Prognostic Impact of Moderate Renal Dysfunction in Acute Coronary Syndromes [21]

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SÉRGIO NABAIS, SÉRGIA ROCHA, JOÃO COSTA, JORGE MARQUES, MÁRCIA TORRES, SÓNIA MAGALHÃES, MIGUEL ÁLVARES PEREIRA, ADELINO CORREIA

Serviço de Cardiologia, Hospital de S. Marcos, Braga, Portugal

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ABSTRACT

Introduction: End-stage renal disease is associated with high cardiovascular mortality. The prognostic importance of milder degrees of renal impairment in patients who have had an acute coronary syndrome (ACS) is less well defined. The purpose of this study was to evaluate the impact of baseline renal dysfunction assessed by estimated glomerular filtration rate (GFR) on mortality in patients admitted with an ACS.

Methods: We studied all patients with an ACS consecutively admitted to an Intensive Cardiac Care Unit over 18 months. The GFR was estimated by means of the four-component Modification of Diet in Renal Disease study equation. Patients were grouped according to their estimated GFR (less than 45.0; 45.0 to 59.9; 60.0 to 74.9; and at least 75.0 ml/min/1.73 m^2). Primary outcome was death from any cause.

Results: The mean age of the 589 study patients was 64.1 years, 73.7% were male, and 49.2% had an ACS with ST-segment elevation. Arterial hypertension, diabetes mellitus, prior myocardial infarction, and Killip class >I were incrementally more common across increasing renal dysfunction strata (p<0.01). The use of reperfusion therapy, beta-blockers, and coronary angioplasty was lower in groups with reduced estimated GFR (p<0.001). Overall six-month mortality was 13.6%. Using the group with an estimated GFR of at least 75.0 ml/min/1.73 m^2 as the reference group yielded odds ratios for six-month mortality that increased with the degree of renal impairment. After adjusting for baseline characteristics, impaired renal function remained associated

RESUMO

Impacto prognóstico da disfunção renal moderada na síndrome coronária aguda

Introdução: A doença renal terminal encontra-se associada a elevada mortalidade cardiovascular. A importância prognóstica de graus mais ligeiros de disfunção renal em doentes que tiveram uma síndrome coronária aguda (SCA) não está definida. O objectivo deste estudo foi avaliar o impacto da disfunção renal basal avaliada pela taxa de filtração glomerular estimada (TFG) na mortalidade em doentes admitidos com uma SCA.

Métodos: Foram estudados todos os doentes com uma SCA admitidos de forma consecutiva numa Unidade de Cuidados Intensivos Cardíacos ao longo de 18 meses. A TFG foi estimada através da equação do estudo Modification of Diet in Renal Disease. Os doentes foram agrupados de acordo com a TFG estimada (<45,0; 45,0 - 59,9; 60,0 - 74,9; e pelo menos 75,0 ml/min/1,73 m^2). Considerou-se como evento primário a morte por qualquer causa.

Resultados: A idade média dos 589 doentes incluídos foi 64,1 anos, 73,7% eram homens e 49,2% tiveram uma SCA com supra-desnivelamento do segmento ST. Verificou-se que a prevalência de hipertensão arterial, diabetes *mellitus* e enfarte do miocárdio prévio, e a apresentação em classe de Killip >I aumentava com o agravamento da disfunção renal (p <0,01). A utilização de terapêutica de reperfusão, beta-bloqueadores e angioplastia coronária percutânea foi inferior nos grupos uma TFG estimada reduzida (p <0,001). A mortalidade global aos seis meses foi de 13,6%. Utilizando o grupo com uma TFG

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with increased mortality. The multivariable-adjusted odds ratio for six-month mortality in patients with mild renal impairment (GFR 60.0 to 74.9 ml/min/1.73 m²) was 2.71 (95% confidence interval [CI] 1.09 to 6.69), compared with 7.53 (95% CI, 3.21 to 17.71) and 8.10 (95% CI, 3.18 to 20.60) in patients with moderate and more severe renal dysfunction, respectively.

