Prognostic impact of renal dysfunction on long-term mortality in patients with preserved, moderately impaired, and severely impaired left ventricular systolic function following myocardial infarction

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Abstract

Objective: The aim of this study was to investigate and compare the prognostic impact of renal dysfunction (RD) at admission in patients with preserved, moderately impaired and severely impaired left ventricular systolic function following ST-elevation myocardial infarction (STEMI).
Methods: We included 2436 patients with STEMI treated with primary percutaneous coronary intervention (pPCI). Patients presenting with cardiogenic shock and those on hemodyalisis were excluded. According to the left ventricular ejection fraction (EF), patients were divided in three groups: preserved left ventricular systolic function – EF >50%, moderately impaired – EF=40%-50% and severely impaired left ventricular systolic function-EF <40%. RD was defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m^2 at admission. The follow-up period was 6 years.
Results: Preserved, moderately impaired and severely impaired systolic function were found in 741 (30.5%), 1367 (56.1%) and 328 (13.4%) patients, respectively. RD was present in 105 (14.2%) patients with preserved systolic function, 247 (18.1%) patients with moderately impaired, and 120 (36.5%) patients with severely impaired systolic function.Regardless of the presence of RD, 6-year mortality rates in patients with preserved, moderately impaired, and severely impaired systolic function were 2.7%, 5.2% and 31.1% respectively. Within each LVEF group, patients with RD had a worse outcome, both in the short- and long-term. In the Mulivariate Cox Analysis, RD remained an independent predictor of 6-year mortality in patients with moderately (HR 2.52, 95% CI 1.54-3.78) and severely impaired systolic function (HR 2.84, 95% CI 1.68-5.34), but not in patients with preserved left ventricular systolic function (HR 0.59, 95% CI 0.14-1.41).
Conclusion: Although patients with RD had higher 6-year mortallity following STEMI regardless of LVEF, RD at admission remained a strong independent predictor for 6-year mortality only in patients with moderately and severely impaired left ventricular systolic function.
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Keywords: renal dysfunction, left ventricular systolic function, prognosis

Introduction

Renal dysfunction (RD) is a strong independent predictor for adverse cardiovascular outcomes in the general population after ST-elevation myocardial infarction (STEMI) (1-7). Another strong and important predictor of short- and long-term outcome following myocardial infarction is left ventricular systolic function (8-12). Introducing the primary percutaneous coronary intervention (pPCI) in treating of patients with STEMI has significantly reduced mortality and the occurrence of complications (8, 9). The percentage of patients with severely impaired left ventricular systolic function (ejection fraction, EF <40%) is also significantly smaller in the pPCI era than in thrombolytic era, as, generally speaking, establish of a normal blood flow through the infracted artery leads to a reduction in the myocardial necrotic zone (8). Therefore, majority patients treated with pPCI have preserved (EF >50%) or moderately impaired (EF=40%-50%) left ventricular systolic function (8). The prognostic impact of renal function in patients with STEMI complicated by heart failure and/or severely impaired left ventricular systolic function (EF <40%) is well known. It has been clearly established that coinciding renal function impairment additionally increases the risk mortality and nonfatal adverse events during short- and long-

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term follow-up, which is considered to be linked to the development of cardiorenal syndrome (5, 9, 10, 13). The prognostic impact of RD in patients with preserved or moderately impaired left ventricular systolic function after STEMI may differ in comparison with those with severely impaired left ventricular systolic function (14, 15). To our best knowledge, the prognostic impact of renal function on long-term patient prognosis in relation to left ventricular systolic function after STEMI has not been analyzed thus far.

The purpose of this study was to evaluate the prognostic impact of RD at admission on long-term overall mortality in patients with severely impaired, moderately impaired and preserved left ventricular systolic function following STEMI.

