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Prognostication of Cardiovascular Outcomes in Patients with Acute Coronary Syndromes

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Introduction

Ischemic heart disease (IHD) is one of the major causes of death in Europe. In order to decrease mortality from IHD, 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 the prognosis [1]. 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) or assessment of the survival function on the basis of the indicators of patients' condition [2–7].

Patients with acute coronary syndromes (ACS) are a heterogeneous population with varying risk of cardiovascular death and recurrent cardiac events in long-term as well as short-term follow-up. Different risk scores (RS) are now available for these patients, based on initial clinical history, ECG, and laboratory tests, which allows for early risk stratification on admission. TIMI, PUPSUIT, GRACE, and EUROSCORE risk models are used. These scores are used for 14 or 30 days prognosis. The GRACE risk model has been validated as a predictor of death or myocardial infarction (MI) in hospital and within 6 months [8–10].

The aim and objectives of the study: (1) to evaluate the informative value of the models in patients with ACS using GRACE (GR) scales; (2) to determine additional informative indicators for short-term and long-term prognosis in ACS patients; (3) to evaluate the prognostic reliability of the designed integrated model.

Patients and methods

The study included 1554 patients who in 2005 were treated for acute coronary syndromes (acute MI with or without ST elevation and unstable angina) in the Department of Cardiology, the Hospital of Kaunas University of Medicine. These clinical syndromes were diagnosed following the WHO diagnostic criteria [11, 12]. The data were collected using the questionnaire of clinical data – anamnesis, co-morbidities and risk factors, clinical indicators, ECG-ST-T shifts, left ventricular function, increase in myocardial damage markers, and pharmacological or interventional treatment; 1,491 patients were interviewed 1 year after inpatient treatment, evaluating their condition, predominant symptoms, and applied treatment. In addition to that, the prognosis of survival was evaluated - i.e. whether the patients survived for one year.

The GRACE risk score was calculated from clinical history, ECG, laboratory values collected on admission in risk stratification both at 30 days and at 1 year. The patients were stratified into low-, medium- and high risk tertiles according to the GRACE risk score [8, 9].

Statistical data analysis

A statistical comparison of baseline characteristics and outcomes was performed using χ^2 test for categorical variables, and the two-tailed Student's test - for continuous variables. We assessed the patents' risk of cardiovascular death (CD) within 1-30 days and within one year, as well as their survival after hospitalization. The risk was assessed separately for patients with ST-elevation (STEMI) and non ST-elevation (NSTEMI) myocardial infarction. To evaluate the risk of cardiovascular death, we used logistic regression; the assessment of risk was performed using crude and adjusted odds ratio (OR) with 95% confidence intervals (CI). The evaluation of complex risk was performed using multivariate logistic regression. The weights of determinants in the RS model were selected proportional to the adjusted odds ratio.

The received operating characteristic (ROC) curves were used to relate the calculated scores to the rate of

cardiovascular death. The area under the ROC curve (C-statistic) and 95% CI were used as a measure of predictive accuracy of RSs. The goodness of fit of the residual sum of square (RSs) was evaluated by the Hosmer-Lemeshow statistic. Statistical analysis was performed using SPSS 13 software.

Results

During the evaluation of the clinical condition of 1,491 patients hospitalized for ACS on admission, 576 patients were found to have MI with ST (STEMI) elevation, and 915 patients had MI without ST or unstable angina pectoris (NSTEMI-ACS) (Table 1). More patients with STEMI, compared to those without NSTEMI, were older and had more severe clinical condition on hospitalization, i.e. more common episodes of ventricular fibrillation, marked clinical signs of heart failure (Killip class III-IV, reduced systolic LV function (EF< 40%), more commonly elevated markers of myocardial damage, and more frequent need for intervention treatment (PCI) on admission.

