Renal function on admission affects both treatment strategy and long-term outcomes of patients with myocardial infarction (from the Polish Registry of Acute Coronary Syndromes)

Michał Hawranek, Marek Gierlotka, Mariusz Gąsior, Bartosz Hudzik, Piotr Desperak, Aneta Ciślak, Matusz Tajstra, Tadeusz Osadnik, Piotr Rozentryt, Lech Poloński

3rd Chair and Department of Cardiology, Medical University of Silesia in Katowice, School of Medicine with the Division of Dentistry in Zabrze, Silesian Centre for Heart Diseases, Zabrze, Poland

Abstract

Background: Impairment of renal function (IRF) is an independent risk factor of myocardial infarction (MI).

Aim: The aim of study was to determine if the presence of IRF affects the choice of treatment strategy in patients with MI, and if long-term mortality rates are influenced by the use of an invasive strategy in patients with MI according to the grade of IRF.

Methods: Data from the PL-ACS Registry of 22,431 patients hospitalised for MI during 2007–2008 with an available estimated glomerular filtration rate (eGFR) with 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula were included. Patients were stratified based on eGFR: \geq 90 (normal); 60–89 (mild IRF); 30–59 (moderate IRF); 15–29 (severe IRF); and < 15 mL/min/1.73 m² (end-stage IRF).

Results: After adjustment, each increase in IRF grade reduced the likelihood of percutaneous coronary intervention by 19% (odds ratio [OR] 0.81; 95% confidence interval [CI] 0.78–0.85; p < 0.001). A higher IRF grade was independently associated with mortality (OR 2.01; 95% CI 1.86–2.18; p < 0.001) and major bleeding (OR 1.42; 95% CI 1.22–1.66; p < 0.001) during hospitalisation, and mortality at 12 (hazard ratio [HR] 1.55; 95% CI 1.49–1.62; p < 0.001) and 36 months (HR 1.50; 95% CI 1.45–1.55; p < 0.001). Invasive treatment was independently associated with improved 12-month prognosis in non-ST-segment elevation MI (NSTEMI) patients with mild-to-severe IRF and in ST-elevation MI (STEMI) patients at all IRF grades.

Conclusions: Invasive procedures were less frequent with worsening renal dysfunction. Invasive treatment was associated with improved 12-month prognosis in STEMI patients regardless of renal function and in NSTEMI patients with eGFR \geq 15 mL/min/1.73 m².

Key words: acute myocardial infarction, coronary artery disease, glomerular filtration rate, renal function

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INTRODUCTION

Epidemiological data indicate that the percentage of patients with impaired renal function (IRF) in the global population ranges from 7% to 29%, depending on the countries or regions analysed [1]. Renal dysfunction is an independent risk factor for cardiovascular disease, which is the main cause of death in that group [2]. The most common manifestation of IRF is reduced estimated glomerular filtration rate (eGFR), which is observed in about 30–50% of patients with myocardial infarction (MI) [3, 4].

The guidelines of the European Society of Cardiology (ESC) on non-ST elevation acute myocardial infarction (NSTEMI) recommend implementation of an invasive diagnostic strategy in moderate to high-risk patients [3]. In patients with eGFR < 60 mL/min/1.73 m², diagnostic catheterisation should be performed within 72 h of presentation, unless other risk factors are present. In patients with ST elevation myocardial infarction (STEMI), renal function should be evaluated as soon as possible, without this causing any delay in decision-making on reperfusion strategy [4]. Moreover,

Address for correspondence:

Michał Hawranek, PhD, MD, 3rd Chair and Department of Cardiology, Medical University of Silesia in Katowice, School of Medicine with the Division of Dentistry in Zabrze, Silesian Centre for Heart Diseases, ul. Skłodowskiej-Curie 9, 41–800 Zabrze, Poland, tel: +48 32 373 38 60, e-mail: mhawranek@poczta.fm **Received:** 25.08.2016 **Accepted:** 01.12.2016 **Available as AoP:** 27.01.2017 Kardiologia Polska Copyright © Polskie Towarzystwo Kardiologiczne 2017 numerous reports suggest that patients with IRF fail to receive optimum treatment in line with ESC recommendations [5–8]. The objective of our study was to determine if the presence of IRF affects the choice of treatment strategy in patients with MI, and if in-hospital and long-term mortality rates are influenced by the use of invasive strategy in patients with MI according to the grade of IRF.

METHODS

A retrospective analysis of data from the Polish Registry of Acute Coronary Syndromes (PL-ACS) was undertaken. PL-ACS is a national, multicentre, prospective observational registry, which includes data on patients hospitalised with ACS in Poland [9]. PL-ACS is a joint project of the Silesian Centre of Heart Diseases in Zabrze and the Polish Ministry of Health, in cooperation with the National Health Fund. The registry was founded in October 2003, and in May 2004 the registry protocol was harmonised with the European Cardiology Audit and Registration Data Standards (CARDS). The institutional review board at each site approved the protocol. The registry was approved by local Ethics Committee and meets the conditions of the Declaration of Helsinki.

This analysis was undertaken in consecutive patients included in the registry in the calendar years 2007–2008. At that time, 260 hospitals were contributing to the registry, including 73 hospitals with access to invasive cardiology units where haemodynamic evaluations were available. Patients with confirmed diagnosis of acute coronary syndrome (ACS) based on clinical symptoms and additional tests were included to the registry, and then classified as having unstable angina, STEMI, or NSTEMI on the basis of electrocardiography and measured levels of markers of myocardial necrosis. Data were collected by the treating physicians and entered into the electronic system of the registry. Data on post-hospitalisation mortality including the date of death were obtained from the National Health Fund. The vital status during 36 months was available for all included patients.

