Research article/Raziskovalni prispevek

EARLY PREDICTORS OF 30-DAY MORTALITY IN NON-ST-ELEVATION ACUTE CORONARY SYNDROME PATIENTS

ZGODNJI DEJAVNIKI TVEGANJA ZA 30-DNEVNO UMRLJIVOST BOLNIKOV Z AKUTNIM KORONARNIM SINDROMOM BREZ DVIGA VEZNICE ST

Suzana Rožič,[1] Melanija Županić,[1] Andreja Sinkovič[2]

[1] Medical Faculty, University Maribor, Slomškov trg 15, 2000 Maribor, Slovenia
[2] Department of Medical Intensive Care, University Clinical Center Maribor, Ljubljanska 5, 2000 Maribor, Slovenia

Abstract

Background *The incidence of non-ST-elevation acute coronary syndrome (ACS), including unstable angina pectoris and non-ST-elevation myocardial infarction (MI), is increasing in comparison to ST-elevation ACS. Our aim was to evaluate predictive role of admission variables for 30-day mortality in non-ST-elevation ACS patients.*

Patients and methods *We retrospectively analysed the data of 415 patients, admitted to University Clinical Center Maribor in 2006 due to non-ST-elevation ACS. Inclusion criteria were rest chest pain, ECG changes (ST-segment depression ≥ 0.1 mV, and/or negative T wave ≥ 0.1 mV and/or pathologic Q and/or non-specific ECG) and/or increased troponin T levels. Predictors of 30-day mortality were analysed by univariate and multivariate logistic regression.*

Results *30-day mortality was 4.3 %. Between nonsurvivors and survivors there were significant differences in mean age, the incidence of arterial hypertension, positive family history of coronary artery disease, in mean admission systolic and diastolic blood pressure, pulse, mean admission troponin T, leukocyte count, CRP, creatinine and the incidence of admission heart failure. Multivariate logistic regression proved that most significant independent early predictor of 30-day mortality was admission heart failure (OR 41.21, 95 % CI 3.50 to 484.66, p = 0.003), followed by admission serum creatinine (OR 0.989, 95 % CI 0.981 to 0.997, p = 0.008) and troponin T (OR 0.263, 95 % CI 0.080 to 0.861).*

Conclusion *Most significant independent predictor of 30-day mortality of patients with non-ST-elevation ACS, being 4.5 %, was heart failure on admission.*

Key words *mortality; non-ST-elevation acute coronary syndrome; predictors*

Izvleček

Izhodišča *Akutni koronarni sindrom (AKS) brez dviga veznice ST je vse pogostejši. Naš cilj je oceniti pomen zgodnjih dejavnikov za smrt znotraj 30 dni pri bolnikih z AKS brez dviga veznice ST.*

Bolniki in metode *Retrospektivno smo obdelali podatke 415 bolnikov, sprejetih v 2006 v Univerzitetni klinični center v Mariboru zaradi AKS brez dviga veznice ST. Ob prsni bolečini v mirovanju so imeli bolniki značilne EKG spremembe (znižanje veznice ST ≥ 0,1 mV in/ali negativni val*

Corresponding author / Avtorica za dopisovanje:

Profesorica dr. sc. Andreja Sinkovič, dr. med., specialist internist, adviser

Department of Medical Intensive Care, University Clinical Center Maribor, Ljubljanska 5, SI-2000 Maribor, phone: +2/3211656, fax.: +2/3312393, e-mail: a.sinkovic@ukc-mb.si

T ≥ 0,1 mV in/ali patološki val Q in/ali nespecifični EKG) in/ali dvig troponina T. Zgodnja napovedna vrednost spremenljivk za 30-dnevno umrljivost je bila ocenjena z univariatno in multivariatno statistično metodo.

Rezultati *30-dnevna umrljivost je bila 4,3 %. Med umrlimi in preživelimi smo ugotavljali statistično pomembene razlike v povprečni starosti, pogostnosti arterijske hipertenzije, pozitivne družinske anamneze koronarne bolezni, povprečni vrednosti sprejemnega sistoličnega in diastoličnega krvnega tlaka, pulza, troponina T, števila levkocitov, CRP in kreatinina ter v pogostnosti srčnega popuščanja ob sprejemu. Multivariantna logistična regresija je pokazala, da je najpomembnejši zgodnji dejavnik tveganja za 30-dnevno umrljivost prisotnost srčnega popuščanja ob sprejemu (OR 41,21, 95 % CI 3,50 do 484,66, p = 0,003), nato sprejemna vrednost kreatinina (OR 0,989, 95 % CI 0,981 do 0,997, p = 0,008) in troponina T (OR 0,263, 95 % CI 0,080 do 0,861, p = 0,027).*

Zaključki *Najpomembnejši neodvisni dejavnik tveganja za 30-dnevno umrljivost bolnikov z AKS brez trajnega dviga veznice ST, ki je bila 4,3 %, je prisotnost srčnega popuščanja ob sprejemu v bolnišnico.*

Ključne besede *umrljivost; akutni koronarni sindrom brez dviga ST; dejavniki tveganja*