Table 1. Baseline characteristics

	STEMI (n=576)	NSTEMI (n=915)	p
Men	66.1	63.9	0.378
Age≥70 years	44.6	34.3	<0.001
Prior CABG	7.3	19.9	<0.001
Prior MI	21.2	34.9	<0.001
Prior stroke/TIA	6.6	5.0	0.201
Renal disease	6.1	5.1	0.438
AH	76.2	83.7	<0.001
CD	16.1	15.7	0.837
Chronic FA	7.6	5.1	0.049
Cardiac arrest	4.9	1.5	<0.001
Killip class III-IV	24.0	8.1	<0.001
EF<40%	45.3	19.6	<0.001
Positive biomarkers (troponin)	68.5	19.8	<0.001
PCI	49.8	20.3	<0.001
CABG	22.7	25.5	0.234
Coronary artery stenosis in 2-3 arteries	49.7	55.8	0.027
GRACE	161(47)*	105(36)*	<0.001

mean (SD)

In the STMI group, 53 (9.2%) patients died during 30 days, 28 (4.9%) patients died within one year due to cardiovascular causes, and 8 (1.4 %) patients died due to co morbidity. 467 (81.1%) patients survived for one year without recurrence of ischemic events.

915 patients had NSTEMI. Of these, 18 (2.0%) died during 30 days, 37 (4.0%) died within one year due to cardiovascular causes, and 6 (0.7%) – due to comorbidity.

GR score in STEMI (NSTEMI) patients ranged from 57 to 293 (26-287), mean 161(105), median 159(99), tertiles 140 and 180 (88 and 114). With GR>180, 19.3% of STEMI patients died within 30 days. With GR>114, 4.4% of NSTEMI patients died within 30 days. With GR>180,

10.6% of STEMI patients died within one year. With GR>114, 10.2% of NSTEMI patients died within one year (Fig. 1). The risk scores in STEMI (NSTEMI) patients who died within 30 days were statistically significantly higher than those in patients who survived for 30 days: GR: 231(165) and 157(101). This table also presents statistically significant standardized risk of these indicators according to the risk score.

The risk of lethal outcome within 30 days in STEMI patients was significantly elevated by high GR scores, chronic atrial fibrillation (AF), while interventional inpatient treatment (PCI or CABG) significantly reduced the risk after adjusting for the GR score. The aforementioned indicators should supplement the GR score when evaluating the risk of STEMI patients within 30 days.
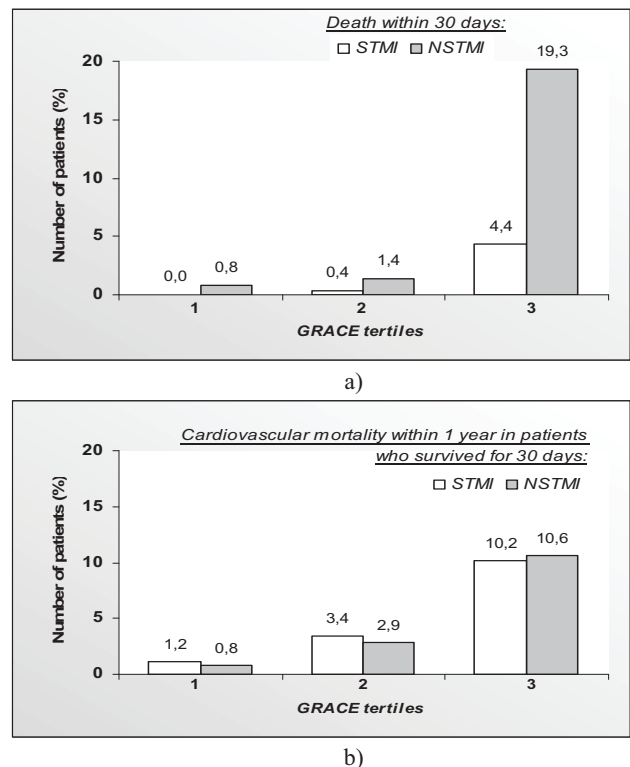

a)

b)

Fig. 1. Incidence of lethal outcome in risk score tertiles

In STEMI patients who survived for 30 days after ACS, 1-year prognosis was significantly improved by interventional inpatient treatment. After adjustment for the GR score, chronic atrial fibrillation (AF) significantly increased the risk, while interventional inpatient treatment reduced it. Ventricular fibrillation (VF) of admission, low systolic blood pressure (SBP), and application of interventional treatment (IT) during hospitalization were the factors that had additional significance.

