

# Impaired renal function in patients with myocardial infarction treated with primary angioplasty and the risk for failed myocardial tissue reperfusion and thus worse long-term outcomes

Upośledzona funkcja nerek u chorych z zawałem serca leczonych pierwotną angioplastyką wieńcową a ryzyko nieskutecznej reperfuzji tkankowej i rokowanie odległe

Dariusz Karwowski<sup>1</sup>, Łukasz Kalińczuk<sup>2</sup>, Krzysztof Majewski<sup>3</sup>, Mariusz Łada<sup>1</sup>, Dariusz Noll<sup>1</sup>, Paweł Radecki<sup>1</sup>, Wojciech Suchcicki<sup>1</sup>, Anna Tyszcza<sup>1</sup>, Marcin Demkow<sup>2</sup>

<sup>1</sup>Department of Invasive Cardiology, Specialist Hospital, Ostrołęka, Poland

<sup>2</sup>Department of Coronary Artery Disease and Structural Heart Diseases, Institute of Cardiology, Warsaw, Poland

<sup>3</sup>Department of Non-Invasive Diagnostics of Cardiovascular Diseases, Specialist Hospital, Ostrołęka, Poland

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## Abstract

**Aim:** The aim was to assess the impact of impaired renal function on myocardial tissue reperfusion in patients with ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (pPCI).

**Material and methods:** Impaired renal function was diagnosed at admission based on abnormal serum creatinine level ( $> 106 \mu\text{mol/l}$ ). Patients with anterior STEMI and maximal single-lead ST-elevation (maxSTPost) exceeding 2 mm up to 90 min post-procedure, as well as patients with inferior STEMI and maxSTPost  $> 1$  mm, were considered to have failed tissue reperfusion. The incidence of death or heart failure (NYHA class  $> 2$ ) was prospectively assessed over a subsequent 12-month period.

**Results:** Primary PCI and maxSTPost measurements were performed in 200 out of 208 consecutive patients ( $63.0 \pm 12.1$  years, 67.5% males) treated between October 2007 and September 2008. Patients with impaired renal function (12.5%) died or developed heart failure more often when compared to the remaining individuals (56.0% vs. 16.0%,  $p < 0.001$ , respectively). Patients with failed reperfusion (15.5%) had higher incidence of one-year mortality and heart failure (35.5% vs. 18.3%,  $p = 0.032$ , respectively). Failed tissue reperfusion was 2.5 times more frequent among patients with impaired renal function, despite a relatively high rate of final TIMI 3 flow as compared to the remaining subjects (32.0% vs. 13.1%,  $p = 0.022$  and 84.0% vs. 92.6%,  $p = 0.239$ , respectively). Impaired renal function and failed reperfusion were independent predictors of death or heart failure (odds ratio (OR) = 4.38, 95% confidence interval (CI) 1.34-14.28,  $p = 0.014$ , and OR = 3.34, 95% CI 1.12-9.88,  $p = 0.029$ , respectively). Impaired renal function was a risk factor for failed tissue reperfusion (OR = 2.98, 95% CI 1.03-8.68,  $p = 0.044$ ).

**Conclusions:** Impaired renal function in patients with STEMI treated with primary PCI is related to the risk for failed myocardial tissue reperfusion, leading in consequence to higher one-year mortality and heart failure.

**Key words:** impaired renal function, myocardial tissue reperfusion, ST-segment elevation resolution

## Streszczenie

**Cel:** Ocena wpływu upośledzonej funkcji nerek, rozpoznawanej w chwili przyjęcia do szpitala, na skuteczność reperfuzji tkankowej u chorych leczonych pierwotną angioplastyką wieńcową (*primary percutaneous coronary intervention* – pPCI) z powodu zawału serca z przetrwałym uniesieniem odcinka ST (*ST-segment elevation myocardial infarction* – STEMI).