Background and aims

Main characteristics of acute coronary syndromes (ACS) are oppressive rest chest pain and new ECG changes. Chest rest pain may vary in intensity and duration and ECG changes mostly involve ST-segment and/or T-wave. According to ECG changes, ACS are devided into two main categories: in ACS with persistent ST-segment elevation and ACS without it. In most case of ACS with persistent ST-segment elevation chest rest pain is usually prolonged (> 30 min) and does not respond to sublingual nitroglicerin application. In ACS with persistent ST-elevation on ECG de novo bundle branch block is the alternative ECG criterium.[1–3]

In non-ST-elevation ACS most common ECG changes are ST-segment depression and/or T-wave inversion, but non-specific ECG changes may be encountered as well. Chest rest pain may be prolonged or shorter than 20 minutes in duration. It can be mostly classified as class IIIA, IIIB or IIIC according to Braunwald's classification of angina pectoris.[2–4]

In both two types of ACS later increase in Troponin T or I levels defines the final diagnosis of acute myocardial infarction (MI), that started with chest pain in addition to ST-changes in ECG.[5]

ACS with ST-segment elevation on ECG is the consequence of transmural ischemia, resulting mostly in acute Q-MI. Non-ST-elevation ACS is mostly the consequence of subendocardial ischemia, resulting later in non Q-MIs.[2, 3, 5] If troponin levels remain normal unstable angina pectoris is the final diagnosis.[4, 5]

ACS is most often the consequence of occlusion or severe stenosis of coronary arteries, caused by acute thrombosis superimposed on ruptured, eroded or inflammed atherosclerotic plaque.[1–3]

Epidemiological clinical studies and registries report an increasing incidence of non-ST-elevation ACS in comparison to ACS with ST-segment elevation.[6–8] In addition, they report better short-term outcome data in non-ST-elevation ACS.[6, 7] However, long-term mortality and/or reinfarction rate are similar or even worse in patients with non-ST-elevation ACS than in ST-elevation ACS patients.[6, 7, 9]

Among predictors of adverse outcome Troponin levels and heart failure on admission and during in-hospital stay in addition to admission ECG changes were most significant according to studies and registries.[6, 7, 10] In addition, there are evidences from clinical studies that white blood cell count, high-sensitivity CRP and changes in haemoglobin level during treatment – in particular anemia due to hemorrhagic complications – have some prognostic value.[6, 11, 18]

Our aim was to assess the importance of admission variables for 30-day mortality of patients with non-ST-elevation ACS, who were admitted to University Clinical Center in 2006.

Patients and methods

We retrospectively analysed the records of all the patients, admitted between January 1st 2006 and December 31st 2006 to the Clinic of Internal medicine of the University Clinical Center Maribor due to ACS. All the data were obtained by the Medis hospital computer programme, by which the data of every in-hospital stay and outpatient visit of every single patient are accessible. As this was a retrospective analysis, we checked the records of all the patients, discharged from the hospital in 2006 with the main diagnosis marked according to International classification of diseases as I20–I25 (ischemic heart disease), in particular I200 (Unstable angina), I21 (acute MI), I210 (acute anterior Q MI), I211 (acute inferior Q MI), I212 (acute Q MI of other locations), I213 (acute Q MI of non-defined location), I214 (acute non-Q MI), I219 (acute undetermined MI), I22 (subsequent MI), I220 (subsequent anterior MI), I221 (subsequent inferior MI), I228 (subsequent MI of other locations) and I229 (subsequent MI of non-defined location). Personal

data of all the patients were protected according to the Law of personal data protection. As only discharge diagnosis I20–I25 were considered, patients with chest pain of noncoronary origin were obviously excluded, when the final – discharge diagnosis was established.

Out of 773 patients with ACS we included only 415 (227 men, 188 women, mean age 67.69 ± 11.77 years), who met the criteria for non-ST-elevation ACS. The inclusion criteria were oppressive chest pain at rest, lasting up to 48 hours before admission and non-ST-elevation ECG changes, i.e. ST-segment depression ≥ 0.1 mV and/or ST-segment depression with slight ST-segment elevation and/or negative T wave ≥ 0.1 mV and/or pathologic Q wave suspective of previous myocardial infarction and/or non-specific changes on ECG with elevated troponin T levels.[2–4]

In all the patients we detected baseline demographic, clinical, and laboratory data, in-hospital treatments and complications as well as 30-day mortality. In case the patient's data were not accessible between the day of discharge and day 30, a telephone call was done to get the information regarding survival/mortality.