Methods

Study population, data collection and definitions

In the present study, data from the prospective Clinical Center of Serbia STEMI Register, for a subgroup of 2,436 consecutive patients, wo were hospitalized between February 2006 and October 2010, were used. The purpose of the prospective Clinical Center of Serbia STEMI Register has been published elsewhere (16). In brief, the objective of the register is to gather complete and representative data on the management and short- and long-term outcomes of patients with STEMI who have undergone primary PCI at the Center. The study protocol was approved by the Local Research Ethics Committee. All consecutive patients with STEMI, aged >18 years, who had been admitted to the Coronary Care Unit after undergoing pPCI at the Center, were included in the Register. For this study, patients with cardiogenic shock at admission and those on haemodialysis were excluded. Coronary angiography was performed via the femoral approach. Aspirin, 300 mg, and clopidogrel, 600 mg, were administered to all eligible patients before pPCI. Selected patients, with visible intracoronary thrombi, were also given the glicoprotein (GP) IIb/IIIa receptor inhibitor tirofiban during pPCI. Flow grades were assessed according to Thrombolysis in Myocardial Infarction (TIMI) criteria. After pPCI, patients were treated according to current guidelines.

Demographic, baseline clinical, angiographic and procedural data were collected and analyzed. Baseline RD was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 at admission. The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) equation.

GFR (mL/min/1.73 m^2) = 175 x $(S_{cr})^{-1.154}$ x $(Age)^{-0.203}$ x (0.742 if female)

Echocardiographic examination was performed within the first 3 days following pPCI. The left ventricular EF was assessed according to the biplane Simpson method, in classical two- and four-chamber apical projections. According to EF, patients were divided into three groups: preserved left ventricular systolic function (EF >50%), moderately impaired left ventricular systolic function (EF=40%-50%) and severely impaired left ventricular systolic function (EF <40%).

Patients were followed-up at 6 years after enrollment. Follow-up data were obtained by scheduled telephone interviews and out-patient visits.

Statistical analysis

Continuous variables were expressed as the median (med), with the interquartile range (IQR) between the 25th and 75th quartiles, whereas categorical variables were expressed as frequency and percentage. Analysis for normality of data (continuous variables) was performed using the Kolmogorov Smirnov test. Baseline differences between groups were analyzed using the Mann-Whitney U test, for continuous variables and the Pearson X^2 test, for categorical variables. The Kaplan-Meier method was used for constructing probability curves for 6-year survival whereas the difference between the groups was tested with the Log Rank test. Multiple logistic regression analysis was used for identifying independent predictors for RD. Multiple cox analysis (backward method, with p<0.10 for entrance into the model) was used for identifying independent risk factors for the occurrence of 6-year all-cause mortality. SPSS statistical software, version 19.0, was applied (SPSS Inc, Chicago, IL, USA).

Results

Out of a total of 2,436 patients, 1,773 (72.8%) were men and 663 (27.2%) were women. The average age of the examined patients was 57 (50-63) years. Preserved, moderately impaired and severely impaired left ventricular systolic function was registered in 741 (30.5%), 1,367 (56.1%) and 328 (13.4%) patients, respectively. RD at admission was registered in 472 (19.3%) patients, whereas the mean eGFR value was 88.5 (67.7, 108.8) ml/min/1.73 m^2; 428 (17.6%) patients had eGFR 30-60 ml/min/1.73 m^2 and 44 (1.8%) patients had eGFR 15-30 mL/min/1.73 m^2. RD was registered in 105 (14.2%) patients with preserved left ventricular systolic function, in 247 (18.1%) patients with moderately impaired left ventricular systolic function and in 120 (36.5%) patients with severely impaired left ventricular systolic function. Demographic characteristics, risk factors, previous cardiovascular diseases or procedures, characteristics on admission, as well as angiographic and procedural characteristics in relation to EF and the presence of RD at admission are shown in Table 1.

