

# Risk stratification according to the type of impaired renal function in patients with acute myocardial infarction treated with percutaneous coronary intervention

Jacek Kowalczyk<sup>1</sup>, Radosław Lenarczyk<sup>1</sup>, Oskar Kowalski<sup>1</sup>, Andrzej Świątkowski<sup>1</sup>, Joanna Stabryła-Deska<sup>1</sup>, Tomasz Kurek<sup>1</sup>, Grzegorz Honisz<sup>1</sup>, Tomasz Kukulski<sup>1</sup>, Mariusz Gąsior<sup>2</sup>, Zbigniew Kalarus<sup>1</sup>

<sup>1</sup> First Department of Cardiology, Silesian Center for Heart Diseases, Medical University of Silesia, Zabrze, Poland

<sup>2</sup> Third Department of Cardiology, Silesian Center for Heart Diseases, Medical University of Silesia, Zabrze, Poland

## Abstract

**Background:** It has been shown that successful reperfusion improves in-hospital and long-term outcome of patients with acute myocardial infarction (AMI). Nevertheless, some patients are still at high risk due to AMI despite achievement of reperfusion. Impaired renal function (IRF) is one of the recently recognised risk factors in this population. However, the prognostic value of different types of IRF in patients with AMI treated with percutaneous coronary intervention (PCI) has not been well characterised.

**Aim:** To evaluate the prognostic value of different types of IRF in AMI patients treated with PCI.

**Methods:** The single centre AMI registry encompassed 1486 consecutive AMI patients treated with PCI, who were followed for a mean of 29.7 months. Subjects with at least 1 measurement of serum creatinine  $>133 \mu\text{mol/l}$  ( $>1.5 \text{ mg/dl}$ ) during hospitalisation were selected ( $n=194$ ; 13.1%) and incorporated into the IRF group. The control group consisted of 1292 (86.9%) subjects with normal renal function. The IRF patients were divided into subgroups: contrast-induced nephropathy – CIN ( $n=90$ ; 6.1%); and chronic kidney disease – CKD ( $n=66$ ; 4.4%). Thirty-eight patients from the IRF group (2.6%) had normal value of serum creatinine on admission and did not match criteria of CIN. Patients with creatinine value  $>133 \mu\text{mol/l}$  on admission were incorporated into the CKD group. CIN was defined as a serum creatinine level  $<134 \mu\text{mol/l}$  on admission and a 25% increase of that parameter, with a value  $>133 \mu\text{mol/l}$  within 48 hours after PCI. Among CIN patients 2 subgroups were identified with respect to coexisting diabetes mellitus: CIN-DM and CIN-nDM (both  $n=45$ ; 3.05%).

**Results:** Remote mortality rate was significantly higher in the IRF group (38.7%) and in particular subgroups – CKD (51.5%), CIN-DM (46.7%), CIN-nDM (28.9%) – than in controls (10.3%,  $p < 0.001$  for all study groups vs. controls). Multivariate analysis identified IRF as an independent predictor of any-cause death in the whole population [hazard ratio (HR) 2.23; 95% CI 1.99–2.47,  $p < 0.001$ ]. All defined types of IRF had a significant and independent influence on remote survival in the study population (CIN-DM – HR 3.52; 95% CI 3.23–3.81; CIN-nDM – HR 2.60; 95% CI 2.29–2.91; CKD – HR 1.98; 95% CI 1.68–2.28).

**Conclusions:** Impaired renal function and all defined types of renal impairment have been shown to worsen the long-term prognosis of AMI patients treated with PCI. The most important risk factor of mortality is CIN in diabetic patients, which is associated with an over 3.5-fold increase of death hazard in this study population.

**Key words:** myocardial infarction (MI), percutaneous coronary intervention (PCI), renal impairment, contrast-induced nephropathy, diabetes

Kardiologia Polska 2007; 65: 635-643

---

## Address for correspondence:

Jacek Kowalczyk MD, I Katedra i Oddział Kliniczny Kardiologii, Śląskie Centrum Chorób Serca, ul. Szpitalna 2, 41-800 Zabrze, tel.: +48 32 271 34 14, fax: +48 32 271 76 92, e-mail: jacekmed@yahoo.com

**Received:** 14 December 2006. **Accepted:** 14 February 2007.

## Introduction

Renal insufficiency is associated with increased cardiovascular morbidity and mortality. It significantly modifies the course of many diseases and the therapeutic approach [1-7].

It has been shown that successful reperfusion improves in-hospital and long-term outcome of patients with acute myocardial infarction (AMI). Nevertheless, some groups of patients are still at high risk due to AMI despite achievement of reperfusion. It is mainly caused by the presence of concomitant diseases and risk factors. Arterial hypertension and diabetes mellitus, with their well-known relationship with coronary artery disease (CAD), are the most important comorbidities in AMI patients [2, 8, 9].

Impaired renal function (IRF) is another recently recognised risk factor in this population [1, 5-7, 10-14]. The increasing number of subjects with AMI who undergo percutaneous coronary intervention (PCI), which is nowadays the best method of treatment in AMI, makes risk stratification of AMI patients with IRF especially important. In addition, IRF has crucial clinical significance because development of nephropathy can be induced or accelerated by a contrast medium used during PCI.