**Materiał i metody:** Upośledzoną funkcję nerek rozpoznawano, gdy stężenie kreatyniny było większe od normy ( $> 106 \mu\text{mol/l}$ ). W czasie do 90 min od pPCI wykonywano 12-odprowadzeniowe badanie elektrokardiograficzne (EKG) i identyfikowano pojedyncze odprowadzenie z najwyższym uniesieniem odcinka ST (maxSTPost). Chorych ze STEMI ściany przedniej i wartością maxSTPost  $> 2$  mm i chorych z zawałem ściany dolnej i wartością maxSTPost  $> 1$  mm zakwalifikowano do grupy z nieskuteczną reperfuzją tkankową. Przeprowadzono prospektywną ocenę kliniczną w ciągu pierwszego roku.

## Corresponding author/Adres do korespondencji:

Dariusz Karwowski MD, Department of Invasive Cardiology, Specialist Hospital, al. Jana Pawła II 120 A, 07-410 Ostrołęka, Poland, tel.: +48 29 765 23 40, fax: +48 29 765 25 30, e-mail: dkarwowski@op.pl

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**Wyniki:** Od 1 października 2007 do 30 września 2008 roku u 205 spośród 208 kolejnych pacjentów przeprowadzono pPCI, a u 200 oceniono maxSTPost (63,0 ± 12,11 roku, 67,5% mężczyzn). Pacjenci z upośledzoną funkcją nerek (12,5%) częściej umierali; częściej też występowała u nich niewydolność serca (56% vs 16% pozostałych pacjentów,  $p < 0,001$ ). Śmiertelność i częstość występowania niewydolności serca w grupie z nieskuteczną reperfuzyją tkankową (15,5%) były znacząco większe (35,5% vs 18,3%,  $p = 0,032$  odpowiednio). U chorych z upośledzoną funkcją nerek 2,5-krotnie częściej rozpoznawano nieskuteczną reperfuzyję tkankową, pomimo stosunkowo dużego wskaźnika skutecznych udrożeń nasierdżiowych w porównaniu z grupą pozostałych pacjentów (odpowiednio 32,0% vs 13,1%,  $p = 0,022$  i 84,0% vs 92,6%,  $p = 0,239$ ). Upośledzona funkcja nerek i brak skutecznej reperfuzyji tkankowej zwiększały niezależnie ryzyko zgonu bądź rozwoju niewydolności serca (odpowiednio iloraz szans (*odds ratio* – OR) = 4,38, 95-procentowy przedział ufności (*confidence interval* – CI) 1,34–14,28,  $p = 0,014$  i OR = 3,34, 95% CI 1,12–9,88,  $p = 0,029$ ). Upośledzona funkcja nerek okazała się czynnikiem ryzyka nieskutecznej reperfuzyji tkankowej (OR = 2,98, 95% CI 1,03–8,68,  $p = 0,044$ ).

**Wnioski:** Upośledzona funkcja nerek u chorego ze STEMI wiąże się z ryzykiem niepowodzenia pPCI w przywróceniu prawidłowej perfuzji na poziomie tkankowym miokardium, co w konsekwencji pogarsza rokowanie odległe.

**Słowa kluczowe:** upośledzona funkcja nerek, reperfuzyja tkankowa miokardium, normalizacja uniesionego odcinka ST

## Background

Impaired renal function is a risk factor for death or development of heart failure in patients with myocardial infarction treated with primary percutaneous coronary intervention (pPCI) [1-3]. The aim of pPCI in acute myocardial infarction with persistent ST-segment elevation (STEMI) is restoration of adequate myocardial tissue perfusion. This determines both the short and long-term prognosis [4, 5]. It has been reported that impaired renal function is associated with increased risk of ineffective tissue reperfusion, and consequently with a worse prognosis in STEMI patients. The assessment of tissue perfusion, however, was based only on the angiographic classification of myocardial perfusion using TIMI Myocardial Perfusion Grade (TMPG) [1, 6]. This method requires proper registration of the angiographic study (appropriate projections and a long duration of cine filming) and experience in the analysis of the degree of opacification of the myocardium [7]. The analysis of the degree of resolution of ST-segment elevation based on the assessment of maximal ST-segment elevation identified in a single ECG lead recorded immediately after the procedure (maxSTPost) allows for an early, non-invasive and objective insight into the status of myocardial reperfusion. Moreover, it is a more reliable diagnostic tool than angiographic assessment [8, 9]. Serum creatinine level is a well-established parameter used to identify patients with impaired renal function [1, 2, 10].