Conclusions: Baseline renal dysfunction, as assessed by estimated GFR, is a potent and easily identifiable determinant of outcome after an ACS. Even mild levels of renal impairment are independently associated with increased mortality after an ACS.

Key words

Acute coronary syndrome; Myocardial infarction; Renal function; Renal failure; Chronic kidney disease; Glomerular filtration rate; Creatinine; Prognosis; Coronary artery disease

estimada de pelo menos 75,0 ml/min/1,73 m² como o grupo de referência obtiveram-se *odds ratios* para a mortalidade aos seis meses que aumentaram à medida que o grau de comprometimento renal também aumentava. Após ajuste para o efeito das características basais, a disfunção renal permaneceu associada a aumento da mortalidade. Na análise multivariável o *odds ratio* para a mortalidade aos seis meses nos doentes com disfunção renal ligeira (TFG estimada entre 60,0 e 74,9 ml/min/1,73m²) foi de 2,71 (intervalos de confiança 95% 1,09 - 6,69), em comparação com 7,53 (IC 95% 3,21 -17,71) e 8,10 (IC 95% 3,18 a 20,60) em doentes com disfunção renal moderada e mais severa, respectivamente.

Conclusões: A disfunção renal basal, avaliada pela TFG estimada, é um determinante importante e facilmente identificável de prognóstico após uma SCA. Mesmo níveis ligeiros de comprometimento da função renal estão associados de forma independente a aumento da mortalidade após uma SCA.

Palavras-Chave

Síndrome coronária aguda; Enfarte do miocárdio; Função renal; Insuficiência renal; Doença renal crónica; Taxa de filtração glomerular; Creatinina; Prognóstico; Doença coronária

INTRODUCTION

Chronic kidney disease (CKD) is defined as persistent kidney damage, as reflected by a glomerular filtration rate (GFR) of less than 60.0 ml per minute per 1.73 m² of body surface area for more than three months [1]. CKD is a poorly recognized but important risk factor for cardiovascular disease [2]. Death from cardiovascular disease is 10 to 30 times higher in dialysis patients than in the general population [3].

During the past 15 years, the burden of cardiovascular disease-related morbidity and mortality in the general population has improved markedly. However, cardiovascular disease-related morbidity and mortality in patients with CKD has remained almost unchanged, perhaps because of poor recognition of the impact of CKD on the biology of cardiovascular disease and, to some extent, the lack of well-designed prospective studies to define the role of treatment of targeted risk factors in patients with CKD [2].

Renal dysfunction has proved to be an important determinant of mortality in the follow-up of patients who have undergone coronary artery bypass grafting [4] or a percutaneous coronary intervention [5], and those who have suffered an acute myocardial infarction [6-9]. Among patients with end-stage renal disease, the two-year mortality rate after myocardial infarction is approximately 50%, twice the mortality rate after myocardial infarction in the general population [10]. However, limited information exists on the risks associated with lesser degrees of renal impairment in patients who have had an acute coronary syndrome (ACS). Most of the

studies that found renal failure was a prognostic factor for ischemic heart disease were performed in selected patients, such as patients from clinical trials or seriously ill patients [4-6, 9, 11, 12], and so the findings cannot be readily generalized. Furthermore, the majority of what is known relates to serum creatinine level, which is an insensitive indicator of renal function owing to nonlinear associations with GFR that vary according to age, gender, race, and lean body mass [7, 13]. Consequently, the United States National Kidney Foundation uses GFR rather than serum creatinine level to define renal dysfunction [1].

The purpose of this study was to quantify the impact of baseline renal dysfunction assessed by estimated glomerular filtration rate (eGFR) on mortality in unselected patients admitted with an ACS.

