Acute coronary syndrome in octogenarian patients: results from the international registry of acute coronary syndromes in transitional countries (ISACS-TC) registry

Olivia Manfrini[1]*, Maria Dorobantu[2], Zorana Vasiljevic[3], Sashko Kedev[4], Božidarka Knežević[5], Davor Miličić[6], Mirza Dilic[7], Dijana Trninic[8], Irfan Daullxhiu[9], Olivija Gustienė[10], Beatrice Ricci[1], Irene Martelli[1], Edina Cenko[1], Akos Koller[11], Lina Badimon[12], and Raffaele Bugiardini[1], on the behalf of the Working Group on Coronary Pathophysiology & Microcirculation of the European Society of Cardiology

[1]*Department of Experimental, Diagnostics and Specialized Medicine, Section of Cardiology, University of Bologna, Bologna, Italy*
[2]*Clinical Emergency Hospital Bucharest, Cardiology Department, University of Medicine and Pharmacy 'Carol Davila' Bucharest, Romania*
[3]*Clinical Center of Serbia, University of Belgrade, Belgrade, Serbia*
[4]*University Clinic of Cardiology, University 'Ss. Cyril and Methodius', Skopje, Macedonia*
[5]*Clinical Center of Montenegro, Center of Cardiology, Podgorica, Montenegro*
[6]*University of Zagreb School of Medicine, Department of Cardiovascular Diseases, University Hospital Centre Zagreb, Croatia*
[7]*Clinical Center University of Sarajevo, 71000 Sarajevo, Bosnia and Herzegovina*
[8]*Clinical Center of Banja Luka, Banja Luka, Republika Srpska, Bosnia and Herzegovina*
[9]*Department of Cardiology, University Clinical Centre of Kosovo, Prishtina, Kosovo*
[10]*Department of Cardiology, Lithuanian University of Health Sciences, Kaunas, Lithuania*
[11]*Department of Pathophysiology and Gerontology, and Szentagothai Research Centre, University of Pecs, Hungary*
[12]*Cardiovascular Research Center, CSIC-ICCC, Hospital de la Santa Creu i Sant Pau, CiberObn-Institute Carlos III, Autonomous University of Barcelona, Barcelona, Spain*

We sought to investigate characteristics, treatment, and outcome of octogenarian patients during hospital stay for acute coronary syndrome (ACS) in a transitional country. This is a cohort study of 437 patients $\geq$ 80 years old, consecutively admitted with a diagnosis of ACS at 14 hospitals in 8 Eastern European countries reporting data to ISACS-TC registry. The primary endpoint was in-hospital mortality. The mean age of the study population was 83.5 years; 50.1% of the patients were women. Females, less frequently than males, had a history of myocardial infarction, smoking habit, and episodes of typical chest pain. But they were more often admitted with left ventricular dysfunction. The rate of reperfusion treatment (29.5%) was very low in patients with ST-elevation myocardial infarction (STEMI). Also, most of the overall study population had a non-invasive approach (women, 79% vs. men, 70.6%; $P = 0.042$). However, when the

* Corresponding author. Tel: +39051347290, Fax: +39051347290,
Email: olivia.manfrini@unibo.it

coronary anatomy was known, there were no differences in the rates of revascularization between genders. There was no difference in the rates of death between male (21%) and female (21.1%) patients. Univariate and multivariate analyses revealed that the independent predictors (*P* < 0.05) of death in octogenarians were systolic blood pressure <100 mmHg (odds ratio [OR], 2.74), Killip class ≥ 2 (OR, 1.71), and STEMI as an index event (OR, 2.01). Evidence-based drugs (beta-blockers, statins, and ACE-inhibitors) had all independent significant protective effect on the hospital outcome. In conclusion, age is relevant in the prognosis of ACS, but its importance should be considered not secondary to other clinical factors.

Introduction

The increase in the number of older persons may have dramatic consequences on public health, the health-care financing and delivery systems, as well as informal care giving.[1] Although more attention has been given to ageing population and their implications in the treatment of ischaemic heart disease in developed countries, greater numbers of older adults and increasing incidence of coronary artery disease place a further strain on the resources in countries with an economy in transition, in which basic public health concerns are yet to be addressed fully.[1]

The ISACS Advisory Committee has identified five roles to promote health and prevent mortality from ischaemic heart disease in older adults: (1) to provide high-quality health information to public health professionals and consumers; (2) to support health-care organizations in prevention efforts; (3) to integrate public health prevention expertise with a cardiology services network; (4) to identify and implement effective prevention efforts; and (5) to monitor changes related to medications and coronary procedures in the health of older adults.

