Original article

The prognostic impact of renal failure in patients with ST-segment elevation acute myocardial infarction

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Abstract

Introduction: Renal insufficiency (RI) is associated with higher morbidity and mortality in patients (P) with coronary artery disease and in P submitted to angioplasty. In ST-segment elevation acute myocardial infarction (STEAMI), this impact has not been well demonstrated.

Aim: To evaluate the impact of RI in P with STEAMI.

Methods: We evaluated 160 P admitted with STEAMI, mean age of 62±14 years, 76% male. We determined creatinine levels on admission. RI was defined as a level >1.5 mg/dl. Analysis of clinical, electrocardiographic and laboratory variables was performed, in relation to the endpoint defined as the occurrence of death at 30-day follow-up.

Results: There were 16 deaths (10%) at 30-day follow-up. P with RI (n=21) were older (68±11 *vs* 61±14 years, p<0.001), more often had diabetes (57 *vs* 24 %, p=0.004) and presented more often with Killip class ≥2 (57 *vs* 12%, p<0.001). The use of statins (62 *vs* 83%, p=0.05) and β-blockers (24 *vs* 65%, p<0.001) was lower in P with RI. Mortality was higher in RI P (62 *vs* 2%, p<0.001). The univariate predictors of death were age ≥75 years, diabetes, Killip class ≥2 on admission, RI, non-use of statins and β-blockers and use of diuretics. In multivariate analysis, independent predictors of death at 30 days were RI (HR 29.6, 95% CI 6.3-139.9, p<0.001) and non-use of β-blockers (HR 0.13, 95% CI 0.02-1.01, p=0.01).

Conclusion: In P admitted for STEAMI, the presence of RI was an independent predictor of death at 30 days whereas the usage of β-blockers was protective.

Key words: ST-segment elevation acute myocardial infarction, renal failure, prognosis

Introduction

Cardiovascular diseases are the leading cause of death in patients with terminal renal insufficiency (RI) [1, 2] and are highly prevalent in patients with the most severe forms of RI [3]. Patients with terminal renal disease who suffer a myocardial infarction (MI) have a mortality that reaches 59.3% in the following year [4, 5]. Those who were submitted to percutaneous coronary angioplasty have higher rates of restenosis [6], and survival after coronary artery bypass grafting is lower than that observed in patients without renal disease [4]. Chronic renal disease was associated with a 40% increased risk of MI, stroke and cardiovascular death among participants of the Heart Outcome and Prevention Evaluation (HOPE) study [7].

There are few studies in patients with less severe forms of RI and coronary disease, although this is a very important population: National Health And Nutrition Examination Survey III [8] identified 9.74% of males and 1.78% of females with a creatinine level ≥1.5 mg/dl. In patients with renal disease and acute MI, the use of aspirin, β-blockers (BB), angiotensin converting enzyme inhibitors (ACEI), statins and antagonists of GP IIb/IIIa receptors is lower when compared with patients with preserved renal function [8-11]. The Global Registry of Acute Coronary

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Events (GRACE) [12] reported that these drugs are used in respectively 95.3%, 86.2%, 65.6%, 54.3% and 28.1% of patients with normal/mildly impaired renal function and 92.7%, 64.9%, 62.1%, 31.6% and 14.6% of patients with severe renal dysfunction (p<0.05 for each class of drugs).

Another important point is the absence of an appropriate characterisation of this high risk population, since those patients are usually excluded from large clinical trials. In the last few years, several risk prediction models have been developed, such as the TIMI risk score for ST-elevation acute myocardial infarction (STEAMI) [13]. These scores are derived from large clinical trial databases, but real-life unselected patient populations seem to differ from those enrolled in clinical trials. In fact, those studies seem to under-represent some of the most important sub-groups of patients, such as the elderly and patients with RI.

More recently, two scores were developed for all acute coronary syndromes, to determine the risk of in-hospital [14] and 6-month [15] mortality. These scores are based on a large scale, multinational registry, with a relatively unselected patient population. The scores included new variables that are characterised by a higher predictive capacity, and one of those variables is renal function [12].

Based on the previously mentioned evidence, the aim of our work was to evaluate the prognostic impact of RI in patients admitted for STEAMI.