The aim of this study was to evaluate the prognostic value of different types of IRF in AMI patients treated with PCI.

## Methods

### Patients

The study population consisted of 1486 consecutive AMI patients treated with PCI between January 1999 and December 2003. The subjects were mainly admitted from referral hospitals (84%) and previous administration of fibrinolytic treatment was allowed. No upper age limit was used. Cardiogenic shock, pulmonary oedema on admission, previous MI and any previous revascularisation procedure were not exclusion criteria.

From the whole AMI population, the IRF patients were selected (n=194; 13.1%). The control group consisted of the remaining 1292 (86.9%) subjects with normal renal function. The IRF group was further divided into subgroups with different types of renal impairment: contrast-induced nephropathy – CIN (n=90; 6.1%); and chronic kidney disease – CKD (n=66; 4.4%). Among CIN patients, 2 subgroups were identified with respect to co-existing diabetes mellitus (DM): CIN-DM and CIN-nDM (each group n=45; 3.05%). Thirty-eight (2.6%) patients from the IRF group had normal value of serum creatinine on admission and did not meet criteria for CIN.

## Definitions

Clinical criteria for AMI evaluated on admission were: chest pain persisting >20 min, ST segment elevation of at least 0.1 mV in two or more successive ECG leads or non-diagnostic ECG with enzymatic confirmation of AMI.

Patients were included in the IRF group if at least 1 measurement of serum creatinine level was above 133  $\mu\text{mol/l}$  (>1.5 mg/dl) during index hospital stay. Subjects with creatinine value >133  $\mu\text{mol/l}$  (>1.5 mg/dl) on admission were included in the CKD group. CIN was defined as a serum creatinine level <134  $\mu\text{mol/l}$  on admission and a 25% increase in it, with a value of >133  $\mu\text{mol/l}$  within 48 hours after PCI. The glomerular filtration rate (GFR) was also calculated using serum creatinine value on admission, according to the abbreviated Modification of Diet in Renal Disease Equation proposed by the National Kidney Foundation [15].

## Data acquisition

The clinical data from all consecutive patients with AMI treated invasively were prospectively recorded in a computerised database as a single centre AMI registry. Recorded data included demographics, clinical characteristics, laboratory values, presence of concomitant diseases, characteristics of AMI, angiography findings, revascularisation procedure and in-hospital mortality. Data concerning long-term outcome were collected in a database of the National Health Fund. The mean follow-up period was 29.7 $\pm$ 14.8 months. These strategies made it possible to collect the data of 99% of the subjects.

## Invasive treatment and medications

All patients were treated with urgent PCI because of AMI. Successful procedure was defined as restoration of TIMI 3 grade flow and residual stenosis <30%. None of the strategies to protect renal function was undertaken in the study population before PCI. All patients received aspirin before the intervention. Heparin was titrated to achieve an activated clotting time of  $\geq$ 250 s. Subjects who underwent stenting were also treated orally with 300 mg of clopidogrel just before the procedure, followed by 250 mg of ticlopidine twice daily or clopidogrel 75 mg per day for at least 6 weeks. Other medication was continued during hospitalisation and after discharge in line with appropriate guidelines [16, 17].

## Statistical analysis

Results are presented as mean  $\pm$ SD or numbers and percentages. Comparison between studied groups was made using Student's t-test for continuous variables and

$\chi^2$  test or Fisher's exact test for categorical variables. In-hospital and long-term outcomes were displayed using Kaplan-Meier survival curves and compared by the log-rank test. Independent predictors of death were identified with a multivariate Cox-regression model and were adjusted for all parameters with a significant univariate association with mortality, which were selected by the use of stepwise selection. Results are presented as hazard ratios (HRs) with 95% confidence intervals (CIs). All tests were double-sided and differences between analysed variables were considered statistically significant when  $p < 0.05$ . The analyses were performed using STATISTICA software (version 6.0, StatSoft, Inc., Tulsa, OK, USA).

## Results

### Baseline characteristics

Considering the whole AMI population treated with PCI, patients with IRF were older, less likely to smoke, and more frequently had hypertension, diabetes mellitus, peripheral vascular disease, history of CAD and previous MI in comparison with the control group (Table I).

Similar analysis performed for specific subgroups with different types of IRF showed the worst baseline profile in CKD and CIN-DM subgroups compared to controls (Table II). Subjects from the two aforementioned subgroups were older, less likely to smoke, with higher prevalence of hypertension and diabetes than the control group. In addition, female gender, history of CAD and previous MI were significantly more common among CIN-DM patients. Patients from the CKD subgroup more often had peripheral vascular disease.

The CIN-nDM patients had similar baseline characteristics to the control group. The only differences were found with respect to age and the presence of diabetes (which was absent in the CIN-nDM subgroup according to the definition).

