

# Independent predictors of in-hospital and 1-year mortality rates in octogenarians with acute myocardial infarction

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Older age is known as a negative prognostic parameter in acute myocardial infarction (AMI) patients. In this study, we aimed to explore age-associated differences in treatment protocols, in-hospital and 1-year mortality. This cohort observational study included 277 consecutive AMI patients, separated into 2 groups according to whether their age was  $\geq 80$  years or not. We found that group I patients (aged  $\geq 80$  years) had a notably lower rate of percutaneous coronary intervention (PCI) performed ( $P < 0.0001$ ) and a notably higher in-hospital death rate ( $P < 0.003$ ). The multivariate logistic regression analysis found that three variables were independent predictors of in-hospital mortality: age  $\geq 80$  years ( $P < 0.0001$ ), LVEF  $< 40\%$  ( $P < 0.0001$ ), and Killip class  $\geq 3$  ( $P < 0.0001$ ). The 1-year death rate was again significantly higher in group I patients ( $P < 0.001$ ) and was independently predicted by the triple-vessel coronary artery disease ( $P = 0.004$ ) and an LVEF  $< 40\%$  at admission ( $P = 0.001$ ). The 1-year readmission rate was superior in group I ( $P < 0.01$ ) and independently predicted by an age  $\geq 80$  years ( $P < 0.001$ ), and an history of congestive heart failure ( $P < 0.0001$ ) or permanent atrial fibrillation ( $P < 0.001$ ). We concluded that patients aged  $\geq 80$  benefit less often from a PCI and have higher rates of in-hospital mortality, as well as of 1-year readmission and mortality rates.

## Keywords

Acute myocardial infarction; Age  $\geq 80$  years; Treatment; Prognosis

## 1. Introduction

Elderly people are a fast-rising part of the population. They represent a rapidly increasing amount of patients with acute coronary syndromes (ACS), including myocardial infarction with ST-elevation (STEMI) and without ST-elevation (NSTEMI). Advanced age is a potent predictor of bad prognosis. The majority of AMI trials have enrolled an unimportant number of elderly subjects, and this explains why incomplete data are available on the management and prognosis of this increasing subset of the ACS population.

Standard therapies are not always applied in the elderly, as evidence of benefit is lacking and the risk of serious side effects is high for this age group [1–3]. These facts can be also explained by some specific clinical characteristics of the elderly at presentation: the symptoms of the ACS are less spe-

cific, the electrocardiographic patterns are more often atypical and the comorbidities may lead to a confounding clinical picture. All these facts may lead to diagnostic incertitude and delayed or conservative therapeutic strategies.

This situation can be found in Romania to, though aggravated by the small number of catheterization laboratories that are able to perform urgent coronary revascularization (23, for a population of 20 million inhabitants). Our retrospective study is the first one done in Romania addressing AMI patients aged  $\geq 80$  years. In-hospital and 1-year mortality, as well as 1-year readmission rate were evaluated in the octogenarians, and compared with those found in the AMI patients aged  $< 80$  years.

## 2. Materials and methods

### 2.1 Subject selection

This is a cohort study. From 1st January to 31st December of 2019, all successive patients that were hospitalized with AMI at Timisoara Institute of Cardiovascular Disease were evaluated for enrolling in the study. In the absence of contraindications, percutaneous coronary intervention (PCI) was performed in the first 12 hours from the symptoms onset in all STEMI and in the high-risk NSTEMI patients. As high-risk NSTEMI patients were stated those with at least one of the following criteria: a GRACE-score  $> 140$ , evolutive changes of the ST-segment/T-wave, or a relative rise or fall in cardiac enzymes [4]. High-risk NSTEMI patients in whom PCI could not be performed in the first 12 hours of the symptoms onset were not enrolled in the study.

The initial evaluation was based on the analysis of the parameters resulting from clinical presentation, cardiac troponin, and resting 12-lead ECG [4, 5]. The diagnosis of AMI with persistent ST-segment elevation (STEMI) was stated in the presence of at minimum 2 of the subsequent 3 parameters: (1) typical angina lasting over 20 minutes; (2) ST-segment elevation  $\geq 1$  mV, lasting over 0.08 sec after the J point, seen in at least 2 contiguous leads; (3) transitory rise in myocardial necrosis markers exceeding twofold the normal laboratory limit [5].

AMI without persistent ST-segment elevation (NSTEMI) was diagnosed in the presence of an appropriate clinical situation (typical angina or angina equivalent) with ST-segment depression or prominent T-wave inversion, without ST-segment elevation and/or positive biomarkers of necrosis (e.g., troponin I  $\geq 1$   $\mu\text{g/L}$  in our laboratory) [6].

The PCI and the adjunctive pharmacological medication was performed according to the ESC guidelines. The patients were administered standard loading doses of 300–600 mg clopidogrel, 300–500 mg aspirin and 5000 IU unfractionated heparin before the PCI. Glycoprotein IIb/IIIa inhibitors were given when the operator considered it necessary. If a coronary stent was implanted, clopidogrel was prescribed for 12 months, associated with aspirin.