Methods

This retrospective study included 160 consecutive patients admitted to our Intensive Care Unit for STEAMI (January – December 2002). STEAMI was defined as the presence of ST-segment elevation in the ECG and the presence of angina for at least a 30-minute duration or elevation of CK-MB levels above the upper normal limit.

The data were obtained from hospital clinical records and when follow-up information did not cover 30 days, a telephone call was made to each patient. Patients were divided into two groups: with or without RI, defined by a serum creatinine level on admission ≥1.5 mg/dl. We evaluated the patient's basal clinical variables: demographic, risk factors, previous coronary artery disease, presence of heart failure on admission (Killip-Kimbal class), medication, infarct location and reperfusion technique.

Using multivariable analysis models, we determined the impact of clinical, demographic and angiographic variables on a 30-day prognosis, defined by the occurrence of death.

In a secondary analysis, we obtained corrected creatinine clearance (corrCrCl) for age and gender, using the Cockcroft-Gault formula [16]:

$$corrCrCl_{male}= (140-age)/Cr \times 72 \times body\ mass\ [kg]$$
$$corrCrClfe_{male}=0.85 \times corrCrCl_{male}$$

Patients were divided into four groups according to corrCrCl levels: normal renal function, with corrCrCl ≥90 ml/min (n=44); mild RI with corrCrCl between 60 and 89 ml/min (n=66); moderate RI with corrCrCl between 30 and 59 ml/min (n=45); severe RI with corrCrCl <30ml/min (n=6).

Statistical analysis

Categorical variables were expressed as frequency and respective percentage and were compared by the Chi-square test with Yates correction. Continuous variables were expressed as mean ± standard deviation and compared using Student's t-test. The survival analysis was performed using Kaplan-Meier curves and by the Log-rank test. By using Cox regression models, which included all variables with potential statistical significance by univariate analysis (p<0.10), we identified independent predictors of outcome. We regarded results with p<0.05 as statistically significant. The statistical analysis was performed using SPSS version 10.0 (Chicago, Illinois).

Results

Of 160 patients studied, 76% were males. The mean age was 62±14 years. No patient was on a dialysis programme. The group with RI (13% of patients) was slightly older, and had a higher prevalence of diabetes (Table I). Heart failure signs on admission were also more prevalent in the group with RI. There were no differences in the previous history of coronary disease, remaining risk factors, coronary angiography results or reperfusion technique. BB and statins were less often used in the group with RI. On the other hand, diuretics were more often prescribed. At 30-day follow-up, mortality was 2% in patients with normal function and 62% in patients with RI (p<0.001).

In univariate analysis, the presence of RI was one of the strongest predictors of outcome (RR 23.8, 95% CI 7.48-75.6) (Table II), with a clear and early separation of survival curves (Log-rank, p<0.001) (Figure 1). When analysing the different levels of corrCrCl, we found that the group with severely compromised renal function had the worst outcome, although moderate RI also had implications on outcome (Figures 2, 3 and 4).

In multivariate analysis, the only independent predictor of outcome was RI (HR 29.6; 95% CI 6.3-139.9; p<0.001) (Figure 5). On the other hand, BB use had

Table I. Population characteristics

(%)	Without RI=139	With RI=21	p
Age (years)	61±14	69±11	<0.001
Male gender	77	67	NS
Risk factors			
Hypertension	54	71	NS
Smoking	42	33	NS
Diabetes	24	57	0.004
Hyperlipidemia	50	33	NS
Previous history			
AMI	9	19	NS
PCI	2	5	NS
CABG	2	5	NS
Anterior location	50	57	NS
Killip class ≥2	12	57	<0.001
Thrombolysis	24	24	NS
Coronary angiography	91	86	NS
Multivessel disease	45	52	NS
PCI	72	62	NS
Medication			
ACEI	78	71	NS
BB	65	24	<0.001
Statin	83	62	0.05
Abciximab	60	43	NS
Diuretic	21	81	<0.001
Death at 30 days	2	62	<0.001

Abbreviations: RI-renal failure; AMI – acute myocardial infarction; PCI – percutaneous coronary interventions; CABG – coronary artery bypass grafting; ACEI – angiotensin converting enzyme inhibitors; BB – β-blockers

