of IHD increases the risk of several cardiovascular events (CE) - cardiac death, myocardial infarction, and stroke. It is possible to evaluate the total risk of CE within a certain period using a binary response (Y=1 – CE occurred, Y=0 – CE did not occur) and then compile a risk score model. However, the effect of the patient's condition on various cardiovascular events differs. For instance, heart failure may increase the risk of cardiac death, but may have no effect on the development of stroke. For this reason, it is expedient to use CE within a certain time period as a nominal value: Y=1 – the patient died of cardiac causes, Y=2 – myocardial infarction developed, and Y=3 – stroke occurred. The modeling of the probabilities of nominal response was performed using multinomial regression: changes in relative probabilities $P\{Y = 0| \mathbf{X} = \mathbf{x}\}$, $P\{Y = 1| \mathbf{X} = \mathbf{x}\}$, .. ., $P\{Y = k| \mathbf{X} = \mathbf{x}\}$, depending on the values $\boldsymbol{x}$ of the multivariate factor $\boldsymbol{X}$, were the following:

$$\begin{cases} P\{Y = 0 \mid X = x\} = 1/(1 + e^{g_1(x)} + e^{g_2(x)} + ... + e^{g_k(x)}), \\ P\{Y = i \mid X = x\} = e^{g_i(x)}/(1 + e^{g_1(x)} ... + e^{g_k(x)}), \end{cases} \quad (1)$$

here i = 1, 2, ...,k, $\boldsymbol{x}$ = ($x^{(1)}$, $x^{(2)}$, ..., $x^{(p)}$) – values of the patient's indicators, and $g_i(\mathbf{x}) = \beta_{i0} + \beta_{i1}x^{(1)} + ... + \beta_{ip}x^{(p)}$, β_{i0}, β_{i1}, ..., β_{ip} – coefficients of multinomial regression. Most frequently, the values of factors used in the multinomial model are binary: x = 1 – the risk factor (RF) is present, and x = 0 – the RF is absent. In such case the value $exp(\beta_{ij})$ indicates the increase in the probability ratio $P\{Y = i| x^{(j)} = 1\}/ P\{Y = 0| x^{(j)} = 1\}$ compared to $P\{Y = i| x^{(j)} = 0\}/ P\{Y = 0| x^{(j)} = 0\}$, when the values of other factors remain constant.

Unknown coefficients β of the model are evaluated using the maximum likelihood method, and their values and the reliability indices of these values – standard deviations and p values – are calculated using statistical software packages SPSS and SAS. The dependence of the probabilities $P\{Y = 0\}$, $P\{Y = 1\}$, ... $P\{Y = k\}$ on a concrete factor is determined by comparing the logarithms of the likelihood function of the model with $g_i(x) = g_i$ and (1): like in logistic regression analysis, statistics G is calculated. If in model (1) all coefficients β with $x^{(i)}$ equal to zero, the distribution of statistics G is χ^2 with $p \times k$ degree of freedom. Statistical packages provide the values of the whole χ^2 criterion of the model and the p value of each coefficient β_{ij}.

The aim of the study was to evaluate the informative determinants of inpatient treatment of acute and chronic coronary syndromes, and to estimate the significance of these values for patients' survival and the risk of cardiovascular events – myocardial infarction and stroke – within the period of one year [1-3].

Patients and methods

The study included 3249 patients who were treated for IHD in Department of Cardiology, Kaunas University of Medicine Hospital acute myocardial infarction (MI), unstable angina pectoris (UAP), stable angina pectoris (SAP), and IHD without the angina syndrome. Clinical syndromes of ischemic heart disease were diagnosed using the diagnostic criteria proposed and approved by the WHO. The data collection questionnaire included the anamnesis, data on concomitant diseases, patients' condition on hospitalization, pharmacological and interventional treatment applied during hospitalization, rehabilitation treatment, and recommended home treatment. 1999 patients were repeatedly inquired after one year, and evaluation of their condition, predominant symptoms, applied treatment during the year, and disease outcomes was performed.