After adjustement for variables defined as predictors in the univariate analysis (age, female gender, previous infarction, diabetes, hypertension, heart failure at admission, anemia at admission and three-vessel disease) we found that independent predictors for RD regardless of EF category were as follows: age (HR 1.20, 95% CI 1.18-1.30; p<0.001), previous infarction (HR 1.38, 95% CI 1.25-2.57; p=0.018), diabetes (HR 1.29, 95% CI 1.10-2.68; p=0.045), hypertension (HR 1.38, 95% CI 1.28-1.68; p=0.050),

Table 1. Clinical and angiographic characteristics of analyzed patients according to the presence of renal dysfunction

Variable	EF >50% eGFR ≥60 mL/min/ 1.73 m² n=636	eGFR <60 mL/min/ 1.73 m² n=105	*P*	EF 40%-50% eGFR ≥60 mL/min/ 1.73 m² n=1120	eGFR <60 mL/min/ 1.73 m² n=247	*P*	EF <40% eGFR ≥60 mL/min/ 1.73 m² n=208	eGFR <60 ml/min/ 1.73 m² n=120	*P*
Age, med (IQR)	54 (48, 71)	75 (68, 77)	<0.001	57 (50, 64)	73 (68, 79)	<0.001	60 (53, 67)	74 (64, 79)	<0.001
Males (%)	487 (76.6)	56 (53.3)	<0.001	880 (82.6)	129 (52.1)	<0.001	156 (75)	65 (54.2)	<0.001
Previous MI (%)	40 (6.3)	12 (11.4)	0.056	106 (9.5)	33 (13.4)	0.067	35 (16.8)	26 (21.7)	0.278
Previous PCI (%)	7 (1.1)	12 (1.9)	0.486	22 (2)	7 (2.8)	0.391	13 (6.3)	4 (3.3)	0.251
Diabetes (%)	92 (14.5)	29 (27.6)	0.001	176 (15.7)	61 (24.7)	0.001	49 (23.6)	38 (31.7)	0.109
Hypertension (%)	386 (60.7)	87 (82.9)	<0.001	685 (61.2)	203 (82.2)	0.001	140 (67.3)	91 (75.8)	0.106
Hyperlipidemia (%)	408 (64.2)	66 (62.9)	0.787	693 (61.9)	147 (59.9)	0.490	118 (56.7)	51 (42.5)	0.018
Smoking (%)	425 (66.8)	34 (32.4)	<0.001	680 (60.7)	82 (25.1)	<0.001	101 (48.6)	33 (27.5)	<0.001
Family history (%)	279 (43.9)	31 (23.5)	0.001	407 (36.3)	49 (19.8)	<0.001	61 (29.3)	24 (20.0)	0.063
Pain duration med (IQR)*	2.5 (1.5, 4)	3.5 (2, 6)	<0.01	2.5 (1.5, 4)	3 (2, 5)	0.020	2.5 (1, 5)	3 (2, 6)	0.037
KillipII and III at admission (%)	12 (1.9)	2 (1.9)	0,99	109 (9.7)	52 (21.1)	<0.001	80 (38.5)	62 (51.7)	0.020
3-vessel disease (%)	122 (19.2)	39 (37.1)	<0.001	260 (23.2)	92 (37.2)	<0.001	76 (36.5)	57 (47.5)	0.051
Stent (%)	612 (96.2)	99 (94.3)	0.879	1066 (95.2)	228 (92.3)	0.079	187 (89.9)	94 (78.3)	0.001
Postprocedural TIMI <3 (%)	1 (0.3)	2 (1.9)	0.922	37 (3.3)	16 (6.5)	0.020	26 (12.5)	29 (24.4)	0.006
Haemoglobin g/L med (IQR)	144 (134,154)	135 (124,151)	<0.001	144 (134,153)	134 (120,146)	<0.001	143 (133,153)	128 (120,141)	<0.001
LVEF med (IQR)	56 (55, 60)	57 (55, 60)	0.882	48 (40, 50)	45 (40, 50)	0.001	33 (30, 35)	30 (25, 35)	<0.001
Creatinine med (IQR)	84 (71, 97)	98 (84, 121)	<0.001	83 (71, 96)	108 (92, 131)	<0.001	84 (72, 99)	112 (96, 147)	<0.001
eGFR med (IQR)	97 (82, 116)	52 (46, 58)	<0.001	95 (81,113)	50 (42, 56)	<0.001	88 (76,106)	48 (38, 55)	<0.001