### Clinical data

Patients with IRF had longer duration of chest pain and higher Killip class on admission, and more often presented with cardiogenic shock, lower ejection fraction and lower mean value of total cholesterol compared to controls (Tables I and III). Similarly, longer time from the onset of symptoms to referral, higher Killip class on

**Table I.** Comparative analysis of demographic and clinical data between IRF group and controls

Parameter	IRF group n=194	Control group n=1292	p
Age [years]	65.4±9.7	57.4±10.6	<0.001
Male	137 (70.6%)	948 (73.4%)	NS
Smoking	99 (51.0%)	898 (69.5%)	<0.001
Hypertension	140 (72.2%)	637 (49.3%)	<0.001
Diabetes	91 (46.9%)	288 (22.3%)	<0.001
Hyperlipidaemia	136 (70.0%)	1005 (77.8%)	<0.05
Peripheral vascular disease	34 (17.5%)	160 (12.4%)	<0.05
History of CAD	110 (56.7%)	625 (48.4%)	<0.05
Previous PCI	12 (6.2%)	81 (6.3%)	NS
Previous CABG	2 (1.0%)	21 (1.6%)	NS
Previous MI	49 (25.3%)	247 (19.1%)	<0.05
Pain duration [hours]	5.9±5.2	4.5±3.5	<0.001
Fibrinolysis	52 (26.8%)	320 (24.8%)	NS
Anterior MI	92 (47.4%)	544 (42.1%)	NS
Killip class on admission	1.8±1.0	1.2±0.6	<0.001
Cardiogenic shock on admission	78 (40.2%)	138 (10.7%)	<0.001
Ejection fraction [%]	39.2±9.9	45.0±8.0	<0.001
In-hospital mortality rate	44 (22.7%)	52 (4.0%)	<0.001
Long-term mortality rate	75 (38.7%)	133 (10.3%)	<0.001

Abbreviations: CABG – coronary artery bypass grafting, CAD – coronary artery disease, IRF – impaired renal function, PCI – percutaneous coronary intervention, MI – myocardial infarction

**Table II.** Comparative analysis of demographic and clinical data within specific subgroups with renal impairment compared to controls

Parameter	CKD n=66	CIN-DM n=45	CIN-nDM n=45	Control group n=1292
Age [years]	65.3±8.5*	67.8±10.3*	62.2±10.6**	57.4±10.6
Male	46 (69.7%)	26 (57.8%)**	38 (84.4%)	948 (73.4%)
Smoking	35 (53.0%)**	18 (40.0%)*	29 (64.4%)	898 (69.5%)
Hypertension	48 (72.7%)*	33 (73.3%)**	28 (62.2%)	637 (49.3%)
Diabetes	31 (47.0%)*	45 (100%)*	0 (0%)*	288 (22.3%)
Hyperlipidaemia	46 (69.7%)	29 (64.4%)**	30 (66.7%)	1005 (77.8%)
Peripheral vascular disease	18 (27.3%)*	9 (20.0%)	5 (11.1%)	160 (12.4%)
History of CAD	39 (59.1%)	30 (66.7%)**	20 (44.4%)	625 (48.4%)
Previous PCI	1 (1.5%)	5 (11.1%)	2 (4.4%)	81 (6.3%)
Previous CABG	1 (1.5%)	1 (2.2%)	0 (0%)	21 (1.6%)
Previous MI	18 (27.3%)	15 (33.3%)**	8 (17.8%)	247 (19.1%)
Pain duration [hours]	6.8±5.9*	6.3±5.7*	5.6±4.8*	4.5±3.5
Fibrinolysis	16 (24.2%)	10 (22.2%)	13 (28.9%)	320 (24.8%)
Anterior wall MI	30 (45.5%)	22 (48.9%)	23 (51.1%)	544 (42.1%)
Killip class on admission	2.1±1.1*	1.8±1.0*	1.7±1.0*	1.2±0.6
Shock on admission	34 (51.5%)*	15 (33.3%)*	18 (40.0%)*	138 (10.7%)
Ejection fraction [%]	37.5±10.6*	38.9±10.0*	40.6±10.1*	45.0±8.0
In-hospital mortality rate	21 (31.8%)*	13 (28.9%)*	7 (15.6%)*	52 (4.0%)
Long-term mortality rate	34 (51.5%)*	21 (46.7%)*	13 (28.9%)*	133 (10.3%)

Abbreviations: CIN-DM – contrast-induced nephropathy in diabetic patients subgroup, CIN-nDM – contrast-induced nephropathy in non-diabetic patients subgroup, CKD – chronic kidney disease subgroup. Rest of abbreviations: see Table I

\*  $p < 0.001$  vs. controls

\*\*  $p < 0.05$  vs. controls

**Table III.** Comparative analysis of laboratory and angiographic findings between patients with impaired renal function and controls

Parameter	IRF group n=194	Control group n=1292	p
Number of affected coronary arteries	2.1±0.8	1.8±0.8	<0.001
Unsuccessful PCI of IRA	44 (22.7%)	118 (9.1%)	<0.001
Number of stents implanted in IRA	0.8±0.7	0.8±0.6	NS
Contrast volume [ml]	221.4±97.2	211.1±94.3	NS
Total cholesterol [mmol/l]	5.5±1.5	5.8±1.2	<0.05
Uric acid [μmol/l]	413.9±117.9	323.3±92.3	<0.001
Proteinuria	45 (23.1%)	151 (11.7%)	<0.001
SCr on admission [μmol/l]	131.6±74.8	87.0±16.2	<0.001
SCr – 24-48 hours after PCI [μmol/l]	165.6±81.	189.1±16.7	<0.001
SCr – maximum value	212.8±120.9	92.4±16.9	<0.001
GFR [ml/min/1.73 m <sup>2</sup> ]	54.0±20.3	80.9±19.0	<0.001