Statistical data analysis

The informative value of separate clinical determinants for the prognostication of unfavorable cardiovascular events -cardiovascular death, myocardial infarction (MI), stroke) was evaluated by applying the multinomial logistic regression method. The informative value of a determinant – the risk of unfavorable events – was evaluated as odds ratios in single-variable multinomial logistic regression with 95% confidence intervals. A determinant was considered to be informative if at least one value of the coefficient *beta p* did not exceed 0.1. The evaluation of the quality of the model was performed using *p* value of the criterion χ^2 and *beta p* values of regression coefficients. The significance level for testing statistical hypothesis was 0.05. The complex effect of determinants on unfavorable events was evaluated using the multivariate multinomial model created by applying the backward stepwise method. We created the total risk score model to assess the significance of the combination of informative parameters for adverse cardiovascular events. Estimated odds ratios (OR) from the final multivariate multinomial regression model were transformed into integer values: 1 point - for OR ≤ 1.75; 2 - for OR between 1.75 and 2.25; 3 - for OR at interval between 2.25 and 2.75, 4 - for OR at interval between 2.75 and 3.25, and 5 - for OR ≥ 3.25. Risk score indices were calculated as a sum of integer values of adjusted odds ratios in final multinomial model. Statistical analysis was performed using SPSS 13 software.

Table 1. Univariate multinomial model for the assessment of the risk of cardiovascular death, myocardial infarction and stroke (model χ^2 p, p value of coefficients beta, odds ratios with 95% confident interval) (PD – pulmonary disease)

	χ^2 p	Cardiovascular EX			MI			Stroke		
		p	OR	CI	p	OR	CI	p	OR	CI
Determinants in the anamnesis										
Myocardial infarction	0.025	0.115	1.338	0.93-1.92	0.014	1.995	1.15-3.47	0.205	1.688	0.75-3.79
Heart failure	0.050	0.017	1.543	1.08-2.20	0.500	1.209	0.70-2.10	0.248	0.605	0.26-1.42
Stroke	0.012	0.005	2.343	1.29-4.25	0.747	0.790	0.19-3.30	0.014	3.950	1.32-11.8
Angina pectoris	0.051	0.325	0.822	0.56-1.21	0.178	1.648	0.80-3.41	0.072	3.794	0.89-16.2
Renal failure	0.190	0.065	2.057	0.96-4.42	0.645	0.625	0.09-4.61		-	
Chronic PD	0.056	0.030	1.885	1.07-3.34	0.701	1.225	0.43-3.46		-	
Age (years): ≤ 70	< 0.001		1			1			1	
(70; 80)		0.006	1.697	1.16-2.48	0.006	2.293	1.27-4.16	0.067	2.196	0.95-5.10
> 80		0.001	2.794	1.53-5.09	0.002	3.912	1.63-9.40	0.300	2.235	0.49-10.2
Determinants on hospitalization										
Heart rate>70	0.001	0.003	1.799	1.23-2.64	0.581	0.855	0.49-1.49	0.016	3.378	1.26-9.09
Atrial fibrillation	0.064	0.019	1.700	1.09-2.65	0.638	1.202	0.56-2.59	0.097	2.204	0.87-5.61
Bundle branch block	0.310	0.054	1.858	0.99-3.49	0.684	0.743	0.18-3.10	0.836	0.808	0.11-6.05
Killip class II-IV	0.039	0.001	3.165	1.56-6.44	0.785	0.757	0.10-5.60	0.616	1.679	0.22-12.7
Determinants of inpatient examination										
EF ≥ 40 %			1			1			1	
< 40 %	0.001	0.001	2.586	1.79-3.73	0.007	2.220	1.25-3.95	0.637	0.771	0.26-2.27
Diagnosis during hospitalization:										
SAP	0.024		1			1			1	
MI		0.238	1.276	0.85-1.91	0.091	1.803	0.91-3.58	0.283	1.653	0.66-4.14
UAP		0.768	0.920	0.53-1.61	0.005	2.861	1.38-5.94	0.436	1.565	0.51-4.82
Painless IHD		0.084	1.732	0.91-3.29	0.463	0.466	0.06-3.58		-	
Stenotic changes in coronary arteries (CA):										
- CA stenoses < 50%	0.02		1			1			1	
- stenoses ≥ 50%, revascularized		0.792	0.899	0.41-1.98	0.369	1.678	0.54-5.20	0.418	0.599	0.17-2.07
- stenoses ≥ 50%, not revascularized		0.255	1.439	0.77-2.70	0.083	2.377	0.89-6.32	0.221	0.517	0.18-1.49
Rhythm on discharge	0.01									
Atrial fibrillation		0.001	3.176	1.56-6.46	0.006	3.951	1.50-10.4	0.705	1.477	0.20-11.2
Pacemaker		0.006	2.261	1.27-4.03	0.446	1.501	0.53-4.26		-	