The analysis included all patients in the PL-ACS registry, who were hospitalised in the period 2007-2008 and had eGFR data available on admission. Patients without eGFR had similar baseline characteristics and long-term prognosis to patients with available eGFR on admission. Subsequently, patients were categorised for NSTEMI and STEMI (diagnosed according to the guidelines [3, 4]), and then stratified into groups based on their eGFR value according to the classification used by Kidney Disease: Improving Global Outcomes (KDIGO) [10]: \geq 90 (normal renal function); 60-89 (mild IRF); 30-59 (moderate IRF); 15-29 (severe IRF); and < 15 mL/min/1.73 m² (end-stage IRF). eGFR was calculated using the 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula: for females with serum creatinine (SCr) \leq 0.7 mg/dL: 144 \times (SCr [mg/dL]/0.7) ^ $(-0.329) \times 0.993$ Age [years] (× 1.159 if black race); for

females with SCr > 0.7 mg/dL: 144 × (SCr [mg/dL]/0.7) ^ (-1.209) × 0.993 ^ Age [years] (× 1.159 if black race); for males with SCr \leq 0.9 mg/dL: 141 × (SCr [mg/dL]/0.9) ^ (-0.411) × 0.993 ^ Age [years] (× 1.159 if black race); for males with SCr with > 0.9: 141 × (SCr [mg/dL]/0.9) ^ (-1.209) × 0.993 ^ Age [years] (× 1.159 if black race) [11].

An invasive strategy was defined as angiography during the primary hospitalisation. Therapeutic decisions were made at the discretion of the operating physician. Outcomes assessed were in-hospital death (from any cause), cardiovascular events, or major bleeding. Cardiovascular events included recurrent MI — a cardiac ischaemic episode meeting the criteria of MI as proposed by ESC/and clearly clinically separate from the baseline ACS at the time of admission - or stroke (haemorrhagic or ischaemic). Stroke was defined as an acute neurological deficit of > 24 h duration. Major bleeding was defined as clinically overt bleeding: i) with an ensuing decrease in haemoglobin to below 5 g/dL (3.1 mmol/L) or absolute decrease of haematocrit by more than 15%; or ii) resulting in haemodynamic disorders; or iii) requiring blood transfusion. Data on all-cause mortality at 30 days, 12 months, 24 months, and 36 months after the index event were also collected.

Statistical analysis

Baseline demographic and clinical characteristics, angiographic findings, in-hospital prognosis, and mortality in the 36-month follow-up period were compared across IRF groups in the NSTEMI and STEMI cohorts of patients. Continuous variables were summarised using arithmetic mean with standard deviation (SD) for normal distribution or median with interquartile range (IQR) for non-normal distribution. Normality of distribution was verified using the Shapiro-Wilk test. Continuous variables following normal distribution were compared using t-Student test, while other than normal were compared using the Mann-Whitney U test. Categorical variables were summarised using frequency tables. For comparison of categorical data the χ^2 test with Pearson modification was used. The Jonckheere-Terpstra test was utilised in the analysis of quantitative variables depending on eGFR values. Qualitative variables were compared using the Cochran-Armitage test for trend. A logistic regression model was used to analyse the factors influencing events during hospitalisation, while factors affecting 30-day, 12-month, and 36-month mortality rates were analysed using a Cox proportional hazards model. Results of the multivariate analysis were summarised as odds ratio (OR) or hazard ratio (HR) with 95% confidence interval (CI). Results were considered statistically significant for p < 0.05. Calculations were undertaken using STATISTICA PL version 10 (StatSoft, Inc., Tulsa, Oklahoma, USA), SPSS version 17.0.1 (SPSS, Inc., Chicago, Illinois, USA), and NCSS version 9 (Kaysville, Utah, USA).



Figure 1. Study design and percentages of patients in particular impairment of renal function stages; NSTEMI — non-ST-elevation myocardial infarction; STEMI — ST-elevation myocardial infarction; eGFR — estimated glomerular filtration rate

RESULTS

In the studied population of 22,431 patients, 11,014 were diagnosed with NSTEMI, while 11,417 had STEMI (Fig. 1). Moderate or higher-grade IRF (eGFR < 60 mL/min/1.73 m²) was present in 36.2% of patients with NSTEMI and in 26.0% of patients with STEMI. Baseline characteristics of the studied population are summarised in Table 1. Regardless of MI category, a trend towards a higher proportion of women and older age of patients was observed with decreasing eGFR. Patients with worse renal function had a higher proportion of existing or previous cardiovascular diseases, more concomitant disorders, and lower left ventricular ejection fraction (Table 1).

The percentage of NSTEMI patients treated invasively decreased from 71.8% in the group with eGFR \geq 90 mL/min/1.73 m² to 35.1% in the severe IRF group (p < 0.001), whereas for patients with STEMI, a decrease in frequency of use of primary percutaneous coronary intervention (PCI) was noted from 85.9% in those with normal renal function to 52.5% in those with end-stage IRF (p < 0.001). It was demonstrated that each single-step increase in IRF grade was associated with a decrease in the likelihood of undergoing PCI during hospitalisation (Fig. 2). This effect was independent of other factors after adjustment for baseline characteristics (Table 2). A trend was identified for progressively less frequent use of most guideline-recommended medications with decreasing eGFR, with the exception of diuretics and low molecular weight heparin (p < 0.001), which were used more frequently in patients with higher grades of IRF (Table 3).