Existing ISACS data may help one to examine whether ongoing coronary programs meet the needs of an ageing population.

Methods

Study population

This is a cohort study of patients ≥80 years old, consecutively admitted with a diagnosis of ACS at 14 hospitals in 8 Eastern European country (Bosnia and Herzegovina, Croatia, Kosovo, Lithuania, Macedonia, Montenegro, Romania, and Serbia), reporting data to the International Survey of Acute Coronary Syndromes in Transitional Countries (ISACS-TC) registry from October 2010 to August 2013. Details of the ISACS-TC registry have been reported previously (NCT01218776).[2,3] Appropriateness of inclusion was judged by a specialist cardiology taking into account clinical history, physical examination, electrocardiogram (ECG), cardiac biomarkers, angiography, and/or postmortem findings.

The index event was categorized as unstable angina or non-ST-segment elevation myocardial infarction (NSTEMI), or ST-segment elevation myocardial infarction (STEMI).

The diagnosis of unstable angina pectoris was based on diagnostic ST-segment changes, and/or T-wave inversion and negative cardiac enzymes; in addition, at least one of the three symptoms: new onset of angina, accelerated angina and angina at rest in the previous 48 h.

NSTEMI was defined as the detection of myocardial markers of necrosis (troponins or creatinkinase MB mass) with typical temporal evolution associated with at least one of the following evidence of ischaemia: (1) typical symptoms of myocardial ischaemia; (2) ST-segment depression ≥0.5 mm in ≥2 contiguous leads or T-wave inversion >1 mm in leads with predominant R waves; (3) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.[4]

The diagnosis of STEMI was made by the detection of positive myocardial markers of necrosis (troponins or creatinkinase MB) with typical temporal evolution associated with at least one of the following evidence of ischaemia: (1) acute onset of prolonged [≥20 min] typical ischaemic chest pain; (2) ST-segment elevation (measured of J-point) of at least 1 mm in two or more contiguous leads, or new left bundle branch block, or development of pathological *Q* waves.

Patients provided written consent to the study. The study was approved by the local research ethics committee from each hospital.

Patients' characteristics

Baseline clinical data were collected prospectively and stored electronically. Information recorded included conventional cardiovascular risk factors, previous and recent cardiovascular history, examinations finding, electrocardiographic data, cardiac enzyme results, and details of in-hospital treatments and outcome. The definitions are reported below.

Cardiovascular risk factors
Diabetes mellitus: Fasting glucose concentration is ≥7 mmol/L (≥126 mg/dL) or if 2-h post-glucose load ≥11.1 mmol/L (≥200 mg/dL) or if the patient requires dietary sugar restriction and/or oral hypoglycaemic drug and/or insulin. *Hypertension*: systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg or the patient currently being treated for hypertension. *Hypercholesterolaemia*: serum total cholesterol ≥200 mg/dL (≥5.18 mmol/L) or LDL-cholesterol ≥130 mg/dL (≥3.33 mmol/L) or current treatment for hypercholesterolaemia.

Cardiovascular findings at hospital admission
We reported: (1) time from the onset of symptoms to admission within 12 h; (2) two or more episodes of chest pain, lasting 20 or more minutes, during the previous 24 h; (3) typical chest pain (heavy or squeezing feeling, or discomfort or tightness or pressure under the sternum or chest bone; pain may radiate to the jaw, neck, arms, back, and epigastrium); (4) heart rate; and (5) systolic blood pressure.

Cardiovascular history
Recent cardiac history (during the last 6 months) was separate from any cardiovascular diseases that took place in the past

(unstable angina, stable angina, myocardial infarction, revascularization, peripheral artery disease, stroke, or transient ischaemic attack, arrhythmias, valvular heart disease, and cardiomyopathy). The diagnosis of left-ventricular failure was made in patients who required diuretic therapy and had radiological signs of interstitial or alveolar pulmonary oedema, or symptoms of breathlessness accompanied by basal crepitations, a third heart sound, or both.

In-hospital treatment

Routine medical therapy (aspirin, clopidogrel/prasugel, ACE-inhibitors, beta-blockers, statins) as well as reperfusion treatment (fibrinolysis, percutaneous coronary intervention (PCI) and coronary artery bypass graft) were reported.