Table II. Univariate analysis

	Relative risk (CI 95%)	P (Log-rank)
Age ≥75 years	3.59 (1.45-8.89)	0.003
Diabetes	5.43 (2.00-14.76)	0.0002
Killip class ≥2	9.97 (3.75-26.5)	<0.001
Creatinine ≥1.5 mg/dl	23.8 (7.48-75.56)	<0.001
Statins	0.42 (0.16-1.07)	0.06
BB	0.05 (0.006-0.35)	<0.001
Diuretics	16.84 (3.98-71.31)	<0.001
Abciximab	0.44 (0.17-1.15)	0.09

Abbreviations: CI – confidence intervals; BB – β-blockers

on RI and coronary artery disease delt with advanced RI in dialysis patients. In this population, Herzog et al. [5] observed a bad outcome in the course of acute MI, with a survival rate of only 41% in the first year and 27% at two-year follow-up. Less severe stages also have a negative impact on survival after surgical revascularisation [19, 20].

Recently, in the GRACE registry, it was validated that serum creatinine on admission is a useful prognostic predictor in patients with acute coronary syndrome [13-15]. Previously, this variable was not considered a predictor, mainly due to the fact that patients with RI were frequently under-represented in large clinical trials.

In our study, RI (defined as serum creatinine on admission ≥1.5 mg/dl, to avoid other variables that might confound this value, particularly the occurrence of
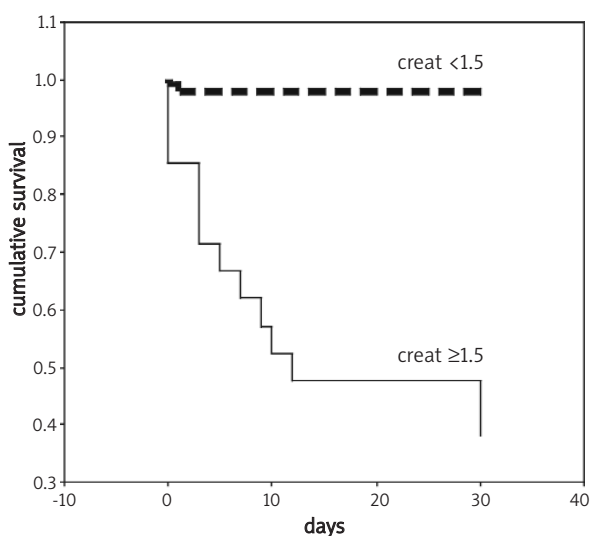
independent protective effects on outcome in this population (HR 0.13; 95% CI, 0.02-1.01, p=0.05).

Discussion

Coronary artery disease is highly prevalent among patients with renal disease, even in less severe stages [3, 7]. The prevalence of renal disease, meanwhile, is increasing in the general population, reaching almost 10%, particularly in males [8]. We may consider it an important public health problem, particularly due to the ominous associated prognosis [4-6]. In patient populations admitted because of acute MI, the percentage of patients with RI varies from 17% to 35% [11, 17-18].

Our study demonstrated that a significant proportion of patients (13%) presenting with STEAMI have abnormal renal function, as well as more adverse basal clinical conditions (particularly the presence of diabetes and heart failure signs on admission). Other authors have already recognised the greater risk of adverse events in patients with chronic RI, such as the case of the HOPE study [7], but the majority of papers

Figure 1. Survival curve for the occurence of death at 30-day follow-up
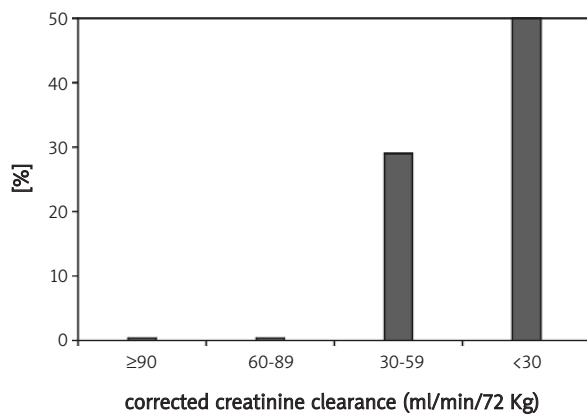
Figure 2. Occurence of death according to renal insufficiency grade