All the patients were treated according to guidelines.[11, 12]

In all the patients standard ECG was recorded on admission, thereafter every 24 hours of hospital stay and at recurrent chest pain. Serum Troponin T (TnT) levels were estimated by immunochemical method (Boehringer, Mannheim – Germany, normal levels up to 0.1 μg/L) on admission, 8–12 hours later and at the discretion of the attending physician, particularly in case of recurrent chest pain.[11] On admission plasma total cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol levels were measured by standard enzymatic methods (Olympus – Japan). Normal plasma levels were for total cholesterol < 5 mmol/L, for triglycerides < 1.7 mmol/L, for HDL-cholesterol > 1 mmol/L in men and > 1.2 mmol/L in women and for LDL-cholesterol < 3 mmol/L as recommended by European guidelines on cardiovascular disease prevention in clinical practice.[11, 13]

Patients received daily oral acetylsalycylic acid (ASA) (100–300 mg tablet), i.v. infusion of standard heparin (SH) or s. c. injection of the recommended dose of low molecular weight heparin (LMWH) for few days, that was prolonged at the discretion of the attending physician.[4, 11, 12] If necessary, the patients were treated by nitroglycerin, clopidogrel, beta-blockers, ACE inhibitors, statins, diuretics, calcium antagonists, dobutamin, etc.[11–13]

Acute ischemic necrosis – non-ST-elevation myocardial infarction (NSTEMI) was confirmed by an increase in TnT level > 0.1 μg/L either on admission and/or 8–12 hours later.[5]

In case of recurrent chest pain and/or hemodynamic instability and/or rhythmic instability within the first 48 hours, the patients were treated with glycoprotein receptor antagonists IIb/IIIa (tirofiban, integrillin, abciximab), followed by early percutaneous coronary angiography and intervention (PCI) or surgical revascularization.[11–13] PCI was associated with clopidogrel therapy – loading dose 300 mg, followed by 75 mg daily.[11, 12, 14] When the patients were asymptomatic during the first 48 hours, coronary angiography with subsequent PCI or surgical revascularization was performed later within the next few days or weeks, in particular if ischemia was detected by exercise testing.[11–13] In case of increased serum creatinine level urine output was carefully measured, most ofter every hour during the ICU-stay. The dose of the medications was adjusted to serum creatinine levels and iv. infusion of fluids administered for renal protection with or without noradrenalin and/or dopamine and/or dobutamine and/or furosemide and/or renal replacement therapy (RRT) was started by the discretion of the treating physician.[11]

Among baseline demographic, clinical and laboratory data gender, age, body mass index (BMI), previous arterial hypertension, diabetes, dyslipidemia, prior myocardial infarction and/or stroke, positive family history of coronary artery disease, smoking, physical activity, admission levels of systolic and dyastolic blood pressure, pulse and heart failure on admission were detected, troponin T levels, the lipid profile, haemoglobin levels, leucocyte count and CRP on admission and during in-hospital stay.

Among in-hospital complication we detected atrial and ventricular arrhythmias, ventricular tachycardias and fibrillation, conduction disturbances such as bundle branch blocks or atrioventricular and sinoatrial blocks, asystole, etc., heart failure of classes II, III and IV according to the NYHA and Killip-Kimball classification, reinfarctions and 30-day mortality.[15, 16] Heart failure on admission was defined when clinical symptoms and signs of Killip class II, III and IV were registered.[11, 15, 16]

Statistical analysis

The retrospectively collected data were analyzed using SPSS for Windows with basic statistical methods. The values were expressed as means ± standard deviations, median levels or percentages. The differences between the groups were tested using chi-square test and two-sided Student's t-test. Multivariate logistic regression was done, using statistically significant variables from univariate analysis. Values $p < 0.05$ were considered statistically significant.[17]

Results

Basic demographic, clinical and laboratory data of all the patients on admission are listed in Table 1. In-hospital complications and laboratory data of all the patients are listed in Table 2. Troponin T on admission was above the 99th percentile of reference level (≥ 0.1 μg/l) in 51 % of all included patients (204/415), troponin T levels after 8–12 hours was increased in 47 % (199/415) of patients and peak troponin T levels (≥ 0.1 μg/l) in 63.4 % (263/415) of patients. Therefore, according to the rise and fall of Troponin T level, NSTEMI was diagnosed in 63.4 % of patients. Rest chest pain was present in 83.4 % of our patients.

Table 1. *Admission demographic, clinical and laboratory data of our patients.*
Razpr. 1. *Demografski, klinični in laboratorijski podatki naših bolnikov ob sprejemu.*

