Contrast-Induced Nephropathy and Acute Renal Failure Following Urgent Cardiac Catheterization: Incidence, Risk Factors, and Prognosis

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Introduction and objectives. The aim was to investigate the incidence and prognosis of, and predictive factors for, acute renal failure following urgent cardiac catheterization.

Methods. The study involved 602 consecutive patients who underwent urgent cardiac catheterization. Acute renal failure (ARF) was defined as an increase in serum creatinine level ≥ 0.5 mg/dL within 72 hours following the procedure. Predictive factors for and the prognosis of ARF were evaluated in an initial cohort of 315 patients, and a risk score was derived. The risk score was validated in a second cohort of 287 patients. The median (interquartile) follow-up time was 1.3 years (0.8-2.0 years).

Results. Seventy-two of the 602 patients (12.0%) developed ARF. In the initial cohort of 315 patients, the following factors were predictors of ARF: cardiogenic shock at admission (odds ratio [OR]= 4.56), diabetes mellitus (OR= 2.98), time to reperfusion >6 hours (OR= 3.18), anterior myocardial infarction (OR= 2.61), baseline serum creatinine level \geq 1.5 mg/dL (OR= 3.51), and baseline serum urea level \geq 50 mg/dL (OR= 3.00). A risk score based on these variables was constructed in which cardiogenic shock = 3 points and each of the remaining variables = 2 points. Patients in the validation cohort were divided into five risk categories: in those with 0 points, the incidence of ARF was 1.2%; with 2-3 points, 8.7%; with 4-5 points, 12.5%; with 6-7 points, 46.2%; and with ≥8 points, 66.7% (P<.0001). Cox regression analysis showed that ARF was a powerful predictor of total mortality (hazard ratio [HR]= 5.97, 95% confidence interval [CI], 2.54-14.03; P<.0001) and of a major cardiovascular event (HR= 3.29, 95% CI, 1.61-6.75; *P*=.001).

Conclusions. The incidence of ARF after urgent cardiac catheterization is high. Cardiogenic shock,

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diabetes mellitus, myocardial infarction location, time to reperfusion, and serum creatinine and urea levels are predictors of ARF. Patients who developed this complication had higher mortality and major cardiovascular events rates.

Key words: *Myocardial infarction. Kidney. Cardiac catheterization.*

Nefropatía inducida por contraste y fracaso renal agudo tras cateterismo cardiaco urgente: incidencia, factores de riesgo y pronóstico

Introducción y objetivos. Nuestro objetivo fue analizar la incidencia, los factores predictores y el pronóstico de la insuficiencia renal aguda (IRA) tras un cateterismo cardiaco urgente.

Métodos. Estudiamos a 602 pacientes consecutivos sometidos a cateterismo urgente. Se definió IRA como un incremento absoluto del valor de creatinina sérica $\geq 0.5 \text{ mg/dl}$ en las 72 h siguientes al procedimiento. En una primera cohorte de 315 pacientes evaluamos los factores predictores y el pronóstico de IRA y elaboramos una clasificación de riesgo, que validamos en una segunda cohorte de 287 pacientes. La mediana (rango intercuartílico) de seguimiento fue de 1,3 (0,8-2) años.

Resultados. De los 602 pacientes, 72 (12%) desarrollaron IRA. En la cohorte de 315 pacientes, los predictores independientes de IRA fueron: shock cardiogénico al ingreso (odds ratio [OR] = 4,56), diabetes mellitus (OR = 2,98), tiempo a la reperfusión > 6 h (OR = 3,18), localización anterior del infarto (OR = 2,61) y valores basales de creatinina \geq 1,5 mg/dl (OR = 3,51) y de urea sérica \geq 50 mg/dl (OR = 3). Se construyó una clasificación de riesgo usando esas variables (shock cardiogénico = 3 puntos; demás variables = 2 puntos); los pacientes de la cohorte de validación fueron clasificados en 5 categorías de riesgo: 0 puntos, el 1,2% de incidencia de IRA; 2-3 puntos, el 8,7%; 4-5 puntos, el 12,5%; 6-7 puntos, el 46,2%; ≥ 8 puntos, el 66,7% (p < 0,0001). En el análisis de regresión de Cox, la IRA resultó ser un poderoso predictor de mortalidad (hazard ratio [HR] = 5,97; intervalo de confianza [IC] del 95%, 2,54-14,03; p < 0,0001) y de eventos cardiovasculares mayores (HR = 3,29; IC del 95%, 1,61-6,75; p = 0,001).

