Kardiologia Polska 2018; 76, 5: 881–888; DOI: 10.5603/KP.a2018.0031 ISSN 0022–9032

ORIGINAL ARTICLE

Risk factors for adverse outcomes of patients with acute coronary syndrome: single-centre experience with long-term follow-up of treated patients

Marcin Grabowski[1], Krzysztof J. Filipiak[1], Grzegorz Opolski[1], Renata Główczyńska[1], Monika Gawałko[1], Paweł Balsam[1], Andrzej Cacko[1], Zenon Huczek[1], Grzegorz Karpiński[1], Robert Kowalik[1], Franciszek Majstrak[2], Janusz Kochman[1]

[1]1st Department of Cardiology, Medical University of Warsaw, Warsaw, Poland

[2]Department of Cardiac Surgery, 1st Department of Cardiology, Medical University of Warsaw, Warsaw, Poland

Abstract

Background: For patients experiencing an acute coronary syndrome (ACS), a crucial time to assess their prognosis and to plan management is at discharge from hospital.

Aim: The aim of the study was to identify risk factors of mortality during post-discharge period following a hospitalisation for ACS.

Methods: We studied 672 consecutive ACS patients hospitalised and discharged alive between 2002 and 2004. The analysis was done with respect to the type of ACS, i.e. unstable angina/non-ST-segment elevation myocardial infraction (UA/NSTEMI; n = 255) vs. ST-segment elevation myocardial infarction (STEMI; n = 417). All patients underwent coronary angiography and, if indicated, primary angioplasty (STEMI: 417 patients; UA/NSTEMI: 157 patients). The Cox proportional hazards regression model was used to evaluate the independent effect of the risk factors on the occurrence of primary endpoint, i.e. all-cause mortality during six-year follow-up. Survival status and date of death were obtained from the National Registry of Population (PESEL database).

Results: A total of 123 patients (18.3%) died within the post-discharge period. The multivariate analysis identified 11 highly significant independent predictors of mortality (in order of predictive strength): diabetes mellitus (all types), higher creatinine level, older age, and more frequent occurrence of: supraventricular arrhythmias during hospitalisation, peripheral artery disease, recurrent angina pectoris with documented ischaemia on electrocardiogram, male sex, prior myocardial infarction, treatment with intra-aortic balloon pump counterpulsation, heart failure, and higher peak levels of creatine kinase-MB.

Conclusions: The risk factors obtained from the medical history and during the hospitalisation improve the risk stratification during the post-discharge period after hospitalisation for ACS.

Key words: acute coronary syndrome, long-term risk, prognosis after discharge

Kardiol Pol 2018; 76, 5: 881–888

INTRODUCTION

Secondary prevention following an acute coronary syndrome (ACS) is a crucial issue because further ischaemic events after the index event are common. Risk prediction tools have identified several risk factors for death and myocardial infarction (MI) following an ACS event [1, 2]. However, most risk scores include hospital mortality in their estimations [3–5], and relatively little attention has been paid to risk assessment at discharge from hospital [6]. This study aimed to identify risk factors of mortality in patients up to six years after discharge following a hospitalisation for ACS.

Address for correspondence:
Marcin Grabowski, MD, PhD, FESC, 1st Chair and Department of Cardiology, Medical University of Warsaw, ul. Banacha 1a, 02–097 Warszawa, Poland, tel: +48 22 599 19 58, fax: +48 22 599 19 57, e-mail: marcin.grabowski@wum.edu.pl