## Aim

The aim of the study was to evaluate the impact of impaired renal function at admission on the effectiveness of tissue reperfusion (assessed as the degree of resolution of ST-segment elevation according to the maxSTPost method), and the assessment of its impact on long-term prognosis of patients with STEMI treated with pPCI.

## Material and methods

### Material

The study included 208 consecutive STEMI patients admitted between 1 October 2007 and 30 September 2008

to the Invasive Cardiology Unit (ICU) of the hospital in Ostrołęka. There were the following criteria for the referral of patients for urgent coronary angiography: chest pain for less than 12 h together with ST-segment elevation  $\geq 0.1$  mV in at least two adjacent limb leads or  $\geq 0.2$  mV in at least two adjacent precordial leads or presumed new left bundle branch block (LBBB). Before coronary angiography, all patients received 4000-5000 units of unfractionated heparin intravenously and a loading dose of aspirin and clopidogrel (300 mg and 600 mg, respectively) followed by 75 mg per day. Abciximab was administered immediately before pPCI in patients with diabetes and anterior STEMI, as well as during the intervention in the case of a large thrombus and in the case of the 'no-reflow' phenomenon. The administration of abciximab was left to the discretion of the physician performing the procedure. Serum creatinine levels were measured in all patients at admission to the ICU. Patients with serum creatinine levels  $> 106$   $\mu\text{mol/l}$  (reference value  $\leq 106$   $\mu\text{mol/l}$ ) formed the group with impaired renal function. Glomerular filtration rate (eGFR) was calculated according to the Modification of Diet in Renal Disease (MDRD) study equation [11]. Serum levels of creatine kinase cardiac specific isoenzyme (CKMB) were measured every 6 h during the first 24 h. Epicardial flow was assessed according to the TIMI scale [12]. Transthoracic echocardiography was performed immediately before discharge, and ejection fraction (LVEF%) as well as left ventricular end-diastolic diameter (LVEDD) were measured.

### The assessment of myocardial tissue reperfusion based on the analysis of the degree of resolution of ST-segment elevation

We analyzed the standard 12-lead ECG registered before, and within 90 min after pPCI. We excluded from the analysis electrocardiograms with LBBB, pre-excitation syndrome, ectopic rhythm or significant artifacts as well as incomplete records which precluded a reliable assessment of the ST segment. Due to these reasons, 5 patients were excluded from the study. We used the methodology proposed by McLaughlin *et al.* [8]. In the infarct zone, we identified a single lead with the maximal ST-segment elevation

(for the anterior wall: leads I, aVL, V1-V6; for the inferior wall: leads II, III, aVF, V5, V6). Measurements of ST-segment elevation were made at 20 ms after the J-point, with respect to the TP segment (considered as the isoelectric line). Measurements were made in the ECG registered both before and after the procedure (maxSTPost). According to the definition, patients with inferior STEMI and maxSTPost > 1 mm as well as patients with anterior STEMI and maxSTPost > 2 mm were considered as patients with failed myocardial reperfusion. Additionally, we compared the corresponding extent of ST-segment elevation measured before and after treatment, and we calculated the relative ST-segment resolution ( $[1 - \text{ratio of maxSTPost and ST-segment elevation before treatment}] \times 100\%$ ).

### Long-term follow-up

All-cause 30-day and 12-month mortality was determined by telephone follow-up. One year after STEMI onset, patients attended a follow-up visit, during which the assessment of functional status according to the NYHA classification was performed and LVEF% and LVEDD were measured [13]. Patients in NYHA class > 2 were considered as having heart failure.