In patients with NSTEMI, worsening IRF was associated with an increased incidence of death (p < 0.001), cerebral stroke (p < 0.001), and major bleeding (p < 0.001), with no influence on recurrent MI (p = 0.054; Fig. 3, Table 3). There were no differences observed in the frequency of target vessel revascularisation (TVR) between different grades of IRF in patients undergoing PCI (p = 0.21). Similarly, in the STEMI group, there was greater incidence of death (p < 0.001), recurrent MI (p = 0.003), cerebral stroke (p < 0.001), and major bleeding (p < 0.001) with worsening IRF, but no difference in the rate of TVR (p = 0.90). After adjustment for clinical factors and the choice of invasive strategy, a statistically independent influence of IRF grade on the incidence of major bleeding, but not recurrent MI or stroke, was demonstrated for the entire studied population (Table 2). A less favourable prognosis with higher grades of renal dysfunction was also noted in long-term follow-up (Fig. 3, Table 2). Mortality rates at 12 months were found to rise with increasing grades of IRF, and were equal to 6.0%, 12.3%, 24.9%, 47.7%, and 45.8%, respectively, for patients with NSTEMI (p < 0.001) and 4.5%, 10.5%, 29.4%, 53.5%, and 58.5% for patients with STEMI (p < 0.001). A similar pattern was demonstrated at 36-month follow-up (p < 0.001). Cox proportional hazard model revealed a strong independent influence of a higher grade of IRF on 12-month and 36-month mortality rates (Table 2).

Mortality rates at 12 months and 36 months were significantly lower for patients undergoing invasive procedures compared with conservative treatment, in all IRF grades, except for end-stage renal failure in the NSTEMI population

					eGFR [ml	./min/1.73	: m²] (n = 22	,431)				
			NSTEMI (n =	11,014)					STEMI (n =	11,417)		·
	≥ 90	60–89	30–59	15–29	< 15	۵.	≥ 90	60–89	30–59	15–29	< 15	۵.
	(n = 2514)	(n = 4516)	(n = 3263)	(n = 553)	(n = 168)		(n = 3681)	(n = 4766)	(n = 2508)	(n = 344)	(n = 118)	
Males (%)	80.7	64.4	45.8	39.2	50.6	< 0.001	82.5	68.5	48.8	36.1	39.8	< 0.001
Median age [years] (IQR)	57 (51–63)	68 (59–75)	75 (69–81)	78 (71–83)	71 (63–79)	< 0.001	55 (50–61)	65 (56–73)	74 (66–79)	77 (71–83)	74 (63–80)	< 0.001
Age > 85 years	0.2	3.2	10.2	16.8	6.0	< 0.001	0.1	2.1	8.4	18.3	11.0	< 0.001
Arterial hypertension (%)	66.1	73.6	79.1	80.5	78.6	< 0.001	55.4	61.8	68.8	65.4	70.3	< 0.001
Diabetes mellitus (%)	19.3	27.5	39.9	49.0	39.3	< 0.001	16.0	20.4	32.5	40.1	30.5	< 0.001
Hypercholesterolaemia (%)	43.9	44.7	39.9	36.9	44.6	< 0.001	41.2	39.6	35.1	31.1	29.7	< 0.001
Obesity (%)	18.7	20.0	23.0	26.0	23.2	< 0.001	16.8	17.9	20.1	19.2	21.2	< 0.001
Smoking history (%)	67.5	53.4	41.7	38.2	47.6	< 0.001	75.4	60.3	45.5	35.8	46.6	< 0.001
Smoking currently (%)	40.1	21.5	10.5	6.9	10.7	< 0.001	52.2	32.9	18.7	12.5	17.8	< 0.001
PAD (%)	5.9	6.0	0.6	9.3	13.1	< 0.001	3.2	4.9	5.5	7.0	5.9	< 0.001
Prior MI (%)	19.8	25.4	31.5	33.6	33.3	< 0.001	10.3	11.6	17.1	18.9	13.6	< 0.001
Prior PCI (%)	12.5	13.7	14.3	13.0	15.5	0.092	7.5	7.0	7.0	7.0	5.9	0.34
Prior CABG (%)	3.9	4.5	4.2	3.4	4.2	0.94	1.1	1.5	1.9	2.4	0.0	0.012
Prior stroke (%)	2.4	4.6	7.0	9.2	7.7	< 0.001	2.1	3.6	5.8	6.7	3.4	< 0.001
Family history (%)	14.2	12.3	11.5	12.3	14.9	0.036	12.8	10.0	9.5	7.8	7.6	< 0.001
SCA prior to admission (%)	0.7	0.8	1.3	0.9	1.2	0.059	1.3	1.6	2.7	4.1	2.5	< 0.001
No coronary chest pain (%)	7.4	11.6	23.3	34.7	26.8	< 0.001	3.3	6.2	13.8	25.9	26.3	< 0.001
Anterior MI (%)	I	I	I	ļ	ļ	I	39.9	40.0	42.1	42.4	42.4	0.072
Killip class I (%)	89.3	80.7	65.2	52.3	54.8	< 0.001	88.6	81.7	66.1	50.0	50.0	< 0.001
Killip class II (%)	8.8	14.2	22.4	28.0	25.6	< 0.001	8.9	12.9	19.1	17.4	22.8	< 0.001
Killip class III (%)	1.2	3.9	9.8	11.9	13.7	< 0.001	0.7	2.1	5.1	11.1	4.2	< 0.001
Killip class IV (%)	0.8	1.2	2.7	7.8	6.0	< 0.001	1.9	3.4	9.6	21.5	16.9	< 0.001
Non-sinus rhythm (%)	4.4	10.8	17.9	22.6	11.9	< 0.001	2.8	5.4	14.1	23.0	18.6	< 0.001
Atrial fibrillation (%)	3.1	8.2	14.1	18.8	7.7	< 0.001	2.0	3.7	9.7	14.5	11.0	< 0.001
ST changes (%)	85.8	87.9	88.8	84.8	86.9	0.10	0.66	98.8	98.0	97.4	97.5	< 0.001
LVEF (%) (IQR)	50 (45–58)	50 (40–55)	45 (35–52)	40 (34–50)	45 (40–50)	< 0.001	50 (44–55)	48 (40–52)	45 (36–50)	40 (31–50)	40 (35–50)	< 0.001
Median creatinine [mg/dL] (IQR)	0.8 (0.7–0.9)	1.0 (0.9–1.1)	1.3 (1.1–1.5)	2.2 (1.9–2.8)	4.9 (4.1–7.1)	< 0.001	0.8 (0.7–0.9)	1.0 (0.9–1.1)	1.3 (1.1–1.5)	2.2 (1.8–2.6)	5.0 (3.7–7.1)	< 0.001
Median eGFR [mL/min/1.73 m ²] (IQR)	100 (94–105)	74 (67–83)	48 (40–54)	24 (20–27)	10 (7–12)	< 0.001	101 (95–107)	76 (69–84)	49 (42–55)	25 (2028)	9 (6–12)	< 0.001
Angiography (%)	71.8	62.8	49.1	35.1	44.6	< 0.001	90.9	85.7	74.2	62.8	55.1	< 0.001
PCI (%) ^a	57.1	47.6	36.6	27.3	36.9	< 0.001	85.9	80.6	68.2	57.9	52.5	< 0.001
CABG during hospitalisation (%)	4.7	4.9	3.5	2.5	4.8	0.006	2.0	2.4	2.2	23	1.7	0.67
CABG after discharge (%)	5.4	6.3	5.2	2.4	4.2	0.021	4.6	4.7	4.0	2.0	3.4	0.064
^a For STEMI patients primary PCI. Median c eGFR — estimated glomerular filtration ra arterv disease: PCI — percutaneous corona	reatinine in mg. ite; IQR — inter arv intervention	/dL to µmol/L, × quartile range; L ; SCA — sudder	:88.4. Data are .VEF — left vent n cardiac arrest:	presented as p tricular ejection STEMI — ST-el	ercentage, mea fraction; MI — levation mvocar	n ± standa myocardial dial infarcti	rd deviation or infarction; NS ⁻ on	median (interq FEMI — non-ST	uartile range); (-elevation myo	CABG — coroni cardial infarctio	ary artery bypas n; PAD — perip	is grafting; heral



