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Reduced glomerular filtration rate in patients with acute STEMI

Khorolets E.V., Shlyk S.V.

Rostov State Medical University Ministry of Health of the Russian Federation, Rostov-on-Don, Russia

Authors

Ekaterina V. Khorolets*, M.D., PhD., associate Professor of the Internal Medicine Department, Rostov State Medical University Ministry of Health of the Russian Federation, Rostov-on-Don, Russia

Sergey V. Shlyk, M.D., doctor of sciences, the Head of the Internal Medicine Department, Rostov State Medical University Ministry of Health of the Russian Federation, Rostov-on-Don, Russia

Abstract

Objective *of this study was to evaluate the characteristics of patients with acute ST-elevation myocardial infarction (STEMI) depending on the glomerular filtration rate (GFR).*

Materials and methods

Patients with STEMI were included. We assessed the changes in their clinical and laboratory characteristics during their hospital stay and evaluated echocardiographic findings depending on the GFR (≥ or<60 ml/min/1.73m^2). In-hospital mortality risk was assessed using the GRACE scale. The statistical analysis was performed using the "Statistica 10.0 for Windows".

Results

Patients with STEMI and reduced GFR comprised 22% of all the patients included, were older, had left atrial and ventricular dilation in the presence of comparable hemodynamic and basic biochemical parameters. Patients with GFR<60 ml/min/1.73m2 were at a higher risk of acute and chronic heart failure and in-hospital mortality according to the GRACE scale. Regardless of GFR the reduction of the concentration of the stimulating growth factor ST2 was noted during inpatient treatment of STEMI. Surgical and pharmacoinvasive STEMI management resulted in the normalization of ST2 concentration in hospitalized patients.

Conclusion

It is important to calculate the GFR in patients with STEMI in order to choose the correct management and assess the risk of complications. The concentration of ST-2 reduced during the hospitalization and returned back to normal values after the percutaneous coronary intervention and pharmacoinvasive therapy regardless of the GFR.

* Corresponding author. Tel. +7 903 433 5477. E-mail: kata_maran@mail.ru

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Introduction

Chronic kidney disease (CKD) is defined as the presence of kidney damage or the loss of kidney function persisting for 3 months or more. In patients with an estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73 m2 CKD can be diagnosed in the absence of kidney damage markers. In clinical practice, the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation is used for GFR estimation.

It is well known that cardiovascular and kidney disease have common risk factors: arterial hypertension (AH); diabetes mellitus (DM); dyslipidemia and obesity. At the same time, patients with kidney disease can have hyperhydration, anemia, phosphate and calcium metabolism disorders, systemic inflammation and hypercoagulation, which, in turn, are the major risk factors for cardiovascular disease (CVD) [1].

Kidney dysfunction is prevalent in 12–17 % of general population, 42.9 % of patients with non-ST-elevation myocardial infarction (NSTEMI) and 30.5 % of patients with ST-segment elevation myocardial infarction (STEMI) [2]. The prevalence of CVD in patients with reduced kidney function is 64 % higher compared with those with preserved kidney function. GFR less than 60 ml/min/1.73 m2 is negatively associated with risk of mortality, cardiovascular complications and hospitalization [3]. The incidence of new cardiovascular complications depends on CKD stage. In patients with CKD stage 2 it was estimated to be 4.8 % and it doubles in patients with CKD stage 3 and 4 [1].

A decline in GFR increases the risk of cardiovascular death in patients with acute coronary syndrome (ACS), acute MI, after thrombolysis, percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). In patients with two CVD risk factors the risk of GFR decline to less than 60 ml/min/1.73 m2 increases 3.7-fold compared with the patients without any risk factors. Approximately 30 % of patients are diagnosed with stage 3–5 CKD after acute MI [1, 2]. A decline in GFR is also seen in 30–40 % of patients with ACS and in 70 % of patients with cardiogenic shock. GFR decline to less than 60 ml/min/1.73 m2 is considered a negative mortality predictor in MI, recurrent MI, heart failure (HF), stroke and bleeding in NSTEMI and STEMI [4].