Received: 11.12.2017 **Accepted:** 16.01.2018 **Available as AoP:** 19.01.2018

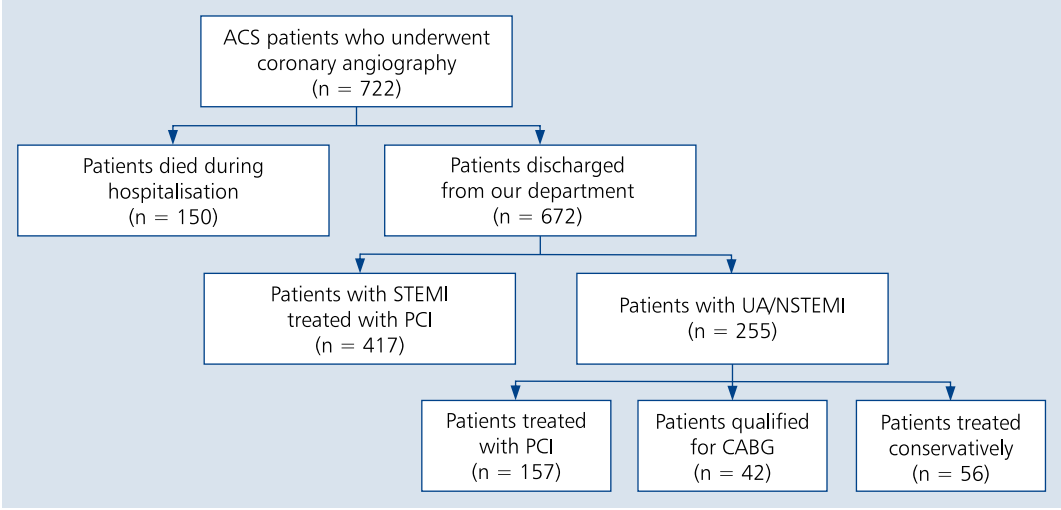

Figure 1. Flow chart of patient enrolment to the study; ACS — acute coronary syndrome; CABG — coronary artery bypass grafting; PCI — percutaneous coronary intervention; STEMI — ST-segment elevation myocardial infarction; UA/NSTEMI — unstable angina/non-ST-segment elevation myocardial infarction

METHODS

We performed a single-centre, prospective study of consecutive patients hospitalised for ACS between 2002 and 2004 in our Department with a 24-h catheter laboratory. All patients underwent coronary angiography and, if indicated, percutaneous coronary intervention (PCI). In total, 672 patients with non-fatal ACS, who survived until hospital discharge, were enrolled, and all of them were followed until 2009. The Third Universal Definition of Myocardial Infarction was used in our study [7]. The patients were classified as having ST-segment elevation myocardial infraction (STEMI) or unstable angina/non-ST-segment elevation myocardial infraction (UA/NSTEMI), according to current guidelines: (i) STEMI: the presence of ST-segment elevation of ≥ 0.2 mV in men aged ≥ 40 years, ≥ 0.25 mV in men aged < 40 years, ≥ 0.15 mV in women in V2–V3 leads and/or ST-segment elevation of ≥ 0.1 mV in two or more standard leads or new left bundle branch block and positive cardiac necrosis markers; and (ii) UA/NSTEMI: the presence of ST-segment depression of ≥ 0.05 mV in two or more standard leads or T-wave flattening or inversion and positive cardiac necrosis markers.

The approval of the ethical committee was obtained before initiation of the study.

Study endpoints

The primary endpoint was defined as all-cause mortality during six years of follow-up. Survival status and date of death were obtained from the National Registry Population.

Statistical analysis

We identified over 78 candidate variables for prediction (medical history on admission, during admission, and at discharge), and these are listed in **Appendix 1 (see journal website)**. From those, the most notable risk factors for post-discharge mortality were developed using Cox proportional hazards model. The statistical approach for factor selection was backward stepwise variable elimination, with a criterion of statistical significance of 5% for variable inclusion. Statistical significance was set at $p < 0.05$.

Only the variables present in at least 90% of subjects listed in the registry were included in the multivariate analysis.

Statistical analysis was performed using MS Windows XP Professional, MS Office 2003 Professional, Statistica 9 PL, and SAS Software 9 (SAS Institute, Cary, NC, USA).

RESULTS

Out of 722 patients with ACS who underwent coronary angiography, 50 patients were excluded from the current analysis because of death during hospitalisation. The final study group included 672 patients (median age, 61 years [range, 52–70 years]; 448 [66.7%] men). The flow chart of patient enrolment to the study is presented in Figure 1. A total of 417 (62.05%) patients were diagnosed with STEMI, and all of them were treated with PCI. The remaining 255 (37.95%) patients presented with UA/NSTEMI; 157 (61.57%) of these patients were treated with PCI, 42 (16.47%) were referred for coronary artery bypass grafting (CABG), and 56 (35.67%) were treated conservatively. Detailed characteristics of the STEMI and UA/NSTEMI groups are presented in **Supplementary Table S1 (see journal website)**.

During the follow-up, 123 (18.3%) patients died: 75 from the STEMI group and 48 from the UA/NSTEMI group. The overall mortality assessed during the follow-up until 2009 was comparable between patients with UA/NSTEMI and STEMI (18.8% vs. 18%, $p = 0.79$). Detailed characteristics of patients

who survived and died during the post-discharge period are presented in Table 1.

From all the candidate variables available, the Cox proportional hazards model identified 11 highly significant independent predictors of six-year mortality (Table 2). All negative predictors of post-discharge survival of patients with STEMI and UA/NSTEMI are shown in Tables 3 and 4, respectively; the only common predictor for both groups was diabetes.