Abbreviations: GFR – glomerular filtration rate, IRA – infarct-related artery, IRF – impaired renal function, SCr – serum creatinine

admission, cardiogenic shock and lower ejection fraction were more frequent among specific subgroups with renal impairment (Table II). Compared with controls, the mean level of total cholesterol was lower only in the CKD and CIN-DM subjects (Table IV).

#### Parameters of renal function

All parameters of renal function were significantly worse in the IRF group and its particular subgroups compared to controls, with the exception of proteinuria frequency in the CIN-nDM subgroup. Lower mean

**Table IV.** Comparative analysis of laboratory and angiographic findings within specific subgroups with renal impairment compared to controls

Parameter	CKD n=66	CIN-DM n=45	CIN-nDM n=45	Control group n=1292
Number of affected coronary arteries	2.3±0.8*	2.3±0.8*	1.8±0.7	1.8±0.8
Unsuccessful PCI of IRA	21 (31.8%)*	8 (17.8%)**	7 (15.6%)	118 (9.1%)
Number of stents implanted in IRA	0.9±0.8	0.8±0.7	0.8±0.6	0.8±0.6
Contrast volume [ml]	205.4±90.1	226.8±99.6	225.4±98.7	211.1±94.3
Total cholesterol [mmol/l]	5.4±1.4**	5.3±1.5**	5.8±1.6	5.8±1.2
Uric acid [μmol/l]	435.2±107.8*	404.0±136.3*	389.8±104.1*	323.3±92.3
Proteinuria	21 (31.8%)*	151 (11.7%)	12 (26.7%)**	5 (11.1%)
SCr on admission [μmol/l]	182.1±109.6*	104.0±20.2*	106.2±20.9*	87.0±16.2
SCr – 24-48 hours after PCI [μmol/l]	189.6±116.3*	172.4±53.9*	167.2±49.7*	89.1±16.7
SCr – maximum value [μmol/l]	228.4±137.8*	217.3±119.3*	220.8±132.7*	92.4±16.9
GFR [ml/min/1.73 m <sup>2</sup> ]	36.2±9.8*	62.1±20.6*	66.3±19.5*	80.9±19.0

Abbreviations: see Tables I-III.

\*  $p < 0.001$  vs. controls

\*\*  $p < 0.05$  vs. controls

estimated GFR and higher concentration of uric acid, serum creatinine evaluated on admission, 24-48 hours after PCI, and its maximum value during hospitalisation were observed in all types of IRF. Patients with IRF, CKD and CIN-DM were more likely to have proteinuria than controls (Tables III and IV).

### Angiographic results

In patients with renal dysfunction and within the CKD and CIN-DM subgroups initial coronarography showed more advanced CAD, assessed as a higher mean number of affected coronary arteries compared to those with normal renal function. Those patients were more likely to have unsuccessful PCI of an infarct-related artery. No significant differences with respect to angiographic results were observed between CIN-nDM patients and controls (Tables III and IV).

All studied groups and subgroups showed no significant differences with respect to the mean contrast volume administered during invasive procedures.

### In-hospital and long-term mortality

From the whole study population, which consisted of 1486 consecutive AMI patients treated with PCI, 208 (14.0%) died during the mean follow-up period of 29.7 months. Remote mortality rate was significantly higher in the IRF group than in the patients who had normal renal function (38.7 vs. 10.3%,  $p < 0.001$ ) (Table I and Figure 1). Additionally, renal dysfunction was associated with excessive mortality, when analysis was performed separately within subgroups with CKD (51.5%), CIN-DM (46.7%) and CIN-nDM (28.9%) (all

**Table V.** Independent predictors of death in the whole population of AMI patients treated with PCI

Parameter	Adjusted hazard ratio (95% CI)	p
Age	1.03 (1.02-1.04)	<0.05
Ejection fraction [%]	0.92 (0.91-0.93)	<0.001
IRF (SCr >133 μmol/l)	2.23 (1.99-2.47)	<0.001
Cardiogenic shock	2.58 (2.34-2.82)	<0.001

Abbreviations: see Table III

**Table VI.** Specific types of renal impairment as independent predictors of death

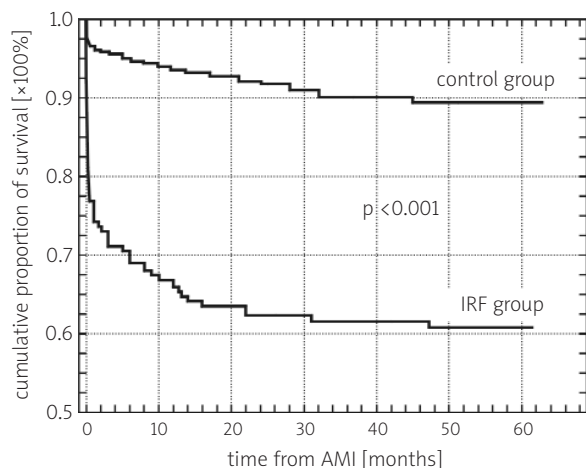
Parameter	Adjusted hazard ratio (95% CI)	p
CIN-DM	3.52 (3.23-3.81)	<0.001
CIN-nDM	2.60 (2.29-2.91)	<0.05
CKD	1.98 (1.68-2.28)	<0.05