PCI improves the outcomes in patients with ACS. At the same time, the use of contrast dyes can cause kidney injury [5]. The evaluation of kidney function in patients with ACS is an important prognostic factor [6]. In CKD, pharmacological and surgical treatment options are limited. Kidney function decline can lead to bleeding in patients taking antithrombotic agents [7, 8, 9] and poor outcomes after myocardial revascularization. CABG intraoperative mortality in such patients rises more than 7-fold.

We used hospital mortality assessment scales and laboratory markers for outcome prediction. One of the commonly used laboratory markers is a stimulating factor 2 (ST-2). ST-2 is a laboratory predicter that can be used for risk stratification in HF as well as for negative outcomes and cardiovascular events prediction [10]. ST-2 levels are not associated with HF specific causes, weight and age [11], change as a response to treatment and therefore can be used for disease progression and treatment effects monitoring [12]. According to KohliP, et al. (2012), ST-2>35 ng/ml in ACS increase the risk of CVD mortality and HF development 3-fold during the first 30 days and at 1-year follow-up.

We suppose that it would be interesting to study STEMI patients while taking into consideration renal function and ST-2 levels.

Objective of this study was to evaluate the characteristics of patients with STEMI depending on the GFR.

Materials and methods

The current study included 150 patients with STEMI. The study was conducted in accordance with Good Clinical Practice standards and Helsinki Declaration Principles. Informed consents were obtained prior to participation. According to The Russian Society of Cardiology (RSC) 2007 guidelines STEMI diagnosis was based on clinical and instrumental (ECG) findings and the presence of laboratory markers: troponin I and CK-MB (creatine kinase myocardial band). Inclusion criteria were age> 45 years, arterial hypertension, acute heart failure grade II–IV according to T. Killip classification, the first 24-hours of presentation. Exclusion criteria were history of liver dysfunction, severe kidney dysfunction, women of

childbearing age, cancer, type I and II diabetes mellitus, connective tissue disease, infections. We evaluated objective clinical findings such as systolic blood pressure (SBP), diastolic blood pressure (SBP), heart rate. Chemistry panel: AST, ALT, urea, creatinine, lipid profile, cardiac necrosis markers, electrolytes. ST-2 plasma level was also evaluated using the immunoferment analysis (Presage ST2 Assay Critical Diagnostics, UC).

All patients with STEMI were examined twice: at admission to cardiology department (visit 1) and at discharge (visit 2). Patients were treated with pharmacologic agents and infusion therapy: prehospital thrombolysis, primary PCI and pharmacoinvasive therapy (thrombolysis+ PCI).

GFR was estimated using the CKD-EPI formula that is based on age, sex, race and creatinine level. We used The Global Registry of Acute Coronary Events (GRACE) score to estimate the risk of in-hospital mortality:<126 — low risk (<2%), 126–154 — moderate risk (2–5%),>154 — high risk (>5%). ECG and echocardiography (to estimate the size of left atrium (LA), right atrium (RA), left ventricle (LV), right ventricle (RV), end-systolic volume (ESV), end-diastolic volume (EDV), stroke volume (SV), ejection fraction (EF), pulmonary artery pressure (PAP), the A wave, the E wave, E/A ratio, tricuspid regurgitation, pulmonary regurgitation) were performed in all patients. All patients were divided into groups depending on the estimated GFR (≥ or<60 ml/min/1.73m2).

The statistical analysis was performed using the "Statistica 10.0 for Windows". Mann-Whitney U-test was used to assess the statistical differences between the groups. Spearman's correlation coefficient was used to measure the association between variables. Numerical data are presented as mean M±m. p<0.05 was considered statistically significant.

