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Impact of the combined presence of left ventricular systolic and renal dysfunction on the 5-year outcome after ST-elevation myocardial infarction

Uticaj istovremenog prisustva sistolne disfunkcije leve komore i renalne disfunkcije na 5-godišnji ishod nakon akutnog infarkta miokarda sa elevacijom ST segmenta

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Abstract

Background/Aim. The coincidence of left ventricular systolic dysfunction (LVSD) and renal dysfunction (RD) is a strong independent predictor of adverse events in the short-term and mid-term follow-ups of patients with ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (pPCI). The aim of this study was primarily to assess the prognostic impact of the LVSD-RD combination on the 5-year all-cause mortality in patients with STEMI treated with pPCI, as well as to assess the prognostic impact of the LVSD-RD combination on the occurrence of major adverse cardiovascular events (MACEs: cardiovascular death, reinfarction, stroke and target vessel revascularization) in these patients. **Methods.** We analyzed 951 patients divided into 4 groups according to the presence of LVSD (ejection fraction < 40%) and/or baseline RD (creatinine clearance < 60 mL/min): group I (no LVSD, no RD); group II (LVSD, no RD); group III (RD, no LVSD); group IV (LVSD+RD). **Results.** The 5-year mortality rates were 2.3%, 17.6%, 11.7% and 38.3%, while the 5-year MACE rates were 8.8%, 28.4%, 18.3% and 44.4% in the groups I, II, III and IV, respectively ($p < 0.001$). The highest percentage of lethal outcomes and MACE was registered in the first year of follow-up in all the groups. The 1-year landmark analysis confirmed that the patients with LVSD-RD combination had the highest percentage of lethal outcomes in the period of 1 to 5 years ($p = 0.028$). There was a strong trend toward the significance in the occurrence of MACE among the analyzed groups in the period of 1 to 5 years ($p = 0.085$). In the Cox regression model the LVSD-RD combination was a strong independent predictor of 5-year mortality and the occurrence of MACE: mortality hazard ratio (HR) 4.5 (95%CI 1.9–10.8); MACE HR 2.5 (95%CI 1.4–4.5). **Conclusion.** The strong negative independent prognostic impact of the LVSD-RD combination persisted in the long-term follow-up of the patients with STEMI treated with pPCI.

Key words:
myocardial infarction; comorbidity; ventricular dysfunction, left; angioplasty, baloon; mortality; prognosis.

Apstrakt

Uvod/Cilj. Istovremeno prisustvo sistolne disfunkcije leve komore (LVSD) i renalne disfunkcije (RD) je snažan nezavisni prediktor pojave neželjenih događaja u kratkoročnom i srednjoročnom praćenju bolesnika sa akutnim infarktom miokarda sa elevacijom ST segmenta (STEMI) koji su lečeni primarnom perkutanom koronarnom intervencijom (pPCI). Cilj ovog rada bio je da se utvrdi, pre svega, prognostički uticaj istovremenog prisustva LVSD i RD na ukupni 5-godišnji mortalitet kod bolesnika sa STEMI koji su lečeni pPCI, kao i da se utvrdi prognostički uticaj LVSD i RD na pojavu značajnih neželjenih kardiovaskularnih događaja [*major adverse cardiovascular events* (MACEs): kardiovaskularni mortalitet, reinfarkt, šlog i hitna revaskularizacija zbog ishemije] kod ovih bolesnika. **Metode.** Analiziran je 951 bolesnik. Bolesnici su bili podeljeni u četiri grupe u zavisnosti od prisustva LVSD (ejekciona frakcija < 40%) i/ili bazalne RD (klirens kreatinina < 60 ml/min): grupa I (bez LVSD, bez RD), grupa II (LVSD, bez RD), grupa III (RD, bez LVSD), grupa IV (LVSD+RD). **Rezultati.** Dobijeni rezultati pokazuju da je 5-godišnji mortalitet iznosio 2,3%, 17,6%, 11,7% i 38.3%, a 5-godišnja pojava MACE 8,8%,