Results

After one year, we knew the outcomes of 1999 patients who in 2005 were treated at the Department of Cardiology for MI, UAP, SAP or IHD without the angina syndrome, and were subsequently discharged. 1819 (91%) patients survived during the one-year period, and 180 (9%) patients died; of these, in 132 (73%) patients death had

cardiovascular causes, in 30 (17%) other causes, and in 18 (10%) cases the cause of death remained unknown. For further analysis, we used data on 1951 patients who survived during the studied period or who died due to cardiovascular causes.

35.5% of the patients had been treated for MI, 17% - for UAP, 41.1% - for SAP, and 6.5% - for IHD without the angina syndrome. 1743 (89.3%) patients survived for 1 year without any cardiovascular events (MI or stroke), 132 (6.8%) patients died , 52 (2.7%) patients had MI within the period of one year, and 24 (1.2%) patients had a stroke. The risk of informative determinants of anamnesis, condition on hospitalization, and inpatient examinations for the aforementioned unfavorable events together with confidence intervals is presented in Table 1.

Table 2. Multivariate multinomial logistic model for the assessment of the risk for adverse cardiovascular events (p of beta, OR, 95% CI of OR) and risk score

Determinant	p	OR	CI	Point
Cardiac death				
EF < 40 %	<0.001	2.214	1.48-3.32	2
Heart rate >70 bpm	0.016	1.619	1.09-2.40	1
Heart failure	0.076	1.411	0.97-2.06	1
Stroke in anamnesis	0.036	1.944	1.04-3.62	2
Atrial fibrillation on discharge	0.140	1.748	0.83-3.72	2
CA stenosis ≥ 50% PTCA performed during hospitalization	0.057	0.525	0.271.02	-2
Age: 70 - 80 years	0.065	1.450	0.98-2.15	1
Age over 80 years	0.054	1.940	0.99-3.81	2
Myocardial infarction				
EF < 40 %	0.085	1.726	0.93-3.21	2
MI in anamnesis	0.112	1.620	0.89-2.94	1
Atrial fibrillation on discharge	0.013	3.737	1.32-10.6	5
UAP during hospitalization	0.003	2.617	1.40-4.90	3
CA stenosis ≥ 50% PTCA performed during hospitalization	0.146	1.902	0.80-4.53	2
CA stenosis ≥ 50% PTCA not performed	0.023	2.079	1.10-3.92	2
Age: 70- 80 years	0.009	2.259	1.22-4.18	3
Age over 80 years	0.001	4.694	1.86-11.8	6
Stroke				
Heart rate >70 bpm	0.020	3.284	1.21-8.92	5
Stroke in anamnesis.	0.024	3.684	1.19-11.4	5
MI in anamnesis	0.182	1.779	0.76-4.15	2
Age: 70- 80 years	0.080	2.165	0.91-5.14	2
Age over 80 years	0.296	2.294	0.48-10.9	2