DISCUSSION

One of the most interesting results of our research is the importance of risk factors rarely reported in other studies. It is well established that age, diabetes, previous MI, time of chest pain onset, tachycardia, hypotension, cardiogenic shock, anterior wall MI, and renal function are independent predictors of poor prognosis in patients with ACS; however, in our study, the prognostic value of these factors during the post-discharge period was reduced, and other clinical parameters (male sex, peripheral vascular disease), adverse events (recurrent angina pectoris with electrocardiographic [ECG] changes, new arrhythmias during hospitalisation), or complications due to invasive treatment were shown to gain importance [8–11]. This is in line with the observation from the GUSTO-I trial [8] among 1891 patients with STEMI, which aimed to assess

Table 1. Characteristics of patients who survived and died during post-discharge period

	Survivors	Dead patients	HR (95% CI)	p
Number of patients	549	123		
MEDICAL HISTORY				
Age [years]	58 [51–68]	68 [61–74]	1.06 (1.04–1.08)	< 0.001
Male sex	363 (66.1%)	85 (69.1%)	1.13 (0.77–1.65)	0.54
Time of onset of symptoms [h]	3 [2–6]	4 [2–7]	1.03 (1.01–0.99)	0.18
De novo angina pectoris < 2 weeks	200 (36.4%)	34 (27.6%)	0.704 (0.47–1.05)	0.08
De novo angina pectoris > 2 weeks < 2 months	40 (7.3%)	7 (5.7%)	0.768 (0.358–1.647)	0.5
De novo angina pectoris < 2 months	240 (43.7%)	41 (33.3%)	0.678 (0.47–0.99)	0.04
Arterial hypertension	313 (57%)	82 (66.7%)	1.484 (1.02–2.16)	0.04
Diabetes	69 (12.6%)	32 (26%)	2.199 (1.47–3.29)	< 0.001
Dyslipidaemia	192 (35%)	48 (39%)	1.150 (0.8–1.65)	0.45
Smoking	235 (42.8%)	36 (29.3%)	0.590 (0.4–0.87)	0.01
Previous MI	121 (22%)	44 (35.8%)	1.765 (1.22–2.55)	0.01
PCI	31 (5.6%)	8 (6.5%)	1.131 (0.55–2.32)	0.74
CABG	17 (3.1%)	5 (4.1%)	1.263 (0.52–3.09)	0.61
Previous stroke	18 (3.3%)	13 (10.6%)	2.815 (1.58–5.0)	< 0.001
Chronic heart failure: NYHA class III/IV	8 (1.5%)	13 (10.6%)	5.323 (2.99–9.47)	< 0.001
PVD	38 (6.9%)	24 (19.5%)	2.808 (1.8–4.39)	< 0.001
Asthma/COPD	26 (4.7%)	9 (7.3%)	1.561 (0.79–3.08)	0.2
SCA prior to hospitalisation	17 (3.1%)	3 (2.4%)	0.769 (0.24–2.42)	0.65
CLINICAL EXAMINATION				
Heart rate [bpm]	75 [65–84]	80 [68–88]	1.003 (0.99–1.01)	0.53
SBP [mmHg]	130 [120–150]	130 [120–155]	1.004 (0.99–1.01)	0.21
DBP [mmHg]	80 [70–90]	80 [70–90]	1.004 (0.99–1.02)	0.49
Pulmonary congestion: Killip class:				
I	508 (92.5%)	97 (78.9%)		
II	34 (6.2%)	24 (19.5%)	1.657 (1.25–2.19)	< 0.001
III	3 (0.6%)	1 (0.8%)		
IV	4 (0.7%)	1 (0.8%)		
Pulmonary congestion: Killip class II–IV	41 (7.5%)	26 (21.1%)	2.836 (1.84–4.38)	< 0.001
Pulmonary congestion: Killip class III–IV	7 (1.3%)	2 (1.6%)	1.184 (0.29–4.79)	0.81
Height [cm]	170 [162–176]	170 [164–176]	1.002 (0.98–1.02)	0.87
Weight [kg]	79.5 ± 25.5	79.9 ± 14.9	1.0 (0.99–1.008)	0.92
	78 [69–86]	78 [70–90]		

→

Table 1 (cont.). Characteristics of patients who survived and died during post-discharge period