Conclusiones. La incidencia de IRA tras un cateterismo urgente es elevada. El shock cardiogénico, la diabetes mellitus, la localización del infarto, el tiempo a la reperfusión y la creatinina y la urea séricas son predictores de IRA. Los pacientes que desarrollaron esta complicación presentaron mayor tasa de mortalidad y de eventos cardiovasculares mayores.

Palabras clave: Infarto de miocardio. Riñón. Cateterismo cardiaco.

ABBREVIATIONS

AMI: acute myocardial infarction ARF: acute renal failure CI: confidence interval HR: hazard ratio OR: odds ratio STEMI: ST segment elevation myocardial infarction

INTRODUCTION

Chronic renal failure has been associated with an increase in mortality in several subgroups of patients with ischemic heart disease; in particular, it has been shown that it worsens prognosis in patients with ST-segment elevation myocardial infarction (STEMI) undergoing fibrinolytic therapy¹ or primary angioplasty.²

The development of acute renal failure (ARF) after elective cardiac catheterization has also been associated with a poor prognosis.³ The causes of ARF after percutaneous coronary revascularization can be very varied, and include contrast-induced nephrotoxicity, hemodynamic alterations, drug-induced toxicity, or atheroembolism. A series of risk factors for ARF have been identified during this type of procedure, such as previous chronic renal failure, diabetes, age, volume of contrast medium, heart failure, and periprocedural hemodynamic alterations.^{4,5}

On the other hand, STEMI patients treated via urgent percutaneous coronary intervention may be at increased risk of contrast-induced nephropathy and ARF after catheterization compared to those undergoing elective procedures.⁶ Factors that may contribute to the development of ARF in this subgroup of patients include hemodynamic alterations within a STEMI setting, the use of high volumes of contrast medium, circulating volume depletion due to sweating and vomiting, and the difficulties involved in providing appropriate prophylaxis for contrast-induced nephropathy. However, there are very few studies that have specifically assessed the evolution of kidney function after urgent catheterization. The aim of this study was to analyze the incidence, risk factors for, and long- and short-term prognosis of ARF in STEMI patients undergoing urgent percutaneous coronary revascularization, and to design a risk classification for this complication.

METHODS

Patients

Between March 2003 and February 2007, a total of 647 STEMI patients admitted to the emergency department of our hospital underwent 669 urgent cardiac catheterization procedures. Patients directly transferred from other hospitals to the cardiac catheterization unit were not included. Patients who died in the first 24 h (n=25) were excluded as well as those in whom, for other reasons, it proved impossible to obtain an appropriate profile of kidney function (n=13) or chronic dialysis patients were finally included in the study. In the case of repeat urgent procedures for STEMI during the study period (n=22), the first procedure was selected or the procedure during which the patient developed ARF.

We selected an initial cohort of 315 patients who had undergone urgent catheterization between March 2003 and August 2005 to investigate the predictive factors for and prognosis of ARF; a second cohort of 287 patients treated between September 2005 and February 2007 was chosen to validate a risk classification derived from the initial cohort.

Variables

This was a retrospective study where demographic, clinical, angiographic, and hemodynamic variables were collected prospectively and stored in our hospital's cardiac catheterization unit database.

Laboratory parameters (including urea and serum creatinine concentrations) were determined at hospital admission (prior to beginning the procedure), and on a daily basis during patient stay in the coronary care unit. All determinations at admission were conducted in the hospital's emergency laboratory; all other serial determinations were conducted in a central laboratory or in the emergency laboratory itself.

Creatinine clearance was estimated by the Cockcroft-Gault formula⁷ and the glomerular filtration rate by the simplified MDRD (Modification of Diet in Renal Disease) equation.^{8,9}

Catheterization and Treatment

In all cases, iohexol was used as the contrast agent (Omnipaque[®], Amersham Health, Carrington Hill, Cork, Ireland). All patients received 250 mg of acetylsalicylic acid prior to catheterization unless contraindicated. Abciximab was administered to all patients in the emergency department or in the cardiac catheterization laboratory prior to beginning the procedure, except for patients who had received fibrinolytic therapy or those presenting other contraindications. Patients undergoing stent implantation were administered a loading dose of 300 mg of clopidogrel, followed by a daily dose of 75 mg.