The inclusion criteria were the confirmed diagnosis of AMI hospitalized within the first 12 hours of the symptoms onset and the absence of exclusion criteria.

Exclusion criteria were: PCI- or CABG- related AMI [7], and the association of diseases worsening the long-term prognosis such as severe primary cardiomyopathy, severe valvular diseases congenital heart diseases, kidney dysfunction, liver cirrhosis, a malignant tumor, and severe infection.

## 2.2 Data extraction

Baseline data were taken from hospital records and comprised gender, age, Killip functional class on admission, medical history, 12 leads resting electrocardiogram, laboratory data, echocardiographic data, and the results of the coronary angiography.

Medical history integrated data regarding obesity, smoking, old myocardial infarction, hypertension, peripheral vascular disease, chronic obstructive pulmonary disease, diabetes, chronic kidney disease, stroke. The laboratory data determined at admission were creatine kinase-MB isoenzyme and cardiac troponin levels, blood cell count, serum hemoglobin, serum glucose, liver enzymes, serum creatinine, serum electrolytes, and lipogram.

Echocardiographic evaluation was done within the first 24 hours of hospitalization, using a VIVID S5 echocardiograph. Mono- and two dimensional echocardiography, as well as pulsed and continuous Doppler imaging, were performed in all patients. Left ventricular ejection fraction (LVEF) was calculated using the Simpson method, evaluating the end-diastolic volume and left ventricular end-systolic volume [8].

Medical treatment reports were accomplished at discharge and 1 year follow up.

The cause of death was determined from hospital records, or by asking the patient's physician for those who died at home.

All causes of readmissions were noted during the 1-year follow-up period. The causes of readmissions were determined by utilizing the hospital records.

## 2.3 Endpoints

The primary endpoint was in-hospital mortality, defined as the death of any cause during the hospitalization for AMI.

Cardiac deaths were considered those due to AMI, heart failure, acute pulmonary edema, cardiogenic shock, ventricular fibrillation, or cardiac rupture.

Noncardiac deaths were considered those having an extra-cardiac cause, such as stroke, acute renal failure, or sepsis.

The secondary endpoints were the 1-year death and readmission rates. 1-year mortality included both cardiac and non-cardiac deaths. 1-year readmissions had as possible causes recurrent myocardial infarction (RMI), stroke, stent thrombosis, and bleeding. RMI was defined according to the Academic Research Consortium (ARC) criteria [9]. Bleeding complications were defined according to the BARC and the TIMI bleeding classification [10, 11]. Stroke was stated as an irreversible neurological impairment, as confirmed by the neurologist, and based on sustaining information, such as brain images.

## 2.4 Statistical analysis

Data were collected and analyzed by means of the MedCalc Statistical Software version 19.1.7 for Windows. Ostend, Belgium. Data are given as mean  $\pm$  SD when normally distributed, and as frequencies and percentages for categorical variables. For comparisons between two groups of continuous data, *t*-tests were used, while for comparisons of categorical data, Chi-square tests were done. To evaluate the contribution of each variable in the studied outcomes, univariate and multivariate logistic regression was used. Variables considered for potential prognostic impact included age, sex, current smoking, obesity, diabetes mellitus, systemic hypertension, chronic obstructive pulmonary disease, chronic kidney disease, peripheral artery disease, history of coronary heart disease and of congestive heart failure, left ventricular ejection fraction (LVEF) at admission, Killip class, laboratory data (serum creatinine, brain natriuretic peptide, peak creatine kinase-MB and troponin-I levels) Multivariate logistic regression analysis with backward stepwise method was used for all initial parameters that were associated with the endpoints in univariate analysis. ROC curves were utilized to determine the optimal sensitivity and specificity of the analyzed parameters. The discrimination ability of the analyzed parameters was estimated by the C-statistic, which is equivalent to the area under the ROC curve. A model with C-statistic  $>0.65$  is considered to have a meaningful discriminatory ability. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using Cox proportional hazards models. The threshold for statistical significance was established at a *p*-value of  $<0.05$ . All *P*-values were results of two-tailed tests.

# 3. Results

## 3.1 Baseline characteristics

Of the 297 patients hospitalized with AMI, 277 were enrolled in the study. The mean age was  $67.38 \pm 13.4$  years (32–95 years). 173 (63%) were males. LVEF at admission was  $44 \pm 13$  %. According to the age, the AMI patients were separated into 2 groups: group I ( $\geq 80$  years, *n* = 63), and

group II (<80 years,  $n = 214$ ). The baseline characteristics, the medical history and the cardiovascular risk factors of the patients are shown in Table 1. Compared with group II, the group I patients were more often women, non-smokers, and presented more frequent systemic hypertension, chronic kidney disease, stroke, congestive heart failure. They had more often a LVEF <40% at admission and a higher Killip functional class.