Endpoint

The primary endpoint was in-hospital mortality. Survival to hospital discharge was recorded for all patients. As potential predictors of death, we assessed age, recent and previous cardiovascular history, clinical findings at hospital admission, as well as in-hospital treatments.

Statistical analysis

We analysed the association between clinical variables and gender, and between clinical variables and age groups: from 80 to 84 years old (young-elderly) vs. 85 years old and older (old-elderly). Values are presented as mean $\pm$ standard deviation and percentage for categorical variables. The normal distribution of the data was tested with the Shapiro–Wilk's test. Comparisons between groups were made either by Student's t-test for continuous or by χ^2 test for categorical variables, as appropriate. Data with skewed distribution of the result were analysed with a non-parametric test (Mann–Whitney test). Predictors of in-hospital mortality were analysed by logistic regression and reported as odds ratio (OR) and 95% confidence interval (95% CI). Multiple logistic regression analysis was performed by introducing all the variables that in the univariate analysis presented a level of significance <0.2. All variables that entered the multiple regression analysis were dichotomized except for age, which was handled as a continuous variable. Statistical evaluation was performed using the STATA 11 (Stata Corporation, TX, USA). Values for $P < 0.05$ were regarded significant.

Results

We studied 437 patients with ACS who were identified prospectively in 14 participating sites from July 2007 through June 2013. Of those, 258 (59%) were admitted for STEMI, 150 (34.3%) for NSTEMI, and 28 (6.4%) for unstable angina. The mean age of the study population was 83.5 years; 50.1% of the patients were women. A total of 73.9% of the patients had hypertension, 25.6% had diabetes, 20.1% had hypercholesterolaemia, and 5.7% of patients were current smokers. *Table 1* shows the baseline demographic, clinical, and procedural characteristics in males and females. Among conventional cardiovascular risk factors, the prevalence of diabetes, hypertension, and dyslipidaemia was similar between genders, but males more frequently than females were smokers or had previous history of smoking. Also, the proportion of patients with a prior diagnosis of stable angina, of peripheral artery disease, of heart failure, and of ischaemic stroke did not

significantly differ between males and females. But, significantly more males than females had a previous myocardial infarction and revascularization.

At hospital admission, 45.8% of patients had 2 or more episodes of chest pain in the previous 24 h and 95.9% of patients showed ECG abnormality. In the clinical presentation, there were a number of gender differences. Females less frequently than males had typical chest pain (75.9% vs. 83.7%, $P = 0.042$) and more frequently than males (42.8% vs. 30.1%, $P = 0.019$) revealed, at physical examination, signs of heart failure (Killip class ≥ 2).

During hospitalization, most of the patients have been treated with guideline-suggested evidence-based therapy (aspirin, beta-blockers, statins, ACE-inhibitors). But, among patients admitted for STEMI, the rate of reperfusion was very low (9.8% lytic therapy and 19.5% primary PCI) and 70.7% of them had conservative treatment ($P < 0.001$), without any significant differences between males and females (*Table 2*). Arrival at the hospital within 12 h from the onset of symptoms was 60.5% of STEMI females and 64.7% of STEMI males ($P = 0.36$). The rate of bleeding and other complication was 12%.

In the overall study population of elderly patient with ACS, coronary angiography was performed in 24.7% of patients. It was significantly ($P = 0.025$) more often in males (29.4%) than in females (21%); and in patients with STEMI vs. non-ST-elevation ACS (29.1% vs. 18.4%, $P = 0.011$). Old men showed more severe coronary atherosclerosis than old women, presenting a number of significant lesions (lumen stenosis $> 50\%$) that was about one-quarter more.

There were only few differences between those patients <85 years old (young-elderly) and those ≥ 85 years old (old-elderly). Comparisons between these two groups are illustrated in *Table 3*. In the old-elderly group the number of females was significantly higher, and the number of patients with diabetes mellitus was significantly lower. Younger patients tended to have ($P = $ ns) invasive procedures more frequently.

Outcome and predictors

The mortality rate was 21%. There was no significant difference between females and males (21.1% vs. 21%, $P = 0.98$), also between young-elderly and old-elderly (19.5% vs. 24.5%, $P = 0.24$). But, as shown in *Figure 1*, the rate of in-hospital mortality increased significantly ($P = 0.022$) from unstable angina (2.2%), through NSTEMI (16.7%) to STEMI (25.2%).