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28,4%, 18,3% i 44, 4% u grupama I, II, III i IV ($p < 0.001$). Najviši procenat smrtnih ishoda i pojave MACE registrovan je u prvoj godini praćenja u svim grupama. Korišćenjem jednogodišnje *landmark* analize potvrđeno je da su bolesnici sa istovremenim prisustvom LVSD i RD imali najviši procenat smrtnih ishoda u periodu između jedne i pet godina ($p = 0,028$). Postojala je snažna tendencija statističke značajnosti za pojavu MACEa između analiziranih grupa u periodu između jedne do pet godina ($p = 0.085$). U Cox regresionom modelu, istovremeno prisustvo LVSD-RD bilo je snažan nezavisni prediktor mortaliteta i pojave MACE u 5-godišnjem praćenju: mortalitet *hazard ratio* (HR) 4,5 [95% interval poverenja (CI) 1,9–10,8]; MACE, HR 2,5 (95% CI 1,4–4,5). **Zaključak.** Snažan negativan, nezavisan prognostički uticaj istovremenog prisustva LVSD-RD održava se u dugoročnom praćenju bolesnika sa STEMI koji su lečeni primarnom PCI.

Ključne reči:
infarkt miokarda; komorbiditet; srce, disfukncija leve komore; angioplastika, balonska; mortalitet; prognoza.

Introduction

Left ventricular systolic dysfunction (LVSD) and renal dysfunction (RD) are strong predictors of short-term and long-term mortality and of major adverse cardiovascular events (MACE) after acute myocardial infarction (AMI) [1–10]. RD is frequently accompanied by coronary disease and cardiac insufficiency. One of the reasons for this lies in the fact that the risk factors are identical, e.g. hypertension or diabetes mellitus [11]. On the other hand, introducing modern therapeutic procedures in AMI treatment, primarily the introduction of primary percutaneous coronary intervention (pPCI) in treatening infarction with ST segment elevation (STEMI), has reduced but not eliminated the risk of LVSD development [12]. This is why even in the pPCI era the group of patients with substantial damage to the myocardium of the left ventricle stands out as the one with a high risk of future adverse events [1, 2]. The coincidence of LVSD and RD (the cardio-renal syndrome) over a longer period of time may lead to further deterioration of the renal and cardiac function *via* complex and as yet insufficiently understood neurohumoral mechanisms [11–18]. The prognostic significance of the combined presence of RD and LVSD for long-term follow-up was analyzed in patients with AMI (STEMI and non-STEMI) in the era before routine pPCI [17, 19]. In the pPCI era, the prognostic significance of the combined presence of LVSD and RD was analyzed during intrahospital and 1-year follow-up and proven that the LVSD-RD combination is the strongest independent predictor of the intrahospital and 1-year mortality and morbidity [20, 21]. Taking into consideration these findings, the authors of this study feel that it would be important to ascertain whether and to what extent does the negative prognostic influence of the LVSD-RD combination persist in long-term follow-up of patients with STEMI treated with pPCI.

The primary aim of this study was to assess the prognostic significance of the combined presence of LVSD and RD on 5-year all-cause mortality in patients with STEMI treated with pPCI, as well as to assess the prognostic significance of the combined presence of LVSD and RD on the occurrence of MACEs (including cardiovascular mortality, non-fatal myocardial reinfarction, non-fatal stroke and target vessel revascularization – TVR) during a 5-year follow-up period.

Methods

In the present study data were used from the prospective Clinical Center of Serbia STEMI Register for a subgroup of 951 consecutive patients, hospitalized between February 2006 and April 2008. The purpose of the prospective Clinical Center of Serbia STEMI Register was published elsewhere [22]. In brief, the objective of the register is to gather complete and representative data on the management and short- and long-term outcome of patients with STEMI undergoing primary PCI in our center. The study protocol was approved by a local research ethics committee. All consecutive patients with STEMI, aged 18 or older, who were admitted to the Coronary Care Unit after undergoing pPCI in our center were included in the Register. For the purpose of this study, patients with cardiogenic shock at admission were excluded. Coronary angiography was performed *via* the femoral approach. Primary PCI and stenting of the infarct-related artery was performed according to the standard technique. Aspirin, 300 mg and clopidogrel, 600 mg, were administered to all eligible patients before pPCI. The selected patients, with visible intracoronary thrombi, were also given the glycoprotein (GP) IIb/IIIa receptor inhibitor, tirofiban during pPCI. Flow grades were assessed according to thrombolysis in myocardial infarction (TIMI) criteria. After pPCI the patients were treated according to current guidelines.

Demographic, baseline clinical, angiographic and procedural data were collected and analyzed. The baseline RD was defined as creatinine clearance (CrCl) < 60 mL/min/m^2 at admission. Creatinine clearance was calculated using the Cockrof-Gault formula:

CrCl = [(140-years)*body weight]/(72*creatinine in mg/dL). The value was multiplied by 0.85 in females.