Admission demographic, clinical and laboratory data Demografski, klinični in laboratorijski podatki ob sprejemu	All Vsi (n = 415)	Nonsurvivors Umrli (n = 18)	Survivors Preživeli (n = 397)	P
Men / women (% men) Moški / ženske (% moških)	227/188 (54.7)	7/11 (38.9)	220 /177 (55.4)	0.226
Mean age ± SD (years) Povprečna starost ± SD (leta)	67.69 ± 11.77	79.78 ± 8.85	67.15 ± 11.60	< 0.001
Mean BMI ± SD, median (kg/m^2) Povprečni ITM ± SD, mediana (kg/m^2)	27.59 ± 4.86	25.42 ± 3.03	27.61 ± 4.87	0.437
Arterial hypertension Arterijska hipertenzija (%)	84.8	64.7	85.6	0.031
Prior diabetes Predhodna sladkorna bolezen (%)	25.1	35.3	24.7	0.390
Prior myocardial infarction Predhodni infarkt srca (%)	30.3	47.1	29.5	0.174
Prior stroke Predhodna možganska kap (%)	7.7	17.6	7.3	0.134
Positive family history of CAD Pozitivna družinska anamneza KBS (%)	35.2	6.7	36.5	0.024
Smoking Kajenje (%)	17.4	31.3	16.7	0.169
Mean systolic BP ± SD, median (mmHg) Povprečni sistolični KT ± SD, mediana (mmHg)	146.90 ± 23.68, 150.0	125.44 ± 28.60, 127.5	147.91 ±22.98, 150.0	< 0.001
Mean dyastolic BP ± SD, median (mmHg) Povprečni diastolični KT ± SD, mediana (mmHg)	87.15 ± 13.20, 85	77.89 ± 18.02, 80.0	87.59 ± 12.90, 86.0	0.002
Mean pulse ± SD, median (min^{-1}) Povprečni pulz ± SD, median (min^{-1})	80.51 ± 21.35, 76.0	100.28 ± 26.10, 100.0	79.59 ± 20.68, 75.0	< 0.001
Heart failure Srčno popuščanje (%)	10.6	55.6	8.5	< 0.001
Mean troponin T ± SD, median (µg/l) Povprečni troponin T ± SD, mediana (µg/l)	0.37 ± 0.66, 0.09	0.87 ± 1.09, 0.34	0.35 ± 0.63, 0.09	0.001
Mean hemoglobin ± SD, median (g/l) Povprečni hemoglobin ± SD, median (g/l)	133.64 ± 18.06, 135.0	128.06 ± 21.40, 127.0	133.88 ± 17.90, 135.0	0.194
Mean leukocyte count ± SD, median (10^9/l) Povprečno število levkocitov ± SD, median (10^9/l)	8.45 ± 3.76, 7.6	10.41 ± 6.25, 9.0	8.37 ± 3.60, 7.6	0.028
Mean serum cholesterol ± SD (mmol/l) Povprečni serumski holesterol ± SD (mmol/l)	4.89 ± 1.34	4.22 ± 0.84	4.91 ± 1.35	0.068
Mean serum triglycerides ± SD (mmol/l) Povprečni serumski trigliceridi ± SD (mmol/l)	1.97 ± 1.48	1.39 ± 0.56	1.99 ± 1.50	0.149
Mean serum LDL-cholesterol ± SD (mmol/l) Povprečni serumski LDL-holesterol ± SD (mmol/l)	2.87 ± 1.05	2.39 ± 0.76	2.89 ± 1.06	0.140
Mean serum HDL-cholesterol ± SD (mmol/l) Povprečni serumski HDL-holesterol ± SD (mmol/l)	1.12 ± 0.29	1.21 ± 0.36	1.12 ± 0.29	0.335
Mean serum CRP ± SD, median (mg/l) Povprečni serumski CRP ± SD, median (mg/l)	15.59 ± 31.42, 5.0	55.38 ± 72.82, 17.0	13.86 ± 27.24, 5.0	< 0.001
Mean serum creatinine ± SD, median (µmol/l) Povprečni serumski kreatinin ± SD, median (µmol/l)	108.05 ± 98.37, 87.0	199.41 ± 167.62, 135.0	104.11 ± 92.61, 86.0	< 0.001

SD – standard deviation, BMI – body mass index, CRP – capsular reactive protein, CAD – coronary artery disease, BP – blood pressure, LDL – low density lipoprotein; HDL – high density lipoprotein

SD – standardna deviacija, ITM – indeks telesne mase, CRP – C-reaktivni protein, KBS – koronarna bolezen srca, KT – krvni tlak, LDL – lipoproteini nizke gostote, HDL – lipoproteini visoke gostote

30-day mortality of our ACS patients with non-ST-elevation was 4.3 % (18/415).

When we compared baseline demographic, laboratory and clinical data between nonsurvivors and survivors, that are listed in Table 1, we observed statistically significant differences in mean age (79.7 ± 8.8 years vs 67.1 ± 11.6 years, p < 0.001), the incidence of arterial hypertension (64.7 % vs 85.6 %, p = 0.031), positive family history of coronary artery disease (CAD) (6.7 % vs 36.5 %, p = 0.024), admission heart failure (55.6 % vs 8.5 %, p < 0.001) and in mean admission systolic (125.4 ± 28.6 mmHg vs 147.9 ± 22.9 mmHg, p < 0.001) and diastolic blood pressure (77.8 ± 18.0 mmHg vs 87.5 ± 12.9 mmHg, p = 0.002), pulse rate (100.2 ± 26.1 min^{-1} vs 79.5 ± 20.6 min^{-1}, p < 0.001), Troponin T (0.8 ± 1.0 µg/l vs 0.3 ± 0.6 µg/l, p = 0.001), serum creatinine (199.4 ± 167.6 µmol/l vs 104.1 ± 92.6 µmol/l, p < 0.001), leucocyte count (10.4 ± 6.2·10^9/l vs 8.3 ± 3.6·10^9/l, p = 0.028) and CRP levels (55.3 ± 72.8 mg/l vs 13.8 ± 27.2 mg/l, p < 0.001).