	Survivors	Dead patients	HR (95% CI)	p
ECG				
ST-segment elevation	342 (62.3%)	75 (61%)	0.94 (0.66–1.36)	0.75
ST-segment depression	277 (50.5%)	59 (48%)	0.94 (0.66–1.34)	0.75
Negative T waves	156 (28.4%)	31 (25.2%)	0.85 (0.56–1.27)	0.42
Sinus rhythm	516 (94%)	108 (87.8%)	1.85 (1.23–2.77)	< 0.001
Regular rhythm	522 (95.1%)	114 (92.7%)	1.43 (0.73–2.83)	0.3
ST-segment elevation in leads II, III, and aVF	206 (37.5%)	38 (30.9%)	0.78 (0.53–1.14)	0.2
ST-segment elevation in leads V_1–V_4	132 (24%)	32 (26%)	1.07 (0.72–1.61)	0.73
LBBB	8 (1.5%)	4 (3.3%)	2.07 (0.77–5.61)	0.15
RBBB	17 (3.1%)	6 (4.9%)	1.48 (0.65–3.36)	0.35
LABORATORY TESTS				
First measurement of troponin level [ng/mL]	2 [0.1–13.5]	4.07 [0.4–33.1]	1.0 (0.998–1.003)	0.93
Highest troponin I level [ng/mL]	16.5 [1.4–50]	50 [3.86–50]	1.001 (1.000–1.002)	0.13
Highest CK-MB isoenzyme level [U/L]	98.5 [23.25–224.5]	94 [26–234.5]	1.001 (1.000–1.002)	0.2
Total cholesterol [mg/dL]	189 [150–220]	189 [151–221]	1.000 (0.99–1.004)	0.94
LDL-C [mg/dL]	111.5 [85–139]	113.5 [79–142]	0.999 (0.99–1.01)	0.81
HDL-C [mg/dL]	43 [36.75–52]	42 [34–52]	0.998 (0.99–1.01)	0.77
Triglycerides [mg/dL]	131 [100–175]	136 [100–180.3]	1.000 (0.99–1.002)	0.7
CRP [mg/L]	9.8 [4.25–24.2]	18.7 [6.6–58.15]	1.003 (1.002–1.01)	< 0.001
Creatinine [mg/dL]	0.91 [0.79–1.08]	1.01 [0.88–1.28]	1.72 (1.47–2.01)	< 0.001
eGFR (Cockroft-Gault) [mL/min/1.73 m^2]	87.5 [68.3–108.4]	71 [53.7–94.1]	0.98 (0.98–0.99)	< 0.001
eGFR (Cockroft-Gault) < 60 mL/min/1.73 m^2	72 (13.1%)	32 (26%)	2.22 (1.49–3.33)	< 0.001
MDRD [mL/min/1.73 m^2]	[66.4–95.8]	[51.7–85.4]	0.98 (0.97–0.99)	< 0.001
MDRD < 60 mL/min/1.73 m^2	80 (14.6%)	39 (31.7%)	2.51 (1.72–3.67)	< 0.001
RISK ASSESSMENT SCALES				
SIMPLE score	19.8 [14.8–25.4]	25.2 [19.2–33.1]	1.05 (1.033–1.062)	< 0.001
GRACE score for in-hospital mortality	119 [101–139]	133 [115.5–155]	1.02 (1.011–1.023)	< 0.001
GRACE score for post-discharge risk of mortality	90 [73–110]	111 [90.5–130]	1.03 (1.02–1.03)	< 0.001
INTERVENTION CHARACTERISTICS				
MV-CAD	145 (26.4%)	59 (48%)	2.35 (1.65–3.35)	< 0.001
LM stenosis	8 (1.5%)	0 (0%)	NA	
LAD stenosis	180 (32.8%)	40 (32.5%)	0.98 (0.67–1.42)	0.9
LCx stenosis	57 (10.4%)	16 (13%)	1.26 (0.75–2.14)	0.38
RCA stenosis	220 (40.1%)	43 (35%)	0.84 (0.58–1.21)	0.35
TIMI flow before PCI	0 [0–2]	0 [0–1]	0.9 (0.76–1.08)	0.27
TIMI flow after PCI	3 [3–3]	3 [3–3]	0.72 (0.59–0.9)	**0.003**
Coronary angioplasty	474 (86.3%)	100 (81.3%)		
POBA	98 (17.9%)	23 (18.7%)	1.08 (0.69–1.7)	0.74
Cardiac stent implantation	360 (65.6%)	67 (54.5%)	0.66 (0.46–0.95)	**0.0238**
Number of cardiac stents implanted	1 [1–2]	1 [1–2]	1.28 (0.88–1.85)	0.2
IABP	6 (1.1%)	5 (4.1%)	3.11 (1.27–7.62)	**0.013**
PHARMACOTHERAPY AT HOSPITAL				
ASA	537 (97.8%)	121 (98.4%)	1.34 (0.33–5.43)	0.68
Antiplatelets other than ASA	492 (89.6%)	106 (86.2%)	0.73 (0.44–1.21)	0.22
GP IIb/IIIa inhibitors	330 (60.1%)	76 (61.8%)	1.05 (0.73–1.52)	0.78

→

Table 1 (cont.). Characteristics of patients who survived and died during post-discharge period