Echocardiographic examination was performed within the first 3 days after pPCI. The left ventricular ejection fraction (LVEF) was assessed according to the biplane Simpson's method in classical two- and four-chamber apical projections. LVEF < 40% was considered as LVSD. LVEF was missing in 10% of patients. The missing data were imputed *via* the single imputation method.

Based on LVEF and estimated glomerular filtration rate (rGFR) values the patients were divided into four groups: group I included patients with no LVSD and no RD; the group II those with LVSD, but no RD; the group III those with RD, but no LVSD, and the group IV those with LVSD and RD.

The primary end-point was all-cause mortality. The secondary end-point was the occurrence of MACEs (including cardiovascular mortality, non-fatal myocardial reinfarction, non-fatal stroke and target vessel revascularization – TVR) [22, 23]. The patients were followed-up up to 5 years after enrolment.

Continuous variables were expressed as the mean ± standard deviation (SD), if the distribution was normal, or median (med) with 25th and 75th quartiles (IQR), if the distribution was skewed, while categorical variables were expressed as frequency and percentage. Analysis for the normality of data was performed using the Kolmogorov-Smirnov test. Baseline differences between the groups were analyzed using the one-way ANOVA test for continuous variables and the Pearson χ^2 test for categorical variables. The Cox regression model (backward method, with $p < 0.1$ for entrance into the model) was used to identify independent risk factors for the occurrence of 5-year all- cause mortality and 5-year MACE. The Kaplan-Meier method was used for constructing the probability curves for 5-year survival and the free interval until the occurrence of the first event in the composite MACE event, while the difference between the groups was tested with the Log- Rank test. One year landmark analysis was performed. The patients who were event-free (no death, no MACE) at the 1-year check-up and had completed the 1-year follow-up were assigned into 4 groups according to the presence of LVSD and/or RD, as previously described. Outcomes for these patients were evaluated up to 5 years after the initial pPCI procedure. The SPSS statistical software version 14.0 was applied (SPSS Inc, Chicago, IL).

Results

Out of a total of 951 patients, 255 (26.8%) were women. The average age of the examined patients was 59.3 ± 11.2 years. A total of 574 (60.3%) patients had the preserved renal and left ventricular systolic function (group I); 81 patients (8.5%) had both LVSD and RD (group IV); 120 (18.5%) patients had only LVSD (group II); and 176 (12.6%) patients had RD (group III). There were no patients on dialysis. The demographic characteristics, risk factors, previous cardiovascular diseases or procedures, characteristics on admission, as well as angiographic and procedural characteristics in relation to the analyzed patient groups are shown in Table 1.

Table 1

Baseline characteristics of the patients according to the presence of left ventricular systlic dysfunctions (LVSD) and /or renal dysfunction (RD)