Figure 2. Percentage of patients with non-ST-elevation myocardial infarction (NSTEMI; A) and ST-elevation myocardial infarction (STEMI; B) treated with angiography and percutaneous coronary intervention (PCI), in different impairment of renal function stages; p value for all trends < 0.0001; eGFR — estimated glomerular filtration rate

(p = 0.41) (**Data are described in Supplementary material online**—**see journal website**). Based on the adjusted data (Fig. 4), an independent improvement in 12-month prognosis with the use of an invasive strategy was demonstrated for IRF grades from normal renal function to severe IRF in NSTEMI patients and for all IRF grades in patients with STEMI.

DISCUSSION

The main objective of this analysis, carried out on a large population of unselected patients with MI included in PL-ACS registry, was to determine whether the choice of therapeutic strategy and/or outcomes varied with renal function. From the results we can conclude that progressively worsening renal function is associated with a greater incidence of adverse cardiovascular events, and this is a consequence of the less favourable clinical and angiographic profile of patients with higher grade IRF as well as an independent effect of IRF on clinical prognosis. The analysis also revealed that some patients with higher-grade renal dysfunction are not treated in accordance with ESC recommendations. In spite of less frequent use of invasive diagnostics and treatment, and increasing mortality rates with worsening eGFR, most patients with MI benefited from implementation of an invasive strategy, at least in terms of 12-month mortality rates, the exception being patients with NSTEMI and end-stage renal failure.

In the randomised clinical trials that have included patients with MI and renal dysfunction, the percentage of patients with moderate or higher grade of IRF (eGFR < 60 mL/min/1.73 m²) ranged from 13.8% to 45.7% [12–18], while in registries from the past five years it ranged from 28.9% to 42.9% [5–8]. The populations of patients with particular IRF grades noted in our analysis are comparable with the data from the GRACE [5], ACS I/II [5], and SWEDEHEART [7] registries. The observed differences between the studies result from the adopted definitions of renal dysfunction and criteria use to select and stratify the analysed population.

Our analysis found that MI patients differ in their clinical and angiographic characteristics, depending on their IRF grade, consistent with the findings of other studies [5-8, 12-16]. In patients with worse IRF, there is a greater percentage of predictors of poorer prognosis. In spite of the absence of statistically significant differences, some baseline factors in the end-stage IRF group in our study were paradoxically more favourable than in the severe IRF group. There are probably two reasons for this finding: 1) a disproportionately low number of patients with end-stage renal failure, and 2) a lack of data on dialysis therapy, after which some patients may have qualified for groups with better renal function due to a temporary decrease in SCr [19]. It is assumed that the mechanism behind more frequent occurrence of adverse events in patients with higher CKD stages is related to advanced progression of atherosclerosis, oxidative stress, increased platelet aggregation, and less frequent utilisation of recommended pharmacological treatment and invasive strategy [20]. The percentages of adverse outcomes during hospitalisation and long-term follow-up are similar to those obtained in other studies [5-8, 15, 21, 22]. In all these studies, eGFR or SCr were potent predictors of death, independent of baseline clinical and angiographic characteristics.