Results

General characteristics of STEMI patients are: age 61.69±0.96 years, SBP 135.42±2.25 mm Hg, DBP 81.86±1.21, HR 81.61±1.51 beats per minute. Laboratory values: ALT 45.03±2.57 IU/L, AST 86.26±8.73 IU/L, urea 9.76±1.44 mmol/l, creatinine 84.45±2.68 mmol/l, eGFR 81.17±1.98 ml/min/1.73m2. Cardiac necrosis markers: troponin I 13.22±1.40 ng/mL, CK-MB 61.63±14.92 IU/l. Lipid profile: total cholesterol 5.74±0.11 mmol/l, low-density lipoproteins (LDL) 2.87±0.06 mmol/l, high-density lipoproteins (HDL) 1.33±0.02 mmol/l, triglycerides (TG) 1.74±0.09 mmol/l. The mean GRACE risk score was 162.26±2.58, which signifies the high risk of in-hospital mortality for STEMI patients.

Of all STEMI patients, 22% had reduced GFR (n=33) and 78% had preserved GFR (n=117). Patients with GFR<60 ml/min/1.73m2 were older — 69.48±2.01(p<0.05) but had similar hemodynamic characteristics: SBP 132.18±5.54 mmHg, DBP 80.21±3.50 mmHg, HR 81.84±3.45 beats per minute compared with the patients with GFR>60 ml/min/1.73m2: 60.26±1.11 years, SBP 135.77±2.43 mmHg, DBP 82.69±1.21 mmHg, HR 81.89±1.67 beats per minute (p>0.05). Patients with reduced GFR were at a higher risk of in-hospital mortality according to the GRACE risk score (181.15±5.84) compared the patients with preserved GFR (159.83±2.79), p<0.05.

Therefore, patients with STEMI and reduced GFR were older and had a higher risk of in-hospital mortality according to GRACE risk score.

We also studied blood chemistry values in STEMI patients with GFR<60 ml/min/1.73m2 and GFR≥60 ml/min/1.73m2. In patients with reduced GFR the laboratory values were as follows: AST 83.46±24.18 IU/L, ALT 41.17±5.50 IU/l, urea 10.38±2.94 mmol/l, CPK 319.78±90.19 IU/l, CK-MB 101.08±61.57 IU/l. In patients with preserved GFR the laboratory values were as follows AST 87.04±8.99 IU/l, ALT 46.09±2.91 IU/l, urea 9.5±1.64 mmol/l, CPK 320.36±37.89 IU/l, CK-MB 49.94±6.65 IU/l. The differences were not statistically significant (p>0.05). In patients with reduced GFR creatinine level was 118.67±7.57 mmol/l, mean GFR 46.09±1.87 ml/min/1.73m2; in patients with preserved GFR — creatinine 75.01±1.97 mmol/l, mean GFR 90.87±1.54 ml/min/1.73m2 and the differences were statistically significant (p<0.05). Lipid levels in patients with reduced GFR were as follows: total cholesterol 5.89± 0.23 mmol/l, LDL 3.11±0.14 mmol/l, HDL 1.40±0.05 mmol/l, TG 1.51±0.12 mmol/l and were similar to those in patients with preserved GFR: total cholesterol 5.70±0.12 mmol/l, LDL 2.80±0.07 mmol/l, HDL 1.31±0.03 mmol/l, TG 3.67±1.32 mmol/l (p>0.05). Troponin I (13.81±3.51 and 13.05±1.51 ng/ml) and sodium (137.84±4.42 and 140.99±0.38 mmol/l) levels were non-specific in both analyzed groups (p>0.05). Potassium level was higher in patients with reduced GFR compared with the patients with preserved GFR (5.60±1.15 mmol/l versus 4.24±0.05 mmol/l, p<0.05).