The decision to institute a hydration schedule after catheterization, the type of fluid therapy and dose, and the need for renal replacement therapy was left to the discretion of the physician responsible for the patient.

Definitions

A cardiac catheterization procedure was defined as urgent when it was perfored for treatment of STEMI within 12 h following symptom onset.

Acute renal failure was defined as an increase in the absolute concentration of creatinine $\geq 0.5 \text{ mg/dL}$ in the 72 h following the procedure compared to creatinine concentrations at hospital admission.¹⁰

Anemia was defined as a baseline hemoglobin concentration <13 mg/dL in men or <12 mg/dL in women.

Cardiogenic shock was defined as systolic blood pressure <85 mm Hg for at least 1 h accompanied by signs of hypoperfusion due to ventricular dysfunction, mechanical complications or right ventricular infarction requiring inotropic support, or intraaortic balloon pump implantation.

Cardiovascular death was defined as unexplained sudden death, death due to acute myocardial infarction (AMI), death after rehospitalization due to heart failure, myocardial ischemia, or death due to hemorrhagic, or embolic stroke.

Reinfarction was defined as the appearance of new symptoms of myocardial ischemia or electrocardiographical changes, accompanied by increases in markers of myocardial necrosis.

Follow-Up and Endpoints

Follow-up data were obtained from the hospital's databases, the patient's medical record, and by telephone interview.

The endpoints analyzed were total mortality and combined major cardiovascular events (cardiovascular death, reinfarction, and percutaneous, or surgical revascularization with objective evidence of previous myocardial ischemia).

Statistical Analysis

Normally distributed continuous variables are presented as mean (SD) and those with a non-normal distribution as median and interquartile range. Discrete variables are presented as percentages.

Comparisons between discrete variables were performed using the χ^2 test or Fisher exact test as required, and

comparisons between continuous variables using the Student t test or Mann-Whitney U test for those with a non-normal distribution. The Kolmogorov-Smirnov test was used to test for normal distribution; this was rejected for all variables except total cholesterol.

Backward stepwise logistic regression analysis was performed to determine the predictive factors for ARF. Variables that were significantly associated with the development of ARF or that showed a tendency (P<.10) toward an association were included in the model. The variables finally included in the model were as follows: age >65 years, sex, diabetes mellitus, hypertension, previous chronic renal failure, treatment with angiotensin-converting enzyme (ACE) inhibitors, and diuretic agents, cardiogenic shock, time to reperfusion >6 h, anterior location of infarction, anemia, creatinine concentration \geq 1.5 mg/dL, and urea concentration \geq 50 mg/dL.

The variables that were identified as independent predictors of ARF by logistic regression analysis were incorporated into a risk score where the scores assigned to each variable were determined according to the value of the odds ratio (OR). This classification was validated in a second cohort of 287 patients.

Death-free survival or combined events in groups with or without ARF were compared using the Kaplan-Meier estimator (log-rank test). Cox regression analysis was conducted to determine the predictive factors for mortality and major cardiovascular events. Initially, a bivariate analysis was performed followed by a multivariate analysis which included those variables with P < .10 from the previous bivariate analysis, as well as others considered clinically relevant. The following variables were included in this analysis: age, sex, smoking habit, diabetes mellitus, hypertension, hypercholesterolemia, background of AMI, chronic renal failure, location of the AMI, cardiogenic shock, ejection fraction, multivessel disease, success of the procedure, time to revascularization, anemia, fasting blood glucose concentration, maximum troponin I concentration, creatinine concentration ≥ 1.5 mg/dL, and urea concentration \geq 50 mg/dL. A *P* value less than <.05 was considered significant.

The statistical analysis was performed using SPSS software, version 14.0 (SPSS, Chicago, Illinois, USA) and STATA software, version 9.1 (STATA, Collage Station, Texas, USA).