The pivotal element in pathophysiology of increased bleeding in the course of CKD among patients with MI is platelet dysfunction and impairment of their interaction with vascular wall [23]. Most anticoagulants recommended for use in the course of MI, being at least partly metabolised in the kidneys, may accumulate in the body, thus increasing the risk of haemorrhagic complications [8, 24, 25]. Data from our analysis confirm the high risk of bleeding in MI patients with IRF. The incidence of major bleeding during hospitalisation increased independently by 42% for each higher grade of IRF. By comparison, Gibson et al. [13] demonstrated that incidence of major bleeding increased by 12% per each 10 mL/min/1.73 m² decline in eGFR. Current ESC recom-

Table 2. Unadjusted and adjust. STEMI patients)	ed odds ratios of in-hospital cardiovascular events	and unadjusted and adjusted hazard ratios for long	g-term mortality (pooled analysis of NSTEMI and
Factor (per single-step	Unadjusted	Adjusted ^a	Adjusted ^b

Factor (per single-step		Unadjusted			Adjusted ^a			Adjusted ^b	
increase of IRF grade)	OR	95% CI	Q	OR	95% CI	٩	OR	95% CI	٩
In-hospital observation:									
Coronary angiography	0.57	0.55-0.59	< 0.001	0.78	0.74-0.81	< 0.001	I	Ι	I
PCI¢	0.63	0.59-0.65	< 0.001	0.81	0.78-0.85	< 0.001	I	I	I
MACE:									
Death	2.75	1.58–2.93	< 0.001	2.05	1.90-2.23	< 0.001	2.01	1.86–2.18	< 0.001
M	1.33	1.12–1.59	0.001	1.04	0.83-1.29	0.74	1.02	0.82-1.27	0.86
Major bleeding	1.79	1.58–2.02	< 0.001	1.38	1.19–1.62	< 0.001	1.42	1.22–1.66	< 0.001
Cerebral stroke	1.82	1.49–2.21	< 0.001	1.33	1.03-1.71	0.025	1.27	1.00–1.61	0.062
TVR ^d	0.90	0.74–1.38	0.34	0.89	0.71-1.12	0.33	I	I	I
	HR	95% CI	d	HR	95% CI	٩	HR	95% CI	٩.
Post-discharge outcomes:									
Death at 30 days	2.29	2.19–2.39	< 0.001	1.66	1.57-1.75	< 0.001	1.61	1.52-1.70	< 0.001
Death at 12 months	2.16	2.09–2.23	< 0.001	1.59	1.53-1.66	< 0.001	1.55	1.49–1.62	< 0.001
Death at 24 months	2.13	2.07–2.19	< 0.001	1.57	1.51-1.63	< 0.001	1.53	1.47–1.59	< 0.001
Death at 36 months	2.09	2.04–2.15	< 0.001	1.54	1.49–1.59	< 0.001	1.50	1.45–1.55	< 0.001
^a Adjusted OR or HR for the following ^b Adjusted OR or HR for the following ^b Adjusted OR or HR taking account of ^c For STEMI patients primary PCI;	parameters: gende o class 3 and 4 on <i>i</i> the parameters as	tr, arterial hypertensio admission, non-sinus listed above (*) plus	n, diabetes mellit rhythm, left venti additionally: angi	us, smoking, obesit icular ejection fract ography (invasive s	y, hypercholesterolaen tion; trategy);	nia, peripheral arte	ery disease, prior N	MI, prior PCI, prior CAE	3G, prior stroke,
^o Recurrent urgent revascularisation of CABG — coronary artery bypass grafti — non-ST-elevation myocardial infarc	the target coronal ing; Cl — confiden tion; OR — odds ra	y artery in patients w ice interval; HR — haz atio; PCI — percutan€	tho have already u zard ratio; IRF — i sous coronary inte	Indergone PCI. mpairment of rena rvention; STEMI —	l function; MACE — m ST-elevation myocard	ajor adverse cardi ial infarction; TVR	ovascular events; — target vessel re	MI — myocardial infar evascularisation	ction; NSTEMI

Table 3. Pharmacological treatment, in-hospital events, and long-term mortality in different impairment of renal function stages

