Renal Function Outcome in Acute Myocardial Infarction as a Prognostic Factor of In-hospital Events and at One-year Follow-up

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Objective

To analyze the role of renal dysfunction at admission or during hospitalization in patients with acute myocardial infarction (AMI).

Methods

Two hundred and seventy-four patients with AMI were assessed between January 2000 and December 2001. Renal function was monitored by serum creatinine (Cr) measurement at admission and peak level during hospitalization. Creatinine clearance (CrCl) was estimated by the Cockcroft-Gault formula. In-hospital and one-year morbidity and mortality were evaluated.

Results

Mean age of the population studied was 62.2 ± 13.5, and 73% of the patients were male. Renal function was more reduced in male patients and in those with systemic arterial hypertension and prior CABG. Multivariate analysis showed higher hospital mortality rates associated with increased peak serum Cr levels (OR: 1.18 95% CI:1.18-2.77 p = 0.006), decreased baseline CrCl (OR:0.96 95% CI:0.93-0.99 p = 0.025) and peak CrCl (OR:0.96 95% CI:0.92-0.99 p = 0.023). Percent difference between baseline CrCl and the lowest CrCl obtained during hospitalization also indicated higher mortality rates (OR: 1.04 95% CI: 1.00-1.07 p = 0.033). No change was observed in the one-year morbidity and mortality from worsening of renal function.

Conclusion

Renal dysfunction at admission and its deterioration during hospitalization have proved to be a major prognostic marker for immediate poor outcome.

Key words

Acute myocardial infarction, renal insufficiency, cardiovascular diseases.

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Currently, acute coronary syndromes (ACS) are the leading cause of mortality in developed countries, and the risk of adverse events is greater in some subgroups that should be identified and properly treated.[1,2] There are several prognostic markers, and renal function deterioration increases the risk of cardiovascular diseases,[3,4] particularly stroke[5] and ACS.[6] Chronic renal failure patients undergoing dialysis are known to have worse prognosis following acute myocardial infarction (AMI) than individuals with normal renal function.[7-9] Few papers, however, have analyzed the role of mild or moderate renal dysfunction in the outcome of patients with acute myocardial infarction.

Previous studies such as GUSTO I, GUSTO II, and In TIME-2, involving a large number of AMI patients, failed to evaluate renal failure as marker of morbidity and mortality.[10-12] In 1999, an investigation aimed at formulating a risk score for long-term prognosis identified moderate increase in urea levels as the mortality marker in a two-year follow-up.[13] Recently, serum creatinine level at admission has proved to be one of the most important markers of hospital mortality in the GRACE registry.[14] No other study analyzed renal function clinical course during hospitalization as marker for worse outcome.

This study was intended to evaluate renal function at admission and its clinical course during hospitalization as prognostic marker for 30-day outcome and at one-year follow-up in patients with ST-segment elevation and non-ST-segment elevation acute myocardial infarction.

Methods

Study population: Three hundred and thirteen patients consecutively admitted to the coronary care unit with a diagnosis of AMI with and without ST-segment elevation between January 2000 and December 2000 were retrospectively evaluated.

Diagnostic criteria: Diagnosis of AMI was based on the World Health Organization criteria and confirmed by the presence of two or three of the following features: chest pain typical of acute coronary insufficiency lasting for at least twenty minutes, electrocardiographic changes consistent with myocardial ischemia and the development of new pathologic Q waves, serial CK-MB levels equal to or greater than twice the upper reference limit. Electrocardiograms performed on admission allowed distinguishing between AMI with and without ST-segment elevation, as well as its location.

Demographic data such as gender, age, and body weight were assessed. The presence of diabetes mellitus (DM) was considered if the patient was previously on oral hypoglycemic agents, insulin or showed fasting plasma glucose $\geq$ 126 mg/dL or $\geq$ 200 mg/dL at any time during hospitalization, making repeat testing necessary. Diagnosis of dyslipidemia (DLP) and systemic arterial hypertension (SAH) was obtained from past history and/or treatment prior to admission and recorded in the medical chart. History of smoking and previous AMI was taken through a medical questionnaire and data from the medical chart.