Characteristics	Group I No LVSD, no RD (n = 574)	Group II LVSD, no RD (n = 120)	Group III RD, no LVSD (n = 176)	Group IV LVSD+RD (n = 81)	*p* value
Age (years), med (IQR)	56 (49–62)	57 (51–64)	71 (65-76)	74 (69–78)	< 0.001
Women, n (%)	120 (20.9)	33 (18.7)	60 (50)	42 (51.8)	< 0.001
Previous MI, n (%)	62 (10.8)	34 (19.3)	19 (15.8)	13 (16)	0.012
Previous AP, n (%)	24 (4.2)	13 (7.4)	7 (5.8)	11 (13.6)	0.004
Previous PCI, n (%)	4 (0.6)	5 (2.8)	1 (0.8)	1 (1.2)	0.127
Previous stroke, n (%)	15 (2.6)	10 (5.7)	7 (5.8)	98 (11.1)	0.001
Diabetes, n (%)	77 (13.4)	41 (23.2)	21 (17.5)	20 (24.7)	0.002
Hypertension, n (%)	350 (60.9)	105 (5.9)	92 (76.7)	61 (75.3)	< 0.001
HLP, n (%)	401 (69.8)	110 (62.5)	77 (64.2)	42 (51.8)	0.031
Smoking, n (%)	375 (65.3)	105 (59.6)	47 (39.2)	22 (27.1)	< 0.001
Pain duration (hours), med (IQR)	2.5 (2–4)	3 (2–5)	3.2 (2–5)	3.5 (2–5)	0.020
Anterior MI, n (%)	194 (33.8)	130 (73.8)	36 (30)	44 (54.3)	< 0.001
HF at admission, n (%)	4 (0.7)	51 (28.9)	2 (1.7)	36 (44.4)	< 0.001
Systolic BP (mmHg) at admission, $\bar{x}$ ± SD	136.4 ± 26.3	133.8 ± 29.9	147.9 ± 26.1	130.4 ± 36.2	< 0.001
HR at admission, $\bar{x}$ ± SD	76.8 ± 15.9	83.1 ± 17.4	74.8 ± 15.3	80.5 ± 21.8	< 0.001
Door to balloon time, minutes, $\bar{x}$ ± SD	160.7 ± 68.5	157.2 ± 74.3	162.3 ± 54.7	167.1 ± 73.6	0.939
3-vessel disease, n (%)	123 (21.4)	56 (31.8)	40 (33.3)	36 (44.4)	< 0.001
Preprocedural flow TIMI 0, n (%)	473 (82.5)	148 (84.1)	100 (83.3)	67 (82.7	0.431
LM stenosis, n (%)	25 (4.4)	13 (7.4)	6 (0.5)	9 (11.1)	0.038
IIb/IIIa blockers, n (%)	259 (45.2)	102 (57.9)	48 (40)	43 (53.1)	0.003
Stent implantation, n (%)	555 (96.7)	161 (91.4	115 (95.8)	70 (86.4)	< 0.001
Postprocedural flow TIMI < 3, n (%)	11 (1.9)	14 (7.9)	4 (3.3)	12 (14.8)	< 0.001
Acute stent thrombosis, n (%)	2 (0.3)	2 (1.1)	0	4 (4.9)	0.358
CK max (U/L), med (IQR)	1795 (968–3185)	2861 (1441–4718)	1800 (917–2968)	1810 (1162–3467)	< 0.001
Troponin I (μg/L), med (IQR)	30.1 (7.4–74.6)	34.1 (6.4–104.7)	31.8 (6.2–113.1)	31.5 (2.2–85.1)	< 0.001
Baseline CrCl (mL/min), $\bar{x}$ ± SD	96.5 ± 21.1	89.4 ± 20.7	49.4 ± 10.1	45.8 ± 12.7	< 0.001
Hgb (g/L), $\bar{x}$ ± SD	144.3 ± 16.6	143.4 ± 19.3	134.4 ± 15.9	129.4 ± 19.6	< 0.001
LVEF (%), $\bar{x}$ ± SD	53.8 ± 6.9	37.5 ± 3.1	52.9 ± 7.3	34.3 ± 5.6	< 0.001

IQR – interquartile range; AP – angina pectoris; HLP – hyperlipidemia; MI – myocardial infarction; HF – heart failure; BP – arterial blood pressure; HR – heart rate; TIMI – Thrombolysis in Myocardial Infarction; LM – left main coronary artery; CK – creatinine kinase; CrCl – creatinine clearance; Hgb – hemoglobin; LVEF – left ventricular ejection fraction; $\bar{x}$ – mean value; SD – standard deviation.

Table 2 shows the adverse events, planned revascularization and therapy in relation to LVSD and/or RD during the entire 5-year follow-up period. The highest percentage of adverse events was registered in the group with LVSD and RD.

The causes of mortality were: cardiovascular causes (fatal reinfarction, progression of heart failure, sudden death, ischemic stroke) in 82 patients and other noncardiovascular causes (cancer, ileus, pneumonia) in 7 patients.

During the follow-up period there was no significant difference between the analyzed groups as far as the referral for planned myocardial revascularization was concerned (patients with multivesel disease). As to the therapy, the only registered difference was in the administration of angiotensin converting enzyme (ACE) inhibitors (group I 76.4%, group II 73.8%, group III 77.5% and group IV 62.9%, $p = 0.032$).

Figure 1a) shows the Kaplan-Meier probability curves for 5-year survival while Figure 1b) shows probability curves for the free interval until the occurrence of MACE in relation to the presence of LVSD and/or RD.

Using 1-year landmark analysis we analyzed 822 patients (group I, n = 539; group II, n = 101; group III, n = 101 and group IV, n = 48) who were event-free (no death, no MACE) at the 1-year check-up after the initial pPCI procedure. In the Figure 2a) the Kaplan Meier probability curves of 5-year survival is shown. The MACE free probability curves according to the presence of LVSD and/or RD using 1-year landmark analysis are shown in Figure 2b).