In STEMI patients, the mortality rate of those treated with reperfusion (fibrinolysis 20.0% or primary PCI 22.0%) and those receiving conservative management (26.5%) was not statistically significant ($P = 0.38$).

Table 4 displays the results of the univariate analysis for predictors of in-hospital mortality. Multivariate logistic regression (*Table 5*) identified systolic blood pressure <100 mmHg, Killip class ≥ 2, and STEMI (as index event) to be independent predictors of death. Conversely, use of evidence-based drugs, such as beta-blockers, statins, and ACE-inhibitors had positive protective effects.

Table 1 Clinical characteristics of the study population according to gender

	Females, $n = 219$	Males, $n = 218$	P-value
Age, year	83.7 ± 3.3	83.3 ± 2.9	0.13
Cardiovascular risk factors			
Diabetes mellitus	26.0	25.2	0.85
History of lipid disorders	17.8	22.5	0.22
History of hypertension	76.3	71.6	0.26
History of smoking	7.4	32.0	<0.001
Past medical history			
Prior stable angina	28.4	26.4	0.79
Peripheral arterial disease	5.0	6.4	0.53
Prior myocardial infarction	12.3	19.7	0.035
Prior revascularization	1.4	1.4	0.92
Prior heart failure	12.8	9.2	0.23
Prior TIA/stroke	6.8	7.8	0.70
Recent unstable angina	17.9	22.5	0.50
Clinical presentation			
Two or more CP in the previous 24 h	42.7	48.7	0.68
Typical chest pain	75.9	83.7	0.072
Killip class ≥2	42.8	30.1	0.019
ECG abnormality	97.2	94.7	0.21
Serum creatinine, μmol/L			
Heart rate, bpm	88.5 ± 25.8	83.5 ± 24.7	0.032
SBP, mmHg	141.4 ± 32.9	136.0 ± 32.4	0.091
Index event			
MI with ST-segment elevation	133 (60.7)	125 (57.3)	0.47
MI without ST-segment elevation	76 (34.7)	74 (33.9)	0.86
Unstable angina	9 (4.1)	19 (8.7)	0.049
In-hospital medications			
Aspirin	200 (91.3)	203 (93.1)	0.48
Beta-blockers	149 (68.0)	153 (70.2)	0.63
Statin	180 (82.2)	184 (84.4)	0.53
ACE inhibitor	167 (76.3)	168 (77.1)	0.84
Diagnostic–therapeutic procedures			
Coronary angiography	46 (21)	64 (29.4)	0.042
Coronary revascularization[a]	80.4	79.7	0.92
Number of significant lesions[a]	1.9 ± 1.2	2.5 ± 1.4	0.039

Data are n (%) or mean ± SD. ACE, angiotensin converting enzyme; CP, chest pain; ECG, electrocardiogram; SBP, systolic blood pressure; TIA, transient ischaemic attack; MI, myocardial infarction.
[a]Values determined from patients having coronary angiography.

Table 2 Management of patients with STEMI

	Females, $n = 133$	Males, $n = 125$	P-value
Conservative treatment	75.2	65.9	0.23
Lytic therapy	7.5	12.2	
Primary PCI	17.3	21.9	
	<85 years old $n = 182$	≥85 years old $n = 74$	P-value
Conservative treatment	70.3	71.6	0.85
Lytic therapy	10.4	8.1	
Primary PCI	19.3	20.3	

STEMI, ST-elevation myocardial infarction; PCI, percutaneous coronary intervention.

Discussion

Octogenarians constitute a fast growing group of cardiovascular patients. This study gives evidence for cardiovascular risk factors, clinical presentation, treatment, and prognosis of 437 very old patients (≥ 80 years) recently admitted to the hospital with ACS in 8 Eastern European Countries. Our main findings, from the ISACS-TC registry, point up gender differences in the clinical presentations and the effects of age on the outcome of very old patients with ACS.