contrast nephropathy) was an important predictor of outcome, as well as age, the presence of diabetes and the presence of heart failure on admission, although after multivariate analysis the only factor that remained as an independent predictor of outcome was RI, showing its important influence. Also the use of medication, particularly BB, was associated with an impact on prognosis, but as a protector, independently associated with a lower risk of death, in a similar way as described in the CAPRICORN trial [21]. As for other drugs, this effect was not as significant, maybe due to the small number of patients and short follow-up duration. Statins also had some benefit, but non-significant. The use of several drugs with a demonstrated effect on outcome, namely aspirin, BB, ACEI and GP IIb/IIIa receptor antagonists, is usually lower in patients with renal failure [9-11]. Also in
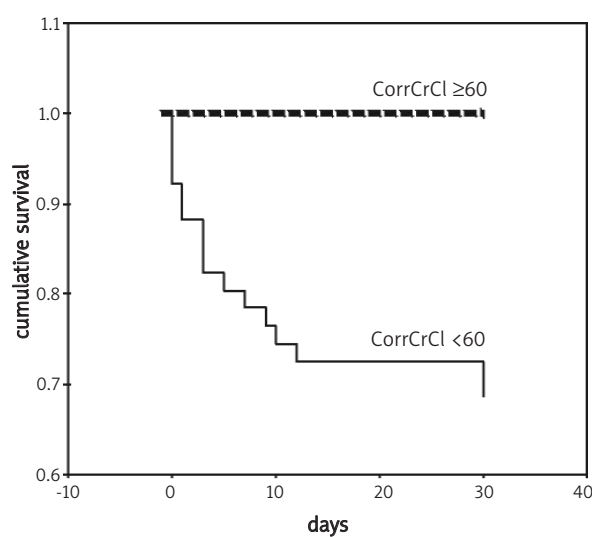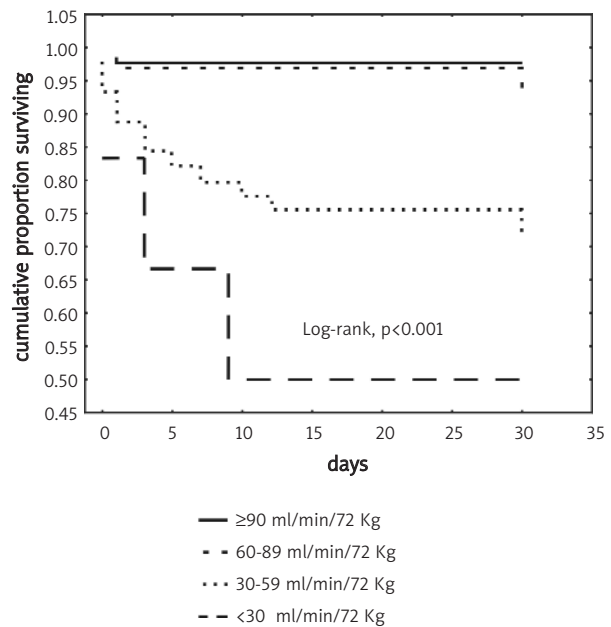

Figure 3. Occurence of death according to corrected creatinine clearence (survival analysis)

our population we reported this fact. The lower use of GP IIb/IIIa receptor antagonist may be due to the reported increased incidence of haemorrhagic complications described in RI patients undergoing primary angioplasty for acute MI [22]. However, in fact, the rise in bleeding risk occurs in all patients, with only a trend towards an interaction between creatinine clearance and major bleeding with abciximab (OR 1.18; p=0.06) and no interaction with minor bleeding [23]. Abciximab is the preferred molecule in the context of primary angioplasty for STEAMI and also the only agent for which clinical data support safety in patients with chronic RI [24]. Therefore, we believe that there is no justification for a dose adjustment in RI patients.