When we compared in-hospital complications and laboratory data between nonsurvivors and survivors, being listed in Table 2, we observed statistically significant differences in the rate of in-hospital heart

Table 2. *In-hospital complications and laboratory data.*

Razpr. 2. *Bolnišnični zapleti in laboratorijski podatki.*

Complications and laboratory data Zapleti in laboratorijski podatki	All Vsi (n = 415)	Nonsurvivors Umrli (n = 18)	Survivors Preživeli (n = 397)	P
Heart failure / Srčno popuščanje (%)	10.1	44.4	8.6	< 0.001
Arrhythmias / Aritmije (%)	13.3	22.2	12.8	0.278
Reinfarction / Reinfarkt (%)	4.1	16.7	3.5	0.032
NSTEMI / NSTEMI (%)	63.9	77.8	63.2	0.316
Mean control serum troponin T ± SD, median (µg/l) / Povprečni kontrolni troponin T ± SD, mediana (µg/l)	0.80 ± 1.0, 0.16	1.2 ± 1.2, 0.83	0.54 ± 0.96, 0.13	0.006
Mean peak troponin T ± SD, median (µg/l) / Povprečni najvišji troponin T ± SD, mediana (µg/l)	1.04 ± 1.41, 0.29	1.54 ± 1.26, 0.88	0.79 ± 1.31, 0.25	0.017
Mean peak creatinine ± SD, median (µmol/l) / Povprečni najvišji kreatinin ± SD, mediana (µmol/l)	124.83 ± 125.58, 94.0	269.88 ± 215.38, 217.0	118.58 ± 116.70, 93.0	< 0.001
Mean peak CRP ± SD, median (mg/l) / Povprečni najvišji CRP ± SD, mediana (mg/l)	31.02 ± 53.75, 8.0	107.56 ± 95.34, 72.0	27.70 ± 48.77, 7.0	< 0.001

NSTEMI – non-ST-elevation myocardial infarction, SD – standard deviation, CRP – capsular reactive protein

NSTEMI – miokardni infarkt brez dviga veznice ST, SD – standardna deviacija, CRP – C-reaktivni protein.

Table 3. *In-hospital treatments of patients.*

Razpr. 3. *Bolnišnično zdravljenje naših bolnikov.*

Treatments Zdravljenje	All Vsi (n = 415)	Nonsurvivors Umrli (n = 18)	Survivors Preživeli (n = 397)	P
Aspirin / Aspirin (%)	88.4	77.8	88.9	0.142
Clopidogrel / Klopidogrel (%)	71.3	44.4	72.5	0.015
Heparin / Heparin (%)	85.1	83.3	85.1	0.740
GP IIb/IIIa inhibitors / Zaviralci GP IIb/IIIa (%)	49.2	11.1	50.9	0.001
Diuretics / Diuretiki (%)	38.1	77.8	36.3	0.001
Noradrenalin / Noradrenalin (%)	1.9	5.6	1.8	0.301
Dobutamine / Dobutamin (%)	2.7	5.6	2.5	0.390
Dopamine / Dopamin (%)	2.2	22.2	1.3	< 0.001
IABC / IABČ (%)	0.2	0	0.2	1.000
RRT / NLZ (%)	1.7	5.6	1.5	0.269
CABG / AKO (%)	5.5	0	5.8	0.613
PCI / PKI (%)	72.3	5.6	75.3	< 0.001

IABC – intraaortic balloon counterpulsation, GP IIb/IIIa – inhibitors of glycoprotein receptors IIb/IIIa, RRT – renal replacement therapy, CABG – aortocoronary bypass grafting, PCI – percutaneous coronary intervention

IABČ – intra-aortna balonska črpalka, GP IIb/IIIa – zaviralci glikoproteinskih receptorjev IIb/IIIa, NLZ – nadomestno ledvično zdravljenje, AKO – aortni koronarni obvod, PKI – perkutana koronarna intervencija

failure (44.4 % vs 8.6 %, p < 0.001), reinfarction rate (16.7 % vs 3.5 %, p = 0.032), mean control troponin T levels after 12 hours of in-hospital stay (1.2 ± 1.2 µg/l vs 0.5 ± 0.9 µg/l, p = 0.006) and mean peak troponin T (1.5 ± 1.2 µg/l vs 0.7 ± 1.3 µg/l, p = 0.017), CRP (107.5 ± 95.3 mg/l vs 27.7 ± 48.7 mg/l, p < 0.001), and creatinine levels (269.8 ± 215.3 mg/l vs 27.7 ± 48.7 mg/l, p < 0.001).

Comparison of in-hospital treatments between nonsurvivors and survivors are listed in Table 3, demonstrating significant differences between nonsurvivors and survivors in the use of clopidogrel (44.4 % vs. 72.5 %, p = 0.015), GPIIb/IIIa inhibitors (11.1 % vs. 50.9 %, p = 0.001), diuretics (77.8 % vs. 36.3 %, p = 0.001), dopamine (22.2 % vs 1.3 %, p < 0.001), and PCIs (5.6 % vs 75.3 %, p < 0.001).