					eGFR [m	1.1.1.7	3 m²] (n = 2	2,431)				
			NSTEMI (n =	11,014)					STEMI (n =	11,417)		
	≥ 90	60–89	30–59	15–29	< 15	ď	≥ 90	60-89	30–59	15–29	< 15	٩
	(n = 2514)	(n = 4516)	(n = 3263)	(n = 553)	(n = 168)		(n = 3681)	(n = 4766)	(n = 2508)	(n = 344)	(n = 118)	
In-hospital pharmacologic t	reatment											
ASA (%)	94.7	93.5	91.9	89.3	88.7	< 0.001	93.8	94.4	91.0	85.2	84.7	< 0.001
Clopidogrel (%)	94.9	93.1	89.4	84.3	94.6	< 0.001	98.2	97.6	94.8	90.4	86.4	< 0.001
Beta-blocker (%)	86.3	85.2	81.5	73.6	76.2	< 0.001	85.3	83.9	76.8	63.4	68.6	< 0.001
ACE-I (%)	80.9	80.9	76.9	66.2	58.9	< 0.001	81.2	79.3	72.2	56.7	50.0	< 0.001
Statin (%)	88.9	86.9	82.6	77.8	74.4	< 0.001	89.1	87.4	79.7	69.2	71.2	< 0.001
Nitrates (%)	27.4	34.0	39.6	39.6	45.8	< 0.001	16.7	19.3	22.1	21.8	23.7	< 0.001
Diuretics (%)	14.2	26.1	47.4	60.9	51.2	< 0.001	12.4	20.4	32.9	44.2	38.1	< 0.001
UFH regardless of PCI (%)	21.8	18.3	17.7	16.6	16.7	< 0.001	32.6	35.0	34.8	28.5	28.5	0.67
LMWH regardless of PCI (%)	26.8	32.0	35.2	38.3	38.1	< 0.001	16.0	16.5	20.9	27.9	28.0	< 0.001
GP IIb/IIIa inhibitor (%)	4.6	3.5	2.9	2.5	3.6	0.001	25.2	21.6	18.2	11.9	17.8	< 0.001
Pharmacologic treatment o	n discharge											
ASA (%)	91.0	89.6	88.0	86.1	91.7	< 0.001	95.2	93.1	90.4	86.8	80.3	< 0.001
Clopidogrel (%)	75.0	74.4	68.4	64.3	68.9	< 0.001	91.6	90.2	80.2	80.6	60.9	< 0.001
Beta-blocker (%)	81.4	79.9	76.9	76.0	79.4	< 0.001	86.6	81.2	78.3	70.6	66.3	< 0.001
ACE-I (%)	77.0	76.3	73.0	63.0	56.1	< 0.001	80.2	79.1	74.0	61.6	48.7	< 0.001
Statin (%)	84.3	82.1	78.5	75.8	75.3	< 0.001	91.0	87.4	80.2	77.6	71.2	< 0.001
Nitrates (%)	19.0	21.8	26.0	26.9	27.8	< 0.001	13.5	13.5	15.4	16.5	11.4	0.026
Diuretics (%)	13.5	24.3	42.6	54.6	41.0	< 0.001	12.8	17.8	31.6	40.1	28.4	< 0.001
In-hospital events												
Death (%)	1.1	2.4	6.8	20.3	17.3	< 0.001	1.0	3.1	12.9	32.0	31.4	< 0.001
Recurrent MI (%)	0.4	0.5	0.5	1.1	1.2	0.054	0.5	0.7	0.7	1.7	3.4	0.003
Cerebral stroke (%)	0.1	0.2	0.6	0.5	1.2	< 0.001	0.2	0.4	0.8	1.2	2.5	< 0.001
TVR ^a (%)	0.5	0.4	0.3	0.4	0.0	0.21	0.9	0.8	0.7	2.0	0.0	0.90
Major bleeding (%)	0.4	0.9	1.5	2.4	2.4	< 0.001	0.5	1.0	2.1	3.2	5.1	< 0.001
Hospitalisation, days (IQR)	4 (2–7)	5 (2–8)	6 (3–10)	7 (2–11)	6 (3-10)	< 0.001	4 (3–7)	5 (3–8)	5 (2–9)	4 (1–10)	5 (1–9)	< 0.001
Post-discharge mortality												
30 days (%)	2.0	4.8	11.0	26.8	22.6	< 0.001	2.2	5.4	18.7	40.7	40.7	< 0.001
12 months (%)	6.0	12.3	24.9	47.7	45.8	< 0.001	4.5	10.5	29.4	53.5	58.5	< 0.001
24 months (%)	8.3	16.9	33.3	59.1	57.7	< 0.001	6.4	13.1	34.7	59.9	61.9	< 0.001
36 months (%)	10.9	20.3	38.9	67.3	66.7	< 0.001	8.6	16.0	39.4	67.2	64.4	< 0.001
^a Recurrent urgent revascularisatior range); ACE-I — angiotensin-conv function; LMWH — low-molecular	of the target co erting enzyme ir weight heparin	oronary artery ir hhibitor; ASA — ; NSTEMI — no	n patients who h - acetylsalicylic ac n-ST-elevation n	ave already ur cid; eGFR — es nyocardial infa	idergone PCI fo stimated glome rction; PCI — p	or NSTEMI o erular filtrati oercutaneou	r primary PCI fo on rate; GP — s coronary inter	or STEMI. Data a glycoprotein; IC vention; STEMI	are presented a R — interquart — ST-elevatior	s percentage ol ile range; IRF – myocardial int	r median (inter — impairment (farction; TVR —	quartile of renal – target
vessel revascularisation; UFH — un	fractionated he	parin										



Figure 3. Percentages of cardiovascular events (recurrent myocardial infarction [MI], cerebral stroke, target vessel revascularisation [TVR], major bleeding) in patients with non-ST-elevation myocardial infarction (NSTEMI; **A**) and ST-elevation myocardial infarction (STEMI; **B**), and mortality rates during hospitalisation, at 12, 24, and 36 months for NSTEMI (**C**) and STEMI (**D**), in different impairment of renal function (IRF) stages; p values for trends provided in the text; eGFR — estimated glomerular filtration rate

mendations on the management of patients with NSTE-ACS and STEMI note that patients with IRF belong to the group at increased risk of major bleeding and thus special care should be taken with anticoagulant and antiplatelet therapy [3, 4]. In our analysis, we noted less frequent use of acetylsalicylic acid, clopidogrel, and unfractionated heparin, and more frequent use of low-molecular weight heparin, in the groups with greater IRF. This suggests some apprehension among physicians concerning the use of anticoagulant and antiplatelet medications in patients with IRF, as has been observed elsewhere [5, 8]. With regard to antiplatelet agents, a sub-analysis of the PLATO study performed in patients with eGFR < 60 mL/min/1.73 m^2 showed that ticagrelor was superior to clopidogrel in reducing a composite endpoint (17.3 vs. 22.0%; HR 0.77; 95% CI 0.65-0.90), including mortality (10.0 vs. 14.0%; HR 0.72; 95% CI 0.58-0.89) over 12-month follow-up, without significantly increasing the risk of major bleeding, bleeding resulting in death, and bleeding not related to coronary artery bypass grafting [17]. Moreover, the absolute benefit of ticagrelor in reducing cardiovascular adverse events compared with clopidogrel was greater in patients with IRF than in those with normal renal function. This may be because clopidogrel has reduced efficacy in patients with impaired renal function [25]. The data available for our

analysis covered the period 2007–2008, when ticagrelor was not yet available for routine clinical use. The ESC recommendations include the possibility of using any of the medications mentioned above, provided appropriate dose adjustments are made to match renal function status [3, 4]. Dosing information was not available for our analysis.