Primary angioplasty was the most often used reperfusion treatment in our study. Elective angioplasty,
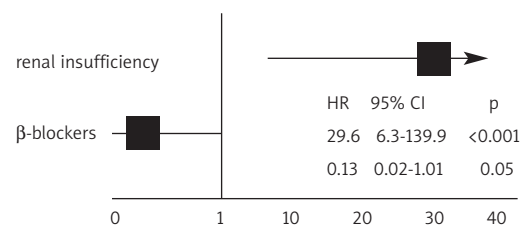

Figure 4. Survival analysis according to renal insufficiency grade (CorrCrCl < and ≥60)

Figure 5. Multivariate analysis for the occurence of death at 30 days. HR – Hazard Ratio; CI – Confidence interval

as such, has a higher rate of complications in patients with RI, particularly with respect to restenosis [6-7, 25]. Also, in the context of primary angioplasty, there is a significant increase in mortality, haemorrhage and restenosis [18]. Either the lower use of drugs, or the worse prognosis associated with myocardial revascularisation procedures in patients with RI, could have contributed to the results found in our population.

In our study, we identified a significant and gradual increase in mortality risk for each stage of RI, suggesting that the clinician should be alert to the presence of RI, due to the higher risk of death. This supports a more aggressive therapeutic approach, with the hope of optimising results, which are still unsatisfactory in patients with RI.

Conclusions

In patients admitted with STEAMI, the presence of RI is an independent predictor of death at 30-day follow-up. The use of BB, in this population, was particularly important, due to their protective effects against death.

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Znaczenie rokownicze niewydolności nerek u chorych z ostrym zawałem mięśnia sercowego z uniesieniem odcinka ST

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Streszczenie

Wprowadzenie: Niewydolność nerek (NN) wiąże się z większą częstością zachorowań i zgonów u pacjentów z chorobą wieńcową oraz poddawanych angioplastyce. Natomiast jej wpływ na rokowanie w przypadku ostrego zawału mięśnia sercowego z uniesieniem ST (STEMI) jest słabiej udokumentowany. Celem naszego badania była ocena wpływu NN na rokowanie chorych z STEMI.

Metody: Ocenie poddaliśmy grupę 160 chorych hospitalizowanych z powodu STEMI w wieku średnio 62±14 lat, z czego 76% stanowili mężczyźni. Pomiaru stężenia kreatyniny dokonywano przy przyjęciu, a za kryterium rozpoznania NN przyjęto stężenie ≥1,5 mg/dl. W odniesieniu do zdefiniowanego punktu końcowego oceny analizowano charakterystykę kliniczną, parametry elektrokardiograficzne i laboratoryjne oraz umieralność w okresie 30-dniowej obserwacji.

Wyniki: W okresie 30 dni zmarło 16 (10%) chorych. Pacjenci z NN (n=21) byli starsi (68±11 *vs* 61±14 lat, p<0,001), częściej cierpieli na cukrzycę (57 *vs* 24 %, p=0,004) oraz byli klasyfikowani w ≥2 klasie wg Killipa (57 *vs* 12%, p<0,001). Osoby z NN rzadziej otrzymywały statyny (62 *vs* 83%, p=0,05) i β-adrenolityki (24 *vs* 65%, p<0,001). Umieralność w grupie chorych z NN była większa (62 *vs* 2%, p<0,001). Analiza jednoczynnikowa wykazała, że czynnikiem prognostycznym zgonu jest wiek ≥75 lat, obecność cukrzycy, klasa ≥2 wg Killipa przy przyjęciu, NN, zaniechanie stosowania statyn i β-adrenolityków oraz stosowanie leków moczopędnych. Niezależnymi czynnikami rokowniczymi w analizie wieloczynnikowej okazały się: NN (HR 29,6, 95% CI 6,3–139,9, p<0,001) oraz stosowanie β-adrenolityków, zmniejszające zagrożenie zgonem w tej populacji (HR 0,13, 95% CI 0,02–1,01, p=0,01).

Wnioski: U chorych hospitalizowanych z powodu STEMI niewydolność nerek jest niezależnym czynnikiem rokowniczym zgonu w okresie pierwszych 30 dni, natomiast β-adrenolityki wywierają wpływ ochronny.

Słowa kluczowe: ostry zawał mięśnia sercowego z uniesieniem ST, niewydolność nerek, rokowanie

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