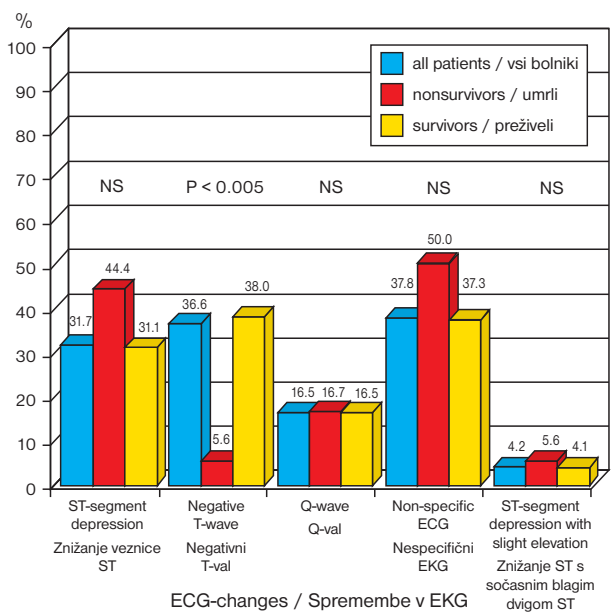

Figure 1. *ECG-changes on admission.*

Sl. 1. *Spremembe v EKG ob sprejemu.*

Table 4. *Multivariate logistic regression of significant clinical and laboratory data on admission.*

Razpr. 4. *Multivariatna logistična regresija statistično pomembnih kliničnih in laboratorijskih podatkov ob sprejemu.*

Admission data / Podatki ob sprejemu	χ^2	P	OR	95 % CI	
				Lower limit Spodnja meja	Upper limit Zgornja meja
Age / Starost	1.461	0.227	0.934	0.835	1.044
Arterial hypertension / Arterijska hipertenzija	2.862	0.091	0.157	0.018	1.341
Positive family history / Pozitivna družinska anamneza	2.330	0.127	0.013	0.000	3.429
Negative T-wave / Negativni T-val	1.455	0.228	0.104	0.003	4.106
Systolic blood pressure / Sistolični krvni tlak	3.704	0.054	1.074	0.999	1.156
Dyastolic blood pressure / Diastolični krvni tlak	0.621	0.431	0.949	0.832	1.082
Pulse / Pulz	0.951	0.330	0.972	0.918	1.029
Heart failure / Srčno popuščanje	8.745	0.003	41.214	3.505	484.660
Troponin T / Troponin T	4.867	0.027	0.263	0.080	0.861
Serum creatinine / Serumski kreatinin	7.138	0.008	0.989	0.981	0.997
Serum CRP / Serumski CRP	0.086	0.770	0.997	0.979	1.016
Leukocyte count / Število levkocitov	1.133	0.287	0.885	0.708	1.108

CRP – capsular reactive protein, χ^2 – chi-square, OR – odds ratio, 95 % CI – 95 % confidence interval.

CRP – C-reaktivni protein, χ^2 – hi-kvadrat, OR – razmerje obetov, 95 % CI – 95 % interval zaupanja

We observed in nonsurvivors the increased admission and control troponin T levels over 0.1 μ/l in 83.3 % (15/18) and increased peak troponin T levels over 0.1 μ/l in 94.4 %. In survivors an increased troponin T on admission was observed in 47.6 % and in 46.3 % after 12 hours of in-hospital stay, but increased peak troponin T level was observed in 61.9 % of survivors. The differences between survivors and non survivors were statistically significant.

Admission ECG changes are presented in Figure 1. A significant difference between nonsurvivors and survivors was observed only in the rate of negative T-wave on admission ECG (5.6 % vs 38.0, $p < 0.005$).

Multivariate logistic regression of variables is presented in Table 4.

Most significant independent predictor of 30-day mortality among admission variables was heart failure on admission, followed by admission serum creatinine and Troponin T level.

Discussion

Our observations were that significant independent early predictors of 30-day mortality in our patients with ACS with non-ST-elevation were heart failure on admission, admission serum creatinine and troponin T level. However, among independent predictors of 30-day mortality heart failure on admission was most significant.

According to other studies and registries we observed some similarities and some differences in epidemiology, treatments and outcome of ACS patients with non-ST-elevation.[6, 7]

During the last few years the incidence and prevalence of ACS with non-ST-elevation has increased when compared to ACS with persistent ST-elevation according to published studies and registries.[6, 7] The same situation is observed in the last few years in University Clinical Center Maribor, covering the area of northeastern part of Slovenia.[8] In 2006 53.7 % (415/773) of total ACS patients fulfilled the criteria for ACS with non-ST-elevation on ECG. This growing incidence of ACS with non-ST-elevation is the consequence of several factors, including older age of population in general, better primary and secondary prevention of CAD, early use of PCI in stable and especially in unstable CAD, increased reinfarction rate and last but not least the use of more sensitive and specific markers of ischemic myocardial necrosis such as troponin T or I.[6–8, 10]