METHODS

Patients

The study population comprised 589 consecutive patients who were admitted to our Intensive Cardiac Care Unit (ICCU) with ACS between July 2003 and December 2004. The inclusion criteria were a history of chest pain at rest or other symptoms suggestive of an ACS, with the most recent episode occurring within 24 h of admission. This could be associated with either transient or persistent ST-segment elevation, ST-segment depression, or T-wave inversion on the electrocardiogram, or elevated levels of biomarkers of myocardial damage. The biomarkers used were cardiac troponin I (cTnI) and creatine kinase MB mass assay (CK-MB), with a threshold for positivity of 0.06 and 3.5 ng/ml, respectively. Although this was a retrospective study, all the clinical and laboratory data were collected prospectively and recorded on a computer database of ACS patients admitted to our institution's ICCU.

Determination of renal function

Serum creatinine levels were measured during the first 12 hours. The GFR was estimated using the four-component Modification of Diet in Renal Disease (MDRD) equation [6, 14] presented below:

Estimated GFR (ml per minute per 1.73 m^2 of body surface area) = 186 x (serum creatinine [mg/dl])$^{-1.154}$ x (age [in years])$^{-0.203}$

For women, the value was multiplied by 0.742.

Patients were categorized into four groups based on eGFR in 15 ml increments (less than 45.0, 45.0 to 59.9, 60.0 to 74.9, and at least 75.0 ml/min/1.73 m^2), incorporating the guidelines of the National Kidney Foundation [1], and each category was analyzed separately. The population was also divided into 2 subgroups according to creatinine concentrations at the time of admission (greater than or less than 1.2 mg/dl for men or 0.9 mg/dl for women, which are the upper limits of this test in our hospital's laboratory).

Outcomes

We defined all-cause mortality as the primary endpoint in the six-month follow-up.

Follow-up

Patients were monitored for at least six months or until the primary endpoint was reached. Follow-up was by telephone, and by review of the databases and medical records of the hospital. Follow-up at six months was complete in 565 (96.0%) patients.

Statistical analysis

Discrete variables were expressed as percentages and comparisons made with the chi-square test. Continuous variables were described as means ± standard deviation and compared with ANOVA. A test for trend across ordered groups was performed for the four eGFR groups. Multivariable logistical regression analysis was performed to identify independent predictors of six-month mortality, including variables that showed potential statistical significance in univariate analysis ($p<0.10$). Kaplan-Meier curves were generated for mortality through six months of follow-up. The log-rank test was used to test the equality of the survival function across groups, and the test for trend of the survival function was performed across the ordered groups. All p values were two-sided, and a p value of less than 0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Baseline characteristics

The study included 589 patients who were admitted consecutively to our ICCU and who met the inclusion criteria. Of these, 434 (73.7%) were men, and mean age was 64.1±12.8 years; 18.5% had suffered a previous infarction, 45.7% had dyslipidemia, 25.0% were diabetic, 24.4% were current smokers, and 57.7% had a history of hypertension. Thirty-one (5.3%) patients had a final diagnosis of unstable angina, 268 (45.5%) had non-ST-segment elevation myocardial infarction, and the remaining 290 (49.2%) had ST-segment elevation myocardial infarction (STEMI).

The baseline estimated GFR was normally distributed. Mean (±SD) estimated GFR was 82.8±30.7 ml per minute per 1.73 m^2 (range, 11.7 to 191.1). A total of 345 (58.6%) patients had an estimated GFR of at least 75.0 ml/min/1.73 m^2, 183 (17.5%) had an estimated GFR of 60.0 to 74.9 ml/min/1.73m^2, 81 (13.8%) had an estimated GFR of 45.0 to 59.9 ml/min/1.73 m^2, and 60 (10.2%) had an estimated GFR of less than 45.0 ml/min/1.73 m^2. One hundred forty-one (24.0%) patients met the estimated GFR criteria for chronic kidney disease (less than 60.0 ml/min/1.73 m^2). There were no patients on chronic dialysis treatment in the cohort. The absolute difference in mean serum creatinine level between groups was 0.1 to 0.8 mg/dl (*Fig. 1*).