Renal function assessment: Renal function was assessed by serum creatinine (Cr) measurement at admission (baseline Cr) and during hospitalization. During hospital stay, the highest Cr value was used (peak Cr). Creatinine clearance (CrCl) was calculated using the Cockcroft-Gault equation.[15]

$$CrCl = \frac{(140 - age) \times body\ weight\ (kg)}{72 \times serum\ Cr} \times (0.85\ for\ females)$$

Renal function outcome was also evaluated, comparing the coefficient of variation between CrCl at admission (baseline CrCl) and the lowest CrCl (lowest CrCl) obtained during hospitalization.

Renal disease patients undergoing dialysis were excluded.

Outcomes during hospitalization and after discharge

The following events were assessed during hospital stay: systolic hypotension (< 90 mm Hg), reinfarction, cardiogenic shock, and death within thirty days. During the one-year follow-up, the presence of one of the following was considered a combined event: reinfarction, CABG, percutaneous coronary intervention (PCI), readmission for unstable angina, and death.

Data were obtained from information included in the medical chart, routine clinical evaluation, or phone calls to patients with no follow-up at the institution.

Statistical analysis: Statistical analysis involved two steps. As the first step, univariate analysis was performed to evaluate the relationship between every potential risk factor or protective factor and death within thirty days and combined events within a year. A statistical significance level of 0.10 was set for the first selection of variables that would be considered for logistic regression models. Fisher's exact test, Student's t test and Mann-Whitney test were used.

As the second step, two logistic regression models were selected, one for the dependent variable 30-day mortality and the other for the dependent variable one-year combined events.

Results

Out of 313 patients admitted with AMI during the study period, 21 were excluded because of inadequate data, 15 with cardiac enzyme elevation following elective percutaneous coronary intervention, 2 with previous chronic renal failure on dialysis, and 1 with myocardial bypass. Two hundred and seventy-four patients, mean age 62.2 ± 13.5, were analyzed, 200 (73%) of them

were male. In 35 (12.8%) patients, only baseline Cr was measured. Most patients (> 95%) underwent coronary angiography, and only parenteral hydration was provided before and after the procedure. No difference was found in worsening of renal function among patients who underwent coronary angiography or not.

Thirty-day mortality was 6.93% (n = 19), and one-year combined events was 29.0% (n = 74). No patient was lost to follow-up in thirty days nor in a year.

Male patients showed better renal function both at admission and during hospital stay (Table 1); mean age for men was 62.5 and for women, 66.0. History of systemic arterial hypertension was correlated with worse renal function at admission and also during hospital stay. Smokers were found to have higher levels of CrCl at baseline as well as higher levels of the lowest CrCl obtained during hospitalization; however, no significant change in renal function was observed in the presence of diabetes mellitus (Table 1).

Mean age of the 19 patients who died within thirty days was significantly higher (70.95 ± 2.38 vs. 62.64 ± 0.85, p = 0.007), and 16 (84.2%) were male (Table 2). No significant difference was observed regarding patients with SAH, DM, DLP, smoking status, and previous AMI. As far as AMI location is concerned, no difference was found between anterior and inferior wall myocardial infarction. Among patients who died within thirty days, 36.8% (p = 0.002) had hypotension and 63.2% (p < 0,001) had cardiogenic shock during hospitalization.

Renal function at admission was reduced in patients that died within thirty days, with higher levels of baseline Cr and lower levels of baseline CrCl (Table 3). In addition, these patients experienced a significant decline in renal function during their hospital stay. No significant difference however was found in creatinine variation percentage.

The logistic regression model using those variables classified in the univariate analysis showed that higher levels of the lowest CrCl obtained during hospitalization have protective value against cardiogenic shock (Table 4), demonstrating that the greater the lowest level of CrCl the lower the mortality rate (OR = 0.97, IC 95% 0.94-0.99, p = 0.036).