### 3.2 Angiographic data and therapeutical interventions

Table 2 describes the findings of the coronary angiography performed within the first 12 hours from the onset of symptoms and the therapeutical interventions. No angiography could be done in 3 (4%) of group I patients and in 1 (0.5%) patients of group II ( $P = 0.03$ ), because of severe kidney failure. Group I patients presented a significantly higher prevalence of 3-vessel coronary disease ( $P = 0.01$ ), and a significantly lower prevalence of myocardial revascularization by PCI (48% vs. 78%,  $P < 0.0001$ ). The rate of coronary artery bypass graft (CABG) was 2% in group I and 3% in group II ( $P = 0.67$ ). Regarding the concomitant medication, diuretics and oral anticoagulants were more often administered in group I patients ( $P < 0.001$ ).

### 3.3 Total mortality

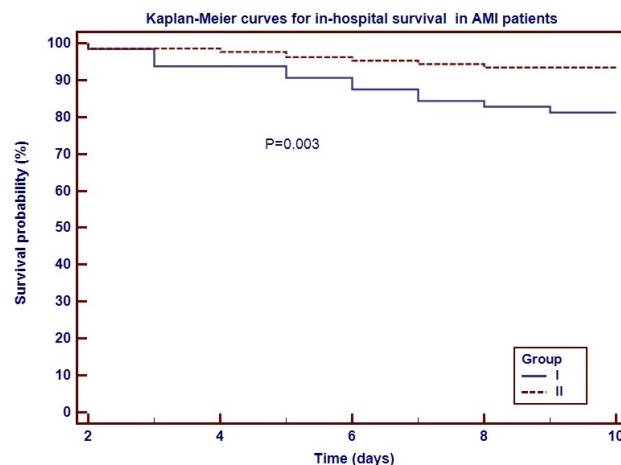
The total all-cause mortality rate was 12.6% ( $n = 35$ ). The number of deaths was 18 (28%) in the octogenarians, besides 17 (8%) in the non-octogenarians,  $P < 0.0001$ . The relative risk for total mortality was 3.5 (95% CI: 1.94 to 6.46,  $P < 0.0001$ ) in the octogenarians with AMI.

### 3.4 In-hospital mortality

During the hospitalization for AMI, 26 patients (9.3%) died, 12 being from group I (19%), and 14 from group II (6.5%),  $P < 0.003$ . Both the cardiac causes of death and the noncardiac causes of death were more often present in group I ( $P < 0.05$ ), as shown in Table 3. The relative risk for in-hospital mortality in the octogenarians was 3.2 for all-cause deaths (95% CI: 2.08 to 5.18,  $P < 0.0001$ ), and 2.9 for cardiac deaths (95% CI: 1.11 to 7.83,  $P = 0.029$ ). Fig. 1 displays the Kaplan-Meier curve for in-hospital survival.

In univariate analysis, the variables associated with in-hospital death were age  $\geq 80$  years ( $P < 0.0001$ ), male sex ( $P < 0.0001$ ), diabetes ( $P < 0.0001$ ), previous myocardial infarction ( $P < 0.001$ ), a Killip class  $\geq 3$  ( $P < 0.0001$ ), an LVEF <40% at admission ( $P < 0.0001$ ), and a three-vessel CAD ( $P < 0.01$ ).

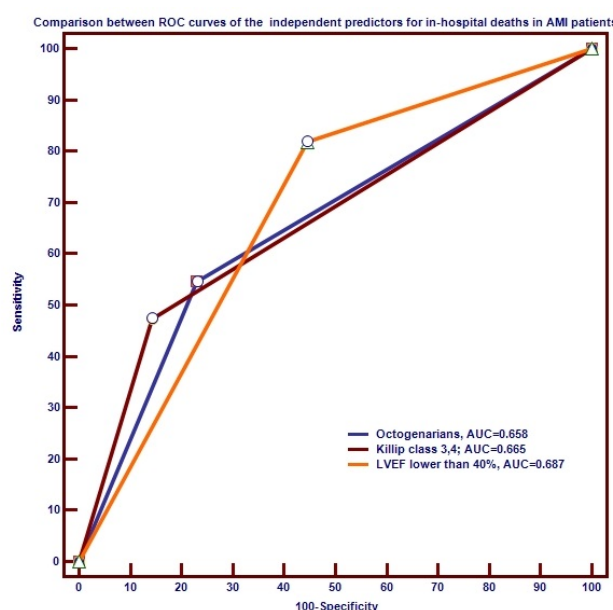
The multivariate logistic regression selected three parameters as independent predictors for in-hospital mortality. These parameters were: an age  $\geq 80$  years [OR = 7.03, 95% CI: 3.05 to 16.20,  $P < 0.0001$ ], a LVEF <40% at admission (OR = 2.1, 95% CI: 0.99 to 4.59,  $P < 0.0001$ ), and a Killip class 3 or 4 (OR = 2.41, 95% CI: 1.06 to 5.51,  $P < 0.0001$ ). When comparing the receiver operating characteristic curves for these variables, as shown in Fig. 2, we found that an LVEF <40% at admission had the best discriminative power, with an AUC of 0.687, followed by the age  $\geq 80$  years (AUC =



**Fig. 1.** Kaplan-Meier curves for in-hospital mortality in AMI patients.

Abbreviations: AMI, acute myocardial infarction.