In NSTEMI patients who survived for 30 days, 1-year prognosis was significantly affected by previous stroke and >70% stenosis of 2-3 coronary arteries (CA).

The prognostic value (with confidence intervals) of informative determinants - the anamnesis, the condition on hospitalization, and inpatient examinations - for the prognostication of the risk of death within 30 days and within one year is presented in Table 2.

In the group of high-risk patients (GR>II tertile) who did not undergo surgery during hospitalization, 14.7% of STEMI, and 13.0% of NSTEMI patients died within one year. The percentage of deaths in the group of patients who did undergo surgery during their hospital stay was lower – respectively, 7.3% and 7.4% (Fig. 2).

Table 2. The assessment of the risk of cardiovascular death (odds ratios with 95% confidence intervals) (* – $p<0.2$)

	30 days				1 year			
	STEMI		NSTEMI		STEMI		NSTEMI	
	OR	CI	OR	CI	OR	CI	OR	CI
Age≥70	2.68	1.41-5.10	4.40	1.35-14.4	5.20	2.32-11.6	4.26	2.21-8.21
Stroke	2.40	0.95-6.09	3.55	0.76-16.5	2.22	0.73-6.74	3.68	1.46-9.28
Renal disease	4.04	1.71-9.51	3.46	0.75-16.1	3.58	1.26-10.1	2.82	1.05-7.58
Adjusted for GRACE	3.32	1.01-11.0	1.65	0.17-15.8	-	-	2.29	0.80-6.57
Chronic AF	4.18	1.91-9.15	3.46	0.75-16.1	4.28	1.71-10.7	0.94	0.22-4.04
Adjusted for GRACE	3,26	1,08-9,89	0.63	0.07-5.58	2.30	1.16-1.60	0.48	0.10-2.25
VF	5.52	2.28-13.4	5.70	0.69-47.1	3.68	1.16-11.7	1.71	0.22-13.5
Killip class III-IV	12.69	6.22-25.9	28.97	8.69-96.6	4.87	2.43-9.75	7.06	3.46-14.4
Adjusted for GRACE	4.07*	0.80-20.6	2.70	0.24-31.0	0.27*	0.06-1.23	2.58*	0.88-7.52
SBP≤100 mmHg	4.16	2.00-8.64	44.28	11.8-166	4.33	1.84-10.2	3.65	1.20-11.1
EF<40%	3.30	1.50-7.26	2.78	0.78-9.94	2.62	1.30-5.27	4.42	2.42-8.10
Interventional treatment during hospitalization+	0.24	0.13-0.45	0.35	0.10-1.29	0.27	0.14-0.57	0.69	0.36-1.34
Adjusted for GRACE	0.31	0.11-0.84	0.40	0.04-3.68	0.29	0.10-0.88	0.86	0.40-1.85
>70% stenoses in 2-3 CA	1.25	0.66-2.41	2.57	0.80-8.25	3.15	1.15-8.58	3.16	1.46-6.87
Adjusted for GRACE	1.11	0.34-3.61	2.01	0.48-8.46	2.77	0.54-14.3	2.66	1.18-5.98
GRACE**	1.43	1.27-1.62	1.49	1.26-1.76	1.38	1.23-1.54	1.24	1.15-1.33
GRACE>median	11.27	2.60-48.9	14.6	1.89-113	10.61	2.41-46.6	4.19	1.89-9.30

+ only data on patients who did not undergo surgery within 1 year following hospitalization were used

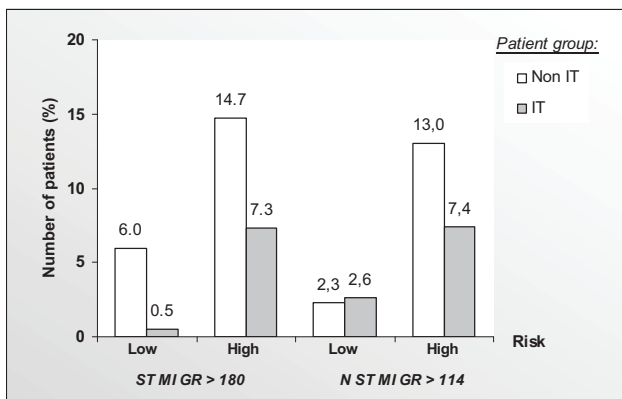** the risk was evaluated when the GRACE score increased by 10 points