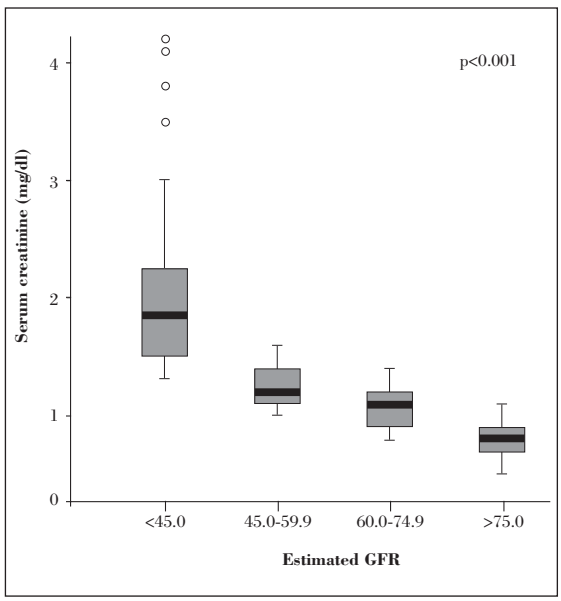

Figure 1. Box-and-whisker plot of serum creatinine level (mg/dl) by estimated glomerular filtration rate (ml/min/1.73 m^2) category.

The proportions of patients with coexisting conditions at baseline increased with decreasing estimated GFR (*Table I*). Patients with lower estimated GFR had higher rates of diabetes, hypertension, previous myocardial infarction, and previous stroke. A lower estimated GFR was also associated with older age and female gender. However, these variables were used in the determination of estimated GFR. Cigarette smoking was less frequent among patients with renal impairment. Patients with renal dysfunction presented less often with ST-segment elevation ACS, had higher heart rates and were more often in Killip class II to IV on admission. The use of cardiovascular pharmacotherapies (aspirin, statins, and angiotensin-converting enzyme inhibitors) before the admission event was more frequent in patients with impaired kidney function (*Table I*).

Regarding management practices, the use of reperfusion therapy (almost always with thrombolytic agents), beta-blockers, coronary angiography, and percutaneous coronary revascularization procedures was lower among patients with impaired renal dysfunction (*Table II*).

Clinical outcomes

Overall in-hospital mortality was 6.1%; six-month mortality was 13.6%. Elevated serum creatinine at presentation was associated with increased mortality in both men and women (*Fig. 2*). *Table III* displays variables associated with six-month overall mortality on univariate analysis. Decreasing estimated GFR was associated with increasing in-hospital and six-month mortality rates (*Table II*). Using the group with an estimated GFR of at least 75.0 ml/min/1.73m^2 as the reference group, the unadjusted odds ratio for six-month mortality for patients in the lowest GFR category (less than 45.0 ml/min/1.73m^2) was 20.00 (95% confidence interval [CI], 9.15 to 43.74), as compared with 15.78 (95% CI, 7.55 to 32.98) and 3.68 (95% CI, 1.60 to 8.47) for patients with moderate and mild renal impairment, respectively (*Table III*). Kaplan-Meier curves show that mortality increased early during the follow-up and continued to separate up to six months of follow-up in patients with moderate and more severe renal dysfunction (*Fig. 3*).

Impaired renal function was associated with increased six-month mortality rates in both non-