0.672) and the Killip class  $\geq 3$  (AUC = 0.665). The differences between the AUCs of the ROC curves were not significant.



**Fig. 2.** Comparison between ROC curves of the independent predictors for in-hospital death in AMI patients.

Abbreviations: AMI, acute myocardial infarction; AUC, area under the curve; LVEF, left ventricular ejection fraction; ROC, receiver operating characteristic.

### 3.5 1-year mortality

251 AMI patients were discharged alive (90%) and followed-up for 1 year. Group I patients received at discharge more often oral anticoagulants ( $P = 0.01$ ) and diuretics ( $P = 0.04$ ). During the follow-up interval further 9 patients died, thus the 1-year mortality was 3.6%. 1-year mortality was notably higher in group I patients (12% vs. 1.5%,  $P < 0.001$ ).

**Table 1. Baseline characteristics of the AMI patients.**

	Group I	Group II	P value
	Age ≥80 years	Age <80 years	
	n = 063	n = 214	
Mean age, years (X ± 1 SD)	83.7 ± 3.5	62 ± 11	<0.0001
Male sex (n, %)	23 (36%)	151 (70%)	<0.0001
Smokers (n, %)	13 (20%)	115 (54%)	<0.0001
Obesity (n, %)	13 (20%)	55 (25%)	0.41
Diabetes mellitus ( n, %)	77 (29%)	64 (30%)	0.87
Hypercholesterolemia ( n, %)	48 (75%)	149 (70%)	0.43
COPD (n, %)	19 (30%)	53 (25%)	0.42
Chronic kindey disease (n, %)	19 (30%)	27 (12%)	<0.001
Systemic hypertension (n, %)	58 (90%)	168 (78%)	0.03
Peripheral artery disease (n, %)	4 (6%)	12 (6%)	1
History of stroke (n, %)	20 (31%)	27 (13%)	<0.001
Old myocardial infarction (n, %)	10 (14%)	24 (11%)	0.51
Previous PCI (n, %)	5 (8%)	15 (7%)	0.78
Previous CABG (n, %)	2 (3%)	3 (1.4%)	0.39
Known congestive heart failure	22 (34%)	28 (13%)	0.0001
STEMI (n, %)	54 (84%)	196 (92%)	0.05
High-risk NSTEMI (n, %)	9 (13%)	18 (8%)	0.22
Killip class at admission	2.6 ± 1	2.2 ± 0.9	<0.003
Heart rate at admission (X ± 1 SD)	82.6 ± 24	79.4 ± 17	0.23
Systolic BP at admission (X ± 1 SD)	124.3 ± 26	130.7 ± 26	0.08
Diastolic BP at admission (X ± 1 SD)	75.2 ± 12.8	77.1 ± 16.	0.38
Atrial Fibrillation at admission (n, %)	22 (34%)	30 (14%)	0.07
- acute (n, %)	12 (19%)	17 (8%)	0.29
- persistent (n, %)	10 (15%)	13 (6%)	0.17
Recenl LBBB at admission (n, %)	1 (1.5%)	4 (1.7%)	0.27
AV block at admission (n, %)	5 (7.5%)	12 (6%)	0.26
- 2nd degree (n, %)	1 (1.5%)	4 (2%)	1
- 3rd degree (n, %)	4 (6%)	8 (4%)	0.19
Ventricular fibrillation at admission (n, %)	6 (9%)	17 (8%)	0.56
LVEF at admission	38 ± 14	47 ± 12	<0.01
<40% (n, %)	47 (73%)	100 (47%)	<0.001
40–49% at admission	9 (14%)	62 (29%)	0.01
≥50% at admission	8 (13%)	52 (24%)	0.06
Scr (mg/dL, mean ± SD)	2.2 ± 1.1	1.72 ± 1.2	0.02
BNP (pg/mL, mean ± SD)	881.69 ± 248.13	834.79 ± 259.99	0.20
CK-MB (μg/L, mean ± SD)	50.01 ± 18.94	51.34 ± 13.36	0.52
Tpn-I (μg/L, mean ± SD)	14.98 ± 2.17	14.69 ± 2.37	0.38

Note: Statistically significant values are written in bold ( $P < 0.05$ ).