Fig. 2. GRACE > II tertile risk for patents with and without interventional treatment (IT) in hospital

We applied multiple logistic regression analysis to calculate additional risk score for the prognosis of later cardiovascular death with respect to inpatient surgical treatment and arrhythmias

$$COR\_GRACE=GR+20(Chronic\ AF) - 30(interventional\ treatment\ in\ hospital). \quad (1)$$

The predictive accuracy of these RS is presented in Table 3. GRACE scores showed a good discriminatory accuracy to predict death at 30 days and at 1 year (C-statistic>0.75). For 1-year cardiovascular death (CD), GRACE RS showed better discriminatory accuracy for patients with STEMI. For MI patients who underwent revascularization when in hospital, the GRACE score was

a better predictor of 1-year CD (C=0.915), compared to those without revascularization (C=0.763).

Table 3. The predictive accuracy and goodness of fit of the risk scores (IT – interventional treatment)

	C (95% CI)	p	C (95% CI)	p
30 days	STEMI		NSTEMI	
GR	0.867 0.78-0.95	0.536	0.950 0.90-1.00	0.990
1 year	STEMI		NSTEMI	
GR	0.809 0.71-0.91	0.637	0.744 0.67-0.82	0.580
IT in hosp.	0.915 0.80-1.03	0.535	0.709 0.59-0.83	0.903
Non IT in hosp.	0.763 0.61-0.92	0.267	0.770 0.68-0.86	0.708
COR-GRACE	0.841 0.74-0.94	0.662	0.741 0.67-0.81	0.062

Adjusted GRACE was a better predictor of 1-year CD for STEMI patients, as increase the C-statistic and p-value of Hosmer-Lemeshow statistic.

Conclusions

1. The prognostic value of the GR scores for 30-day mortality was higher in NSTEMI patients (C=0.95).
2. The prognostic value of the GR score was better for STEMI patients who were had intervention treatment during their hospital stay (C=0.915) than for those who did not (C=0.763).
3. Following adjustment of the GR scores, the prognostic value improved for STEMI patients as increase the C-statistic and p-value of Hosmer-Lemeshow statistic.

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Ischemic heart disease is the leading cause of death in Europe among males over 45 years of age and females older than 65. The aim of the study: to evaluate the informative value of the models in ACS patients using GRACE (GR) risk score, to identify additional informative indicators for short-term and long-term prognosis following ACS, and to evaluate the prognostic reliability of the integrated model. The study included 1491 patients who in 2005 were treated for ACS in the Department of Cardiology, the Hospital of Kaunas University of Medicine. We devised an adjusted prognostic index for making short and long-term prognosis in patients with acute coronary syndromes (STEMI and NSETMI). Following adjustment of the GR scores, the prognostic value improved for STEMI patients. Ill. 2, bibl. 12, tabl. 3 (in English; abstracts in English and Lithuanian).

M. R. Babarskienė, J. Venclovienė, D. Lukšienė, I. Milvidaitė. Kardiovaskulinių baigčių prognozė persirgusiems ūminiais koronariniais sindromais // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2011. – Nr. 4(110). – P. 77–80.

Išeminės širdies ligos sąlygoti ūminiai koronariniai sindromai (ŪKS) yra pagrindinė vyrų, vyresnių nei 45, ir moterų vyresnių nei 65 metai, mirties priežastis. Atliekamų mokslinių studijų, tikslas išaiškinti veiksnius, galinčius pabloginti artimąją ir tolesnę prognozę po ŪKS ir, nustačius požymius, aktyviai koreguoti gydymą. Darbe įvertinta 1491 paciento, sirgusio ŪKS ir gydyto KMUK Kardiologijos klinikoje, klinikinė eiga ir tolesnė prognozė po vienų metų. Įvertinus galimų baigčių tikimybę pagal GRACE sistemą, ligoniams pasiūlytas modifikuotas rizikos įvertis. Il. 2, bibl. 12, lent. 3 (anglų kalba; santraukos anglų ir lietuvių k.).