RESULTS

Baseline Characteristics and Incidence of Acute Renal Failure

Of the 602 patients, 72 (12%) fulfilled the criteria for ARF after cardiac catheterization. In the initial cohort of 315 patients, 36 (11.4%) subjects developed ARF. Of this initial cohort, 266 (84.4%) patients were men and mean age (SD) was 61 (12) years. Fifteen (4.8%) patients

were in cardiogenic shock at the time of the procedure. Primary angioplasty comprised 96.8% of the procedures, the remainder being urgent procedures indicated after the failure of fibrinolytic treatment. The median (interquartile range) volume of the contrast medium was 300 (230-393) mL.

Tables 1 and 2 show the baseline characteristics of the patients who developed ARF compared to those who did not present this complication. Patients fulfilling criteria for ARF were more often women, older, and more often had a history of diabetes, hypertension, peripheral vascular disease, and chronic renal failure. A trend was observed in this group toward a higher percentage of treatment with diuretics and ACE inhibitors or angiotensin II receptor antagonists. These patients more frequently presented with anterior AMI and were in cardiogenic shock at admission. They also had significantly lower hemoglobin concentrations and a worse baseline renal function profile.

Predictive Factors for Acute Renal Failure and Risk Classification

In the logistic regression analysis, the predictive factors for ARF were cardiogenic shock at admission, diabetes mellitus, time to reperfusion >6 h, anterior AMI, creatinine concentration \geq 1.5 mg/dL, and serum urea concentration \geq 50 mg/dL (Table 3). All the variables presented similar OR values (around 3) except for cardiogenic shock. With the aim of constructing an operational risk score, while still taking into account the relative proportion of the odds ratio, a value of 3 points was assigned to cardiogenic shock and 2 points to the remaining variables; the score was calculated as the sum of these values. The patients in the second cohort were classified into 5 categories according to their scores (0, 2-3, 4-5, 6-7, and ≥8 points). Figure 1 shows the result of this stratification in which a significant increase can be observed in the risk of ARF per each increase in score (P<.0001).

Prognosis of Acute Renal Failure

In-Hospital Evolution

Of the patients who presented ARF, 22.2% (n=8) required renal replacement therapy at admission. Continuous veno-venous hemofiltration was employed in all these patients.

The patients fulfilling criteria for ARF had worse inhospital outcome, with a higher percentage of cardiogenic shock and intraaortic balloon pump implantations at admission, more episodes of serious ventricular arrhythmia or cardiorespiratory resuscitation, greater incidence of respiratory failure necessitating mechanical ventilation, and greater in-hospital mortality (Table 4).

	Without ARF (n=279)	ARF (n=36)	Р
Men, %	86	72.2	.032
Age, median (IR), y	60 (49-69)	67 (61-74)	.001
Age ≥65 years, %	38.4	61.1	.009
BMI, median (IR)	27.8 (25.8-30.1)	27.3 (25.5-30.1)	.89
Diabetes mellitus, %	22.2	47.2	.001
Smoking habit, %	38.4	25	.12
Hypertension, %	32.3	52.8	.015
Hypercholesterolemia, %	37.6	33.3	.62
History of heart disease			
AMI, %	8.6	16.4	.12
Unstable angina, %	7.9	8.3	1.00
Coronary angioplasty, %	7.6	8.3	.75
Coronary revascularization surgery, %	3.2	2.8	1.00
No history of heart disease			
Stroke, %	2.5	5.6	.28
Peripheral vascular disease, %	4.3	13.9	.03
Chronic renal failure, %	3.6	13.9	.019
Previous treatment			
ACE inhibitors or ARA-II, %	6.8	16.7	.05
Statins, %	11.1	19.4	.17
Diuretic agents, %	2.2	8.3	.07
Insulin, %	3.9	5.6	.65
Oral antidiabetic agents, %	8.6	19.4	.07

^aARF indicates acute renal failure; ARA-II, angiotensin II receptor antagonists; AMI, acute myocardial infarction; ACE inhibitors, angiotensin-converting enzyme inhibitors; BMI, body mass index; IR, interquartile range.