### Statistical analysis

Continuous variables with normal distribution were presented as means  $\pm$  standard deviations. In case of a non-normal distribution, data were presented as medians with interquartile ranges. Data were compared using either Student's *t* test or the Mann-Whitney test, where appropriate. Categorical variables were presented as percentages and were compared using either the Fisher test or the  $\chi^2$  test. The primary endpoint included: (1) failed myocardial tissue reperfusion, and (2) death or heart failure symptoms during the first year after the procedure. To identify independent variables predicting the end point, we used a multivariate logistic regression model, in which the following parameters were entered simultaneously: age, sex, history of diabetes, history of myocardial infarction, presence of hypertension, history of smoking, anterior STEMI, time from onset of pain to the opening of the vessel, normal flow in the infarct-related artery before the procedure and TIMI 3 flow after the intervention, the extent of the maximal ST-segment elevation in a single lead ECG measured before treatment, and the following variables evaluated at admission: heart rate, systolic blood pressure and Killip class > 1. A value of  $p < 0.05$  was considered statistically significant.

## Results

Two hundred patients ( $63.0 \pm 12.1$  years, 67.5% males) were studied. Anterior STEMI was diagnosed in 48.5% of patients, 3.5% of patients had cardiogenic shock, and 21.5% presented with symptoms of heart failure at admission (Killip class > 1). The median time from the onset of chest pain to the opening of the artery was 240 min (range: 148-

416 min). In 25% of patients, coronary angiography revealed a patent infarct-related artery (TIMI flow > 1). A stent was implanted in the infarct-related artery in 91.5% of patients. In 43% of cases, abciximab was administered. Normal epicardial flow (TIMI 3 flow) in the infarct-related artery was restored in 91.5% of patients.

The median serum creatinine level was 79.5 mmol/l (range: 61.8-88.3 mmol/l), and the mean eGFR value was  $84.5 \pm 28.9$  ml/min/1.73 m<sup>2</sup>. Impaired renal function at admission was diagnosed in 12.5% ( $n = 25$ ) of patients. Patients with impaired renal function were older and more often presented with symptoms of acute heart failure. The diagnosis of anterior STEMI and the time from the onset of symptoms to the opening of the artery did not differ significantly between the groups, while serum troponin levels measured at admission were higher in patients with impaired renal function. The extent of the maximal ST-segment elevation measured before the procedure was similar in both groups (Table 1). There were no differences in the stent implantation rate and the use of abciximab between the groups (92.0% vs. 91.4% and 32.0% vs. 44.6%,  $p = 0.284$ ). TIMI 3 flow in the infarct-related artery was restored in 84.0% of patients with impaired renal function and in 92.6% of the remaining ones ( $p = 0.239$ ).

Failed myocardial tissue reperfusion was found in 15.5% of patients ( $n = 31$ ). This phenomenon occurred three times more often in patients with anterior infarct (23.7% vs. 7.8% in the remaining patients,  $p = 0.003$ ) and three times more often in patients without normal epicardial flow restoration (41.2% vs. 13.1%,  $p = 0.007$ , respectively). The median extent of the maximal ST-segment elevation measured before the intervention in patients with failed reperfusion was 2-fold higher than the corresponding value measured in patients with successful myocardial reperfusion (4.0 mm [3.0-7.0] vs. 2.0 mm [2.0-3.0],  $p < 0.001$ ). The time from the onset of pain to the opening of the infarct-related artery was longer in the first group but the difference was not statistically significant (309 min [199-459] vs. 236 min [143-402],  $p = 0.175$ , respectively). The percentage of patients admitted with cardiogenic shock (3.2% vs. 3.6%,  $p = 1.0$ , respectively), as well as the incidence of diabetes (32.3% vs. 26.0%,  $p = 0.511$ , respectively), was similar in both groups. Blood pressure values and heart rate, assessed at admission, did not differ between the groups ( $p = 0.338$  and  $p = 0.288$ , respectively). Coronary angiography performed immediately after admission revealed a normal patent infarct-related artery in 6.5% and 13.6% of patients, respectively ( $p = 0.381$ ). A similar percentage of patients in both groups received abciximab (48.4% vs. 42.0%,  $p = 0.557$ , respectively). Patients with impaired renal function were 2.5 times more likely to have failed tissue reperfusion (32.0% vs. 13.1% in patients with normal renal function,  $p = 0.022$ ). The relative normalization of ST-segment elevation was significantly lower in patients with impaired renal function (50.0% [23.8-66.7] vs. 66.7% [50.0-100.0],

