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Original Article

Impact of Acute Renal Failure on In-Hospital Outcomes Following Percutaneous Treatment of Acute Myocardial Infarction

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ABSTRACT

Background: Acute renal failure (ARF) is a possible complication after percutaneous coronary intervention (PCI). The objective of this study was to evaluate the occurrence and prognostic impact of ARF after PCI in patients with ST segment elevation myocardial infarction (STEMI). **Methods:** Single-center registry evaluating in-hospital outcomes of 501 patients admitted with STEMI undergoing primary, rescue or late PCI. The incidence and predictors of ARF after PCI were evaluated. **Results:** Mean age was 60.7 ± 12.6 years and 67% were male. The populaton had high cardiovascular risk characteristics, with 30% of diabetics and 7.4% with preexisting chronic kidney disease (CKD). The left anterior descending artery was the culprit vessel in 49.4% of the cases and 15% of patients had Killip class III or IV. ARF was observed in 24.7% of patients, who were significantly older, had more diabetes, history of CKD or heart failure, had higher enzyme elevation and lower ejection fraction when compared to those without ARF. In-hospital mortality was higher in patients who developed ARF (29% vs. 4.8%; P < 0.01). Independent predictors of ARF were age > 76 years, previous CKD, Killip class III or IV, need of vascular surgery or blood transfusion. **Conclusions:** Acute renal failure after PCI in STEMI was a frequent complication and was

RESUMO

Impacto da Insuficiência Renal Aguda na Evolução Hospitalar Após Tratamento Percutâneo do Infarto Agudo do Miocárdio

Introdução: A insuficiência renal aguda (IRA) é uma complicação possível após intervenção coronária percutânea (ICP). O objetivo deste estudo foi avaliar a ocorrência e o impacto prognóstico da IRA pós-ICP em pacientes com infarto agudo do miocárdio com supradesnivelamento do segmento ST (IMCSST). **Métodos**: Registro unicêntrico, que analisou a evolução hospitalar de 501 pacientes admitidos com IMCSST submetidos à ICP primária, de resgate ou tardia. Foram avaliados a incidência e os preditores de IRA pós-ICP. **Resultados**: A idade média foi 60,7 ± 12,6 anos e 67% eram do gênero masculino. A população apresentava características de alto risco cardiovascular, sendo 30% diabéticos e 7,4% com doença renal crônica (DRC) preexistente. A artéria descendente anterior foi a principal artéria culpada (49,4%) e 15% dos pacientes se apresentaram em Killip III ou IV. A IRA ocorreu em 24,7% dos pacientes, que, quando comparados àqueles sem IRA, eram significativamente mais idosos, diabéticos, com DRC e insuficiência cardíaca, além de apresentarem maior elevação enzimática e menor fração de ejeção. A mortalidade hospitalar foi maior nos pacientes que desenvolveram IRA (29% vs. 4,8%;

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associated with increased in-hospital mortality.

DESCRIPTORS: Renal insufficiency. Percutaneous coronary intervention. Myocardial infarction.

P < 0,01). Os preditores independentes de IRA foram idade > 76 anos, DRC prévia, Killip III ou IV, necessidade de cirurgia vascular ou transfusão sanguínea. **Conclusões**: A disfunção renal aguda após ICP no IMCSST foi uma complicação frequente e associada com aumento da mortalidade hospitalar.

DESCRITORES: Insuficiência renal. Intervenção coronária percutânea. Infarto do miocárdio.

Coronary artery disease is a major cause of mortality in developed countries. Although mortality after acute myocardial infarction (AMI) have been reduced in recent decades, there are still subgroups of patients who are at higher risk of complications and death, such as those with kidney dysfunction.[1-3]

Patients undergoing percutaneous coronary intervention (PCI) after AMI represent a population at high risk for developing acute renal failure (ARF), since many conditions can favor its occurrence, such as hypotension, ventricular dysfunction, the use of drugs with nephrotoxic potential, and inability to start prophylactic measures in the context of the emergency. Some trials have demonstrated that renal dysfunction is an independent predictor of risk of death in AMI.[4-6] PCI also has the potential to cause renal dysfunction induced by the use of contrast medium. Its occurrence in diagnostic and therapeutic examinations has been related to an increase in in-hospital morbidity and mortality, prolonged hospital stay, development of chronic renal failure, and dialysis.[7-9]

The aim of this trial was to evaluate the impact of ARF on in-hospital outcomes of patients with AMI with ST-segment elevation (STEMI) treated percutaneously.