TABLE 2. Clinical Angiographic, Hemodynamic, and Laboratory Data ^a

	Without ARF (n=279)	ARF (n=36)	Р
 Anterior AMI, %	39.8	64.7	.006
Cardiogenic shock at admission, %	0.7	11.1	.002
Time, median (IR), min			
Initial pain at hospital admission	112 (60-196)	147 (107-227)	.047
Door to balloon time	68 (53-98)	92 (63-180)	.006
Cardiac catheterization time	38 (29-53)	44 (36-60)	.016
Time to reperfusion	199 (144-294)	273 (189-415)	.001
Time to reperfusion >6 h, %	20.1	35.3	.049
Primary angioplasty, %	97.1	94.4	.38
Access route, %			
Femoral artery only	58.5	61.1	.097
Radial artery only	38.3	30.6	
Both	2.2	8.3	
Number of diseased vessels, %			
1 vessel	52.9	47.2	0.75
2 vessels	26.6	33.3	
3 vessels	19.8	19.4	
Complete revascularization, %	61.4	48.6	.15
Aortic systolic pressure, median (IR), mm Hg	120 (105-140)	115 (95-155)	.95
LVEDP, median (IR) mm Hg	25 (18-30)	30 (25-35)	.002
LVEF, median (IR), %	61 (51-70)	47 (41-60)	.0001
LVEDV, median (IR), mL	146 (120-203)	128 (104-171)	.11
Volume of contrast medium, median (IR), mL	294 (227-387)	320 (274-386)	.11
Volume of contrast medium >350 ml, %	33.8	38.9	.55
IABP implantation at admission, %	2.5	13.9	.007
Anemia at admission, %	8.2	25	.005
Urea concentration at admission, median (IR), mg/dL	42 (35-50)	54 (42-69)	<.0001
Urea concentration at admission ≥50 mg/dL, %	26.2	58.3	<.0001
Creatinine concentration at admission, median (IR), mg/dL	1.0 (0.8-1.1)	1.1 (0.9-1.4)	.26
Creatinine concentration at admission \geq 1.5 mg/dL, %	6.8	22.2	.006
GFR (MDRD) <60 mL/min/1.73 m2, %	17.2	36.1	.007
CrCl (Cockroft-Gault) <60 mL/min, %	14.4	33.3	.004
Troponin I concentration at admission, median (IR), ng/mL	0.1 (0.0-0.7)	0.4 (0.1-3.4)	.001
Maximum troponin I, median (IR), ng/mL	54.7 (17.7-109.1)	110.0 (71.0-197.5)	<.0001
Fasting blood glucose concentration, median (IR), mg/dL	114 (96-144)	151 (130-223)	<.0001
Total cholesterol, mean (SD), mg/dL	194 (45)	182 (49)	.46
Triglycerides, median (IR), mg/dL	134 (96-194)	189 (142-219)	.053

^aIABP indicates intraaortic balloon pump; GFR, glomerular filtration rate; CrCl, creatinine clearance; SD, standard deviation; LVEF, left ventriclular ejection fraction; AMI, acute myocardial infarction; ARF, acute renal failure; MDRD, Modification of Diet in Renal Disease; LVEDP, left ventricular end-diastolic pressure; IR, interquartile range; LVEDV, left ventricular end-diastolic volume.

On the other hand, ICU stay and total hospital stay were significantly longer in the patients with ARF; in fact, the medians were double that of the group of patients who did not present compromised renal function (Table 4).

Long-Term Follow-Up

The median follow-up time was 1.3 (0.8-2) years. Total mortality and the major cardiovascular event rate were strikingly higher in the patients who developed ARF (Figure 2). Cardiovascular mortality and the ischemic revascularization rate were also significantly higher in the

1030 Rev Esp Cardiol. 2007;60(10):1026-34

TABLE 3. Logistic Regression Analysis: IndependentPredictive Factors for Acute Renal Failure AfterUrgent Cardiac Catheterizationa

	OR	95% CI	Р
Cardiogenic shock	4.56	1.08-19.29	.039
Diabetes mellitus	2.98	1.31-6.79	.009
Time to reperfusion >6 h	3.18	1.30-7.77	.011
Anterior AMI	2.61	1.15-5.95	.022
Creatinine concentration \geq 1.5 mg/dL	3.51	1.10-11.26	.035
Serum urea concentration \geq 50 mg/dL	3	1.33-6.75	.008

^aCl indicates confidence interval; OR, odds ratio.