Table 3 Differences between young-elderly and old-elderly patients

	<85 years old $n = 302$	≥85 years old $n = 135$	P-value
Age, year	81.8 ± 1.4	87.3 ± 2.6	<0.001
Males	52.9	42.2	0.039
Risk factors			
Diabetes mellitus	28.5	19.3	0.041
History of lipid disorders	19.5	21.5	0.63
History of hypertension	73.2	75.6	0.60
History of smoking	22.5	13.3	0.029
Past medical history			
Prior stable angina	27.5	31.2	0.46
Peripheral arterial disease	5.3	6.7	0.57
Prior myocardial infarction	17.5	12.6	0.19
Prior revascularization	3.3	2.2	0.53
Prior heart failure	10.3	12.6	0.47
Prior TIA/stroke	6.6	8.9	0.40
Recent unstable angina	19.3	22.2	0.69
Clinical presentation			
Two or more CP in the previous 24 h	49.5	37.5	0.17
Typical chest pain	81.6	75.8	0.38
Killip class ≥ 2	36.8	36.2	0.92
Time from symptom onset to admission, within 12 h	61.3	63.7	0.62
ECG abnormality	96.5	94.7	0.37
Heart rate, bpm	87.2 ± 26	83.8 ± 23.6	0.21
SBP, mmHg	138.7 ± 33.1	138.9 ± 31.9	0.94
Index event			
MI with ST-segment elevation	60.9	54.8	0.23
MI without ST-segment elevation	32.8	37.8	0.31
Unstable angina	6.3	6.7	0.88
In-hospital medications			
Aspirin	92.5	92.6	0.85
Beta-blockers	62.6	55.6	0.16
Statins	84.1	81.5	0.49
ACE inhibitor	76.8	76.3	0.90
Diagnostic–therapeutic procedures			
Coronary angiography	83 (27.5)	27 (20.0)	0.096
Coronary revascularization[a]	79.3	84.1	0.45
Number of significant lesions[a]	2.2 ± 1.2	2.3 ± 1.6	0.90

Data are n (%) or mean ± SD. ACE, angiotensin converting enzyme; CP, chest pain; ECG, electrocardiogram; TIA, transient ischaemic attack; SBP, systolic blood pressure; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.
[a]Values determined by patients having coronary angiography.

Women

The proportion of women in this study population was very high, similar and even superior to that of men, as in the subgroup of old-elderly. This is consistent with previous studies[5–9] and somehow expected, because women commonly live longer than man. However, till now, it was still unclear which details that characterized ACS in young females were shared with old females. This is the case of typical angina. Heavy or squeezing feeling, discomfort, tightness, or pressure under the sternum or chest bone, which may radiate to the jaw, neck, arms, back, and epigastrium was less prevalent in elderly women than elderly men, as described for younger females.[5] Conversely, STEMI, as index event, results much more often in elderly women than in younger patients.[5–9]

Cardiovascular risk profile in octogenarians

This study shows that the prevalence of all conventional cardiovascular risk factor but hypertension was very low. The population of octogenarian patients with ACS may present many differences with the classic cohort of ACS patients.[6–12] Our population had an elevated incidence of patients with hypertension, but a very low incidence of smokers or former smokers and of patients with dyslipidaemia and diabetes mellitus. This observation gives origin to the idea that perhaps the octogenarian status can be achieved more easily without conventional cardiovascular risk factors (patients with risk factors died of ischaemic heart disease before). Furthermore, in old patients hypertension could be a pathophysiological response to decreased elastic artery compliance, reduced plasma
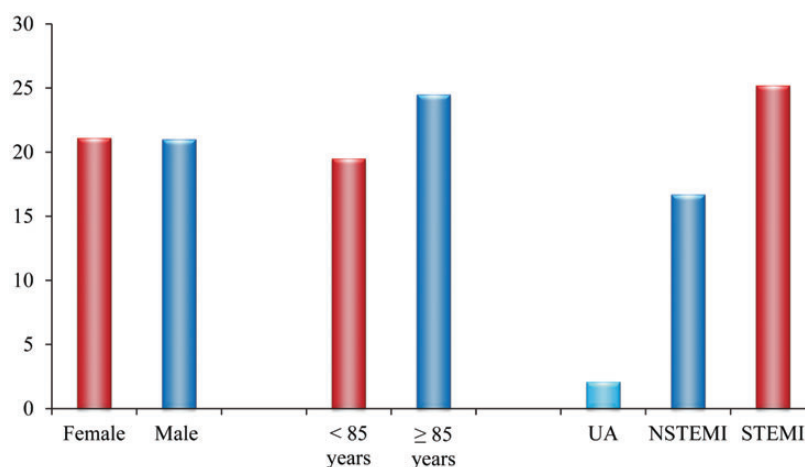
Figure 1 The rate of in-hospital mortality increased significantly (*P* = 0.022) from unstable angina (2.2%), through NSTEMI (16.7%) to STEMI (25.2%). There was no significant difference in the rate of in-hospital mortality between females and males (21.1% vs. 21%, *P* = 0.98), also between young-elderly (≤85 years old) and old-elderly (19.5% vs. 24.5%, *P* = 0.24). NSTEMI: non-ST-elevation myocardial infarction, STEMI: ST-elevation myocardial infarction.