METHODS

Study population

STEMI patients undergoing primary, rescue, or late PCI were evaluated in a single center, Instituto do Coração, Hospital das Clinicas, School of Medicine, Universidade de São Paulo (InCor/HCFMUSP), São Paulo, Brazil, from January 2008 to March 2011.

Data collection

Data from in-hospital evolution were prospectively collected during the index hospitalization, following the completion of previously standardized forms; all patients signed an informed consent to participate in a PCI study. The data collection included clinical characteristics, laboratory test results, and data from the invasive procedure and clinical outcome until hospital discharge. Patients who developed ARF, with or without a history of chronic renal disease, were analyzed.

Procedures

In all procedures, unfractionated heparin at a dose of 70 to 100 U/kg was previously administered, so that an activated clotting time between 250 and 300 seconds was obtained, except for those who were already using low molecular weight or unfractionated heparin at the admission to Hemodynamics, when the dose was adjusted according to the half-life of the drug used or to the results of the activated clotting time. The patients received dual antiplatelet therapy with acetylsalicylic acid and clopidogrel. During the diagnostic and therapeutic procedures, care was taken to minimize the volume of contrast and avoid drugs with nephrotoxic potential. At the discretion of the physician and according to the clinical condition, the patients received periprocedural saline hydration.

The choice of the route, techniques, materials, and diagnostic and interventional methods was left at the surgeon's discretion. All angiograms were analyzed by the Department of Interventional Cardiology, InCor/HCFMUSP. Image acquisition was performed using two or more angiographic projections of the stenosis after administration of vasodilators.

Definitions

The diagnosis of STEMI was conducted in light of the occurrence of a persistent ST elevation > 1 mm in two contiguous leads, or of a new left bundle branch block on the electrocardiogram in patients with a clinical picture suggestive of myocardial ischemia.

ARF was defined as a 25% baseline increase in serum creatinine or an absolute increase of 0.5 mg/dL in serum creatinine assessed in the first seven days after the completion of the procedure.[10] Initial tests of creatinine were obtained from previous values in patient's medical record or from tests collected in the emergency room, at hospital admission.

PCI was defined as a primary procedure when it was performed in the acute phase of AMI (< 12 hours or between 12 and 24 hours in the presence of symptoms)

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using balloon catheter or stent, without previous use of fibrinolytics, aiming to restore the antegrade coronary flow. Rescue PCI was considered as the procedure performed when the fibrinolytic agent was not successful in reperfusion of the ischemic muscle (resolution of ST elevation < 50% in the first 60 minutes of administration). The clinical picture was defined as a late PCI when the procedure was performed > 24 hours after the onset of symptoms.

Death was defined as death from any cause. The vascular complications evaluated were pseudoaneurysm, arteriovenous fistula, significant hematoma at the access site (defined by a diameter ≥ 10 cm), and significant bleeding (defined as a fall in hemoglobin > 2 g/dL or which required blood transfusion).

Statistical analysis

Continuous variables were described as mean ± standard deviation and compared using the Wilcoxon test. Categorical variables were represented as percentages and compared with chi-squared test. The clinical and angiographic characteristics presented were included in a regression model to detect predictors of ARF following the procedure.

All tests were two-tailed and a P value < 0.05 was considered significant. The analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 17.0 (SPSS Inc., Chicago, Estados Unidos).