In the univariate analysis, male patients and smokers were less prevalent among those who had combined event within a year when compared with event-free patients (64.9% vs. 75.1%; p = 0.065 e 27.0% vs. 41.4%; p = 0.031).

In addition, renal function variables showed no significant difference with respect to combined event incidence within a year. Therefore, logistic regression of these factors was not studied.

Discussion

Risk factors for developing coronary artery disease also appear as markers of poor renal function. Male gender and history of SAH, congestive heart failure, previous AMI, and myocardial revascularization are associated with renal dysfunction in several studies.[16-21] Likewise, data from literature consistently demonstrate that smokers have better renal function than non-smokers, but with no plausible explanations.[16-21] Our study showed no significant decline in renal function in DM patients, probably because the sample of patients with DM was small compared to other populations studied.

Patients undergoing dialysis after AMI have higher mortality rates in follow-ups ranging from 30 days to 27 months.[16-18] McCullough *et al*. analyzed 817 patients with AMI and demonstrated that non-dialysis patients with CrCl < 47 mL/min at admission had worse in-hospital outcomes with regard to events such as left ventricular

Table 1 – Analysis of renal function variables according to gender and past history, represented by mean + standard error

		Baseline Cr (mean)	Peak Cr (mean)	Baseline CrCl (mean)	Lowest CrCl (mean)
Gender	Male	1.3±0.5	1.6±0.7	68.0±26.0	60.0±25.6
	Female	1.2±0.6	1.4±1.3	56.0±25.0	50.1±25.8
	p	**<0.001**	**<0.001**	**<0.001**	**0.007**
SAH	No	1.1±0.3	1.3±0.4	71.0±26.0	63.7±26.7
	Yes	1.3±0.6	1.6±1.1	62.0±26.0	54.1±25.1
	p	**0.005**	**0.003**	**0.009**	**0.009**
DM	No	1.3±0.5	1.5±1.0	65.0±26.0	56.3±25.3
	Yes	1.3±0.5	1.5±0.8	65.0±27.0	58.6±27.4
	p	0.895	0.383	0.887	0.513
Smoking	No	1.3±0.5	1.6±1.0	59.0±24.0	50.2±23.8
	Yes	1.2±0.5	1.4±0.6	76.0±25.0	69.8±25.2
	p	0.052	**0.001**	**<0.001**	**<0.001**
DLP	No	1.3±0,4	1.5±0,6	66.0±27.0	57.7±26.0
	Yes	1.3±0,6	1.6±1,3	64.0±25.0	56.0±26.1
	p	0.664	0.666	0.537	0.616

Table 2 – Univariate analysis of demographic data, past history, and post-infarction clinical course with 30-day death and one-year combined events. Age is represented by mean ± standard error

	30-day death (N= 19)	non-30-day death (N= 255)	p	1-year events (N= 74)	1-year event-free (N= 200)	p
Age (years)	70.95 ± 2.38	62.64 ± 0.85	**0.007**	64.39 ± 1.39	62.78 ± 1.00	NS
Gender (%)						
Male	84.2	72.2	NS	64.9	75.1	0.065
Female	15.8	27.8		35.1	24.9	
Past history (%)						
DM	36.8	31.4	NS	33.8	30.4	NS
SAH	68.4	68.6	NS	74.3	66.3	NS
Smoking	15.8	37.3	NS	27.0	41.4	0,031
DLP	26.3	40.0	NS	39.2	40.3	NS
Previous AMI	47.4	37.3	NS	43.2	34.8	NS
Changes in ECG (%)						
Anterior ST-elevation	36.8	29.0	NS	29.7	28.7	NS
Inferior ST- elevation	42.1	39.6	NS	44.6	37.6	NS
No- ST- elevation	21.1	31.0	NS	25.7	33.1	NS
Post-infarction in-hospital outcome (%)						
Reinfarction	0	3.1	NS	-	-	-
Hypotension	36.8	9.4	**0.002**	-	-	-
Cardiogenic shock	63.2	4.7	**< 0.001**	-	-	-