Over 1.7-fold increase in the risk of death was observed in patients who during hospitalization were found to have atrial fibrillation, pulse rate over 70 bpm, and arrhythmias. MI in the anamnesis and older age increased the risk of death by twofold. Meanwhile, the risk of a stroke within the period of one year was by nearly 4-fold increased by previous stroke and angina pectoris, and pulse rate >70 on hospitalization increased such risk by 3.38 times. Age over 70 years increased the risk of stroke by twofold. Low (<40) ejection fraction increased the risk of death and MI by 2.2 times. Persistent atrial fibrillation on discharge increased the risk of death by 3.18 times, and the risk of MI – even by 3.95 times. The risk of MI increased by 2.86 times in the presence of UAP during hospitalization, compared to SAP, while pharmacological treatment alone (without intervention treatment) increased such risk by 2.38 times.

We used determinants whose model *p* value did not exceed 0.05 to create multivariate multinomial logistic regression model and to determine risk values for the evaluation of the risk of unfavorable events (Table 2).

According to the risk values, the patients were distributed into low, moderate, and high risk groups for each unfavorable event (Table 3). Table 3 presents the distribution of patients in the risk groups for cardiac death, myocardial infarction, and stroke, the incidence of these unfavorable events, and the increase in risk, compared to the low risk group. The risk of cardiac death in high risk group increased in 6.86, compare with low risk group. The risk myocardial infarction in high risk group increased in 43.8, compare with low risk group. The risk of stroke in high risk group increased in 10.6, compare with low risk group.

Table 3. Distribution of patients in risk groups for cardiac death, myocardial infarction, and stroke, the incidence of these events, and the increase in the risk for these events compared to the low risk group

Risk group	Patients, %	Event, %	OR	95% CI
Cardiac death				
Low <1	22.2	2.7	1	
Moderate 1-3	61.9	6.0	2.33	1.22-4.44
High >3	16.0	15.8	6.86	3.49-13.5
Myocardial infarction				
Low <2	21.4	0.2	1	
Moderate 2-7	68.3	2.4	10.3	1.40-75.3
High > 7	10.3	9.5	43.8	5.82-329
Stroke				
Low < 3	38.7	0.7	1	
Moderate 3-9	58.2	1.8	2.69	1.01-7.21
High > 9	3.1	6.9	10.6	2.78-40.8

Conclusions

1. The model that was based on the regression analysis using combinations of informative determinants for the prognostication of lethal outcome and cardiac events helps to stratify patients into high, moderate, and low risk groups for a one-year time period.
2. The created regression models according to risk groups help to substantiate the application of the individualized pharmacological or interventional treatment tactics and to recommend combined measures of secondary prophylaxis.

References

1. **Anand S. S., Xie C. C., Franzosi M. G., Joyner C., Chrolavicius S., Fox K.A., et al.** Differences in the management and prognosis of women and men who suffer from acute coronary syndromes // J. Am. Coll. Cardiol. – 2005. – No. 46(10). – P. 1845–1851.
2. **Goldberg A., Southern D., Galbraith D., Traboulsy M., Knudtson M., Ghali W.** Coronary dominance and prognosis

of patients with acute coronary syndrome. Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) // Am. Heart. J. – 2007. – No. 154(6). – P. 1116–1122.

3. **Maurin T., Zaller M., Cottin Y., Touzery C., Beer J.C., L'Huillier I., et al.** Long-term prognosis of patients with acute coronary syndrome abd moderate coronary artery stenosis // Cardiol. – 2003. – No. 99(2). – P. 90–95.

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Ischemic heart disease (IHD) is the major cause of death in Europe among males over 45 years of age and among females aged over 65 years. In order to decrease mortality from IHD and to increase life expectancy in the affected population, studies have been undertaken to identify factors and mechanisms that cause IHD and promote its progression, and to clarify the relationships of these factors with the clinical course of the disease, the treatment and prognosis. The aim of the study was to evaluate the informative determinants of inpatient treatment of acute and chronic coronary syndromes, and to estimate the significance of these values for patients' survival and the risk of cardiovascular events – myocardial infarction and stroke – within the period of one year. The study included 3249 patients who were treated for IHD in Kaunas University Cardiological department acute myocardial infarction (MI), unstable angina pectoris (UAP), stable angina pectoris (SAP), and IHD without the angina syndrome. Clinical syndromes of ischemic heart disease were diagnosed using the diagnostic criteria proposed and approved by the WHO. The data collection questionnaire included the anamnesis, data on concomitant diseases, patients' condition on hospitalization, pharmacological and interventional treatment applied during hospitalization, rehabilitation treatment, and recommended home treatment. 1999 patients were repeatedly inquired after one year, and evaluation of their condition, predominant symptoms, applied treatment during the year, and disease outcomes was performed. Bibl. 3 (in English; summaries in English, Russian and Lithuanian).