Table I
Baseline characteristics of the patients according to estimated GFR

Characteristic	GFR <45.0 ml/min/1.73 m² (n=60)	GFR 45.0-59.9 ml/min/1.73 m² (n=81)	GFR 60.0-74.9 ml/min/1.73 m² (n=183)	GFR ≥75.0 ml/min/1.73 m² (n=345)	P
Age (years)	74.0±9.4	74.1±7.5	66.9±12.0	59.3±11.9	<0.001
Creatinine (mg/dl)	2.0±0.7	1.2±0.2	1.1±0.1	0.8±0.1	<0.001
eGFR (ml/min/1.73 m²)	32.7±8.4	52.6±4.4	68.1±4.1	102.9±21.7	<0.001
Female (%)	51.7	54.3	29.1	14.5	<0.001
ST-segment elevation ACS (%)	30.0	50.6	46.6	53.0	0.011
Diabetes mellitus (%)	51.7	34.6	22.3	18.8	<0.001
Hypertension (%)	66.7	69.1	62.1	52.2	0.009
Dyslipidemia (%)	38.3	40.7	56.3	44.9	0.076
Current smoking (%)	8.3	9.9	17.5	32.8	<0.001
BMI >30 (%)	25.0	12.3	24.2	21.1	0.26
Prior myocardial infarction (%)	31.7	23.5	21.4	14.2	0.005
Prior PCI (%)	5.0	7.4	4.9	3.2	0.37
Prior CABG (%)	5.0	4.9	1.9	3.2	0.62
History of angina (%)	8.3	7.4	4.9	6.7	0.83
Prior stroke (%)	6.7	17.3	4.9	4.9	0.001
History of PVD (%)	1.7	3.7	1.9	0.9	0.30
Baseline medication (%)					
Aspirin	31.7	27.2	27.2	17.7	0.02
Beta-blocker	25.0	16.0	18.4	14.2	0.19
Statin	38.3	23.5	24.3	20.0	0.006
ACE inhibitor	46.7	34.6	25.2	18.0	0.02
Killip class >I on admission (%)	61.7	42.0	25.2	12.8	0.001
Blood pressure (mmHg)					
Systolic	135.2±31.6	136.5±28.8	137.2±26.0	138.4±24.2	0.8
Diastolic	73.5±21.8	75.2±15.6	77.1±16.3	78.7±15.5	0.08
Heart rate (bpm)	86.1±22.1	81.2±22.1	78.1±17.6	73.7±17.7	<0.001

eGFR: estimated glomerular filtration rate; ACS: acute coronary syndrome; BMI: body mass index (weight in kg divided by square of height in meters); PVD: peripheral vascular disease

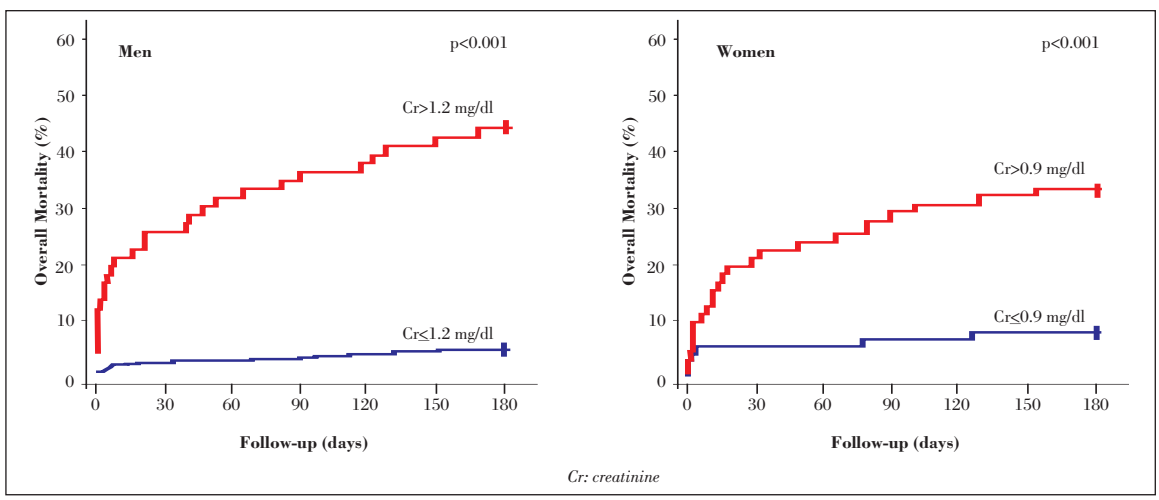

Figure 2. Kaplan-Meier curves for overall mortality in men and women with acute coronary syndromes stratified according to admission serum creatinine concentrations.