Abbreviations: see Table II

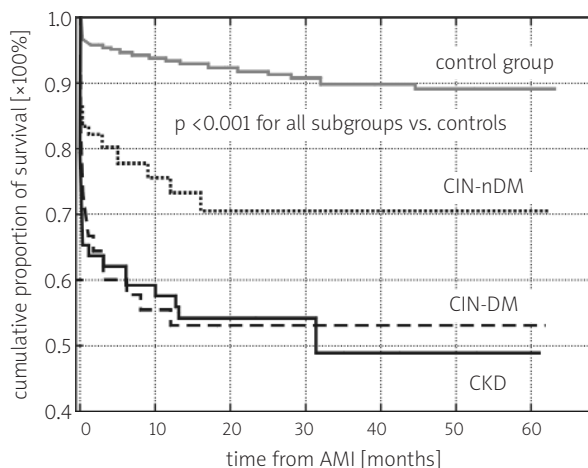
$p < 0.001$  for a particular study group vs. controls) (Table II and Figure 2). Furthermore, in-hospital mortality rate was significantly higher both in the whole IRF group (22.7%) and in specific subgroups (CKD – 31.8%, CIN-DM – 28.9%, CIN-nDM – 15.6%) compared to controls (4.0%; all  $p < 0.001$ ) (Tables I and II).

### Prognostic implications of IRF and its specific types

Multivariate analysis identified IRF as an independent predictor of total mortality in the whole population (HR 2.23; 95% CI 1.99-2.47,  $p < 0.001$ ), and likewise in



**Figure 1.** Kaplan-Meier curves of cumulative survival stratified by coexisting IRF  
 Abbreviations: AMI – acute myocardial infarction, IRF – impaired renal function



**Figure 2.** Remote survival curves for specific types of renal dysfunction  
 Abbreviations: AMI – acute myocardial infarction, CIN-DM – contrast-induced nephropathy in diabetic patients, CIN-nDM – contrast-induced nephropathy in non-diabetic patients, CKD – chronic kidney disease subgroup

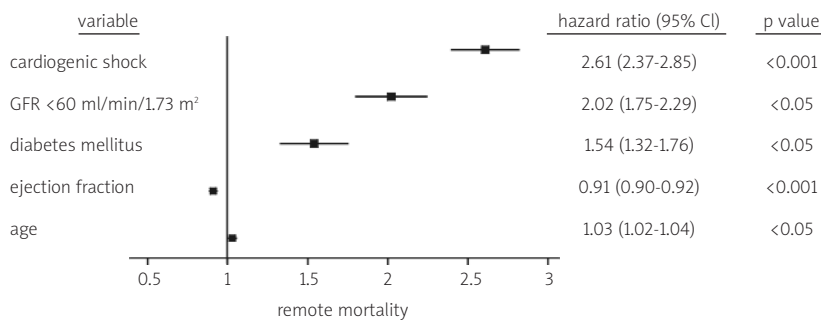
subgroups with advanced age (HR 1.03; 95% CI 1.02-1.04,  $p < 0.05$ ), lower ejection fraction (HR 0.92; 95% CI 0.91-0.93,  $p < 0.001$ ) and cardiogenic shock (HR 2.58; 95% CI 2.34-2.82,  $p < 0.001$ ) (Table V). Similarly, all types of renal impairment had a significant and independent effects on remote survival (Table VI). The worst outcomes were associated with CIN in diabetics. In this population, the hazard ratio for death during the observation period was increased 3.5-fold (HR 3.52; 95% CI 3.23-3.81,  $p < 0.001$ ). The presence of CIN in patients without diabetes mellitus resulted in HR 2.60 (95% CI 2.29-2.91,  $p < 0.05$ ), and CKD was associated with HR 1.98 (95% CI 1.68-2.28,  $p < 0.05$ ).

The separate multivariate analysis which was performed for various death stratifiers revealed that GFR  $< 60$  ml/min/1.73m<sup>2</sup> was an independent and

significant risk factor in the study population, associated with over 2-fold increase of death hazard (Figure 3).

**Discussion**

Previous studies documented that renal insufficiency is associated with increased risk for cardiovascular diseases and for adverse outcomes. Both end-stage renal disease and mild to moderate renal insufficiency have been shown to worsen the prognosis of patients with different forms of CAD. Recently published reports showed that renal impairment is common among patients with acute coronary syndromes and is associated with higher risk for death, even in subjects who were treated with the most effective method of reperfusion such as PCI [5, 6].