Outcome prediction in hospitalized patients is an important problem. We evaluated the correlation between GFR and the risk of ACS, chronic heart failure and GRACE risk score. GFR was inversely correlated

with acute heart failure severity in STEMI patients (r=–0.48, p=0.001), with stage of CHF progression (r=–0.23, p=0.038), in-hospital mortality according to GRACE risk score (r=-0.48, p=0.0001) and with poor outcome during in-hospital treatment (r=-0.40, p=0.043).

We also calculated GFR in patients with different STEMI management approaches: there were no statistical difference between the filtration rate in patients who undergone thrombolysis (75.41±6.25 ml/min/1.73m2) compared with patients who undergone primary PCI (87.04±3.14 ml/min/1.73m2) and with patients who undergone both thrombolysis+PCI (74.85±6.96 ml/min/1.73m2). Patients with PCI had higher GFR compared with those who undergone pharmacoinvasive treatment (thrombolysis+PCI), p<0.05.

As such, GFR estimation plays a major role in choosing the adjust management and medication dosages in STEMI patients and is important for better prognosis in such patients.

Assessment of ST-2 levels in hospitalized patients was also important for outcome prediction. The mean ST-2 level in all the patients with STEMI at admission was 70.48±7.80 ng/ml and 35.25±4.70 ng/ml at discharge (p<0.05). ST-2 concentration was positively correlated with troponin I levels (r=0.21, p<0.05) and inversely correlated with LVEF (r=0.21, p<0.05). These data confirm the association between ST-2 concentration and the extent of myocardial damage. Normalization of ST-2 levels during the treatment period signifies a better prognosis for STEMI patients.

Mean levels of ST-2 in hospitalized patients in STEMI patients with GFR<60 ml/min/1.73m2 and GFR≥60 ml/min/1.73m2 are shown in Figure 1. ST-2 concentrations were similar at the first (p>0.05) and second (p>0.05) visits in both groups of patients with STEMI. At the same time ST-2 levels decreased in groups with GFR<60 ml/min/1.73m2 (p<0.05) and GFR≥60 ml/min/1.73m2 (p<0.05) during hospital stay. Therefore, ST-2 levels decreased in STEMI patients during hospitalization independently from GFR.

STEMI patients were divided into two groups depending on the treatment approach: pharmacologic therapy, primary PCI, prehospital thrombolysis, thrombolysis+ PCI. ST-2 levels were similar at the first 24 hours of treatment in all groups (p>0.05) (Figure 2). ST-2 levels decreased during in-hospital treatment in the pharmacologic therapy group (p<0.05), PCI (p<0.05) and thrombolysis+ PCI groups (p<0.05) groups. The levels of ST-2 normalized in patients in the primary PCI and thrombolysis+ PCI groups and didn't change in thrombolysis group (p>0.05). At the second visit, ST-2 levels were different in patients who have undergone thrombolysis comparing with those who had primary PCI (p<0.05) or thrombolysis+ PCI (p<0.05).

Therefore, normal ST-2 levels were reached during in-hospital treatment in STEMI patients who have undergone primary PCI or thrombolysis+ PCI. Those who only received pharmacologic therapy and prehospital thrombolysis failed to reach normal ST-2 levels while still at the hospital.

Echocardiography findings in STEMI patients with preserved and reduced GFR are presented in Table 1.