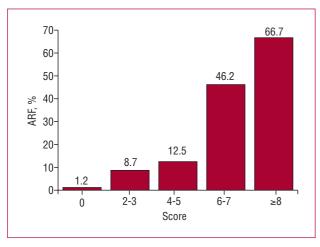


Figure 1. Risk stratification for acute renal failure (ARF) in the validation cohort according to the score.

group that presented ARF; furthermore, a nonsignificant trend was observed toward a greater incidence of reinfarction during follow-up in this group (Table 5). No discharged patient required renal replacement therapy after the index hospitalization. Finally, 3 patients in the group that developed ARF required cardiac transplantation during follow-up, in contrast to none in the group not presenting this complication.

Cox multivariable regression analysis demonstrated that the development of ARF was a strong independent predictor of total mortality (adjusted hazard ratio [HR]=5.97; 95% confidence interval [CI], 2.54-14.03; P<.0001) and of major cardiovascular events (adjusted HR=3.29; 95% CI, 1.61-6.75; *P*=.001).

DISCUSSION

Incidence of Acute Renal Failure

Although the risk of ARF after percutaneous coronary revascularization in the general population is low (0.6%-3%), depending on the definition used),¹⁰ the incidence can be considerably higher in risk subgroups, especially in the setting of STEMI; thus, Rihal et al⁶ identified AMI as an independent predictor of ARF after cardiac catheterization.

In our study, 12% of the patients fulfilled criteria for ARF. In a CADILLAC trial substudy,² the reported incidence of contrast-induced nephropathy after primary angioplasty was just 4.6%. The difference between these results and ours may be due to the exclusion of patients with known previous renal failure or those in cardiogenic shock, as well as to the lack of daily measurements of renal function, given that only creatinine concentrations at admission and discharge were assessed. Taken together,

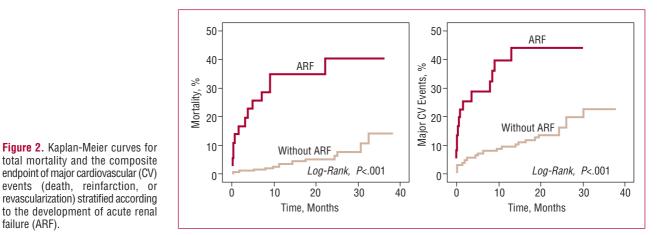


TABLE 4. In-Hospital Events in Patients With and Without Acute Renal Failure

	Without ARF (n=279)	ARF (n=36)	Р
In-hospital mortality, %	0.7	13.9	.0003
Cardiogenic shock, %	3.6	36.1	<.0001
In-hospital reinfarction, %	2.2	8.3	.071
Serious ventricular arrhythmias or cardiorespiratory failure, %	1.8	11.4	.011
Respiratory failure with need for mechanical ventilation, %	2.2	17.1	.0007
Time of ICU stay, median (IR), days	2 (2-3)	4 (3-10)	<.0001
Time of hospital stay, median (IR), days	6 (5-8)	12 (8-22)	<.0001

^aARF indicates acute renal failure; IR, interquartile range.

failure (ARF).

	Unadjusted HR	95% CI	Р
Total mortality	7.95	3.77-16.74	<.0001
Major cardiovascular events ^b	3.90	2.10-7.24	<.0001
Cardiovascular mortality	8.32	3.20-21.64	<.0001
Reinfarction	2.59	0.96-6.94	.059
Revascularization	2.91	1.14-6.01	.024

TABLE 5. Long-Term Prognosis of Acute Renal Failure After Urgent Catheterization^a

^aHR indicates hazard ratio; CI, confidence interval.

^bCardiovascular death, reinfarction, or revascularization.

this may have led to underestimating the true incidence of ARF. Marenzi et al¹¹ reported an incidence of contrastinduced nephropathy of 19% in a group of 208 patients who had undergone primary angioplasty.

There was a high incidence of ARF in our study even in patients with normal renal function; in fact, 77.8% of the patients who developed ARF had creatinine concentrations at admission <1.5 mg/dL, and 63.9% had a glomerular filtration rate of >60 mL/min/1.73 m² assessed by the simplified MDRD equation. It is possible that the use of a low-osmolality contrast medium may have affected the incidence of ARF in our study.¹²

Predictive Factors for Acute Renal Failure and Risk Classification

Identifying patients at high risk of renal dysfunction after urgent cardiac catheterization is of utmost importance, given its prognostic implications.