Table 4 Predictors of in-hospital mortality

	OR	95% CI	*P*-value
Age, year	1.05	0.98–1.13	0.13
Age ≥ 85	1.33	0.82–2.16	0.25
Males	1.00	0.63–1.59	0.98
Risk factors			
Diabetes mellitus	1.11	0.63–1.79	0.82
History of lipid disorders	0.51	0.25–1.03	0.31
History of hypertension	0.69	0.33–1.09	0.12
History of smoking	0.98	0.46–3.09	0.71
Clinical history			
Prior stable angina	0.51	0.18–1.46	0.21
Peripheral arterial disease	1.19	0.46–3.09	0.71
Prior myocardial infarction	0.57	0.28–1.18	0.13
Prior revascularization	0.93	0.19–4.48	0.93
Prior heart failure	0.72	0.32–1.61	0.43
Prior TIA/stroke	1.27	0.55–2.93	0.57
Recent unstable angina	0.41	0.11–1.46	0.17
Clinical presentation			
Two or more CP episodes in the previous 24 h	1.20	0.49–2.93	0.69
Typical chest pain	0.86	0.46–1.59	0.65
Killip class ≥ 2	1.86	1.16–3.01	0.011
Time from the onset of symptom to admission within12 h	1.26	0.78–2.05	0.34
ECG abnormality	1.98	0.44–8.83	0.37
Heart rate, bpm	0.99	0.98–1.01	0.48
SBP, mmHg	0.97	0.95–0.98	< 0.001
Index event			
MI with ST-elevation	1.89	1.15–3.12	0.012
MI without ST-elevation	0.66	0.39–1.09	0.10
Unstable angina	0.27	0.06–1.17	0.08
In-hospital medications			
Aspirin	0.30	0.14–0.61	<0.001
Beta-blockers	0.56	0.35–0.86	0.012
Statins	0.19	0.12–0.31	<0.001
ACE inhibitor	0.19	0.11–0.32	< 0.001
Diagnostic–therapeutic procedures			
Coronary angiography	0.61	0.35–1.09	0.087
Coronary revascularization	0.87	0.48–1.57	0.65
Number of significant lesions	0.73	0.44–1.23	0.21

ACE, angiotensin converting enzyme; CP, chest pain; ECG, electrocardiogram; SBP, systolic blood pressure; TIA, transient ischaemic attack; MI, myocardial infarction; OR, odds ratio; CI, confidence intervals.

Table 5 Multivariate predictors of mortality

	OR	95% CI	P-value
Age, year	1.03	0.95–1.14	0.36
Male	1.16	0.66–2.05	0.59
SBP ≤ 100 mmHg	2.74	1.28–5.88	0.009
Killip class ≥2	1.71	1.01–3.70	0.029
STEMI	2.01	1.06–3.84	0.032
Unstable angina	0.68	0.13–3.45	0.64
Aspirin	0.54	0.21–1.14	0.20
Beta-blockers	0.38	0.21–0.67	0.001
Statin	0.37	0.18–0.72	0.004
ACE inhibitors	0.28	0.15–0.53	<0.001
Coronary revascularization	0.92	0.44–1.84	0.82

SBP, systolic blood pressure; STEMI, ST-elevation myocardial infarction; ACE, angiotensin converting enzyme; OR, odds ratio; CI, confidence intervals.

renin activity, and increased salt sensitivity. However, such high prevalence of hypertension in very old patients with ACS also raises the suspicion that hypertension could play a key and major role in the pathogenesis of ACS in the very elderly patients and opens the door to call attention for positive preventive actions. Indeed, randomized controlled intervention trials have demonstrated that treatment of systolic hypertension in very old patients may reduce the rates of cardiovascular mortality.[13]