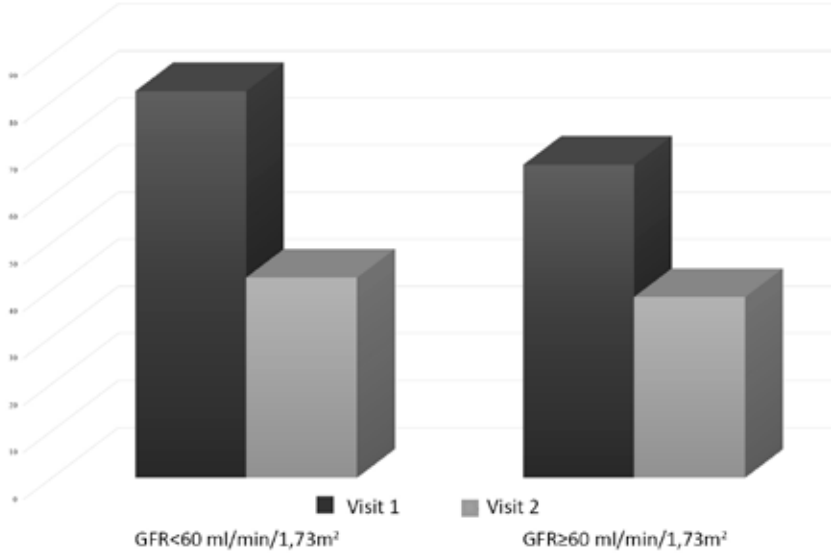

Figure 1. Mean ST-2 levels on visit 1 and 2 in patients with GFR<60 ml/min/1,73m² and GFR≥60 ml/min/1,73m² (p<0,05).

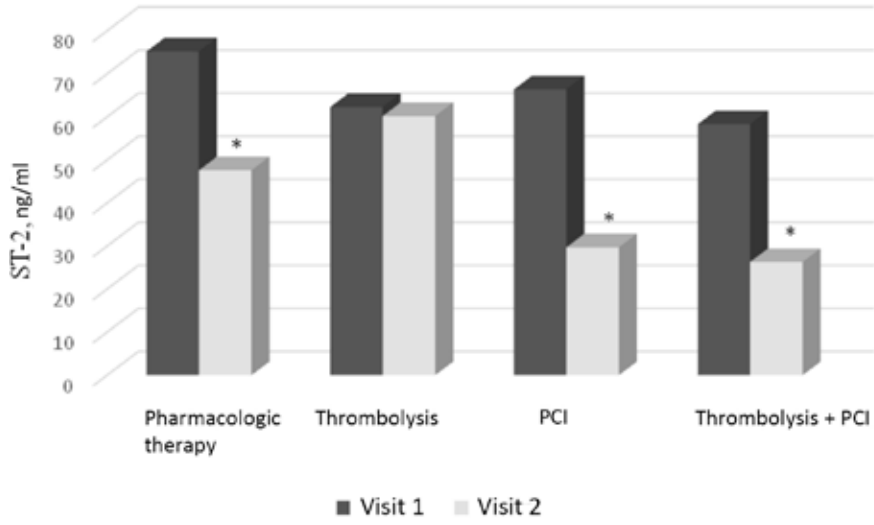

Figure 2. ST-2 levels in STEMI patients with different treatment approaches. **Note:** Visit 1 — ST-2 levels are similar in all groups (p>0,05); * — p<0,05 at visit 2.

STEMI patients with reduced GFR had higher LA, LV end-systolic dimension (ESD), LV end-diastolic dimension (EDD), LV ESV, LV EDV (p<0.05) compared with those with preserved GFR. At the same time, other values of stroke volume and ejection fraction, pulmonary artery pressure, the A wave, the E wave, E/A ratio and RV and RA parameters were similar in both groups. GFR reduction was positively correlated with pulmonary artery pressure (r=–0.20, p<0.02) and E peak decrease (r=0.23, p<0.007). Shortening of early diastolic filling time deceleration (E peak) is considered to be the predictor of increased mortality in patients with acute MI.

Patients with STEMI and reduced GFR also had larger LA and LV, although the sizes of RV and RA were unchanged.