European Society of Cardiology guidelines for NSTE-ACS recommend an invasive strategy in patients at moderate to high risk of ischaemic events [3]. However, as described earlier, these recommendations are based on sub-analyses from randomised studies and data from observational registries. In the FRISC II study, in which patients with SCr > $150 \,\mu$ mol/L were excluded from analysis, patients with mild and moderate IRF, who underwent revascularisation had a significantly lower rate of death or recurrent MI during the two-year follow-up compared with patients who were treated conservatively [14]. Moreover, absolute benefits from revascularisation were greater in patients with creatinine clearance < 69 mL/min than in those with creatinine clearance > 90 mL/min (7.8% vs. 0.4%). A sub-analysis of data from the TACTICS-TIMI 18 study revealed that, during six-months of follow-up, the benefits of invasive management are similar for patients with mild or moderate IRF and for those with normal renal function [12]. In an analysis of non-selected patients included



Figure 4. Mortality rates at 12 months in different impairment of renal function stages, depending on treatment strategy in patients with non-ST-elevation myocardial infarction (**A**) and ST-elevation myocardial infarction (**B**). Hazard ratio (HR) adjusted for the following parameters: age, gender, arterial hypertension, diabetes mellitus, smoking, obesity, hypercholesterolaemia, peripheral artery disease, prior myocardial infarction, prior percutaneous coronary intervention, prior coronary artery bypass grafting, prior stroke, cardiac arrest prior to admission, Killip class 3 and 4 on admission, non-sinus rhythm, left ventricular ejection fraction; CI — confidence interval

in the GRACE and ACS I/II registries, Wong et al. [5] proved that in-hospital revascularisation was associated with better 12-month prognosis regardless of degree of renal dysfunction. However, the methodology applied in that analysis did not incorporate a multivariate model for each IRF grade, as was used in our study. An analysis of data from 23,262 unselected NSTEMI patients in the SWEDEHEART registry demonstrated that, compared with conservative management, use of an invasive strategy was associated with an independent improvement in 12-month survival by 36% in mild IRF (95% CI 0.52-0.80) and by 32% in moderate IRF (95% CI 0.54-0.86) [7]. However, the benefit of invasive management was not seen in patients with severe (HR 0.91; 95% CI 0.51-1.61; p = 0.7) or end-stage IRF (HR 1.61; 95% CI 0.51-1.61; p = 0.2). Our study confirmed the independent reduction of long-term mortality with invasive vs. conservative treatment in NSTEMI patients with mild and moderate IRF, but invasive management was not found to impact on long-term outcomes in the end-stage IRF group. Contrary to most registries, our

study found that patients with severe IRF had significantly greader benefit in 12-month follow-up when they receive invasive rather than conservative treatment.

In the case of STEMI patients, the decision regarding invasive reperfusion must be made before any evaluation of renal function is possible, because of the proven benefits of such treatment [4]. Studies in STEMI patients indicate that IRF is associated with a less favourable prognosis, both in patients receiving invasive treatment and in the entire STEMI population [15, 16]. Likewise, in our analysis, prognosis was significantly worse in patients with higher-grade IRF. However, the overall benefits of an invasive strategy in STEMI patients outweigh the adverse events and appear quite promising.

Limitations of the study

PL-ACS is a prospective observational registry, but not all of the hospitals providing treatment to patients with ACS in Poland participate in data collection. The main limitation of the study was the fact that patients were treated in 2007–2008, which can make it difficult to transfer the presented results to contemporary practice, particularly in the context of greater availability of invasive treatment of patients with NSTEMI and new antiplatelet agents. Additionally, a potential weakness of our analysis is its retrospective nature. The number of patients with severe and end-stage IRF was relatively small compared with the other groups, which may have compromised the statistical power of the model. The key limitation, however, is the fact that some relevant measurements and information, such as troponin types, history of dialysis treatment, or data concerning type of kidney injury (acute/chronic) were not collected. Not all patients in the PL-ACS registry had data on eGFR on admission, and they were excluded from the analysis. Therefore, even after adjustment of the data, the real results of the analysis may have been different from the presented ones due to the potential effect of data not included in the registry. There is no information on co-morbidities that also may be related to IRF (acute infections, anaemia, dementia, psychotic state, etc.). For this reason, the obtained trend towards improvement in prognosis following implementation of an invasive strategy in NSTEMI patients with severe IRF should be interpreted with caution.

CONCLUSIONS

In conclusion, the percentages of patients who qualified for invasive management tend to decrease with worsening renal function in both NSTEMI and STEMI populations. Implementation of an invasive strategy is associated with independent improvement in 12-month prognosis for STEMI regardless of patients' renal function status and for NSTEMI if eGFR is \geq 15 mL/min/1.73 m². Further investigations should be conducted to verify these findings.