One-year landmark analysis confirmed that the highest percentage of the patients with a fatal outcome was in the LVSD+RD group. The patients with LVSD+RD combination had also the highest MACE rate in the period between 1 and 5 years of follow-up. There was no statistically significant difference in the occurrence of MACE among the examined groups in the period between one and five years, but there was a strong trend toward significance.

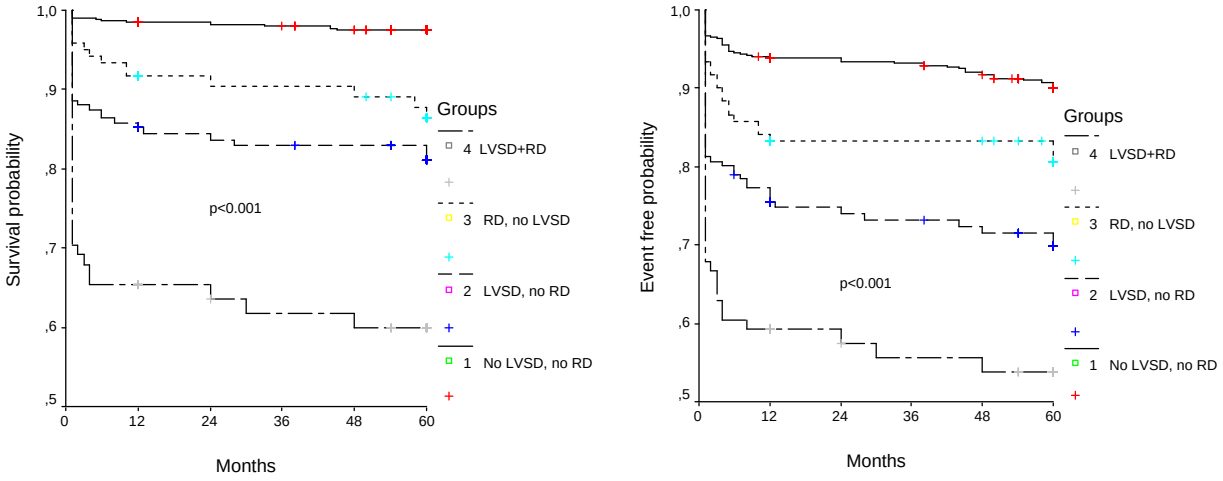
The causes of a lethal outcome in the period between one and five years of follow-up were: malignant diseases – lung cancer and gastric cancer (n = 5); myocardial reinfarction (n = 3); sudden cardiac death (n = 3); ischemic stroke (n = 1); unknown causes n = 2.

Table 2

Adverse events during the entire 5-year follow-up period

Event	Group I No LVSD, no RD (n = 574)	Group II LVSD, no RD (n = 120)	Group III RD, no LVSD (n = 176)	Group IV LVSD + RD (n = 81)	*p* value
Overall mortality, n (%)	13 (2.3)	31 (17.6)	14 (11.7)	31 (38.3)	< 0.001
MACE, n (%)	51 (8.8)	50 (28.4)	22 (18.3)	36 (44.4)	< 0.001
Cardiovascular death, n (%)	11 (1.9)	28 (15.9)	12 (10)	31 (38.3)	< 0.001
Nonfatal reinfarction, n (%)	21 (3.6)	17 (9.6)	4 (33.3)	6 (7.4)	< 0.001
Nonfatal stroke, n (%)	4 (0.7)	3 (1.7)	6 (5)	3 (3.7)	< 0.001
TVR, n (%)	23 (4.1)	12 (6.8)	5 (4.2)	5 (6.2)	0.161
Subacute stent thrombosis, n (%)	14 (2.4)	20 (11.4)	3 (2.5)	6 (7.4)	< 0.001
Late stent thrombosis, n (%)	5 (0.9)	3 (1.7)	1 (0.8)	1 (1.2)	0.943