RESULTS

From January 2008 to March 2011, 501 patients consecutively admitted with STEMI were evaluated, and their clinical characteristics were summarized in Table 1. The patients were predominantly male (67%) with a mean age of 60.7 ± 12.6 years; 29.7% were diabetic. Chronic renal disease was observed in 7.4% of the trial population. Regarding the type of procedure, primary PCI was performed in 59.2%, rescue PCI in 15.3%, and late PCI in 25.5% of cases. The time elapsed between the onset of symptoms and hospital admission (pain-to-door time) was 5 hours and 12 minutes, with no statistical difference between patients who developed ARF and those who preserved normal renal function (P = 0.27). The left anterior descending artery was the location most related to the infarction (49.4%), followed by the right coronary (39.8%) and left circumflex artery (10.8%). Regarding the hemodynamic presentation at hospital admission, most patients were in Killip class I (75%), however, about 15% of the patients had already been presented in Killip class III or IV. Glycoprotein IIb/IIIa inhibitors were used in approximately one-third of cases.

ARF after PCI occurred in 124 (24.7%) patients. Comparatively, patients who developed ARF were older, diabetic, and more often had a history of chronic renal disease and heart failure. In this group, a lower left ventricle ejection fraction (40.2% vs. 47%; P < 0.01) was also observed, and a greater increase in cardiac enzymes (peak CK-MB: 255.8 IU/L vs. 213.3 IU/L; P = 0.01). There was no difference between the two groups with regard to time of onset of symptoms and hospital admission (pain-to-door time) or the type of PCI (primary, rescue, or late) performed, as shown in Table 1.

In relation to in-hospital outcomes, it was observed that patients with ARF had significantly higher mortality than patients without loss of renal function (29% vs. 4.8%; P < 0.01). Among the deaths, 87.3% occurred from cardiovascular causes and 34% of patients had infectious complications that contributed to the outcome. It was also observed that patients with ARF had a greater need for transfusions, without significant increase in the incidence of fistulas, pseudoaneurysms, or bleeding at the access site (Table 2). There was also a tendency, although not statistically significant, for a higher incidence of hemorrhagic stroke (1.6% vs. 0%; P = 0.06). Among patients who developed ARF, approximately 12% required dialysis during the in-hospital period.

The following factors were identified as independent predictors of occurrence of ARF during the in-hospital period: age > 76 years, history of chronic renal disease, Killip class III or IV at initial presentation, and vascular surgery or need for blood transfusion (Table 3). Patients presenting preserved left ventricular systolic function with an ejection fraction > 60% had a lower occurrence of ARF.

DISCUSSION

ARF is a possible complication after coronary diagnostic or therapeutic procedures, and its development has been associated with prolonged hospital stay, persistent renal dysfunction, and early and late mortality. Observational clinical trials have demonstrated that renal dysfunction is an independent risk factor for death in patients with AMI.[4-6,11] In the GRACE registry, an increase of 1 mg/dL in the initial creatinine increased the risk for in-hospital death by 20%.[12]

The present study observed that ARF is a frequent complication after PCI in patients hospitalized with STEMI, occurring in almost one-quarter of patients. Sadeghi et al.[6] and Lanza et al.[13] found ARF in 18% and 15.3% post-AMI patients, respectively. In the present study, it was observed that the main independent predictors of occurrence of ARF were age > 76 years, history of chronic renal disease, Killip class III or IV at hemodynamic presentation, and a need to perform vascular surgery or blood transfusions. The presence of an ejection fraction > 60% was an independent protective factor for ARF. Marenzi et al.[14] studied 208 patients with AMI and observed a post-PCI incidence

TABLE 1
Clinical and procedural characteristics

Characteristics	Global (n = 501)	ARF (n = 124)	Without ARF (n = 377)	P value
Male,%	67.8	67.9	67.8	0.90
Age, years	60.7 ± 12.6	65.6 ± 12.9	59.1 ± 12.1	< 0.01
Diabetes, %	29.7	38.7	26.8	0.03
Hypertension, %	75.5	81.5	73.5	0.17
Dyslipidemia, %	70.3	72.6	69.8	0.25
Current smoking, %	42.6	35.5	44.8	0.09
FH of early CAD, %	29.5	21.8	32.1	0.07
Prior CRF, %	7.4	20.2	3.2	< 0.01
Prior renal transplantation, %	0.8	0.8	0.8	> 0.99
PAD, %	7	12.1	5.3	0.03
Heart failure, %	12.4	21	9.5	< 0.01
Prior PCI, %	13.9	12.1	14.6	0.72
Previous CABG, %	5.8	9.7	4.5	0.09
Killip				< 0.01
I	75.2	45.5	85.1	
II	9	12.2	8	
III	3.8	10.6	1.6	
IV	12	31.7	5.3	
Pain-to-door time, minutes	312 ± 272	349 ± 288	301 ± 249	0.27
Target artery, %				0.07
LAD	49.4	54.0	47.8	
RCA	39.8	39.5	40.0	
LCx	10.8	6.5	12.2	
LVEF, %	45.7 ± 11.6	40.2 ± 10.7	47.6 ± 11.3	< 0.01
PCI type, %				0.40
Primary	59.2	61.3	58.3	
Rescue	15.3	15.3	15.4	
Late	25.5	23.4	26.3	
Use of GP IIb/IIIa%	33.1	30.6	33.9	0.50