Mehran et al¹³ assessed predictive factors for contrastinduced nephropathy and developed a risk classification in patients undergoing elective percutaneous coronary revascularization procedures. Patients treated for AMI or in shock were excluded. Contrast-induced nephropathy was defined as an increase of $\geq 25\%$ or ≥ 0.5 mg/dL in serum creatinine concentrations 48 h after the procedure. The predictors of contrast-induced nephropathy incorporated in the risk score were arterial hypotension, intraaortic balloon pump use, congestive heart failure, baseline serum creatinine concentration >1.5 mg/dL, age >75 years, anemia, diabetes, and volume of contrast medium.

However, information is limited within the setting of urgent cardiac catheterization, given that many studies that have assessed the predictive factors for ARF after cardiac catheterization have excluded patients with AMI. Marenzi et al¹¹ identified age \geq 75 years, intraaortic balloon pump use, anterior infarction, volume of contrast medium, and time to reperfusion as predictors of contrast-induced nephropathy after primary angioplasty.

Baseline renal function is a strong predictor of ARF after the procedure. Sadeghi et al² reported an incidence of contrast-induced nephropathy in patients undergoing primary angioplasty which was almost 3 times higher in a group with previous renal failure than in the cohort presenting normal baseline renal function. In our study,

baseline creatinine concentrations $\geq 1.5 \text{ mg/dL}$ were independently associated with the development of ARF. The baseline renal function not only depends on creatinine concentration, but also varies with age, sex, and muscle mass, although the estimated glomerular filtration rate or creatinine clearance may be used for a more accurate assessment. However, Mehran et al¹³ did not observe significant differences between the models that used serum creatinine concentration and creatinine clearance as predictors of contrast-induced nephropathy. With the aim of obtaining a more workable score, we decided to use serum creatinine concentration instead of creatinine clearance. High urea concentrations were also associated with the development of ARF. In the setting of AMI, increased urea concentrations may reflect a renal response to systemic hypoperfusion, rather than intrinsic renal alterations as such.

Cardiogenic shock at admission, time to reperfusion, and anterior AMI were also predictors of ARF. The maximum troponin I concentrations used to estimate AMI size were also significantly higher in the group that developed ARF. The harmful effect of sustained hypotension on renal function is well known,⁴ and our results confirm that prerenal factors in a STEMI setting play a determining role in the pathogenesis of ARF after urgent cardiac catheterization.

Although the volume of contrast medium was higher in the group fulfilling criteria for ARF, this association was not statistically significant even in the univariate analysis. The volume of contrast medium was similar to that reported in previous studies,¹¹ even though left ventriculography was performed in 80% of the patients in our study. However, due to the high incidence of ARF in these patients, it seems advisable to avoid this whenever left ventricular function can be assessed by alternative methods.

Prognosis of Acute Renal Failure

The patients who developed ARF had worse in-hospital outcome; during index admission, mortality in this group was 13.9% in contrast to just 0.7% in the group which did not fulfill criteria for ARF. Similarly, Marenzi et al¹¹ reported a hospital mortality of 31% in patients presenting compromised renal function after primary angioplasty, in

contrast to 0.6% in the population that did not develop renal failure.

Patients who survive an episode of ARF after a percutaneous revascularization procedure may remain at risk of long-term events.¹⁴ In our study, total mortality and the major cardiovascular events rate during follow-up were strikingly higher in the group that developed ARF. Although ARF may be a marker of hemodynamic deterioration and other comorbidities—that in turn are important in the prognosis of these patients—it was a strong predictor of mortality and major cardiovascular events after adjusting for these variables.

In the setting of primary or rescue angioplasty, standard prophylactic treatment for ARF cannot be administered,¹⁵ and few studies have evaluated alternative interventions in this area. Standard hydration by saline infusion does not seem to have a significant beneficial effect on the incidence of ARF.¹¹ In the RAPPID¹⁶ study, a rapid protocol of intravenous N-acetylcisteine proved effective in preventing contrast-induced nephropathy in patients with previous renal dysfunction. In the setting of primary angioplasty, a study reported that Nacetylcysteine reduces the incidence of renal failure, in a dose-dependent manner and improves in-hospital outcome.¹⁷ In another recent study,¹⁸ a rapid hydration protocol with sodium bicarbonate and N-acetylcisteine was effective in preventing contrast-induced nephropathy in patients undergoing urgent cardiac catheterization. Despite these promising results, the need for infusing high volumes of serum during fluid therapy in a relatively short period suggests the need for further studies, especially in patients in cardiogenic shock or with signs of heart failure.