In addition to rest chest pain present in majority of our cases (83.4 %), among ECG changes ST-segment depression and T-wave inversion predominated. T-wave inversion was even significantly less likely present in nonsurvivors than in survivors at 30 days. However, among our included patients non-specific ECG changes were registered in 37.1 %, but in Euro heart survey in 2002 only in 6.5 % of all ACS patients.[7] This striking difference may be the consequence of prior myocardial infarctions or other cardiovascular abnormalities or prior use of PCIs. Therefore, nonspecific ECG changes may even be the consequence of transmural ischemia, but classified as ACS with non-ST-elevation at discharge.[7]

Troponin T level, which is the most specific and sensitive marker of ischemic necrosis, was increased in approximately 50 % patients on admission, but during in-hospital stay even in more than 60 %, suggesting ischemic necrosis in more than 60 % of included patients, what is significantly more likely than in Euro Heart Survey from 2002, where they estimated the development of myocardial infarction in approximately 35 % patients – approximately 26.9 % non-Q wave myocardial infarction and 7.9 % Q-wave MI.[7] In approximately 40 % of our patients we did not register any increase in troponin T level and therefore, no MI in contrast to app. 65 % in Euro Heart Survey ACS in 2002.[7]

Baseline demographic data, such as age, diabetes, smoking, etc. as well as the incidence of chest pain, the mean level of systolic and diastolic blood pressure were similar to those in Euro Heart Survey ACS and Grace registry.[6, 7] However, in our patients we observed more likely arterial hypertension and positive family history of CAD and less likely gender dif-

ference as only 54.7 % of our patients were men and the rest women.[6, 7, 9]

When we compared our data to Grace registry and Euro Heart Survey ACS we observed in our patients similar rate of arrhythmias, reinfarctions, but less likely heart failure.[6,7] In comparison to registries our patients were treated during in-hospital stay more likely with clopidogrel, GPIIb/IIIa inhibitors and PCIs, but there was a similar use of aspirin, heparins and CABG.[6, 7] There are evidences that the use of early PCI procedures and concomitant use of triple antiplatelet therapy with aspirin, clopidogrel and GPIIb/IIIa as it was done in our patients is associated with better short-term and long-term survival of patients with ACS in general.[11, 12]

In spite of contemporary treatments 30-day mortality of our ACS patients with non-ST-elevation on ECG was 4.3 % (18/415) in comparison to 3.5 % in Euro Heart Survey ACS.[7]

In general, comorbidities and classical risk factors of atherosclerosis, if present on admission, indicate earlier and more severe CAD and they increase the risk of short- and long-term mortality.[6, 7, 11] Our population was older, had more arterial hypertension and more likely positive family history of CAD. When we compared nonsurvivors to survivors we observed several significant differences in baseline demographic, laboratory and clinical data, but also in in-hospital complications and treatments. Our nonsurvivors with non-ST-elevation ACS were significantly older than survivors, as their mean age was almost 80. They majority of them were women with comorbidities such as arterial hypertension, diabetes, prior stroke and MI. Admission heart failure, characterized by the presence of Killip classes II, III and IV, was even diagnosed in nearly 56 % of nonsurvivors in contrast to 8.5 % in survivors. The data about previous heart failure are not available; however, the data about 47 % of prior MI in nonsurvivors together with high percentage of admission heart failure may point to the pre-existing left ventricular dysfunction, that may not be symptomatic until new ischemic necrosis developed.[6, 11]

Nevertheless, when multivariate logistic regressional statistical testing of admission data was performed most significant independent predictor of 30-day mortality was heart failure on admission, followed by admission creatinine and troponin T level. Classical risk factors of atherosclerosis such as arterial hypertension, diabetes or age were not among independent predictors of mortality.

According to registries and several studies heart failure is usually the leading cause of mortality, but also the most significant risk and predictor of mortality.[6–8] Heart failure in ACS patients is the consequence of extensive ischemic necrosis, or reinfarction, or both.[2, 3, 11] Admission, control (8–12 hours after admission) and peak mean troponin T levels were significantly increased in nonsurvivors than survivors, indicating larger ischemic necrosis in nonsurvivors. However, only admission troponin T remained independent predictor of 30-day mortality.

Significant differences in treatments between nonsurvivors and survivors were observed in the use of antiplatelet agent clopidogrel, PCIs, diuretics and dopamine, as well as in nonsignificant differences in the use of noradrenalin, dobutamine and intra-aortic-baloon counterpulsation (IABC). Less frequent use of PCIs in nonsurvivors was the consequence of different factors, in particular of severe pre-existing CAD and the older age of nonsurvivors. In addition, in our non-ST-elevation ACS patients, who died within 30 days, we observed – besides older age – more frequently also other co-morbidities such as renal failure with increased admission serum creatinine levels, as well as increased mean white blood cell count and CRP levels, suggesting an active inflammatory process. Increased admission serum creatinine level was among significant independent predictors of 30-day mortality and the use of diuretics and iv. dopamine more likely in nonsurvivors was the consequence of both complications – heart failure and renal failure.