*Hours from symptom onset to first medical contact
EF - ejection fraction; eGFR - estimated glomerular filtration rate

Table 2. Therapy at discharge

Variable	EF>50% eGFR ≥60 mL/min/ 1.73 m² n=636	eGFR <60 mL/min/ 1.73 m² n=105	*P*	EF 40%-50% eGFR ≥60 mL/min/ 1.73 m² n=1120	eGFR <60 mL/min/ 1.73 m² n=247	*P*	EF<40% eGFR ≥60 mL/min/ 1.73 m² n=208	eGFR <60 mL/min/ 1.73 m² n=120	*P*
Aspirin (%)	602 (99.5)	99 (99.6)	0.522	1051 (99)	204 (99)	0.935	200 (96.1)	110 (92)	0.582
Clopidogrel (%)	636 (100)	105 (100)	0.99	1120 (100)	247 (100)	0.999	208 (100)	120 (100)	0.999
Beta blockers (%)	580 (95.9)	95 (96.9)	0.615	1021 (95.9)	214 (96)	0.286	161 (77.4)	86 (73)	0.729
ACE inhibitors (%)	506 (83.6)	90 (91.8)	0.036	945 (89.1)	208 (92.1)	0.185	153 (73.2)	89 (74)	0.665
Statins (%)	575 (95)	87 (88.5)	0.036	1009 (95.1)	211 (93.4)	0.068	202 (97)	113 (94)	0.371
Diuretics (%)	36 (6.0)	10 (10.2)	0.114	132 (12.4)	54 (26.1)	<0.001	148 (71.1)	86 (74)	0.688

EF - ejection fraction; eGFR - estimated glomerular filtration rate

heart failure at admission (HR 1.54, 95% CI 1.25-2.28; p=0.027) and anemia (hemoglobin level <130 g/L in males and <120 g/L in females) at admission (HR 1.24, 95% CI 1.12-1.57; p=0.028).

Therapy at discharge is shown in Table 2.

Over a 6-year follow-up, there were 196 (8.3%) deaths overall. Regardless of the presence of RD, 6-year mortality rates in patients with preserved, moderately impaired and severely impaired left ventricular systolic function were 2.7%, 5.2% and

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Table 3. In-hospital mortality and mortality during follow-up

Variable	EF>50% eGFR ≥60 mL/min/ 1.73 m² n=636	eGFR <60 mL/min/ 1.73 m² n=105	*P*	EF 40%-50% eGFR ≥60 mL/min/ 1.73 m² n=1120	eGFR <60 mL/min/ 1.73 m² n=247	*P*	EF<40% eGFR ≥60 mL/min/ 1.73 m² n=208	eGFR <60 mL/min/ 1.73 m² n=120	*P*
In-hospital mortality	1 (0.01)	1 (0.09)	0.684	7 (0.6)	13 (5.3)	<0.001	29 (13.9)	58 (48.3)	<0.001
1-month mortality	2 (0.03)	2 (1.9)	0.146	12 (1.1)	19 (7.7)	<0.001	28 (13.5)	59 (49.2)	<0.001
1-year mortality	7 (1.1)	2 (1.9)	0.965	19 (1.7)	29 (11.7)	<0.001	37 (17.8)	61 (50.1)	<0.001
6-year mortality	16 (2.6)	4 (3.8)	0.345	30 (2.8)	40 (16.1)	<0.001	40 (19.2)	62 (51.2)	<0.001

EF - ejection fraction; eGFR - estimated glomerular filtration rate

31.1% respectively. Within each EF group, patients with RD had a worse outcome, both in the short- and long term, (Table 3).