Abbreviations: AMI, acute myocardial infarction; ACEI, Angiotensin-converting enzyme inhibitor; ARB, Angiotensin receptor blocker; AV, atrio-ventricular; BNP, Brain natriuretic peptide; BP, blood pressure; CABG, Coronary artery bypass grafting; CCB, Calcium antagonists; CK-MB, Creatine kinase-MB; E/A - the ratio of peak velocity blood flow in early diastole to peak velocity flow in late diastole; LBBB, left ventricular blood pressure; LVEF, Left ventricular ejection fraction; LW/WH, Low molecular weight heparin; NSTEMI, acute myocardial infarction without ST-segment elevation; PCI, Percutaneous coronary intervention; Scr, Serum creatinine; STEMI, acute myocardial infarction with persistent ST-segment elevation; Tpn-I, Troponin-I.

The relative risk for death during the 1-year follow-up in the elderly group was 7.8 (95% CI: 2.03 to 30.29,  $p = 0.002$ ). Fig. 3 displays the Kaplan-Meier curve for the 1-year survival in the two AMI patient groups. The most frequent causes of death were recurrent myocardial infarction as well as congestive heart failure (Table 3).

The 1-year mortality risk was associated in univariate analysis with triple-vessel disease ( $P = 0.002$ ), Killip class  $\geq 3$  ( $P = 0.028$ ), LVEF  $< 40\%$  at admission ( $P = 0.0009$ ) and age  $\geq 80$  years ( $P = 0.04$ ).

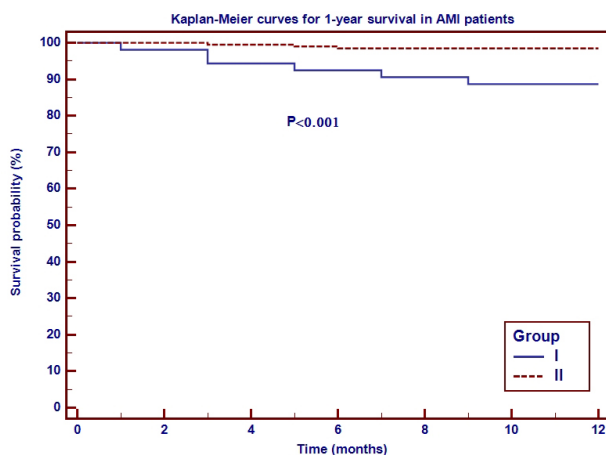


**Table 2. Angiographic data and therapeutical interventions.**

	Group I	Group I	P value
	Age $\geq 80$ years	Age $< 80$ years	
	n = 63	n = 214	
Door to balloon time (min)	83 $\pm$ 14	80 $\pm$ 10	0.06
Radial approach n (%)	19 (52%)	102 (48%)	0.57
Angiographic findings- number of diseased vessels	61 (96%)	213 (99.5%)	<b>0.03</b>
One	23 (36%)	104 (49%)	0.06
Two	7 (11%)	48 (22%)	0.05
Three	21 (32%)	38 (18%)	<b>0.01</b>
Left main trunk	10 (16%)	23 (11%)	0.28
Interventional revascularization:	32 (50%)	174 (81%)	<b>&lt;0.0001</b>
PCI	31 (48%)	167 (78%)	<b>&lt;0.0001</b>
CABG	1 (2%)	7 (3%)	0.67
Concomitant drug therapy			
Clopidogrel	63 (100%)	210 (98%)	0.25
Aspirin	62 (97%)	210 (98%)	0.63
Betablockers	48 (76%)	175 (82%)	0.29
Statin	60 (95%)	206 (96%)	0.72
ACEI/BRA	46 (72%)	156 (73%)	0.87
CCB	16 (25%)	64 (30%)	0.44
Diuretics	42 (65%)	54 (25%)	<b>&lt;0.0001</b>
Oral anticoagulants	22 (35%)	30 (14%)	<b>0.0002</b>

Note: Statistically significant values are written in bold ( $P < 0.05$ ).

Abbreviations: ACEI, Angiotensin-converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, Angiotensin receptor blocker; AV, atrio-ventricular; BNP, Brain natriuretic peptide; BP, blood pressure; CABG, Coronary artery bypass grafting; CCB, Calcium antagonists; CK-MB, Creatine kinase-MB; E/A - the ratio of peak velocity blood flow in early diastole to peak velocity flow in late diastole; LBBB, left ventricular blood pressure; LVEF, Left ventricular ejection fraction; LW/WH, Low molecular weight heparin; NSTEMI, acute myocardial infarction without ST-segment elevation; PCI, Percutaneous coronary intervention; Scr, Serum creatinine; STEMI, acute myocardial infarction with persistent ST-segment elevation; Tpn-I, Troponin-I.

**Fig. 3. Kaplan-Meier curves for 1-year mortality in AMI patients.**

Abbreviations: AMI, acute myocardial infarction.

The multivariate logistic regression selected two parameters as independent predictors for the 1-year mortality: the triple-vessel CAD (OR = 3.3, 95% CI: 1.47 to 7.75,  $P = 0.004$ ) and an LVEF  $< 40\%$  at admission (OR = 5.0, 95% CI: 1.85 to 13.91,  $P = 0.001$ ). The comparison of the ROC curves for these parameters (Fig. 4) showed no significant differences

regarding the AUCs (0.662 for LVEF  $< 40\%$  ROC curve, 0.643 for the triple-vessel disease ROC curve,  $P = 0.75$ ).