Contemporary guidelines recommend early invasive treatment in non-ST-elevation ACS patients, in particular in high-risk groups, presenting with age over 65 years, increased troponins, heart failure on admission, etc. However, according to trials, elderly are less likely to receive invasive treatment due to failed early benefit compared to younger patients. Therefore, according to European guidelines, in the elderly treatment decisions should be tailored according to estimated life expectancy, patient wishes, and comorbidities to minimize risk and improve outcomes. Therefore, in the elderly patients invasive procedures, including PCIs, as well as insertion of IABC, should be started only after careful evaluation of their inherited risk of procedure-related complications and this was the case in our nonsurvivors.[11]

Our conclusions are that ACS with non-ST-elevation on ECG is becoming more frequent clinical syndrome in our area with an early mortality rate of 4.3 %. Heart failure, troponin T level on admission as well as renal failure with increased serum creatinine on admission are most significant independent predictors of 30-day mortality of these ACS patients.

References

1. Štajer D, Koželj M, Ploj T, Pavčnik D, Milčinski M, Gužič-Salobir B, et al. Bolezni srca in žilja. In: Kocijančič A, Mrevlje F, Štajer D, eds. Interna medicina. Ljubljana: Littera picta, 2005. p. 53–290.
2. Antman EA, Braunwald E. Acute myocardial infarction. In: Braunwald E, Zipes DP, Libby P, eds. Heart disease. A textbook of cardiovascular medicine. 6th edition, Philadelphia: W. B. Saunders Company; 2001. p. 1114–231.
3. Kenda MF, Fras Z, Kranjec I, Noč M, eds. Akutni koronarni sindrom. Ljubljana: Združenje kardiologov Slovenije; 2002.
4. Cannon C, Braunwald E. Unstable angina. In: Braunwald E, Zipes DP, Libby P, eds. Heart disease. A textbook of cardiovascular medicine. 6th ed. Philadelphia: W. B. Saunders Company; 2001. p. 1232–71.
5. Thygesen K, Alpert JS, White HD on behalf of the joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. Eur Heart J 2007; 28: 2525–38.
6. Fox KAA, Goodman SG, Klein W, Brieger D, Steg PG, Dabbous O, et al. for the GRACE Investigators. Management of acute coronary syndromes. Variations in practice and outcome. Findings from the Global Registry of Acute Coronary Events (GRACE). Eur Heart J 2002; 23: 1177–89.

7. Hasdai D, Behar S, Wallentin L, Danchin N, Gitt AK, Boersma E, et al. A prospective survey of the characteristics, treatment and outcomes of patiens with acute coronary syndromes in Europe and the Mediterranean basin. The euro heart survey of acute coronary syndromes (Euro heart survey ACS). Eur Heart J 2002; 23: 1177–89.
8. Svensek F, Sinkovic A, Pehnec Z. Acute coronary syndromes in the elderly treated at the General Hospital Maribor in 2002 and 2003. Slov Kardiol 2005; 2: 8–12.
9. Sinkovic A, Marinsek M, Svensek F. Women and men with unstable angina and/or nin ST-elevation myocardial infarction. Wien Klin Wochenschr 2006; 118 Suppl 1: 52–7.
10. Sinkovic A, Pogacar V. Risk stratification in patients with unstable angina and/or non-ST-elevation myocardial infarction by Troponin T and plasminogen-activator-inhibitor-1 (PAI-1). Thromb Res 2004; 114: 251–7.
11. Bassand JP, Hamm CW, Ardissino D, Boersma E, Budaj A, Aviles FF, et al. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. The Task Force for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of the European Society of Cardiology. Eur Heart J 2007; 28: 1598–660.
12. Silber S, Albertsson P, Aviles FF, Camici PG, Colombo A, Hamm C, et al. Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Guidelines for percutaneous coronary interventions. The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Eur Heart J 2005; 26: 804–47.
13. De Backer G, Ambrosioni E, Borch-Johnsen K, Brotons C, Cifkova R, Dallongeville J, et al. European guidelines on cardiovascular disease prevention in clinical practice. Third joint task force of European and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of eight societies and by invited experts). Eur J Cardiovasc Prev Rehabil 2003; 10 Suppl 1: 1–78.
14. CURE investigators. Effects of pre-treatment with clopidogrel and aspirin followed by longterm therapy in patients undergoing percutaneous coronary intervention: The PCI-CURE study. Lancet 2002; 358: 527–33.
15. Lown B, Graboys TB. Sudden death. An ancient problem newly percieved. Cardiovasc Med 1977; 2: 219–29.
16. Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two years experience with 250 patients. Am J Cardiol 1967; 20: 457–64.
17. Jekel JF, Elmore JG, Katz DL, eds. Epidemiology, biostatistics and preventive medicine. 1st ed. Philadelphia: W. B. Saunders Company; 1996.
18. De Servi S, Mariani M, Mariani G, Mazzone A. C-reactive protein increase in unstable coronary disease. JAM Coll Cardiol 2005; 46: 1496–1502.

Arrived 2008-05-09, accepted 2008-08-08