	Survivors	Dead patients	HR (95% CI)	p
UFH/LMWH	539 (98.2%)	121 (98.4%)	1.26 (0.31–5.08)	0.75
ACE inhibitors	493 (89.8%)	111 (90.2%)	1.1 (0.6–1.99)	0.76
β-adrenolytics	514 (93.6%)	107 (87%)	0.56 (0.33–0.94)	**0.03**
Statins	483 (88%)	109 (88.6%)	1.131 (0.648–1.975)	0.66
ADVERSE EVENTS DURING HOSPITALISATION				
Re-infarction	6 (1.1%)	3 (2.4%)	2.05 (0.65–6.45)	0.22
SCA	19 (3.5%)	7 (5.7%)	1.62 (0.76–3.48)	0.21
Recurrent angina pectoris with ECG changes	16 (2.9%)	13 (10.6%)	3.21 (1.81–5.7)	< 0.001
Recurrent angina pectoris without ECG changes	37 (6.7%)	6 (4.9%)	0.71 (0.31–1.62)	0.4186
Stroke	1 (0.2%)	0 (0%)	NA	
Ventricular arrhythmias	12 (2.2%)	8 (6.5%)	2.65 (1.29–5.42)	**0.008**
Supraventricular arrhythmias	25 (4.6%)	20 (16.3%)	3.15 (1.95–5.08)	< 0.001
Pulmonary oedema	3 (0.5%)	3 (2.4%)	2.92 (0.93–9.19)	0.07
Cardiogenic shock	8 (1.5%)	4 (3.3%)	1.99 (0.73–5.37)	0.18
Significant bleeding	19 (3.5%)	7 (5.7%)	1.53 (0.72–3.28)	0.27
HOSPITALISATION PERIOD				
Duration [days]	9 [7–12]	11 [9–16]	1.04 (1.02–1.06)	< 0.001
Discharged home	494 (90%)	107 (87%)	0.77 (0.45–1.3)	0.32
CABG referral	45 (8.2%)	11 (8.9%)	1.1 (0.59–2.05)	0.76
PHARMACOTHERAPY AT HOSPITAL DISCHARGE				
ASA	485 (88.3%)	101 (82.1%)	0.64 (0.4–1.02)	0.06
Antiplatelets	404 (73.6%)	79 (64.2%)	0.67 (0.46–0.96)	**0.03**
Anticoagulants	27 (4.9%)	15 (12.2%)	2.53 (1.47–4.34)	< 0.001
ACE inhibitors	494 (90%)	107 (87%)	0.78 (0.46–1.32)	0.36
Statins	513 (93.4%)	110 (89.4%)	0.64 (0.36–1.15)	0.13
β-adrenolytics	511 (93.1%)	108 (87.8%)	0.59 (0.34–1.01)	0.05

Continuous variables are presented as median (interquartile range), and categorical variables are presented as absolute numbers (percentages). P values are given for differences between the ST-segment elevation myocardial infraction (STEMI) and the unstable angina/non-ST-segment elevation myocardial infraction (UA/NSTEMI) patients.
Conversion factors to SI units are as follows: for total cholesterol — 0.0259; HDL-C — 0.0259; LDL-C — 0.0259; triglicerydes — 0.0113; troponin I — 1.0.
ACE — angiotensin-converting-enzyme; ASA — acetylsalicylic acid; CABG — coronary artery bypass grafting; CI — confidence interval; COPD — chronic obstructive pulmonary disease; CK-MB — creatinine kinase-MB; CRP — C reactive protein; DBP — diastolic blood pressure; ECG — electrocardiography; eGFR — estimated glomerular filtration rate; GP — glycoprotein; HDL-C — high-density lipoprotein cholesterol; HR — hazard ratio; IABP — intra-aortic balloon pump; LAD — left anterior descending artery; LBBB — left bundle branch block; LCx — left circumflex artery; LDL-C — low-density lipoprotein cholesterol; LM — left main coronary artery; LMWH — low molecular weight heparin; MDRD — glomerular filtration rate using the Modification of Diet in Renal Disease Study equation; MI — myocardial infarction; MV-CAD — multivessel coronary artery disease; NA — non-applicable; NYHA — New York Heart Association; PCI — percutaneous coronary intervention; POBA — plain old balloon angioplasty; PVD — peripheral vascular disease; RBBB — right bundle branch block; RCA — right coronary artery; SCA — sudden cardiac arrest; SBP — systolic blood pressure; TIMI — thrombolysis in myocardial infarction; UFH — unfractionated heparin

long-term outcome and determine its predictors among 30-day survivors of cardiogenic shock. The strongest predictors of higher mortality during 11-year follow-up included age, shock, higher Killip class, cerebrovascular disease, prior MI, prior CABG, hypertension, diabetes, and anterior location of MI. Interestingly, among patients with cardiogenic shock who survived 30 days after STEMI, the annual mortality rates of 2% to 4% approximated those of patients without shock [8]. This phenomenon is defined by some authors as "the calm after the storm", analogously to an "electrical storm", which in itself can be a complication in high-risk patients [9, 12].