Causes of mortality in all analyzed groups were predominantly cardiovascular (n=183, 93.3% of all deaths). Cardiovascular causes included fatal re-infarction, progression of heart failure, sudden death, and ischemic stroke. Noncardiovascular causes of death (such as cancer, ileus, pneumonia) were registered in 13 patients (6.7% of all deaths).

Figure 1 shows Kaplan-Meier probability curves for 6-year survival in patients with preserved (curve a), moderately impaired (curve b) and severely impaired (curve c) left ventricular systolic function in relation to the presence of RD at admission.

After adjustment for variables defined in the univariate analysis as predictors of mortality, RD at admission remained an independent predictor of all-cause mortality during a 6-year follow-up in patients with moderately and severely impaired left ventricular systolic function, but not those with preserved left ventricular systolic function (Table 4).

Discussion

Results of this study have shown that the prognostic impact of RD at admission on the long-term survival of patients with STEMI differs depending on left ventricular systolic function, i.e. in patients with preserved left ventricular systolic function, RD had no prognostic impact, however, in those with moderately or severely impaired left ventricular systolic function it had a strong independent prognostic impact. The prognostic impact of RD was similar, albeit somewhat stronger, in patients with severely impaired left ventricular systolic function, in whom the presence of RD increased 6-year mortality by three times, whereas in patients with moderately impaired left ventricular systolic function the existence of RD increased the 6-year mortality by approximately 2.5 times. Results of this present study have also confirmed that upon STEMI, in the pPCI era larger percentage of patients have preserved or moderately impaired left ventricular systolic function. The total percentage of patients with RD at admission is similar or somewhat smaller than data found in literature (2, 7), whereas the largest percentage of patients with RD at admission was registered in the group with EF <40%.

The present study differs from other studies analyzing the prognostic impact of RD upon STEMI published to date, because it separately identifies and analyzes the subgroup of patients with EF=40%-50%. It is a known fact that mortality upon STEMI rapidly increases in patients with EF <40%, whereas patients with EF >50% have a good prognosis in the short-term and long-term follow-up (8). Therefore, prognostically speaking, there is a "gap" for a large group of patients whose EF is between 40 and 50 percent. These patients were, in earlier studies, commonly attached to the patient group with preserved systolic function (17, 18). Identifying the group of patients with EF=40%-50% as a separate group is something that can only be seen in recent studies dealing with heart failure. Clinical characteristics and prognosis of patients with EF=40%-50% are most commonly somewhere in between that with EF >50% and those with EF <40% (8, 12, 15, 17), this has also been observed in this present study.

With respect to pathophysiology, the EF value of 40%-50% means that there is a primarily moderate systolic dysfunction of the left ventricle, with a lesser impairment of diastolic function (14, 18). Because moderately impaired systolic function is considered to be the initial step toward further deterioration of the said function, simultaneous existence of RD represents the first step toward the development of cardiorenal syndrome (11, 17). This particular conclusion may be the explanation for similar prognostic impact of RD during long-term monitoring of patients in the present study with EF 40%-50% and EF <40%.

In literature, the prognostic impact of renal function in relation to the EF value is most frequently analyzed in patients with heart failure. Accordingly, in a study by Löfman et al. (15), which included patients with heart failure with varying etiology, the prognostic impact of chronic kidney disease (CKD) in patients with preserved EF (>50%), mid-range EF (40%-50%) and reduced EF (<40%) was analyzed. In this study, in the absence of CKD, patients with preserved EF had a higher short-term and long-term mortality than those with moderately and severely impaired

Table 4. Association between RD and 6-year mortality according to EF (Univariate analysis and Multiple Cox analysis)