**Figure 3.** Independent predictors of remote mortality in the whole population of AMI patients treated with PCI  
 Abbreviations: CI – confidence interval, GFR – glomerular filtration rate

Moreover, Masoudi et al. [6] demonstrated progressive increase in mortality rates with increasing severity of renal insufficiency. It has been shown that coexisting renal dysfunction in patients with MI negatively affects their prognosis [1, 11]. Even in subjects who underwent successful PCI because of AMI, the in-hospital mortality among IRF patients was markedly increased, as shown by Yamaguchi et al. [14]. Similarly, Sadeghi et al. [7] found that renal insufficiency at baseline in AMI patients treated with PCI was independently associated with a striking increase of mortality both at 30 days and at one year.

In the present study, 13.1% of AMI patients treated with PCI had various forms of impaired renal function. This study was designed as a non-randomised, single centre observational analysis and could have potentially underestimated the frequency of renal dysfunction in the study population. The published studies evaluated numerous populations and used different criteria for definition of renal impairment, and therefore reported prevalence of renal dysfunction varies significantly. The majority of them examined different sets of subjects (with acute coronary syndromes or stable angina pectoris), and different treatment regimes (from invasive to conservative). The highest prevalence (33-41%) was noticed in the elderly and/or diabetic subjects, which is understandable because age and diabetes mellitus are established risk factors of renal dysfunction [6, 11, 18]. Only a few studies have included such a homogeneous and highly selected population as the one assessed in our study [4, 11, 18]. Divergences in prevalence of IRF could also be associated with the use of various definitions of renal impairment with respect to serum creatinine or GFR. Although GFR is a better parameter to estimate renal function, in the presented study the well-established and simple bedside tool serum creatinine was used to identify different types of IRF, especially contrast-induced nephropathy.

Similarly to other studies, in this highly selected group of AMI patients treated with PCI in one centre, the presence of IRF was associated with a remarkable increase in short-term and remote mortality. Moreover, despite many significant differences between the IRF group and controls, IRF remained an independent risk factor for total mortality in the whole population after adjustment for other factors influencing survival. Its predictive power with the hazard ratio of 2.23 was inferior only to the presence of cardiogenic shock.

The role of specific types of renal dysfunction in risk stratification of patients with AMI treated invasively has not yet been well established. The first principal finding of the presented study is that all defined types of IRF in AMI

patients treated with PCI are significant and independent risk factors of any-cause death. The highest mortality rate was observed in the CKD patients, with a total mortality rate of 51.5% during a mean of 29.7 months of observation. Surprisingly, after adjustment for other important death stratifiers, CIN remained the strongest independent risk factor among different types of IRF in diabetic patients, instead of CKD. A potential explanation of this finding may be the highest prevalence of cardiogenic shock in the CKD patients (51.5%). After adjustment for cardiogenic shock and other significant risk factors, CKD remained an independent, but still less powerful death stratifier than CIN-DM.

Our data showed that cardiogenic shock is the strongest risk factor of death among all identified predictors for this study population. An important and strong relationship between cardiogenic shock, impaired renal function and their influence on remote mortality was confirmed by the authors of the American College of Cardiology National Cardiovascular Data Registry [19]. They identified renal dysfunction as the most unfavourable predictor among six independent risk factors of death in a group of 483 AMI patients with cardiogenic shock treated with PCI. Serum creatinine level  $>2$  mg/dl on admission was associated in their population with almost 6-fold increase of death hazard [19]. Basic scientific studies revealed that one of the most important factors which enhance renal impairment is renal hypoperfusion, which is the consequence of hypovolaemia or shock [20]. The exposure to nephrotoxic media, like contrast media used during PCI, could additionally intensify renal impairment. These findings suggest that cardiogenic shock can play an important role in the development of renal dysfunction and it should be taken into consideration.

The second principal finding, based on the above presented data, is that special attention should be paid to diabetic patients who have normal values of serum creatinine on admission and develop CIN after PCI. A potential explanation of this phenomenon could be synergic effects of diabetes and contrast toxicity in causing renal impairment. Contrast-induced nephropathy, as a new risk factor in patients receiving contrast media, is still little explored despite the increasing number of studies. Moreover, in view of its clinical importance, the results of numerous CIN-prevention strategies and methods of its therapy are still disappointing and inconsistent [7, 20]. It seems that identification of protective factors and methods acting against development of CIN will benefit especially diabetic patients. Further progress in this area will have important clinical implications.

## Conclusions

Impaired renal function and all defined types of this impairment have been shown to worsen the long-term prognosis of AMI patients treated with PCI. The most important risk factor of mortality is contrast-induced nephropathy in diabetic patients, which is associated with over 3.5-fold increase of death hazard.