Another example of the so-called "depletion" of the prognostic value of some risk factors important during the in-hospital period is a lack of statistical difference in pulse and blood pressure values between patients who survived and those who died after ACS. In a study by Eagle et al. [10], a reduction of 20 mmHg in systolic blood pressure had a less significant prognostic value in the GRACE score for post-dis-

Table 2. Multivariate analysis of post-discharge mortality in the whole study group

Risk factors	HR	95% CI	p
Age (every year)	1.06	1.03–1.08	< 0.001
Male sex	2.002	1.25–3.21	0.0040
Diabetes	2.71	1.65–4.44	< 0.001
Previous MI	1.76	1.14–2.73	0.011
Chronic heart failure (NYHA class III/IV)	2.32	1.08–5.002	0.031
Peripheral vascular disease	2.59	1.49–4.498	< 0.001
Maximum CK-MB isoenzyme (every 1 U/L)	1.001	1.000–1.003	0.037
Creatinine (every 1 mg/dL)	1.582	1.31–1.91	< 0.001
Insertion of IABP	3.094	1.22–7.88	0.018
Recurrent angina with ECG changes	2.949	1.43–6.07	0.003
Supraventricular arrhythmias during hospitalisation	2.697	1.52–4.78	< 0.001

CI — confidence interval; CK-MB — creatinine kinase-MB; ECG — electrocardiography; HR — hazard ratio; IABP — intra-aortic balloon pump; MI — myocardial infraction; NYHA — New York Heart Association

Table 3. Multivariate analysis of post-discharge mortality in ST-segment elevation myocardial infraction (STEMI) group

Risk factors	HR	95% CI	P
Age (every year)	1.07	1.04–1.1	< 0.001
Male sex	2.6	1.3–5.21	0.007
Diabetes	2.47	1.25–4.89	0.009
Percutaneous coronary intervention	4.69	1.33–16.53	0.016
Chronic heart failure (NYHA class III/IV)	6.93	2.17–22.15	0.001
Peripheral vascular disease	4.3	2.08–8.89	< 0.001
Maximum CK-MB isoenzyme (every 1 U/L)	1.002	1 –1.003	0.036
Creatinine (every 1 mg/dL)	2.07	1.31–3.26	0.002
Statin recommendation	3.26	1.01–10.57	0.049
Supraventricular arrhythmias during hospitalisation	3.53	1.75–7.1	< 0.001
Discharged home	0.34	0.16–0.75	0.008

Abbreviations — see Table 2

Table 4. Multivariate analysis of post-discharge mortality in patients with unstable angina/non-ST-segment elevation myocardial infraction (UA/NSTEMI)

Risk factors	HR	95% CI	P
Diabetes	2.86	1.32–6.19	0.0078
Dyslipidaemia	2.57	1.14–5.81	0.0229
Maximum troponin I value (every 1 ng/mL)	1.01	1.01–1.02	< 0.001
Glomerular filtration rate using the MDRD formula (every 1 mL/min/1.73 m^2)	0.95	0.934–0.97	< 0.001
Resuscitated SCA	11.61	3.744–36.02	< 0.001
Recurrence of angina with ischaemia on ECG	6.43	2.268–18.23	< 0.001
Ventricular arrhythmias during hospitalisation	8.92	1.88–42.4	0.006

Abbreviations — see Tables 1 and 2

charge evaluation (hazard ratio [HR] 1.1, 95% confidence interval [CI] 1.08–1.20) than in the in-hospital evaluation (odds ratio [OR] 1.3); moreover, in the analysis of the validation cohort it did not obtain statistical significance (HR 1.0; 95% CI 0.92–1.19). In addition, an increase in heart rate of more than 30 bpm had prognostic value only in in-hospital evaluation of the GRACE score (HR 1.30; 95% CI 1.23–1.47) [10].

The importance of heart rate may vary depending on the assessment period, but also on the range of heart rate. A study by Bangalore et al. [13] evaluated 139,194 patients with UA/NSTEMI in the CRUSADE quality improvement initiative. Patients with systolic blood pressure lower than 90 mmHg (4030 patients) were excluded to avoid the confounding effect of cardiogenic shock. An adjusted OR was calculated using a reference OR of 1 for a heart rate of 60 to 69 bpm, after controlling for baseline variables. Compared with a reference group, patients with higher heart rate on presentation had up to a 2.2-fold increased risk of all-cause mortality and up to 1.9-fold increased risk of stroke. There was a J-shaped relationship between presenting heart rate and in-hospital primary outcome, all-cause mortality, and stroke, such that the event rates increased at both high and very low heart rate. However, there was no J-shaped relationship between presenting heart rate and risk of re-infarction [13].

An example of the risk factors differentiating STEMI and UA/NSTEMI populations is the type of biochemical myocardial necrosis marker — creatine kinase-MB (CK-MB) for patients with STEMI and troponin I for those with NSTEMI. This can be explained by the characteristics of a given indicator. In the STEMI population, where the markers of myocardial necrosis concentrations are higher, dynamic changes of CK-MB correlate better with the extent of myocardial damage and the effectiveness of reperfusion therapy than troponins. However, in patients with UA/NSTEMI, in whom the most important is the biochemical confirmation of MI, troponin I showed higher sensitivity for predicting mortality.