	Univariate analysis		Multiple Cox analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
EF >50%				
RD	1.61 (0.55-2.90)	0.367	0.59 (0.14-1.41)	0.461
eGFR 30-60 mL/min/1.73 m^2	1.08 (0.89-1.98)	0.898	0.98 (0.89-1.01)	0.887
eGFR 15-30 mL/min/1.73 m^2	0.98 (0.89-1.01)	0.999	0.87 (0.85-1.02)	0.998
Age (years)	1.05 (1.01-1.09)0	0.027	1.05 (1.01-1.08)	0.025
Diabetes	2.23 (1.05-5.95)	0.050		
Hypertension	2.35 (1.05-7.11)	0.042		
Heart failure at admission	6.29 (1.31-10.17)	<0.001	4.79 (1.83-10.12)	0.038
Peak CK	1.01 (1.02-1.04)	0.010		
3-vessel diasease	1.95 (1.10-4.99)	0.040		
EF 40-50%				
RD	2.94 (1.97-1.39)	<0.001	2.52 (1.54-3.78)	0.001
eGFR 30-60 mL/min/1.73 m^2	3.04 (2.34-10.94)	<0.001	2.22 (1.52-5.35)	0.001
eGFR 15-30 mL/min/1.73 m^2	4.32 (3.95-31.5)	<0.001	3.64 (1.35-7.57)	<0.001
Age (years)	1.09 (1.06-1.11)	<0.001	1.04 (1.01-1.07)	0.002
Previous MI	1.45 (1.31-2.93)	0.050		
Diabetes	2.68 (1.60.4.40)	0.001		
Hypertension	1.78 (1.03-2.78)	0.048		
Heart failure at admission	5.10 (3.04-8.59)	<0.001	3.20 (1.93-5.33)	<0.001
Sytolic blood pressure at admission (mm Hg)	1.01 (0.98-1.02)	0.871		
Heart rate admission /min	1.02 (1.01-1.03)	0.060		
Peak CK	1.02 (1.01-1.04)	0.030		
3-vessel disease	2.14 (1.31.3.50)	0.002		
Post-procedural flow TIMI<3	3.45 (1.56-5.64)	0.001	1.90 (0.96-3.05)	0.097
EF <40%				
RD	6.76 (4.21-10.89)	<0.001	2.84 (1.68-5.34)	<0.001
eGFR 30-60 mL/min/1.73 m^2	3.34 (2.15-7.18)	<0.001	2.62 (1.95-3.59)	<0.001
eGFR 15-30 mL/min/1.73 m^2	13.01 (3.25-20.9)	<0.001	3.72 (2.80-10.14)	<0.001
Age (years)			1.05 (1.01-1.07)	0.001
Previous MI	1.44 (0.92-2.51)	0.042		
Diabetes	1.39 (1.27-2.35)	0.037		
Hypertensio	1.25 (1.15-1.95)	0.050		
Heart failure at admission	3.46 (2.11-5.68)	<0.001	1.93 (1.29-2.91)	
Systolic blood pressure at admission (mm Hg)	1.01 (0.99-1.03)	0.001		
Heart rate at admission/min	1.01 (0.99-1.03)	0.002		
Peak CK	1.02 (1.01-1.04)	0.020		
3-vessel disease	2.14 (1.32-3.46)	0.002		
Post-procedural flow TIMI<3	5.34 (2.87-9.95)	<0.001	2.07 (1.36-3.15)	<0.001

EF- ejection fraction; MI - myocardial infarction; RD - renal dysfunction (eGFR<60 mL/min/1.73 m^2); eGFR- estimated glomerular filtration rate; CK - creatinine kinase

left ventricular systolic function. However, CKD was an independent predictor of 5-year mortality in all three groups of patients, with a similar prognostic impact in patients with EF=40-50% and EF<40% (15). In addition it was found that CKD was more frequent in patients with preserved EF, but was prognostically least significant, in the sense of a lesser impact on long-term mortality, than in patients with EF <40% and EF=40%-50%. A larger percentage of patients with CKD in the group with EF >50% was attributed by the authors to the fact that the group with EF >50% was older and with a higher percentage of hypertension and diabetes (15). Overall it can be said that data in literature regarding the prevalence and prognostic impact of CKD in pa-