## References

- Anavekar NS, McMurray JJ, Velazquez EJ, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl J Med* 2004; 351: 1285-95.
- Gerstein HC, Pogue J, Mann JF, et al. The relationship between dysglycaemia and cardiovascular and renal risk in diabetic and non-diabetic participants in the HOPE study: a prospective epidemiological analysis. *Diabetologia* 2005; 48: 1749-55.
- Mann JF, Gerstein HC, Yi QL, et al. Development of renal disease in people at high cardiovascular risk: results of the HOPE randomized study. *J Am Soc Nephrol* 2003; 14: 641-7.
- Naidu SS, Selzer F, Jacobs A, et al. Renal insufficiency is an independent predictor of mortality after percutaneous coronary intervention. *Am J Cardiol* 2003; 92: 1160-4.
- Al Suwaidi J, Reddan DN, Williams K, et al. Prognostic implications of abnormalities in renal function in patients with acute coronary syndromes. *Circulation* 2002; 106: 974-80.
- Masoudi FA, Plomondon ME, Magid DJ, et al. Renal insufficiency and mortality from acute coronary syndromes. *Am Heart J* 2004; 147: 623-9.
- Sadeghi HM, Stone GW, Grines CL, et al. Impact of renal insufficiency in patients undergoing primary angioplasty for acute myocardial infarction. *Circulation* 2003; 108: 2769-75.
- Deedwania PC. Diabetes and hypertension, the deadly duet: importance, therapeutic strategy, and selection of drug therapy. *Cardiol Clin* 2005; 23: 139-52.
- Guzder RN, Gatling W, Mullee MA, et al. Prognostic value of the Framingham cardiovascular risk equation and the UKPDS risk engine for coronary heart disease in newly diagnosed Type 2 diabetes: results from a United Kingdom study. *Diabet Med* 2005; 22: 554-62.
- Walsh CR, O'Donnell CJ, Camargo CA Jr, et al. Elevated serum creatinine is associated with 1-year mortality after acute myocardial infarction. *Am Heart J* 2002; 144: 1003-11.
- Shlipak MG, Heidenreich PA, Noguchi H, et al. Association of renal insufficiency with treatment and outcomes after myocardial infarction in elderly patients. *Ann Intern Med* 2002; 137: 555-62.
- Wright RS, Reeder GS, Herzog CA, et al. Acute myocardial infarction and renal dysfunction: a high-risk combination. *Ann Intern Med* 2002; 137: 563-70.
- West AJ, Dixon SR, Kahn JK, et al. Effectiveness of primary angioplasty for acute myocardial infarction in patients on dialysis. *Am J Cardiol* 2004; 93: 468-70.
- Yamaguchi J, Kasanuki H, Ishii Y, et al. Prognostic significance of serum creatinine concentration for in-hospital mortality in patients with acute myocardial infarction who underwent successful primary percutaneous coronary intervention (from the Heart Institute of Japan Acute Myocardial Infarction [HIJAMI] Registry). *Am J Cardiol* 2004; 93: 1526-8.
- National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; 39 (2 Suppl 1): S1-266.
- Van de Werf F, Ardissino D, Betriu A, et al. Management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. *Eur Heart J* 2003; 24: 28-66.
- Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction – executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction). *Circulation* 2004; 110: 588-636.
- Nikolsky E, Mehran R, Turcot D, et al. Impact of chronic kidney disease on prognosis of patients with diabetes mellitus treated with percutaneous coronary intervention. *Am J Cardiol* 2004; 94: 300-5.
- Klein LW, Shaw RE, Krone RJ, et al. Mortality after emergent percutaneous coronary intervention in cardiogenic shock secondary to acute myocardial infarction and usefulness of a mortality prediction model. *Am J Cardiol* 2005; 96: 35-41.
- Goldenberg I, Matetzky S. Nephropathy induced by contrast media: pathogenesis, risk factors and preventive strategies. *CMAJ* 2005; 172: 1461-71.



# Stratyfikacja ryzyka w zależności od rodzaju nieprawidłowej funkcji nerek u pacjentów z ostrym zawałem serca leczonych przezskórną interwencją wieńcową

Jacek Kowalczyk<sup>1</sup>, Radosław Lenarczyk<sup>1</sup>, Oskar Kowalski<sup>1</sup>, Andrzej Świątkowski<sup>1</sup>, Joanna Stabryła-Deska<sup>1</sup>, Tomasz Kurek<sup>1</sup>, Grzegorz Honisz<sup>1</sup>, Tomasz Kukulski<sup>1</sup>, Mariusz Gąsior<sup>2</sup>, Zbigniew Kalarus<sup>1</sup>

<sup>1</sup> I Katedra i Oddział Kliniczny Kardiologii, Śląskie Centrum Chorób Serca, Zabrze

<sup>2</sup> III Katedra i Oddział Kliniczny Kardiologii, Śląskie Centrum Chorób Serca, Zabrze

## Streszczenie

**Wstęp:** Współczesne leczenie zawału serca jest ukierunkowane przede wszystkim na przywrócenie drożności i normalizację przepływu krwi w tętnicy odpowiedzialnej za zawał oraz maksymalne skrócenie czasu potrzebnego do uzyskania takiego efektu. Najskuteczniejszymi metodami leczenia przyczynowego są zabiegi przezskórnej rewaskularyzacji (PCI). Niestety nie zawsze wysoka skuteczność zabiegów rewaskularyzacyjnych bądź farmakologicznej reperfuzji przekłada się na dobre wyniki odległe. Jest to spowodowane w głównej mierze licznymi schorzeniami współistniejącymi i czynnikami ryzyka występującymi w tej grupie chorych. Dlatego szczególną uwagę poświęca się wyodrębnieniu chorych wysokiego ryzyka i prewencji wtórnej poprzez modyfikację i intensyfikację ich leczenia farmakologicznego oraz zmianę stylu życia i czynników środowiskowych. Nieprawidłowa funkcja nerek (IRF) jest jednym z niedawno wyodrębnionych czynników ryzyka w tej populacji chorych, a znaczenie prognostyczne różnych jej rodzajów u pacjentów z ostrym zawałem mięśnia sercowego (AMI) leczonych PCI jest wciąż słabo poznane.