**Table 1.** Selected clinical, electrocardiographic and angiographic parameters, compared between patients with impaired versus normal renal function at admission**Tabela 1.** Porównanie wybranych zmiennych pomiędzy grupą chorych z upośledzoną i prawidłową funkcją nerek przy przyjęciu

Parameter	Impaired renal function at admission (n = 25, 12.5%)	Patients with normal creatinine levels at admission (n = 175, 87.5%)	Value of p
Age [years]	68.6 ±9.6	62.3 ±12.2	0.014
Males, % (n)	68.0 (17)	67.4 (118)	1.0
Anterior STEMI, % (n)	52.0 (13)	48.0 (84)	0.831
Time from onset of pain to admission to ICU [min]	265 (124-487)	240 (130-425)	0.833
Time from onset of pain to admission to opening of the artery [min]	275 (148-515)	240 (148-404)	0.331
Maximal ST-segment elevation measured in a single ECG lead before the intervention [mm]	2.0 (2.0-5.0)	2.0 (1.0-3.75)	0.460
maxSTPost [mm]	1.9 ±1.7, 1.0 (1.0-2.0)	1.1 ±1.3, 1.0 (0.0 -2.0)	0.010
Diabetes, % (n)	28.0 (7)	26.9 (47)	1.0
Smoking history, % (n)	28.0 (7)	47.4 (83)	0.086
Previous myocardial infarction, % (n)	24.0 (6)	14.9 (26)	0.248
Lipid disorders, % (n)	52.0 (13)	58.9 (103)	0.524
Hypertension, % (n)	60.0 (15)	54.3 (90)	0.670
Troponin T level at admission [ng/ml]	0.18 (0.03-1.65)	0.10 (0.03-0.41)	0.020
Troponin T level at admission > 0.03 ng/ml, % (n)	76.0 (19)	59.8 (104)	0.130
Heart rate at admission [beats/min]	86 ±31	82 ±23	0.587
Systolic blood pressure at admission [mm Hg]	135 ±42	159 ±29	0.010
Serum creatinine level at admission [μmol/l]	128.4 (115.1-148.4) min 115.1 – max 682.0	70.9 (62.0-79.7) min 35.4 – max 106.0	< 0.001
eGFR at admission [ml/min/1.73 m <sup>2</sup> ]	41.4 ±14.0 min 6.0 – max 65.0	90.1 ±25.1 min 48.0 – max 227.0	< 0.001
Serum creatinine level at discharge [μmol/l]	115.1 (93.0-150.6) min 70.9 – max 177.1	70.9 (62.0-79.7) min 35.4 – max 141.7	< 0.001
Killip-Kimball class > 1 at admission, % (n)	56.0 (14)	16.6 (29)	< 0.001
Cardiogenic shock at admission, % (n)	24.0 (6)	0.6 (1)	< 0.001
TIMI > 1 flow before the intervention, % (n)	24.0 (6)	25.1 (44)	1.0
TIMI 3 flow before the intervention, % (n)	8.0 (2)	13.1 (23)	0.746
LVEF% measured before discharge, % (n)	44 ±12 (15)	49 ±10 (170)	0.135
LVEDD measured before discharge [cm], (n)	5.3 ±0.60 (15)	5.3 ±3.8 (170)	0.982
LVEF% measured after 1 year, % (n)	48 ±11 (9)	51 ±8 (136)	0.397
LVEDD measured after one year [mm] (n)	5.4 ±0.4 (9)	5.2 ±0.6 (135)	0.291

$p = 0.046$ , respectively). Infarct size, assessed by the peak CKMB level, was significantly larger in patients with impaired renal function (252 IU/l [86-431] vs. 183 IU/l [97-295],  $p = 0.024$ , respectively).