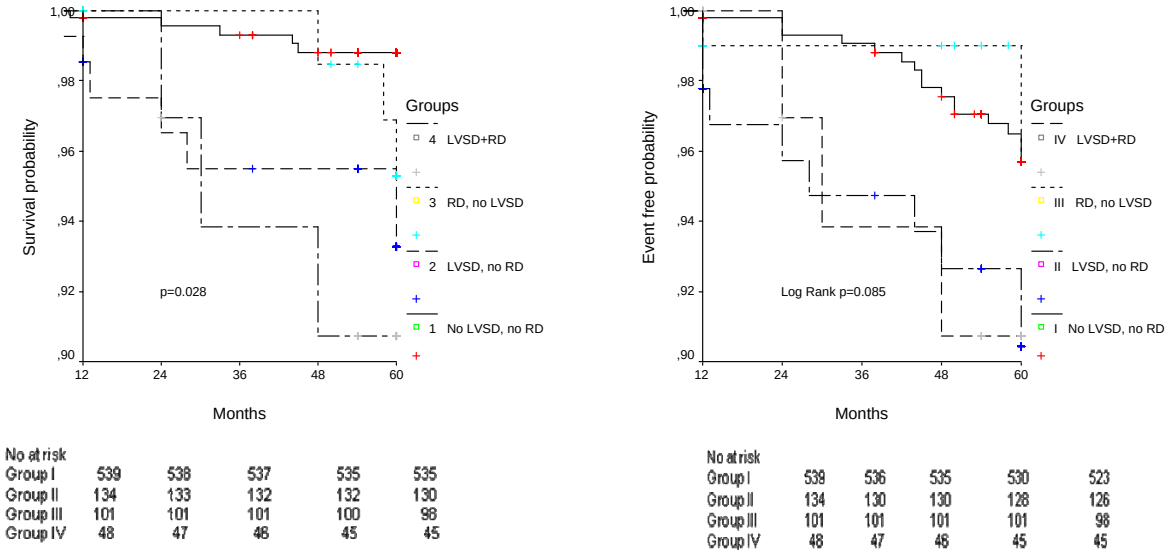
LVSD – left ventricular systolic dysfunction; RD – renal dysfunction; MACE – major adverse cardiovascular events (including cardiovascular death, nonfatal reinfarction, nonfatal stroke and TVR); TVR – target vessel revascularization.



a) **b)**

Fig. 1 – a) Kaplan Meier estimating the 5-year all-cause mortality, and b) MACE free probability according to the presence of LVSD and/or RD.

MACE – major adverse cardiovascular events; LVSD – left ventricular systolic dysfunction; RD – renal dysfunction.



a) **b)**

Fig. 2 – a) Kaplan Meier estimating the 5-year all-cause mortality, and b) MACE free probability according to the presence of LVSD and/or RD using 1-year landmark analysis.
For abbreviations see under Figure 1.

Table 3 shows the unadjusted hazard ratios (95% confidence interval) for the occurrence of all-cause mortality and MACE during follow-up (Cox regression model).

After adjustment to variables defined in the univariate analysis, as predictors of mortality and MACE, LVSD, RD and LVSD+RD remain independent predictors of all-cause mortality and MACE during a 5-year follow-up, as shown in Table 4. In the Cox regression model for 5-year all-cause mortality, adjustment was made for the following variables: age, prior myocardial infarction, diabetes, heart failure on admission, systolic blood pressure on admission, heart rate on admission, anterior infarction, peak creatinine kinase (CK), 3-vessel disea-

Table 3

Unadjusted hazard ratios (HR) [(95% confidence interval (95% CI)] for all-cause mortality and major adverse cardiovascular events (MACE)

All cause mortality	30 days	1 year	5 years
No LVSD, no RD	1.0	1.0	1.0
LVSD, no RD	11.4 (4.5–28.3)	9.7 (4.6–20.8)	8.3 (4.4–15.4)
RD, no LVSD	4.9 (1.6–15.1)	5.4 (2.2–13.2)	5.4 (2.5–11.2)
LVSD+RD	33.5 (13.7–43.3)	24.3 (11.4–51.5)	20.2 (10.6–38.7)
MACE			
No LVSD, no RD	1.0	1.0	1.0
LVSD, no RD	4.9 (2.9–8.1)	4.1 (2.6–6.5)	3.5 (2.5–5.2)
RD, no LVSD	2.1 (1.1–4.2)	2.7 (1.6–4.8)	2.2 (1.3–3.6)
LVSD+RD	9.6 (5.7–16.4)	7.8 (4.8–12.7)	6.2 (4.1–9.6)

LVSD – left ventricular systolic dysfunction; RD – renal dysfunction.