Limitations

Although the demographic, clinical, angiographic, and hemodynamic data were collected prospectively, this was a retrospective analysis with the limitations inherent to this type of studies. Furthermore, the small sample size may have limited the power of our study to detect a significant association between ARF and the volume of contrast medium. In addition, the serial analysis of serum creatinine concentrations in 2 different laboratories may have had an influence on assessing the incidence of ARF. Finally, the study design makes it impossible to determine the relative importance of atheroembolism in relation to the administration of contrast medium or hemodynamic alterations in the development of renal dysfunction.

CONCLUSIONS

The incidence of ARF after urgent catheterization is high. In these patients, diabetes, location of AMI, time to reperfusion, creatinine and urea concentrations, and cardiogenic shock were independent predictors of ARF. The patients who develop ARF after urgent cardiac catheterization have a poor prognosis, with worse in-hospital outcome, longer hospital stays, and greater long-term mortality rates and incidence of major cardiovascular events. More studies are needed to assess the efficacy of therapeutic interventions designed to minimize the risk of developing ARF after urgent cardiac catheterization.

REFERENCES

- Wright RS, Reeder GS, Herzog CA, Albright RC, Williams BA, Dvorak DL, et al. Acute myocardial infarction and renal dysfunction: a high-risk combination. Ann Intern Med. 2002;137:563-70.
- Sadeghi HM, Stone GW, Grines CL, Mehran R, Dixon SR, Lansky AJ, et al. Impact of renal insufficiency in patients undergoing primary angioplasty for acute myocardial infarction. Circulation. 2003;108:2769-75.
- McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW. Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. Am J Med. 1997;103:368-75.
- Dangas G, Iakovou I, Nikolsky E, Aymong ED, Mintz GS, Kipshidze NN, et al. Contrast-induced nephropathy after percutaneous coronary interventions in relation to chronic kidney disease and hemodynamic variables. Am J Cardiol. 2005;95:13-9.
- Goldenberg I, Matetzky S. Nephropathy induced by contrast media: pathogenesis, risk factors and preventive strategies. CMAJ. 2005;172:1461-71.
- Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. Circulation. 2002;105: 2259-64.
- Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16:31-41.
- Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130: 461-70.
- Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function — measured and estimated glomerular filtration rate. N Engl J Med. 2006;354:2473-83.
- Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney Int Suppl. 2006; 100:S11-5.
- Marenzi G, Lauri G, Assanelli E, Campodonico J, de MM, Marana I, et al. Contrast-induced nephropathy in patients undergoing primary angioplasty for acute myocardial infarction. J Am Coll Cardiol. 2004;44:1780-5.
- Aspelin P, Aubry P, Fransson SG, Strasser R, Willenbrock R, Berg KJ. Nephrotoxic effects in high-risk patients undergoing angiography. N Engl J Med. 2003;348:491-9.
- Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol. 2004;44:1393-9.
- McCullough P. Outcomes of contrast-induced nephropathy: experience in patients undergoing cardiovascular intervention. Catheter Cardiovasc Interv. 2006;67:335-43.
- Solomon R, Deray G. How to prevent contrast-induced nephropathy and manage risk patients: practical recommendations. Kidney Int Suppl. 2006;100:S51-3.

Rev Esp Cardiol. 2007;60(10):1026-34 1033

- Baker CS, Wragg A, Kumar S, de Palma R, Baker LR, Knight CJ. A rapid protocol for the prevention of contrast-induced renal disfunction: the RAPPID study. J Am Coll Cardiol. 2003;41:2114-8.
- 17. Marenzi G, Assanelli E, Marana I, Lauri G, Campodonico J, Grazi M, et al. N-acetylcysteine and contrast-induced nephropathy in primary angioplasty. N Engl J Med. 2006;354:2773-82.
- Recio-Mayoral A, Chaparro M, Prado B, Cozar R, Mendez I, Banerjee D, et al. The reno-protective effect of hydration with sodium bicarbonate plus N-acetylcysteine in patients undergoing emergency percutaneous coronary intervention: the RENO Study. J Am Coll Cardiol. 2007;49:1283-8.