The overall mortality in the entire cohort was 8.5% ( $n = 17$ ) and 13% ( $n = 26$ ) at the 30-day and the 1-year follow-up, respectively. In patients with impaired renal function, 30-day mortality and 1-year mortality were higher than in the remaining patients (40.0% vs. 4.0%,  $p < 0.001$ , and 52.0% vs. 7.4%,  $p < 0.001$ , respectively). Death or heart failure symptoms within the first year after the procedure occurred in 21% of patients ( $n = 42$ ). Patients with impaired

renal function were significantly more likely to die or develop heart failure (56.0% vs. 16.0% in the remaining patients,  $p < 0.001$ ). The comparison of long-term prognosis of patients with failed tissue reperfusion after the intervention vs. patients with normal myocardial perfusion revealed that patients in the first group had a significantly higher risk of death or development of heart failure (35.5% vs. 18.3%,  $p = 0.032$ ). In patients with poor prognosis, we observed a trend toward a higher degree of maximal ST-segment elevation measured before the intervention (3.76 ±3.90 mm vs. 3.08 ±2.19 mm in the remaining patients,  $p = 0.110$ ). Impaired renal function at admission

was associated with a 3-fold increase of the risk for failed tissue reperfusion ( $p = 0.044$ , Table 2). Impaired renal function at admission and failed tissue reperfusion were found to be risk factors for death or development of heart failure at 1-year follow-up (Table 3).

## Discussion

Our results of the treatment of 200 consecutive patients with STEMI undergoing primary coronary angioplasty in the non-academic center showed that ineffective myocardial tissue reperfusion was associated with poor long-term prognosis. Moreover, they indicated that the

presence of impaired renal function at admission to hospital was a risk factor for failure of primary coronary angioplasty to restore normal tissue perfusion, which in turn was associated with greater myocardial damage and increased risk of death or development of heart failure at the long-term follow-up.

The mean age of the study group, the time from the onset of symptoms, the incidence of anterior location of myocardial infarction and the incidence of cardiogenic shock – all these parameters were in close agreement with the corresponding parameters of the baseline characteristics of patients in similar studies conducted world-

**Table 2.** Univariate and multivariate predictors of death and/or heart failure incidence during 12-month follow-up  
**Tabela 2.** Parametry przewidujące wystąpienie złożonego punktu końcowego (zgonu bądź niewydolności serca) w ciągu 12-miesięcznej obserwacji

Parameter	Univariate analysis			Multivariate analysis*		
	Odds ratio	95% Confidence interval	Value of $p$	Odds ratio	95% Confidence interval	Value of $p$
Age [years]	1.11	1.07-1.15	< 0.001	1.11	1.06-1.17	< 0.001
Time from onset of pain [min]	1.003	1.001-1.005	0.001	1.003	1.001-1.005	0.029
Anterior-wall myocardial infarction	2.26	1.12-4.58	0.023	–	–	0.593
Killip class > 1 atm admission	8.35	3.88-17.99	< 0.001	4.34	1.61-11.68	0.004
Maximal elevation of ST segment measured in a single lead before the intervention [mm]	–	–	0.097	1.20	1.02-1.41	0.032
Diabetes	2.54	1.24-5.20	0.011	3.99	1.33-10.04	0.012
Normal flow in the infarct-related artery before the intervention	–	–	0.088	–	–	0.142
TIMI flow < 3 after the intervention	5.11	1.84-14.24	0.002	–	–	0.198
Impaired renal function at admission	6.68	2.75-16.22	0.001	4.38	1.34-14.28	0.014
Failed myocardial tissue reperfusion	2.45	1.07-5.63	0.035	3.34	1.12-9.88	0.029
Systolic blood pressure at admission [mm Hg]	0.98	0.97-0.99	0.021	0.98	0.96-0.99	0.046
Heart rate at admission	–	–	0.102	–	–	0.960