Table 4

Multivariable Cox regression model for 5-year overall mortality and major adverse cardiovascular events (MACE)

Variable	5-year overall mortality		5-year MACE	
	HR (95% CI)	*p*	HR (95% CI)	*p*
LVSD + RD	4.5 (1.9–10.8)	< 0.001	2.5 (1.4–4.5)	0.003
LVSD	4.4 (2.1–9.2)	< 0.001	2.2 (1.4–3.4)	0.003
RD	3.4 (1.5–7.8)	0.004	1.7 (1.1–2.9)	0.050
HF at admission	3.5 (2.0–6.0)	< 0.001	2.5 (1.6–3.8)	< 0.001
Postprocedural flow TIMI < 3	2.8 (1.6–4.9)	< 0.001	2.5 (1.6–4.0)	< 0.001
Age (years)	1.03 (1.01–1.06)	< 0.001	1.01 (1,0–1.03)	0.040
3-vessel disease	1.5 (1.1–2.4)	0.050	ns	
Previous infarction	ns		1.8 (1.2–2.6)	0.002

LVSD – left ventricular systolic dysfunction; RD – renal dysfunction; HF – heart failure; HR – hazard ratio; CI – confidence interval; TIMI – Thrombolysis in Myocardial Infarction.

se, left main stenosis, and post-procedural TIMI flow grade < 3. In the Cox regression model for the 5-year occurrence of MACE, adjustment was made for the following variables: age, previous infarction, previous stroke, diabetes, heart failure on admission, anterior infarction, 3-vessel disease, and post-procedural TIMI flow grade < 3.

Discussion

The results of this study show that the patients with STEMI treated with pPCI, who had a combined presence of LVSD and RD, had a significantly greater all-cause mortality and occurrence of MACE during a 5-year follow-up period as compared to patients with preserved left ventricular systolic function and preserved renal function, and in comparison with patients with only LSVD or RD. The highest percentage of lethal outcomes and MACE was registered in the first year of follow-up in all the groups. One-year landmark analysis confirmed that the patients with LVSD+RD had the highest percentage of lethal outcomes in comparison with all the other examined groups in the period 1 and 5 years. A statistically significant difference in the occurrence of MACE between the analyzed groups in the period 1–5 years of follow-up was not found, but there was a strong trend toward a significance. The LVSD+RD combination was the strongest independent predictor of all-cause 5-year mortality and the occurrence of MACE – the patients with the LVSD+RD combination had a 4.5 times greater risk of 5-year mortality and a 2.5 times greater risk of the occurrence of MACE in the 5-year follow-up period as compared to patients with preserved left ventricular systolic function and with preserved renal function.

It has previously been published that the LVSD+RD combination is the strongest independent predictor of mortality and the progression of cardiac and renal insufficiency after pPCI during hospitalization [20]. During a 1-year follow-up period of patients with a first time myocardial infarction treated with pPCI, the risk of mortality and MACE was increased by approximately 5 times in the group with the LSVD+RD combination in comparison with the patients with preserved cardiac and renal function, i.e. the LVSD+RD combination was also the strongest independent predictor for the occurrence of adverse events during the 1-year follow-up period [21]. The results of the present study confirm these findings and show that the LVSD+RD combination remains the strongest independent predictor of mortality and the occurrence of MACE in a longer period of time, at least 5 years after pPCI.

The results of the present study are consistent with the results of the study by Palmer et al. [19] who analyze the prognostic significance of the renal and cardiac function in over 1,000 consecutive patients who suffered myocardial infarction, over a 10-year follow-up period. In this study, the coincidence of VRD and cardiac dysfunction increased the risk of lethal outcome and the occurrence of cardiac insufficiency by 5 to 10 times in the 10-year follow-up period as compared to patients with intact renal and cardiac function. As opposed to the present study, where only the patients with STEMI were analyzed, in the study by Palmer et al. [19] non-STEMI patients were also included (around 18% of the studied patients), there were no patients treated with pPCI, thrombolytic therapy was applied in 58% of the patients, while intrahospital PTCA was performed on 20% of the patients. In this study the left ventricular systolic (dys)function was analyzed in two ways: as the N-terminal–probrain natriuretic peptide (NT-pro BNP) value and as the LVEF (LVSD was considered to be LVEF < 50%). The results obtained when the decreased eGFR < 60 mL/min) was analyzed in combination with an increased NT-proBNP (10-year mortality was 60%) did not differ from the results obtained by combining eGFR < 60 mL/min and LVEF < 50% (10-year mortality was 58%) [19].