Table 1. **Echocardiography findings in STEMI patients with GFR<60 ml/min/1,73m² and GFR≥60 ml/min/1,73m²**

Value	GFR<60 ml/min/ 1.73m2 M±m	GFR≥60 ml/min/ 1.73m2 M±m	p
LA, mm	45.03±2.20	41.48±0.65	<0.05
LV ESD, mm	44.41± 2.12	40.98±0.64	<0.05
LV EDD, mm	56.41±1.74	53.48±0.52	<0.05
ESV, ml	83.45±3.61	73.14±1.48	<0.05
EDV, ml	148.29±5.25	137.86±1.78	<0.05
SV, ml	67.48±2.24	64.36±0.77	>0.05
LVEF, %	46.32±2.12	47.06±0.74	>0.05
PAP, mmHg	35.96±2.66	32.77±0.90	>0.05
E, cm/sec	48.80±2.72	51.52±1.19	>0.05
A, cm/sec	62.09±2.91	60.68±1.28	>0.05
E/A	4.15±3.29	1.84±0.91	>0.05
RA, mm	35.87±2.32	33.24±0.65	>0.05
RV, mm	32.38±2.4	30.58±0.67	>0.05
TV V max, cm/sec	250.06±7.52	245.38±2.95	>0.05
TR, st	1.06±0.04	1.95±0.90	>0.05
PA, mm	29.16±2.47	27.12±0.76	>0.05
PR, st	0.81±0.07	1.92±0.93	>0.05

Note:
LA — left atrium,
LV ESD — left ventricular end-systolic dimension;
LV EDD — left ventricular end-diastolic dimension;
ESV — end-systolic dimension;
EDV — end-diastolic volume;
SV — stroke volume;
LVEF — left ventricular ejection fraction;
PAP — pulmonary artery pressure;
E — E peak;
A — A peak;
RA — right atrium;
RV — right ventricle;
TV — tricuspid valve;
TR — tricuspid regurgitation;
PA — pulmonary artery;
PR — pulmonary regurgitation.

Discussion

It is well known that in STEMI reperfusion should be performed as early as possible. GFR estimation is an important safety factor for patients with MI. Kidney function assessment can guide physicians when choosing appropriate dosing of antiplatelet agents and contrast agents. Patients with acute MI and CKD often receive high doses of antiplatelet agents during the first 48 hours after the event and that leads to the higher risks of bleeding and other complications [13]. GFR estimation determines if it is possible to perform coronary angiogram, if the drug doses should be changed and what complications are possible.

Our results are similar to those of previous studies reporting that the reduced GFR is a predictor for increased mortality in MI [1]. Contrast-induced nephropathy after PCI are associated with negative outcomes in patients with MI [13]. In our study patients with reduced GFR were at higher risk of in-hospital

mortality according to the calculated GRACE risk score and poor prognosis. Pharmacoinvasive approach had negative influence on GFR compared with primary PCI in patients with STEMI.

GFR depends on a number of clinical and laboratory values [1]. One of the CVD development predictors is ST-2. ST-2 levels are not influenced by gender, age or GFR [11] and its concentration in healthy adults is around 18 ng/ml. Concentration>35 ng/ml is associated with increased risk of CVD complications [14]. Increase in ST-2 correlates with HF severity and doesn't depend on other biomarkers [15]. According to the literature reviewed, ST-2 levels decrease during in-hospital treatment of STEMI patients with both reduced and preserved GFR. The use of primary PCI and pharmacoinvasive leads to normalization of ST-2 levels and improves the prognosis.

Patients with acute MI require the complex assessment of risk factor and objective and laboratory findings for the choice of appropriate safe therapeutic approach. GFR is an outcome predictor in patients receiving pharmacologic and invasive MI treatment [1, 2, 4].

Conclusion

Glomerular filtration rate estimation is necessary for hospitalized patients with acute myocardial infarction as it can guide the choice of appropriate treatment and drug dose changes. STEMI patients with reduced GFR were older, tended to have hyperkalemia with higher in-hospital mortality according to GRACE risk score and dilation of left atrium and ventricle on echocardiography. ST-2 concentration decreased during in-hospital treatment in patients with both reduced and preserved GFR. Surgical and pharmacoinvasive approaches led to ST-2 normalization during in-hospital treatment and thus resulted in better prognosis.

Conflict of interest: none declared.

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