\*The following parameters were entered simultaneously in the regression model: age (1), gender (2), diabetes history (3), history of myocardial infarction (4), presence of hypertension (5), smoking history (6), anterior location of STEMI (7), time from onset of pain to the opening of the vessel (8), normal flow in the infarct-related artery before the procedure (9) and TIMI 3 flow after the procedure (10), maximal ST-segment elevation in a single ECG lead measured before the intervention (11), myocardial tissue reperfusion (12), and the following evaluated at admission: heart rate (13), systolic blood pressure (14) and Killip class > 1 (15)

**Table 3.** Risk factors for failed myocardial tissue reperfusion  
**Tabela 3.** Czynniki ryzyka braku reperfuzy tkankowej po zabiegu

Factor	Univariate analysis			Multivariate analysis*		
	Odds ratio	95% Confidence interval	Value of $p$	Odds ratio	95% Confidence interval	Value of $p$
Anterior wall myocardial infarction	3.69	1.56-8.72	0.003	–	–	–
Maximal ST-segment elevation in a single ECG lead measured before the intervention [mm]	1.42	1.21-1.66	< 0.001	1.40	1.20-1.64	< 0.001
TIMI < 3 flow after the intervention	4.64	1.61-13.34	0.005	4.83	1.47-15.83	0.009
Impaired renal function at admission	6.68	2.75-16.22	0.001	2.98	1.03-8.68	0.044

\*The following parameters were entered simultaneously in the regression model: age (1), gender (2), diabetes history (3), history of myocardial infarction (4), presence of hypertension (5), smoking history (6), anterior location of STEMI (7), time from onset of pain to the opening of the vessel (8), normal flow in the infarct-related artery before the procedure (9) and TIMI 3 flow after the procedure (10), maximal ST-segment elevation in a single ECG lead measured before the intervention (11), and the following evaluated at admission: heart rate (12), systolic blood pressure (13) and Killip class > 1 (14)

wide [1, 6, 14]. In the current study, there were 12.5% of patients with impaired renal function. This percentage ranges from 15% to 35% in other populations of patients admitted with STEMI [2, 3, 14, 15]. In the group of patients in the VALLIANT study (Valsartan in Acute Myocardial Infarction Trial), this percentage was quite high (33%) but more than 70% of patients in this study presented with symptoms of acute heart failure [3]. The Japanese authors reported a similar, when compared to our study, proportion of patients with renal dysfunction (15.8%) in a group of 1500 patients with STEMI admitted up to 12 h from the onset of pain [2]. Similarly, in the CADILLAC study (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications), this percentage was slightly higher and equaled 18% [14]. In the GRACE registry (Global Registry of Acute Coronary Syndromes), which studied patients with acute ST-segment elevation in at least two contiguous leads, this group constituted 28% of patients. It is interesting, however, that reperfusion therapy in the GRACE study was performed in only 65% of patients. In addition, there was no information about the time from the onset of symptoms to admission [15]. It should be noted here that serum creatinine level measured at admission could be considered as a reliable indicator of renal function if the blood sample is obtained within 5 h from the onset of symptoms of myocardial infarction, which is one of the clinical conditions that can potentially lead to renal hypoperfusion [16]. In our study, in the group of patients with impaired renal function, the median time from the onset of chest pain to admission was 4.4 h. The mean value of eGFR in this group was  $41 \pm 14$  ml/min/1.73 m<sup>2</sup>, indicating renal dysfunction in stage 3 of renal failure according to the National Kidney Foundation (NKF), and argues for chronic kidney disease in these patients [11].

In our study, patients with impaired renal function were older, admitted to the ICU later from the onset of the pain and more often presented with symptoms of acute heart failure. However, our results demonstrated that impaired renal function at admission in patients with STEMI was associated with a 4.38-fold increase in risk of death or development of heart failure over a follow-up period of 12 months (95% CI 1.34-14.28,  $p = 0.014$ ) independently from age, duration of symptoms, location of the infarct, hemodynamic status at admission, and the presence of diabetes. In the CADILLAC trial, the risk of death within a year after the procedure was 1.98 times higher in patients with impaired renal function [14]. In the analysis of the ANIN Myocardial Infarction Registry, death or heart failure symptoms at the short-term follow-up were 3.81-fold more likely in patients with elevated creatinine levels at admission (95% CI 2.99-4.87,  $p < 0.001$ ) [10].