Research highlights

- 1. The percentages of patients who qualified for invasive management tend to decrease with worsening renal function in both NSTEMI and STEMI populations.
- 2. In patients with STEMI, the invasive treatment was associated with improved 12-month prognosis regardless of renal function.
- 3. Implementation of an invasive strategy is associated with independent improvement in 12-month prognosis for NSTEMI if eGFR is \geq 15 mL/min/1.73 m².
- 4. An invasive strategy appears to be more beneficial than conservative treatment for patients with NSTEMI and severe IRF.

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Funkcja nerek przy przyjęciu wpływa na strategię leczenia i wyniki długoterminowe pacjentów z zawałem serca (dane z Polskiego Rejestru Ostrych Zespołów Wieńcowych)

Michał Hawranek, Marek Gierlotka, Mariusz Gąsior, Bartosz Hudzik, Piotr Desperak, Aneta Ciślak, Matusz Tajstra, Tadeusz Osadnik, Piotr Rozentryt, Lech Poloński

III Katedra i Oddział Kliniczny Kardiologii, Śląski Uniwersytet Medyczny w Katowicach, Wydział Lekarski z Oddziałem Lekarsko-Dentystycznym w Zabrzu, Śląskie Centrum Chorób Serca, Zabrze

Streszczenie

Wstęp: Upośledzenie funkcji nerek (IRF) jest niezależnym czynnikiem ryzyka u pacjentów z zawałem serca (MI). Najczęstszą manifestacją IRF jest zredukowana wartość wskaźnika filtracji kłębuszkowej (eGFR), którą obserwuje się u 30–50% chorych z MI.

Cel: Celem pracy było określenie wpływu IRF na wybór strategii leczenia pacjentów z MI oraz związku między rokowaniem wewnątrzszpitalnym i długoterminowym a wdrożeniem strategii inwazyjnej w zależności od stopnia IRF.

Metody: Przeanalizowano dane kolejnych pacjentów z rejestru PL-ACS hospitalizowanych z powodu MI w latach 2007–2008 z dostępnym wynikiem eGFR przy przyjęciu. Pacjentów podzielono na podstawie eGFR: \geq 90 (prawidłowa funkcja nerek); 60–89 (łagodne IRF); 30–59 (umiarkowane IRF); 15–29 (ciężkie IRF); i < 15 ml/min/1,73 m² (schyłkowe IRF). Wartość eGFR obliczono z użyciem formuły 2009 CKD-EPI (*Chronic Kidney Disease Epidemiology Collaboration*). Dane dotyczące śmiertelności odległej, włączając daty zgonów, zostały uzyskane z oficjalnych danych Narodowego Funduszu Zdrowia. Dane z obserwacji odległej były dostępne dla wszystkich włączonych do badania pacjentów.

Wyniki: W badanej populacji obejmującej 22 431 chorych, u 11 014 rozpoznano MI bez uniesienia odcinka ST (NSTEMI), natomiast u 11 417 pacjentów MI z uniesieniem odcinka ST (STEMI). Wraz z nasileniem upośledzenia filtracji kłębuszkowej obserwowano mniej korzystną charakterystykę kliniczną i angiograficzną. Odsetek osób z NSTEMI leczonych inwazyjnie spadał z 71,8% w grupie z eGFR \ge 90 ml/min/1,73 m² do 35,1% w grupie z ciężkim IRF (p < 0,001). Podobną zależność stwierdzono u pacjentów ze STEMI, wśród których odsetek pierwotnej przezskórnej interwencji wieńcowej (PCI) spadał z 85,9% w grupie z prawidłową wartością eGFR do 52,5% u chorych ze schyłkowym IRF (p < 0,001). Po skorygowaniu wzrost stopnia IRF powodował redukcję prawdopodobieństwa przeprowadzenia PCI o 19% (iloraz szans [OR] 0,81; 95% przedział ufności [CI] 0,78–0,85; p < 0,001). Większy stopień IRF był niezależnie związany z wyższym ryzykiem zgonu wewnątrzszpitalnego (OR 2,01; 95% CI 1,86–2,18; p < 0,001), dużego krwawienia (OR 1,42; 95% CI 1,22–1,66; p < 0,001), śmiertelności 12-miesięcznej (współczynnik ryzyka [HR] 1,55; 95% CI 1,49–1,62; p < 0.001) oraz 36-miesięcznej (HR 1,50; 95% CI 1,45–1,55; p < 0,001). Leczenie inwazyjne było niezależnie związane z poprawą rokowania 12-miesięcznego pacjentów z NSTEMI z łagodnym do ciężkiego IRF oraz ze STEMI niezależnie od IRF.

Wnioski: Wraz z gorszą funkcją nerek obserwuje się rzadsze przeprowadzanie procedur inwazyjnych. Leczenie inwazyjne wiąże się z lepszym rokowaniem 12-miesięcznym wśród pacjentów ze STEMI niezależnie od funkcji nerek oraz z NSTEMI z eGFR \geq 15 ml/min/1,73 m².

Słowa kluczowe: angioplastyka, funkcja nerek, wskaźnik filtracji kłębuszkowej, zawał serca

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Adres do korespondencji:

dr n. med. Michał Hawranek, III Katedra i Oddział Kliniczny Kardiologii, Śląski Uniwersytet Medyczny w Katowicach, Wydział Lekarski z Oddziałem Lekarsko--Dentystycznym w Zabrzu, Śląskie Centrum Chorób Serca, ul. Skłodowskiej-Curie 9, 41–800 Zabrze, tel: +48 32 373 38 60, e-mail: mhawranek@poczta.fm Praca wpłynęła: 25.08.2016 r. Zaakceptowana do druku: 01.12.2016 r. Data publikacji AoP: 27.01.2017 r.