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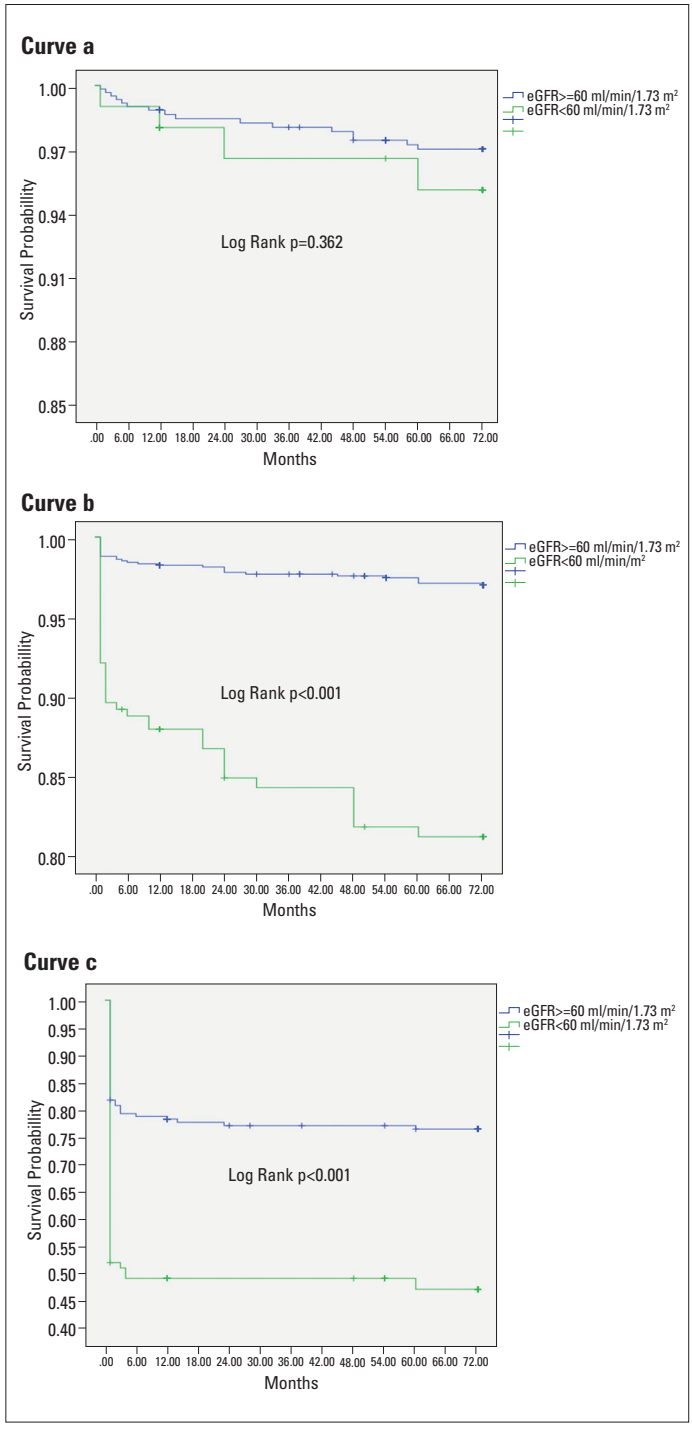

Figure 1. Kaplan-Meier curves estimating the 6-year survival probability according to RD in patients with preserved EF (curve a), moderately impaired EF (curve b) and severely impaired EF (curve c)

tients with EF >50% is inconsistent (8, 12, 15). Thus, in a study analyzing the prognostic impact of left ventricular systolic function in patients with STEMI, no significant difference was found in the prevalence of baseline CKD amongst patients with EF >50%, EF=40-50% and EF <40% (8). In the Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) it was demonstrated that among patients with EF >50%, there was a smaller percentage of those with CKD and a lesser impact of CKD on mortality tahn that in patients with EF=40%-50% and EF <40 (11).