**Cel:** Określenie wpływu IRF i jej poszczególnych rodzajów na wewnątrzszpitalne i odległe wyniki leczenia PCI chorych z AMI.

**Metodyka:** Jednośrodkowym rejestrem objęto 1486 kolejnych chorych z AMI poddanych PCI. Średni okres obserwacji odległej wyniósł 29,7 mies. Pacjenci, u których stwierdzono kreatyninemię  $>133 \mu\text{mol/l}$  ( $>1,5 \text{ mg/dl}$ ) na którymkolwiek etapie hospitalizacji, zostali włączeni do grupy IRF ( $n=194$ ; 13,1%). Grupę kontrolną utworzyło 1292 chorych bez cech jawnej dysfunkcji nerek. Pacjenci z grupy IRF zostali podzieleni na: podgrupę nefropatii indukowanej kontrastem – CIN ( $n=90$ ; 6,1%) oraz podgrupę podwyższonej kreatyninemii przy przyjęciu – CKD ( $n=66$ ; 4,4%). Pozostałych 38 chorych z grupy IRF (2,6% całej populacji badanej) to pacjenci z prawidłową kreatyninemią przy przyjęciu, którzy nie spełniają kryteriów rozpoznania nefropatii indukowanej kontrastem. Pacjenci z wyjściową kreatyniną  $>133 \mu\text{mol/l}$  w surowicy krwi zostali włączeni do podgrupy z podwyższoną kreatyninemią przy przyjęciu. Nefropatia indukowana kontrastem została zdefiniowana jako kreatyninemia przy przyjęciu  $<134 \mu\text{mol/l}$  z 25% wzrostem jej wartości, która przekroczyła  $133 \mu\text{mol/l}$  w ciągu 48 godz. od PCI. Podgrupę CIN podzielono dodatkowo na CIN-DM, tj. ze współistniejącą cukrzycą, oraz bez cukrzycy – CIN-nDM (obie podgrupy jednakowo liczebne –  $n=45$ ; 3,05%).

**Wyniki:** Śmiertelność wewnątrzszpitalna w grupie IRF osiągnęła wartość 22,7%, co w porównaniu z 4% w grupie kontrolnej stanowi różnicę znamioną statystycznie ( $p < 0,001$ ). Całkowita śmiertelność odległa w okresie obserwacji średnio 29,7 mies. była istotnie wyższa w grupie IRF (38,7%) oraz w poszczególnych podgrupach: CKD (51,5%), CIN-DM (46,7%), CIN-nDM (28,9%) w porównaniu z grupą kontrolną (10,3%,  $p < 0,001$  dla wszystkich grup vs kontrola). Wieloczynnikowa analiza wykazała, że IRF jest niezależnym czynnikiem ryzyka zgonu w badanej populacji [współczynnik ryzyka zgonu (HR) 2,23; 95% CI 1,99–2,47,  $p < 0,001$ ]. Również wszystkie zdefiniowane w niniejszej pracy rodzaje nieprawidłowej funkcji nerek miały istotny i niezależny wpływ na całkowite przeżycie w badanej populacji (CIN-DM – HR 3,52; 95% CI 3,23–3,81; CIN-nDM – HR 2,60; 95% CI 2,29–2,91; CKD – HR 1,98; 95% CI 1,68–2,28).

**Wnioski:** Nieprawidłowa funkcja nerek i wszystkie jej rodzaje istotnie oraz niezależnie od innych czynników pogarszają rokowanie zarówno wewnątrzszpitalne, jak i odległe pacjentów z AMI leczonych PCI. Najsilniejszym czynnikiem ryzyka zgonu okazała się CIN u chorych ze współistniejącą cukrzycą, której wystąpienie wiązało się z ponad 3,5-krotnym wzrostem ryzyka zgonu.

**Słowa kluczowe:** zawał serca (MI), przezskórna interwencja wieńcowa (PCI), nieprawidłowa funkcja nerek (IRF), nefropatia indukowana kontrastem, cukrzyca

Kardiologia Polska 2007; 65: 635-643

## Adres do korespondencji:

dr n. med. Jacek Kowalczyk, I Katedra i Oddział Kliniczny Kardiologii, Śląskie Centrum Chorób Serca, ul. Szpitalna 2, 41-800 Zabrze, tel.: +48 32 271 34 14, faks: +48 32 271 76 92, e-mail: jacekmed@yahoo.com

Praca wpłynęła: 14.12.2006. Zaakceptowana do druku: 14.02.2007.