Another risk factor with a different prognostic value for patients with STEMI and NSTEMI in our analysis was the type of arrhythmias that occurred during hospitalisation. In the multivariate model, an important prognostic indication in patients with STEMI was supraventricular arrhythmias (relative risk [RR] 3.5), whereas in patients with UA/NSTEMI it was ventricular arrhythmias (RR 8.9). Our observations of the relationship between prognosis and occurrence of ventricular arrhythmias in UA/NSTEMI are consistent with reports from the GRACE registry. In the registry, the proportion of patients who developed ventricular arrhythmias during hospitalisation was 6.9% (1.8% with ventricular tachycardia [VT], 5.1% with ventricular fibrillation or cardiac arrest). Patients with STEMI were more likely to have ventricular arrhythmias (12%) than those with NSTEMI (4.9%) or UA (3.1%, $p < 0.001$). Several demographic and clinical variables were associated with the occurrence of ventricular arrhythmias, including ST-segment deviation, Killip class, age, initial cardiac markers, serum creatinine level, heart rate, and history of selected comorbidities. Ventricular arrhythmias during hospitalisation for ACS were associated with higher in-hospital mortality in the whole study group (OR 46.5, 95% CI 40.7–52.9) as well as in the STEMI and UA/NSTEMI subgroups (OR 31.8, 95% CI 26.7–27.8 and OR 80.8, 95% CI 65.8–99.2), with a higher impact observed in patients with UA/NSTEMI. Nevertheless, the adverse effect of ventricular arrhythmias on the prognosis for up to six months after discharge, excluding in-hospital mortality, was only significant in the UA/NSTEMI group (OR 1.46, 95% CI 1.01–2.10), and not in the STEMI group (OR 1.29; 95% CI 0.96–1.75) [14]. These results are in line with our findings. Moreover, the rates of ventricular arrhythmias without sudden cardiac arrest (SCA) and with resuscitated SCA were 3% and 3.9%, respectively. The frequency of ventricular arrhythmias was higher in the STEMI group than in the UA/NSTEMI group, with a significant difference in resuscitated SCA (5.3% vs. 1.6%, $p = 0.0156$) and no significant difference in ventricular arrhythmias without SCA (3.8% vs. 1.6%, $p = 0.0931$) [13]. Recent studies indicate that milder forms of ventricular arrhythmia may also be important in patients with UA/NSTEMI. The MERLIN-TIMI 36 trial [15] confirmed that non-sustained VT is common in patients with NSTEMI, and even short episodes of VT lasting from four to seven beats are independently associated with the risk of sudden cardiac death (SCD) during the subsequent year. A total of 6345 (97%) patients had continuous ECG recordings evaluable for analysis. Compared with patients with no VT ($n = 2764$), there was no increased risk of SCD in patients with only ventricular triplets ($n = 1978$, 31.2%; 1.4% vs. 1.2%); however, the risk of SCD was higher in patients with VT lasting from four to seven beats ($n = 1172$, 18.5%; SCD 2.9%, adjusted HR 2.3, $p < 0.001$) and in patients with VT lasting at least eight beats ($n = 431$, 6.8%; SCD 4.3%, adjusted HR 2.8, $p = 0.001$). This effect was independent of baseline characteristics and ejection fraction. VT occurring within the first 48 h after admission was not associated with SCD [15].

Other interesting clinical prognostic parameters are recurrence of angina pectoris with ischaemia on ECG for the UA/NSTEMI group and hospital discharge for the STEMI group. In the case of angina pectoris with ischaemia on ECG, this indicator may reflect two clinical situations. First, it can identify patients enrolled in the first hours of the conservative strategy who had recurrence of pain, and second, it identifies patients who have not undergone PCI due to advanced coronary lesions or while awaiting cardiac surgery for angina pectoris with ischaemic changes. This situation is probably more common in the UA/NSTEMI group than the STEMI group, so this factor was identified in the model. Hospital discharge as a risk factor in the NSTEMI group can be explained by the fact that those patients were more likely to be referred to cardiac surgery departments due to complications of ACS (myocardial rupture,

coronary artery perforation), to the co-operating departments of medicine for longer follow-up and optimisation of pharmacotherapy, or referred for CABG surgery.

Because the main purpose of the study was to assess the long-term outcome of patients with ACS hospitalised and discharged from a particular referral centre with 24-h catheter laboratory in collaboration with centres without an interventional cardiology unit, this was a single-centre study. Such analysis may be more appropriate than the use of clinical trial data, which initially represents the population excluding the most at-risk patients.

The smaller number of patients with UA/NSTEMI is also a limitation for statistical analysis. On the other hand, regarding the purpose of the study, data for the whole population seem to be largely useful and universal.

Another limitation is no division of the ACS group without persistent ST-segment elevation into UA and NSTEMI subgroups. It is well-known that the UA subgroup has a better prognosis. However, given the common definition of these populations in the standards for the diagnosis and treatment of ACS, and the fact that the UA group is a minority, especially in reference centres to which patients are referred for interventional treatment, the common denotation of these populations is, in our opinion, useful in practice. It should also be noted that the distinction between UA and NSTEMI patients would be very difficult due to the data collection period, especially between 2002 and 2003 when the new division of ACS was introduced into practice.