Management and outcome

Revascularization of very elderly patients showed a trend of decreased mortality for patients undergoing PCI and/or CABG.[14] However, the estimated benefit of invasive procedure and revascularization during the acute phase of ACS is still a matter of debate in elderly. The most powerful predictor of in-hospital mortality for PCI has been shown to be an emergent case.[14]

The study population of the ISACS registry had a very low rate of invasive management, comparing with recently published data from Western Countries.[15–17] In the Belgian STEMI registry, 76.9% of patients aged ≥80 years had PCI, vs. 19.6% placed in our cohort of 8 Eastern European Countries. Moreover, female gender was associated with lower use of invasive evaluation; although, when the coronary anatomy was known the revascularization was performed in a similar manner, and gender did not influence old-patient's outcome. The mortality rate of our cohort was 2.2% for patients with unstable angina, 16.7% for patients with NSTEMI, and 25.2% for patients with STEMI. In STEMI patients, the mortality rate was 20.0% for those receiving fibrinolysis, 22.0% for those who underwent primary PCI and 26.5% for those receiving conservative treatment and no reperfusion (differences were not statistically significant). The rate of death was slightly higher to those recently published by other European countries. In the Belgian STEMI registry, in-hospital mortality was 17.8% (without significant difference regarding conservative vs. thrombolysis vs. primary PCI).[15] While, in the Eindhoven area (the Netherlands), the rate of in-hospital death for STEMI

patients undergoing primary PCI was 16.3%, but the study did not explore other treatment options (no reperfusion and fibrinolysis).[17]

Our findings, particularly in relation to prognosis, are relevant to treatment decision.[18] Determinants of outcome are complex. Previous studies demonstrated that age is one of the most important determinants of death.[10,11] However, those studies refer to younger study cohorts. Our data show that age was unhelpful in defining the risk of death in very old (>80 years old) patients with ACS. Systolic blood pressure < 100 mmHg, STEMI as the index event, and the development of left-ventricular failure were the most important negative determinants of prognosis for our cohort, which emphasizes that in planning risk-based management, consideration of age independently of clinical status seems to be inappropriate.

Only limited data are available about the safety, efficacy and outcome of treatments in octogenarian patients with ACS. Randomized clinical trials are under-powered. And most registry studies refer to selected populations. Our findings lend support for vigorous treatment of elderly patients with ACS as a way of improving the outcome. Not all elderly patients have a poor outcome and the use of evidence-based drugs in this study population is excellent both in terms of absolute and relative risk.

Limitation

The endpoint of the present study was in-hospital mortality in very elderly patients. The study did not find any advantage of revascularization over conservative treatment for patients of ≥80 years old, even in the sub-group of STEMI patients. Short-term outcome must be placed in the context of long-term benefits that might be offered by invasive management.[19,20]

Acknowledgements

References

1. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet* 1997;**349**:1269–1276.
2. Bugiardini R, Manfrini O, Majstorovic Stakic M, Cenko E, Boytsov S, Merkely B, Becker D, Dilić M, Vasiljević Z, Koller A, Badimon L. Exploring In-hospital Death from Myocardial Infarction in Eastern Europe; From the International Registry of Acute Coronary Syndromes in Transitional Countries (ISACS-TC); on the behalf of the Working Group on Coronary Pathophysiology & Microcirculation of the European Society of Cardiology. *Curr Vasc Pharmacol* 2013. [Epub ahead of print].
3. Bugiardini R, Badimon L, Manfrini O, on the behalf of the ISACS-TC Investigators. Rationale and design of the ISACS-TC (International Survey of Acute Coronary Syndromes in Transitional Countries) Project. *Eur Heart J Suppl* 2014;**16**.
4. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Writing Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Thygesen K, Alpert JS,

White HD, Jaffe AS, Katus HA, Apple FS, Lindahl B, Morrow DA, Chaitman BA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasché P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S, ESC Committee for Practice Guidelines (CPG). Third universal definition of myocardial infarction. *Eur Heart J* 2012;**33**:2551–2567.

5. Vaccarino V, Badimon L, Corti R, de Wit C, Dorobantu M, Manfrini O, Koller A, Pries A, Cenko E, Bugiardini R. Presentation, management, and outcomes of ischaemic heart disease in women. *Nat Rev Cardiol* 2013;**10**:508–518.

6. Bugiardini R, Yan AT, Yan RT, Fitchett D, Langer A, Manfrini O, Goodman SG; Canadian Acute Coronary Syndrome Registry I and II Investigators. Factors influencing underutilization of evidence-based therapies in women. *Eur Heart J* 2011;**32**:1337–1344.