Table II
Management, angiographic and echocardiographic features, and outcomes of patients according to estimated glomerular filtration rate

Characteristic	GFR <45.0 ml/min/1.73 m² (n=60)	GFR 45.0-59.9 ml/min/1.73 m² (n=81)	GFR 60.0-74.9 ml/min/1.73 m² (n=183)	GFR ≥75.0 ml/min/1.73 m² (n=345)	P
In-hospital medication (%)					
Aspirin	100	98.8	99.0	99.7	0.52
Beta-blocker	61.7	67.9	82.5	91.0	<0.001
Statin	85.0	87.7	91.3	91.9	0.57
ACE inhibitor	86.7	84.0	88.3	87.0	0.99
Reperfusion therapy¶	7.1	34.2	64.4	58.1	<0.001
Procedure (%)					
Cardiac catheterization	35.6	33.3	59.8	69.9	<0.001
PCI	5.0	4.9	12.6	20.6	<0.001
CABG	6.8	7.4	11.8	10.5	0.63
Three vessel / left main CAD (%)	22.7	44.8	34.4	22.0	0.022
Left ventricular systolic dysfunction (%)	68.3	61.3	54.4	52.9	0.11
Discharge medication (%)					
Aspirin	95.7	100.0	98.0	95.8	0.27
Beta-blocker	67.4	75.7	88.0	86.9	<0.001
Statin	89.1	88.6	93.0	93.2	0.49
ACE inhibitor	93.5	81.4	90.0	84.9	0.17
In-hospital mortality (%)	21.7	16.0	2.9	2.0	<0.001
Six-month mortality (%)	42.9	37.2	12.1	3.6	<0.001

ACE: angiotensin-converting enzyme; ¶ In ST-segment elevation acute coronary syndromes; CAD: Coronary artery disease

Table III
Univariate analysis - variables with potential statistical significance (p<0.10)

Variable	OR (95% CI)	P
Age (per year)	1.10 (1.07-1.14)	<0.001
Current smoking	0.23 (0.09-0.55)	<0.001
Diabetes	2.83 (1.72-4.66)	<0.001
Dyslipidemia	0.57 (0.34-0.94)	0.029
Female	1.92 (1.16-3.19)	0.01
Heart rate	1.03 (1.02-1.04)	<0.001
Killip class	3.02 (2.21-4.14)	<0.001
eGFR 60.0-74.9 ml/min/1.73 m²¶	3.68 (1.60-8.47)	0.002
eGFR 45.0-59.9 ml/min/1.73 m²¶	15.78 (7.55-32.98)	<0.001
eGFR <45.0 ml/min/1.73 m²¶	20.00 (9.15-43.74)	<0.001
LVSD	1.54 (0.97-2.46)	0.068
Hypertension	1.56 (0.93-2.59)	0.090

eGFR: estimated glomerular filtration rate; LVSD: left ventricular systolic dysfunction; ¶The group with an estimated glomerular filtration rate of at least 75.0 ml/min/1.73 m² served as the reference group

Table IV
Multivariate analysis - independent predictors of six-month mortality

Variable	OR (95% CI)	P
Age (per year)	1.05 (1.01-1.08)	0.01
Killip class	1.50 (1.02-2.21)	0.04
eGFR 60.0-74.9 ml/min/1.73 m²¶	2.71 (1.09-6.69)	0.032
eGFR 45.0-59.9 ml/min/1.73 m²¶	7.53 (3.21-17.71)	<0.001
eGFR <45.0 ml/min/1.73 m²	8.10 (3.18-20.60)	<0.001

eGFR: estimated glomerular filtration rate; ¶The group with an estimated glomerular filtration rate of at least 75.0 ml/min/1.73 m² served as the reference group