ARF = acute renal failure; FH CAD = family history of coronary artery disease; CRF = chronic renal failure; PAD = peripheral arterial disease; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; LAD = Left anterior descending artery; RCA = right coronary artery; LCx = left circumflex artery; LVEF = left ventricular ejection fraction; GP = glycoprotein.

TABLE 2
In-hospital outcomes and complications

Events	Global (n = 501)	ARF (n = 124)	Without ARF (n = 377)	P value
Mortality,%	10.8	29	4.8	< 0.01
Ischemic stroke,%	0.8	1.6	0.5	0.25
Hemorrhagic stroke,%	0.4	1.6	0	0.06
Pseudoaneurysm,%	1.6	1.6	1.6	> 0.99
AV fistula,%	0.2	0.8	0	0.24
Vascular surgery,%	1.7	4.0	1.1	0.03
Bleeding by access route, %	3.7	5.6	3.1	0.16
Transfusion,%	2.8	8.1	1.1	< 0.01

AV = arteriovenous.

TABLE 3
Independent predictors of acute renal failure (n = 501)

Predictors	Odds Ratio	95% CI	P value
Age > 76 years	2.54	1.44-4.50	< 0.01
CRD	6.47	2.45-17.09	< 0.01
LVEF > 60%	0.95	0.93-0.98	< 0.01
Killip III	7.07	1.87-26.69	< 0.01
Killip IV	6.53	3.20-13.33	< 0.01
Blood transfusion	4.51	1.01-20.16	0.05
Vascular surgery	7.45	1.61-34.54	0.01

CRD = chronic renal disease; LVEF = left ventricle ejection fraction.

of ARF of 19%, reporting a high risk among older patients with renal dysfunction at hospital admission and greater enzymatic elevation – findings similar to those observed in the present study.They also observed an increased risk for patients with lower left ventricle ejection fraction, greater delay for myocardial reperfusion, and for patients with anterior wall AMI, possibly related to the higher contrast volume reported by the investigator to treat this territory and/or by a greater hemodynamic compromise.

Worsening of renal function has been associated with an increased risk of bleeding and of vascular access-related complications after PCI.[15] Some trials suggest a relationship between the occurrence of bleeding and increased mortality in patients with AMI.[16,17] In the context of primary PCI, in which there is a particularly high risk due to the need for aggressive anticoagulation and antiplatelet therapy, the incidence of vascular complications in this subgroup of patients with renal dysfunction remains uncertain.[18] In the present study, no significant increase in complications related to arterial access (pseudoaneurysms, fistulas, or significant bleeding at the access site) was observed in patients with impaired renal function after coronary intervention: 8.0% in patients with ARF and 4.7% in those without renal dysfunction. However, the need for blood transfusion due to bleeding of other origin was an independent predictor of renal failure in these patients (OR = 4.51, 95% CI 1.01-20.16; P = 0.05).