To identify the group of patients with ineffective myocardial reperfusion, we used the methodology used in the analysis of the results of the CADILLAC trial (maxST-

Post) [8]. It is based solely on the analysis of the ST segment after the intervention. The reliability of this simple tool in the assessment of tissue perfusion was confirmed in studies with positron emission tomography [17]. Interestingly, the maximal values of ST-segment elevation measured both before and after the intervention were significantly higher in patients classified by us in the group of patients with failed myocardial reperfusion. When we compared the above data and calculated the relative ST-segment resolution, we found that the relative ST-segment resolution was lower in patients with ineffective myocardial reperfusion (according to the criteria used in our study). This confirmed that the extent of maxSTPost was not only a simple reflection of the extent of ST-segment elevation measured before treatment. Additionally, it should be emphasized that we used multivariate analysis models to examine the clinical significance of failed tissue reperfusion, and to assess whether impaired renal function was an independent predictor of ineffective tissue reperfusion. In these models, the extent of ST-segment elevation measured before the intervention was one of the variables included in the models. In the current study, 15.5% of patients met electrocardiographic criteria for high risk for failure to achieve tissue reperfusion (high-risk maxSTPost). In the CADILLAC trial, these criteria were present in about 20% of patients [8]. In the analysis of the results of the ANIN Myocardial Infarction Registry, the incidence of this phenomenon, namely failed reperfusion assessed on the basis of analysis of the ST segment in a single ECG lead after the intervention, was approximately 25% [9].

In our study group, impaired renal function was associated with a 2.98-fold increase in risk for failed tissue reperfusion (95% CI 1.03-8.68,  $p = 0.044$ ), independently of other well-established risk factors for this phenomenon (Table 3). In the work by Lin Zhao *et al.*, elevated creatinine level ( $> 114.8$  mmol/l) was associated with a 3.93-fold increase (95% CI 1.13-6.84) in the risk for failed tissue reperfusion assessed on the basis of angiography (TMPG). Elevated creatinine levels were also associated with a significantly lower degree of the resolution of the sum of ST-segment elevation [1]. It is interesting that in the work by Gibson *et al.*, there was no correlation between elevated creatinine levels at admission and the degree of TMPG. However, this population of patients was treated with fibrinolytic therapy only [18]. It should be noted that impaired renal function is associated with increased proinflammatory and prothrombotic activity as well as increased oxidative stress and endothelial dysfunction [3, 19]. All these factors are involved in the pathogenesis of the 'no-reflow' phenomenon [20].

In our study, failed tissue reperfusion was associated with larger extent of myocardial damage by enzymatic estimation and with more severely impaired left ventricular contractile function, assessed both at discharge and at follow-up. Consequently, failure of tissue reperfusion was

a risk factor for death or development of heart failure at 1-year follow-up (OR 3.34, 95% CI 1.12-9.88,  $p = 0.029$ ). In the CADILLAC trial, patients at high risk according to maxSTPost, corresponding to the group of patients with ineffective myocardial reperfusion in our study, had a 3.23-fold increase in risk of death or reinfarction over a follow-up period of 12 months (95% CI 1.74-5.99,  $p = 0.0002$ ) [8]. In the analysis of the results of the ANIN Myocardial Infarction Registry, patients with persistent ST-segment elevation after the procedure, at high risk according to Schröder, had a 3.3-fold increase in risk of death at 12-month follow-up (95% CI 1.4-7.8,  $p = 0.007$ ) [9].

## Conclusions

Impaired renal function at admission to hospital had a negative impact on the effectiveness of tissue reperfusion in patients with STEMI treated with pPCI. This may be one of the pathomechanisms responsible for poor outcome in this population.

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