Table 3 – Univariate analysis of renal function variables with 30-day death and one-year combined events, represented by mean ± standard error

	30-day death N= 19	non-30-day death N= 255	p	1-year events N= 74	1-year event-free N= 200	p
Baseline Cr (mg/dL)	1.56 ± 0.09	1.25 ± 0.03	**< 0.001**	1.30 ± 0.07	1.26 ± 0.03	NS
Peak Cr (mg/dL)	2.19 ± 0.28	1.49 ± 0.06	**< 0.001**	1.63 ± 0.18	1.40	NS
Baseline CrCl (mL/min)	46.45 ± 3.71	66.54 ± 1.64	**< 0.001**	64.67 ± 3.08	67.0 ± 2.0	NS
Lowest CrCl (mL/min)	38.29 ± 4.76	58.29 ± 1.73	**0.003**	56.48 ± 3.3	59.0 ± 2.0	NS
Variation (%)	20.18 ± 5.84	11.12 ± 0.91	NS	12.84 ± 1.7	10.4 ± 1.1	NS

Table 4 – Logistic regression model for 30-day death variable

	OR	95% CI	p
Lowest CrCl	0.97	0.93-0.99	0.036
Cardiogenic shock	15.2	4.57-50.4	0.024

failure, ventricular arrhythmias, reinfarction and death, when compared to dialysis patients.[17]

Possible explanations for worse outcomes following AMI in patients with mild-to-moderate renal function deterioration suggest that endothelial dysfunction, increased oxidative stress, and high levels of homocysteine are early seen in renal disease.[22]

Management of acute coronary syndromes (ACS) in patients with renal dysfunction should be better observed, offering them the best therapeutic options available. Previous studies analyzed the usefulness of treatments known to improve patient outcome after AMI, such as beta-blockers, antiplatelet agents, statins, glycoprotein IIb/IIIa inhibitors, thrombolytics, and angioplasty in renal dysfunction patients. It has been proved that patients with deteriorated renal function receive optimal treatment less frequently than those with normal renal function.[4,16,20, 23,24]

In the GRACE registry, an increase of 1 mg/dL in baseline Cr was associated with a 1.2-fold increase in hospital death risk.[14] This elevation in Cr levels has been

shown to have higher prognostic value than cardiac enzyme levels at admission, since at present markers of myocardial necrosis are given more importance than renal function.

In another GRACE registry publication, using the adapted classification of the National and Kidney Foundation recommendations, in-hospital mortality was greater among patients with moderately or severely decreased baseline CrCl.[25] Patients with baseline CrCl between 30-60 mL/min had a two-fold higher mortality rate, and patients with baseline CrCl $\leq$ 30 mL/min, a four-fold higher mortality rate than patients with CrCl > 60 mL/min[21].

Papers available in the literature used only renal function at admission, failing to analyze its outcome during hospitalization. In our sample, patients with improved CrCl levels during hospitalization had lower 30-day mortality, with a decline of 3% in mortality for every one-unit increase in the lower CrCl. In like manner, worsening of renal function in patients who progressed to death within thirty days may be related to greater incidence of cardiogenic shock; however, no difference was found regarding incidence of anterior wall AMI with ST-segment elevation, a fact that denotes higher severity, demonstrating the important role of renal function outcome in acute myocardial infarction.

Thus, careful renal function monitoring, as well as elimination or correction of factors that decrease glomerular filtration rate during hospitalization, such as dehydration and use of nephrotoxic substances, may reduce morbidity and mortality in AMI patients.

Conclusion

Renal function deterioration during hospitalization in the acute phase of myocardial infarction was found to be a major marker of 30-day mortality. This suggests that proper monitoring of renal function with serial serum Cr measurement and CrCl calculation may be relevant in the treatment of patients with AMI to reduce short-term morbidity and mortality.

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