### 3.6 1-year readmission

During the 1-year follow-up phase, 22 patients (8.7%) were rehospitalized. The relative risk for 1-year readmissions was 2.7 in the octogenarians when compared with those aged  $< 80$  years (95% CI: 1.22 to 5.99,  $P = 0.01$ ). The readmission rate was higher in the octogenarians ( $P < 0.01$ ), and congestive heart failure (CHF) was a significantly more frequent cause of readmission in these patients ( $P = 0.02$ ), as shown in Table 4. Fig. 5 displays the Kaplan-Meier curves for the 1-year readmissions in the two AMI patient groups.

The readmission rate was notably associated in univariate analysis with the history of CHF ( $P < 0.0001$ ), permanent atrial fibrillation ( $P < 0.001$ ), and an age  $\geq 80$  years ( $P < 0.001$ ). All these variables were identified by the multivariate logistic regression as independent predictors for 1-year readmission. The comparison between the ROC curves showed no significant differences between their discriminative capacities (Fig. 6).

**Table 3. Comparison regarding mortality rates and death causes of AMI patients.**

	Group I	Group II	P value
	Age $\geq 80$ years	Age $< 80$ years	
	n = 63	n = 214	
<b>Total mortality</b>	18 (28%)	17 (8%)	<b>&lt;0.0001</b>
<b>In hospital mortality</b>	12 (19%)	14 (6.5%)	<b>&lt;0.003</b>
Cardiac causes	7 (11%)	8 (3.7%)	<b>0.02</b>
Ventricular fibrillation	3 (5%)	3 (1.4%)	0.08
Electromechanical dissociation	1 (1.5%)	1 (0.4%)	0.34
Cardiogenic shock	2 (3%)	3 (1.5%)	0.43
Acute pulmonary edema	1 (1.5%)	1 (0.4%)	0.34
Noncardiac causes	5 (8%)	6 (2.8%)	<b>0.04</b>
Acute renal failure	2 (1.1%)	2 (0.9%)	0.88
Bleeding	1 (0.7%)	1 (0.5%)	0.85
Stroke	1 (0.3%)	1 (0.5%)	0.63
Sepsis	1 (0.3%)	2 (0.9%)	
Discharged patients	Group I	Group I	P value
	Age $\geq 80$ years	Age $< 80$ years	
	n = 51	n = 200	
Medication at discharge			
Clopidogrel	41 (80%)	170 (85%)	0.38
Aspirin	44 (86%)	168 (84%)	0.72
Betablockers	33 (64%)	146 (73%)	0.20
Statin	42 (81%)	172 (86%)	0.37
ACEI/BRA	37 (72%)	156 (78%)	0.36
Oral anticoagulants	13 (26%)	24 (12%)	<b>0.01</b>
CCB	20 (40%)	62 (31%)	0.22
Diuretics	20 (40%)	52 (26%)	<b>0.04</b>
<b>1-year mortality</b>	6 (12%)	3 (1.5%)	<b>0.0004</b>
<b>Causes:</b>			
Recurrent myocardial infarction	2 (4%)	2 (1%)	0.12
Congestive heart failure	2 (4%)	1 (0.5%)	<b>0.04</b>
Stroke	1 (2%)	-	<b>0.04</b>
Bleeding	1 (2%)	-	<b>0.04</b>

Note: Statistically significant values are written in bold ( $P < 0.05$ ).

Abbreviations: ACEI, Angiotensin-converting enzyme inhibitor; ARB, Angiotensin receptor blocker; CCB, Calcium antagonists.

## 4. Discussion

During the last decades the incidence of AMI, as well as its mortality, has decreased essentially in developed countries [12, 13]. These favorable tendency reflects a change for the better in many issues that affect the prognosis in patients with AMI [14]. Advanced age, as a circumstance we cannot influence, has a negative prognostic impact value in most studies [15]. One of the most potent variables that improve survival in AMI patients is the myocardial revascularization by PCI [16].

Our study is the first one performed in Romania addressing AMI patients aged  $\geq 80$  years. All patients included in our study were treated at an academic tertiary hospital, able to provide 24 hours/7 days cardiovascular catheterizations and to ensure the urgent coronary revascularization interventions for the western region of Romania. All reperfusion procedures were done only by PCI, within the first 12