In the study by Schou et al. [17] the influence of the eGFR and the wall motion score index (WMI) on the prognosis of patients with myocardial infarction or cardiac insufficiency during a 10-year follow-up period was analyzed. This study show a significant interaction between the values for eGFR and WMI. The highest percentage of 10-year mortality was registered in patients with eGFR < 60 mL/min/m^2 and LVSD low (WMI < 1.4), while the lowest one in patients with eGFR > 60 mL/min/m^2 and a preserved left ventricular systolic function, which coincides with the results of the present study. As opposed to the presented study, however, in the study by Schou et al. [17], patients with decreased eGFR (< 60 mL/min/m^2) and a preserved left ventricular systolic function had higher mortality than patients with LVSD and a preserved renal function. Also, the study by Schou et al. [17] examined a different population of patients, i.e. in addition to patients with myocardial infarction, patients with cardiac insufficiency were also included. All of the studied patients were treated in 1990s and early 2000s, when the treatment of myocardial infarction (and cardiac insufficiency) differed from the treatment of today, which the authors themselves stated as one of the limitations of the study [17].

The finding related to the highest percentage of analyzed adverse events in the first year of follow-up in the present study is not unusual. In a study by Kümler et al. [1], which followed up patients with LVSD after myocardial infarction for a period of up to 17 years, it was also found that the highest percentage of lethal outcomes occurred in the first year after myocardial infarction and that it then became stabilized and much lower.

Clinically speaking, taking into consideration the results of the present study and the aforementioned studies as well as the well-known fact that neurohormonal mechanisms contribute to the development and progression of chronic cardiorenal syndrome [11, 24], it is important to make a note of the fact that as of the moment when the patient is hospitalized onwards, all patients with LVSD and RD should be advised to take medication which can, to a certain extent, modify and block these mechanisms, and this primarily relates to ACE inhibitors and beta blockers [11, 17, 25]. But, at this moment there is no ideal therapeutic strategy that would improve the prognosis of patients with LVSD and RD [24, 26, 27]. The reason for this lies not only in the complex interactions between the heart and the kidneys but also in the fact that some of the risk factors for coronary disease and a decreased CrCl are un-

changeable, primarily the age of the patient [27]. In some studies, the glomerular filtration rate was not an independent predictor of mortality when age was also included into the regression model [27, 28], while in others this was not the case, and both the patient's age and the renal function were independent predictors of mortality and other adverse events [19–21]. In the present study the LVSD+RD combination proves to be the strongest independent predictor of the occurrence of all-cause mortality and MACE after adjusting other variables, including age.

Study limitations

The study is observational, prospective, including consecutive patients, and limiting a possible selection bias. There are no data on follow-up echocardiographic examinations during the follow up of the patients with LVSD that would have shown whether there was a certain degree of recovery of the myocardial contractility. On the other hand, the coincidence of RD may influence the deterioration of the systolic function and the remodeling of the left ventricle [18]. Basal renal function can be the indicator of the chronic state or acute deterioration. As the present study excluded patients with cardiogenic shock at admission, the authors considered the risk of acute renal function deterioration minimized. The renal function during follow-up of the patients with LVSD+RD, to determine the progression of RD, was not evaluated, however, during a 5-year follow-up the development of terminal renal insufficiency did not occur and none of the patients was started on hemodialysis. The renal function was assessed with the use of the Cockroft-Gault formula [28], which has its limitations. As far as antiplatelet therapy is concerned, all of the patients in the study received clopidogrel (loading dose including the follow-up period), there were no patients receiving new antiplatelet drugs (prasugrel or ticagrelor), which may have a more potent antiplatelet effect and can therefore reduce the occurrence of MACE [8]. The study was not designed to evaluate whether changing pharmacological treatment would have impact on the long-term outcome in patients with LVSD+RD.

Conclusion

Patients with the combined presence of left ventricular systolic dysfunction and renal dysfunction have a significantly higher mortality upon percutaneous coronary intervention during a 5-year follow-up period, as well as during a follow-up period of 1 and 5 years as compared to patients with normal renal and cardiac function, patients with only left ventricular systolic dysfunction or those with only renal dysfunction. The combined presence of left ventricular systolic dysfunction and renal dysfunction is the strongest independent predictor of all-cause mortality and the occurrence of major adverse cardiovascular events in a 5-year follow-up period. The results of the present study confirms the strong negative independent prognostic impact of the left ventricular systolic dysfunction and renal dysfunction combination, and shows that this negative impact persisted in the long-term follow up of patients with ST-elevation myocardial infarction treated with percutaneous coronary intervention.

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