И. Венцловиене, М. Р. Бабарскиене. Прогнозирование исходов ишемической болезни сердца в течении одного года // Электроника и электротехника. – Каунас: Технология, 2009. – № 5(93). – С. 103–106.

Ишемическая болезнь сердца является главной причиной смерти среди мужщин старше 45 лет и женщин более 65 лет. Многообразие клинических факторов, характеризующих состояние больных ишемическими синдромами сердца и влияющих на исход заболевания, роль отдельных симптомов на исход болезни является необходимым условием при оценке тяжести заболевания, лечебной тактики и определения прогноза. Цель работы − установить информативность и значительность отдельных клинических и инструментальрых признаков в периоде стационарного лечения у больных ишемическими синдромами (острым инфарктом миокарда) для прогнозирования летального исхода, развития инфаркта миокарда, инсульта в течение одного года. Анализированы данные 1999 больных, которые лечились в Кардиологической клинике Каунасского Медицинского Университета. Используя математические методы логистической мультиномной регресии, с доверительными интервалами 95 % были установлены информативные признаки для прогнозирования исходов в течении одного года и разработаны модели прогнозирования исходов больных в трёх группах риска. Библ. 3 (на английском языке; рефераты на английском, русском и литовском яз.).

J. Venclovienė, M. R. Babarskienė. Išeminiais sindromais sergančių ligonių kardiovaskulinių įvykių prognozės vertinimas vienų metų laikotarpiu // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2009. – Nr. 5(93). – P. 103–106.

Išeminė širdies liga (IŠL) Europoje yra pagrindinė vyrų, vyresnių negu 45 metų amžiaus, ir moterų, vyresnių negu 65 metų amžiaus, mirties priežastis. Norint sumažinti gyventojų mirtingumą nuo IŠL, prailginti sergančiųjų gyvenimo trukmę, tyrinėjami veiksniai bei mechanizmai, sukeliantys IŠL ir skatinantys ją progresuoti, jų sąsają su klinikine ligos eiga, gydymo taktika ir prognoze. Tyrimo tikslas – įvertinti ūminių ir lėtinių koronarinių sindromų stacionarinio gydymo informatyvius požymius ir jų reikšmę išgyvenamumui ir kardiovaskulinių įvykių – miokardo infarkto, insulto išsivystymo rizikai vienų metų laikotarpiu. Atsitiktinės atrankos būdu buvo atrinkti 3249 pacientai, kurie gydėsi KMU Kardiologijos klinikoje dėl IŠL – ūminio miokardo infarkto (MI), nestabiliosios krūtinės anginos (NKA), stabiliosios krūtinės anginos (SKA), IŠL be angininio sindromo Išeminės ligos klinikiniai sindromai buvo diagnozuoti pagal PSO nurodytus ir aprobuotus diagnostinius kriterijus. Į duomenų rinkimo anketą buvo įtraukti anamnezės duomenys, gretutinės ligos, būklė stacionarizavimo metu, stacionare taikytas medikamentinis ir intervencinis gydymas, reabilitacinis gydymas bei rekomenduotas gydymas namuose. 1999 pacientai buvo pakartotinai apklausti po vienų metų, įvertinta jų savijauta, vyraujantys simptomai, metų laikotarpiu taikytas gydymas bei baigtys. Bibl. 3 (anglų kalba; santraukos anglų, rusų ir lietuvių k.).