A study by Moukarbel et al. (9) analyzed the prognostic impact of CKD in high-risk patients with myocardial infarction (EF <40%). The total 23-month mortality was approximately 18%; the reduction in renal function led to an increase in mortality in these patients; whereas CKD was an independent predictor of mortality. This study did not analyze the prognostic impact of CKD in patients with EF >40% (9). Similarly, during the average folow-up of aproximatly 24.7 months results of a study by Anavekar et al. show CKD to be an independent predictor of mortality and other adverse events in patients who had suffered myocardial infarction complicated by heart failure, systolic dysfunction of the left ventricle, or both, with the risk of occurrence of adverse events increasing with a decrease in eGFR (5). In this study, as well as in the present study, it has been demonstrated that the greatest risk of mortality in patients with CKD is in the first 30-180 days upon infarction. The negative prognostic impact of CKD remains unchanged independently of therapy with ACE inhibitors, i.e., sartans (5).

There are multiple pathophysiological mechanisms that can account for the negative prognostic impact of impaired renal function in patients with acute myocardial infarction and/or heart failure. Firstly, the existence of comorbidities that may be risk factors for coronary disease and RD (hypertension, diabetes, as well as older age). Secondly, complications of advanced RD, such as hypercalcemia, anemia and disorders of the blood coagulation system, increase the risk of atherosclerotic disease progression, when they co-occurr with traditional risk factors. Hypervolemia, as a part of advanced RD, may exacerbate symptoms of heart failure, independent of EF values (7). Sympathetic and numerous neurohormonal mechanisms, inflammation, free radicals, and other factors can significantly influence the development and progression of cardiorenal syndrome (17, 19, 20). Consequently, it has often been noted in literature that patients with RD less frequently receive therapy (beta blockers, ACE inhibitors, sartans, aldosterone antagonists, etc.) that improve the prognosis upon STEMI, particularly in patients with EF <40% (7). There are data suggesting that treatments that improve clinical outcome in patients with EF<40% also seem to benefit those with EF 40%-50% (14). Consdering that there are studies indicating a strong negative prognostic impact of RD in patients with EF=40%-50%, as well as in patients with simultaneous occurrence of RD and mild – to- moderate left ventricular systolic function impairment, independent of the cause, it should be insisted that therapy with ACE inhibitors (or sartans), beta blockers and aldosteron antagonists should be introduced as soon as possible (14, 15).

Study limitations

This is an observational prospective study - however it has included consecutive patients limiting possible selection bias. We did not use other measurs for determining systolic function such as myocardial deformation imaging. However, many cor-

nerstone clinical trials so far have used EF to stratify patients and have demonstrated its benefit in determining the outcome benefit of therapy (8, 9, 11, 17). There are no data on follow-up echocardiographic examinations to show whether there has been a certain degree of recovery or deterioration in the myocardial contractility. Renal (dys)function at admission can be an indicator of a chronic state or acute deterioration.Renal function was not evaluated during follow-up, however, during the 6-year follow-up, development of terminal renal insufficiency did not occur and none of the patients was started on hemodialysis. Renal function was assessed with the use of the MDRD equation which also has its limitations (19, 21). We did not measure the rates of urinary albumin or protein excretion, factors that may influence the independent impact of RD on cardiovascular outcomes. Patients were treated with clopidogrel; there were no patients treated with more recently developed antithrombotic drugs (ticagrelor was not available for routine administration to patients at the time of their entry into the register); this could have influenced the prognosis of the patients, i.e., reduced the occurrence of cardiovascular mortality, as there are data indicating that the efficacy of clopidogrel is decreased in patients with RD (2). The study was not designed to evaluate whether changing pharmacological treatment would have impact on the long-term outcome in analyzed patients.

Conclusion

Patients with STEMI and RD at admission have higher 6-year mortality, independently of EF values, than those with preserved renal function. Approxmately half of the patients in the pmary PCI era have moderately impaired left ventricular systolic function upon STEMI. RD at admission was an independent predictor of 6-year mortality only in patients with EF=40%-50% and EF <40%. The negative prognostic impact of RD at admission was similar in both groups of patients, although it as somewhat stronger in those with EF <40%.

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