Another limitation is the fact that the data obtained from the PESEL database did not provide an opportunity to analyse the causes of death. It was also impossible to provide data on the occurrence of non-fatal complications.

In conclusion, we documented marked differences in the risk of post-discharge mortality after an ACS event. The risk factors obtained both from the medical history and during the hospitalisation increased the power of the risk stratification model.

References

1. Bueno H, Fernández-Avilés F. Use of risk scores in acute coronary syndromes. Heart. 2012; 98(2): 162–168, doi: 10.1136/heartjnl-2011-300129, indexed in Pubmed: 22156037.
2. Hamm CW, Bassand JP, Agewall S, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2011; 32(23): 2999–3054, doi: 10.1093/eurheartj/ehr236, indexed in Pubmed: 21873419.
3. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. JAMA. 2000; 284(7): 835–842, indexed in Pubmed: 10938172.
4. Boersma E, Pieper KS, Steyerberg EW, et al. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation. Results from an international trial of 9461 patients. The PURSUIT Investigators. Circulation. 2000; 101(22): 2557–2567, indexed in Pubmed: 10840005.
5. Fox KAA, Dabbous OH, Goldberg RJ, et al. Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE). BMJ. 2006; 333(7578): 1091–1094, doi: 10.1136/bmj.38985.646481.55, indexed in Pubmed: 17032691.
6. Eagle KA, Lim MJ, Dabbous OH, et al. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. JAMA. 2004; 291(22): 2727–2733, doi: 10.1001/jama.291.22.2727, indexed in Pubmed: 15187054.
7. Thygesen K, Alpert JS, Jaffe AS, et al. Third Universal Definition of Myocardial Infarction. Circulation. 2012; 126(16): 2020–2035, doi: 10.1161/cir.0b013e31826e1058.
8. Singh M, White J, Hasdai D, et al. Long-term outcome and its predictors among patients with ST-segment elevation myocardial infarction complicated by shock: insights from the GUSTO-I trial. J Am Coll Cardiol. 2007; 50(18): 1752–1758, doi: 10.1016/j.jacc.2007.04.101, indexed in Pubmed: 17964038.
9. Hochman JS, Apolito R. The calm after the storm: long-term survival after cardiogenic shock. J Am Coll Cardiol. 2007; 50(18): 1759–1760, doi: 10.1016/j.jacc.2007.07.046, indexed in Pubmed: 17964039.
10. Eagle KA, Lim MJ, Dabbous OH, et al. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. JAMA. 2004; 291(22): 2727–2733, doi: 10.1001/jama.291.22.2727, indexed in Pubmed: 15187054.
11. Tomaszuk-Kazberuk A, Kozuch M, Malyszko J, et al. Which method of GFR estimation has the best prognostic value in patients treated with primary PCI: Cockcroft-Gault formula, MDRD, or CKD-EPI equation? A 6-year follow-up. Ren Fail. 2011; 33(10): 983–989, doi: 10.3109/0886022X.2011.618922, indexed in Pubmed: 22013931.
12. Lenarczyk R, Pruszkowska P, Morawski S, et al. Ultra-fast, high density 3D mapping (Rhythmia Mapping System) and catheter radiofrequency ablation for electrical storm – early single centre experience. Heart Beat J. 2017; 1: 35–40, doi: 10.24255/hbj/68137.
13. Bangalore S, Messerli FH, Ou FS, et al. The association of admission heart rate and in-hospital cardiovascular events in patients with non-ST-segment elevation acute coronary syndromes: results from 135 164 patients in the CRUSADE quality improvement initiative. Eur Heart J. 2010; 31(5): 552–560, doi: 10.1093/eurheartj/ehp397, indexed in Pubmed: 19793769.
14. Avezum A, Piegas LS, Goldberg RJ, et al. Magnitude and prognosis associated with ventricular arrhythmias in patients hospitalized with acute coronary syndromes (from the GRACE Registry). Am J Cardiol. 2008; 102(12): 1577–1582, doi: 10.1016/j.amjcard.2008.08.009, indexed in Pubmed: 19064008.
15. Scirica BM, Braunwald E, Belardinelli L, et al. Relationship between nonsustained ventricular tachycardia after non-ST-elevation acute coronary syndrome and sudden cardiac death: observations from the metabolic efficiency with ranolazine for less ischemia in non-ST-elevation acute coronary syndrome-thrombolysis in myocardial infarction 36 (MERLIN-TIMI 36) randomized controlled trial. Circulation. 2010; 122(5): 455–462, doi: 10.1161/CIRCULATIONAHA.110.937136, indexed in Pubmed: 20644019.

Cite this article as: Grabowski M, Filipiak KJ, Opolski G, et al. Risk factors for adverse outcomes of patients with acute coronary syndrome: single-centre experience with long-term follow-up of treated patients. Kardiol Pol. 2018; 76(5): 881–888, doi: 10.5603/KP.a2018.0031.