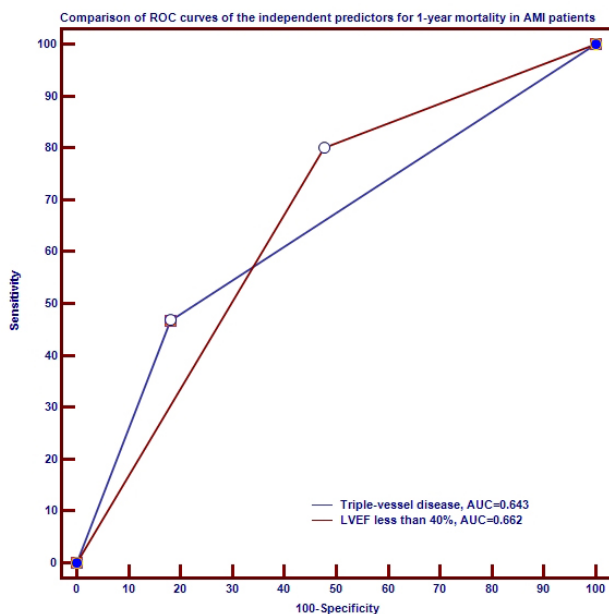
hours from the symptoms onset, in a considerable group of successive patients with a diagnosis of STEMI or high-risk NSTEMI.

The principal results of the present study were that AMI patients aged  $\geq 80$  years were less frequently treated by PCI within the first 12 hours from the symptoms onset and they have a worse prognosis when compared with the younger patients. The risk of in-hospital death was 3 times higher in the elderly. This statistic might be justified by the higher frequency of comorbidities, and the higher severity of the AMI in the elderly. Our study identified three independent predictors for all cause in-hospital death risk AMI patients: the age  $\geq 80$  years, the LVEF  $\leq 40\%$  at admission, and the Killip class 3 or 4. Similar findings were reported by Nicolau in a  $\geq 70$  years AMI population [17], as well as by Ielasi in  $\geq 75$  years STEMI patients [18]. In STEMI patients that underwent primary PCI and received everolimus-eluting or bare-

**Table 4. Comparison regarding 1-year readmission of AMI patients.**

	Group I	Group II	<i>P</i> value
	Age $\geq$ 80 years	Age < 80 years	
	n = 51	n = 200	
<b>1-year readmissions</b>	9 (18%)	13 (6.5%)	<b>&lt;0.01</b>
<b>Causes:</b>			
Recurrent myocardial infarction	2 (4%)	3 (1.5%)	0.25
Congestive heart failure	3 (6%)	2 (1%)	<b>0.02</b>
3rd Atrio-Ventricular block	2 (4%)	3 (1.5%)	0.25
Stroke	1 (2%)	2 (1%)	0.55
Bleeding	1 (2%)	3 (1.5%)	0.80

Note: Statistically significant values are written in bold ( $P < 0.05$ ).

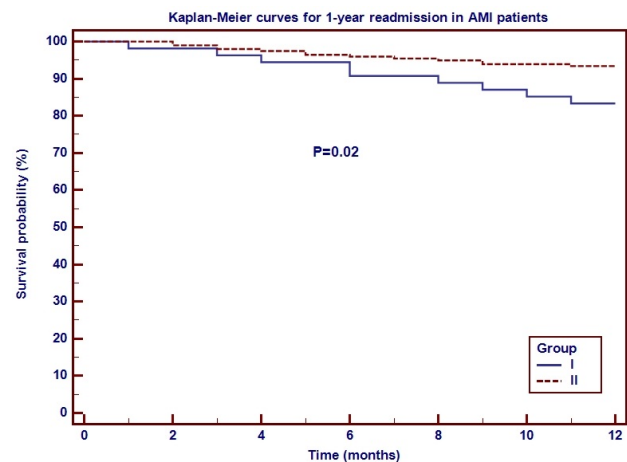


**Fig. 4. Comparison between ROC curves of the independent prognosticators for 1-year mortality in AMI patients.**

Abbreviations: AMI, acute myocardial infarction; AUC, area under the curve; LVEF, left ventricular ejection fraction; ROC, receiver operating characteristic.

metal stent, advanced age ( $\geq 75$  years) was the most powerful independent predictor of a worse outcome, concerning both the patient and the device related outcomes (all-cause and cardiac deaths) [18]. Regardless of the worse expected prognosis in the elderly, the frequency of coronary angiography in our study was found to be notably smaller in this high-risk AMI subgroup ( $P = 0.03$ ), due to the higher prevalence of chronic kidney failure. Further, interventional revascularization by a PCI was done less frequent in the elderly ( $P < 0.0001$ ). Coronary artery by-pass graft was performed in about 2% of all AMI patients, regardless of the age-group.

On the subject of the concomitant medication, the diuretics and the oral anticoagulants were more often prescribed in the elderly, as they presented more frequently atrial fibrillation and heart failure, respectively. Although the elderly re-