In this study, in-hospital mortality was significantly higher in patients who developed loss of renal function after PCI (29% vs. 4.8%; P < 0.01). Similarly, several authors have found a significant increase in early and late mortality in patients with post-PCI loss of renal function in AMI.[6,11,14,19] Rihal et al.,[9] defining ARF as an increase in creatinine ≥ 0.5 mg/dL, observed that patients with renal dysfunction had an in-hospital mortality of 22%, compared with 1.4% in those with normal renal function. Sadeghi et al.[6] demonstrated that patients with renal dysfunction at any time during the hospital stay after primary PCI had a significant increase in 30-day mortality (RR = 13.8; 95% CI 7.3-26.2) and at one year (RR = 7.4; 95% CI 4.7-11.7). Some authors argue that this increased mortality persists even after a long period of observation. Amin et al.[20] reported that the worsening of renal function was associated with a higher risk of death in patients with AMI, even after 4 years (HR = 1.64; 95% CI 1.23-2.19). An increased mortality was also observed in patients with previous chronic renal failure to the procedure. Gruberget al.[21] reported that patients who had an increase of 25% in baseline creatinine had an in-hospital mortality of 14.9%, compared with 4.9% for those without additional renal dysfunction.

Brown et al.[11] demonstrated that both transient and persistent changes in renal function are associated with a worse prognosis in short and long term. Some trials have shown that up to 45 to 50% of patients who develop renal dysfunction may be unable to return to normal renal function after between two and four weeks of evolution.[11,22] Wi et al.[22] showed that patients with transient renal dysfunction after PCI in an AMI scenario presented, in two years, lower risk of death or dialysis compared to those with persistent renal dysfunction (17.9% vs. 34.1%; P = 0.013). However, even those with transient renal dysfunction had a higher rate of events compared with those without renal dysfunction (17.9% vs. 6.3%; P < 0.001).

Some trials have suggested that patients with renal disease are less likely to receive pharmacological therapies or to undergo CABG when compared to those with preserved renal function.[23,24] In addition, patients with deterioration of their renal function presented a higher number of risk factors compared to the group of patients who maintained normal renal function, such as advanced age, diabetes, and previous chronic heart failure.[20] Lazaros et al.[19] also observed that patients in whom renal function deteriorated during the in-hospital period showed a more important and less completely treated coronary artery disease, with greater degree of myocardial necrosis and of neurohormonal activation – factors that may contribute to a worse outcome in these patients.

Mehran et al.[25] developed a scoring system to assess the risk of ARF after PCI, including clinical and procedural variables: hypotension, intra-aortic balloon, congestive heart failure, chronic renal disease, diabetes, age > 75 years, anemia, and volume of contrast. In an AMI scenario, Wi et al.[26] showed that the Mehran risk score was a significant independent predictor of persistent renal dysfunction and of late adverse cardio and cerebrovascular events in patients who underwent PCI.

If the patient has risk factors, some authors suggest the adoption of preventive measures against the development of renal dysfunction.[27] One of the most importantis proper hydration. The most effective protocol has not been well defined yet, but one trial showed that an infusion of isotonic saline at the rate of 1 mL/kg/h for 48 hours was associated with a significant reduction in the incidence of renal failure (3.7%) compared to unrestricted oral rehydration (34%).[27] N-acetylcysteine, although representing an inexpensive pharmacological intervention and virtually without side effects, had its indication challenged after the negative results of the ACT trial,[28] and is no longer routinely recommended for prevention of nephropathy after percutaneous procedures. Nephrotoxic drugs also increase the risk of nephropathy; the recommendation is for their discontinuation at least 24 hours prior to procedure , when possible. Furthermore, the use of a smaller amount of low- or iso-osmolar contrast is associated with a lower incidence of renal complications.[29]

Study limitations

This non-randomized, observational study was conducted at a single referral center in this institution's cardiology service. Furthermore, the trial presented limitations in the evaluation of ischemia time, because it was not possible to measure the door-to-balloon time – an important variable, due to its association with mortality. Additionally, the calculation of creatinine clearance was not performed, because it was not possible to obtain information regarding the amount of contrast used and the dosage of potentially nephrotoxic medications – known predictors of ARF after procedures using iodinated contrast.

CONCLUSIONS

The occurrence of acute renal failure after percutaneous coronary intervention in patients with acute myocardial infarction with ST segment elevation is a frequent complication, and is associated with increased mortality in this group of patients. Advanced age, the presence of chronic renal disease prior to the procedure, a clinical presentation in Killip class III or IV, and the need for vascular surgery or blood transfusion were the main independent predictors of acute renal failure in this study. Monitoring renal function in acute myocardial infarction may contribute significantly to the risk stratification and treatment of these patients.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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