7. Bugiardini R, Estrada JL, Nikus K, Hall AS, Manfrini O. Gender bias in acute coronary syndromes. *Curr Vasc Pharmacol* 2010;**8**:276–284.

8. Poon S, Goodman SG, Yan RT, Bugiardini R, Bierman AS, Eagle KA, Johnston N, Huynh T, Grondin FR, Schenck-Gustafsson K, Yan AT. Bridging the gender gap: insights from a contemporary analysis of sex-related differences in the treatment and outcomes of patients with acute coronary syndromes. *Am Heart J* 2012;**163**:66–73.

9. Tatu-Chitoiu G, Cinteza M, Dorobantu M, Udeanu M, Manfrini O, Pizzi C, Vintila M, Ionescu DD, Craiu E, Burghina D, Bugiardini R. In-hospital case fatality rates for acute myocardial infarction in Romania. *CMAJ* 2009;**180**:1207–1213.

10. Boersma E, Pieper KS, Steyerberg EW, Wilcox RG, Chang WC, Lee KL, Akkerhuis KM, Harrington RA, Deckers JW, Armstrong PW, Lincoff AM, Califf RM, Topol EJ, Simoons ML. 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**:2557–2567.

11. Granger CB, Goldberg RJ, Dabbous O, Pieper KS, Eagle KA, Cannon CP, Van De Werf F, Avezum A, Goodman SG, Flather MD, Fox KA; Global Registry of Acute Coronary Events Investigators. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med* 2003;**163**:2345–2353.

12. Barakat K, Wilkinson P, Deaner A, Fluck D, Ranjadayalan K, Timmis A. How should age affect management of acute myocardial infarction? A prospective cohort study. *Lancet* 1999;**353**:955–959.

13. Staessen JA, Gasowski J, Wang JG, Thijs L, Den Hond E, Boissel JP, Coope J, Ekbom T, Gueyffier F, Liu L, Kerlikowske K, Pocock S, Fagard RH. Risks of untreated and treated isolated systolic hypertension in the elderly: meta-analysis of outcome trials. *Lancet* 2000;**355**:865–872.

14. Peterson ED, Alexander KP, Malenka DJ, Hannan EL, O'Conner GT, McCallister BD, Weintraub WS, Grover FL; American Heart Association Chronic CAD Working Group. Multicenter experience in revascularization of very elderly patients. *Am Heart J* 2004;**148**:486–492.

15. Vandecasteele EH, De Buyzere M, Gevaert S, de Meester A, Convens C, Dubois P, Boland J, Sinnaeve P, De Raedt H, Vranckx P, Coussement P, Evrard P, Beauloye C, Renard M, Claeys MJ. Reperfusion therapy and mortality in octogenarian STEMI patients: results from the Belgian STEMI registry. *Clin Res Cardiol* 2013;**102**:837–845.

16. Paul SD, O'Gara PT, Mahjoub ZA, DiSalvo TG, O'Donnell CJ, Newell JB, Villarreal-Levy G, Smith AJ, Kondo NI, Cararach M, Ferrer L, Eagle KA. Geriatric patients with acute myocardial infarction: Cardiac risk factor profiles, presentation, thrombolysis, coronary interventions, and prognosis. *Am Heart J* 1996;**131**:710–715.

17. Moonen LA, van 't Veer M, Pijls NH. Procedural and long-term outcome of primary percutaneous coronary intervention in octogenarians. *Neth Heart J* 2010;**18**:129–134.

18. Pozzati A, Bugiardini R, Borghi A, Ottani F, Muzi A, Morgagni G, Puddu P. Transient ischaemia refractory to conventional medical treatment in unstable angina: angiographic correlates and prognostic implications. *Eur Heart J* 1992;**13**:360–365.

19. Graham MM, Ghali WA, Faris PD, Galbraith PD, Norris CM, Knudtson ML. Survival after coronary revascularization in the elderly. *Circulation* 2002;**105**:2378–2384.

20. Manfrini O, Slucca M, Pizzi C, Colombo A, Viecca M, Bugiardini R. Effect of percutaneous coronary intervention on coronary blood flow at rest in myocardial sites remote from the intervention site in patients with stable angina pectoris. *Am J Cardiol* 2008;**101**:776–779.