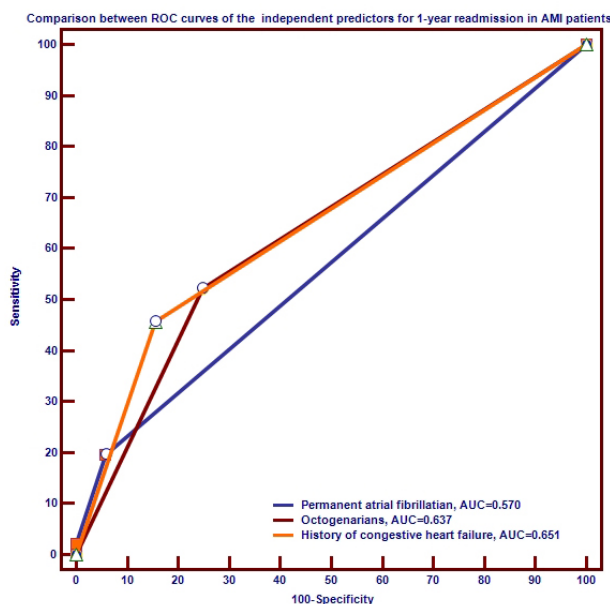


**Fig. 5. Kaplan-Meier curves for 1-year readmission in AMI patients.**

Abbreviations: AMI, acute myocardial infarction.

ceived more often oral anticoagulants, the in-hospital bleeding rate in the octogenarians was not importantly different from that of the younger AMI patients, probably because the radial approach represents the preferred method of vascular access in our hospital. At discharge, the proportion of patients receiving oral anticoagulants was again higher among the elderly, and their 1-year mortality rate due to bleeding or stroke was higher ( $P = 0.04$ ). Beside the higher prevalence of oral anticoagulant treatment, group I patients were more often female and had more frequent chronic kidney disease, facts that are increasing the risk factors for bleeding. Advanced age is also related with vascular calcification and fragility, factors that are increasing the bleeding events [19].

A parallel with earlier published statistics is difficult because of the significantly poorer catheterization and revascularization rates in octogenarian AMI patients. Mehta *et al.* [20] estimated in-hospital mortality in STEMI patients aged  $\geq 70$  years and assessed a smaller mortality rate than those found in our study concerning octogenarians (14.4% in PCI-treated patients vs. 19%). Ishihara evaluated the outcome of a large group of AMI patients according to age ( $\geq 70$  vs.  $< 70$  years). Although all patients underwent cardiac catheterization in the first 24 hours after admission, the in-hospital



**Fig. 6. Comparison between ROC curves of the independent prognosticators for 1-year readmission in AMI patients.**

Abbreviations: AMI, acute myocardial infarction; AUC, area under the curve; ROC, receiver operating characteristic.

death rate was significantly higher in the elderly (11.7% vs. 5.0%) [21].

In our study, the 1-year mortality was 12% in the elderly, while the 1-year readmission rate was 18%. Both the 1-year mortality and the 1-year readmission rate were significantly higher in the elderly ( $P < 0.001$ , and  $P < 0.01$ , respectively). The most frequent causes of 1-year death and/or readmission were aggravated heart failure and recurrent myocardial infarction, suggesting that the AMI in elderly patients is the result of more extensive atherosclerosis and a more advanced CAD.

The results from the literature regarding the post-discharge prognosis in the elderly AMI patients are discordant [22, 23]. In a considerable research, Sui found that octogenarians have a greater risk of mortality and heart failure during the first months following the AMI. But, after a few months, the prognosis of the elderly patients became similar to that of those aged  $< 80$  years [24]. In our study, the analysis of the Kaplan-Meier 1-year mortality and 1-year readmission curves suggest a rather uniform time-distribution of the events in both AMI age-categorized patients.

## 5. Limitations

The current study was an observational cohort study, that included unselected, successive patients with a confirmed diagnosis of AMI admitted in a single center with a readily available catheterization laboratories to perform urgent coronary revascularization. This center provides urgent coronary revascularization for the western region of Romania.

The angiographic results were not evaluated in a blinded

manner or by an independent lab, but all angiographies were performed by experienced doctors licensed in interventional cardiology.

We did not use the competing risk analysis, that provides a more interpretable estimate for the survival experience of multiple competing events compared to the traditional Kaplan Meier product-limit method. Although the amount of elderly patients was not great, the event rate was high enough to allow multivariable analyses.

## 6. Conclusions

Patients aged  $\geq 80$  years have a more severe prognosis after an AMI and benefit less often from a PCI. When compared with a younger AMI group, these patients have greater in-hospital and 1-year mortality rates, as well as a higher 1-year readmission rate. Age  $\geq 80$  years, LVEF  $< 40\%$ , and Killip functional class  $\geq 3$  were independent prognosticators for in-hospital mortality. 1-year mortality was predicted by an LVEF  $< 40\%$  and a triple-vessel CAD, while 1-year readmission by the age  $\geq 80\%$ , and the history of permanent atrial fibrillation or congestive heart failure.

## Author contributions

FC and DAB contributed to the conception and design of the study, collected data, wrote and revised the manuscript; AG and BB, revised the manuscript, and insured software and data validation; MCT analyzed the data and supervised the manuscript.

## Ethics approval and consent to participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the ethical principles for medical research involving human subjects stated by World Medical Association in the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Victor Babes University of Medicine and Pharmacy Timisoara, Romania (approval number 2018-0036).

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## Conflict of interest

The authors declare no conflict of interest.

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