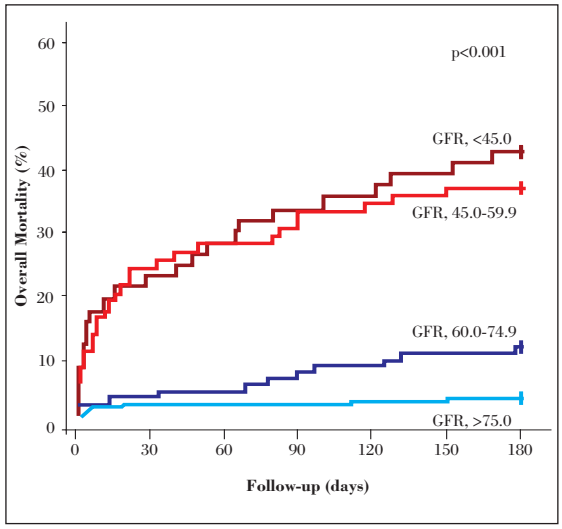

Figure 3. Kaplan-Meier curve for overall mortality in patients with acute coronary syndromes stratified according to estimated glomerular filtration rate (ml/min/1.73 m²) on admission.

ST-segment elevation ACS and STEMI (*Fig. 4-A*). In addition, six-month mortality rates increased with declining estimated GFR when patients were stratified by the presence or absence of a history of hypertension or diabetes, which are known cardiovascular risk factors and independent predictors of renal disease development and progression (*Figs. 4-B and 4-C*). Furthermore, impaired renal function was associated with increased mortality in the follow-up of patients with and without signs of heart failure on admission (*Fig. 4-D*).

Mildly to more severely impaired renal function was associated with increased six-month mortality in a multivariate model including variables that showed potential statistical significance in univariate analysis (p<0.10) (*Table IV*). In the group with the lowest estimated GFR, the adjusted odds ratio for six-month mortality was 8.10 (95% CI, 3.18 to 20.60), compared with 7.53 (95% CI, 3.21 to 17.71) in the group with an estimated GFR of 45.0 to 59.9 ml/min/1.73 m², and 2.71 (95% CI, 1.09 to 6.69) in the group with mild renal impairment (GFR 60.0 to 74.9 ml/min/1.73 m²). Considered as a continuous variable, for baseline estimated GFR values below 91.0 ml/min/1.73 m², the multivariate-adjusted odds ratio for six-month mortality for each 10-unit reduction in estimated GFR was 1.29 (95% CI, 1.10 to 1.52).

DISCUSSION

This single-center observational study extends previous reports regarding the association of renal dysfunction and increased mortality among patients who have had an acute coronary syndrome [6, 7, 15]. In the presence of non-ST-segment elevation and ST-segment elevation ACS, reduced estimated GFR on presentation is associated with increased mortality, independent of other conventional risk factors.

Onset of CKD is associated with an increased tendency for the development of cardiovascular disease-related events [16, 17]. Persons with CKD are predisposed to three types of cardiovascular disease - atherosclerosis, arteriosclerosis, and cardiomyopathy - compared with age- and gender-matched persons with normal kidney function [2].

Glomerular filtration rate is accepted as the best overall measure of kidney function [18]. It is measured as the urinary or plasma clearance of an ideal filtration marker such as inulin or alternative exogenous markers. However, this method is complex, expensive, and difficult to perform in routine clinical practice [18]. Several reliable equations incorporating clinical variables to estimate GFR are available. In this study, we used GFR estimated with the four-component MDRD study equation [14], which is more accurate and provides a better assessment of renal function in elderly patients and women [6, 19]. This equation does not require the weight of the subject, an advantage over other formulae for estimating filtration. Furthermore, a recent American Heart Association science advisory recommends that all adult patients with cardiovascular disease be screened for renal disease using GFR estimated by the MDRD study equation and a test for microalbuminuria [20].

The use of estimated GFR revealed wider differences in renal function than those evident from serum creatinine levels. Differences in the levels of serum creatinine between groups appeared small, whereas the differences in mortality after an ACS were large (*Figs. 1 and 3*). In agreement with recent studies [6, 15], approximately one-quarter (24%) of the patients met the estimated GFR criteria for chronic kidney disease.

Previous large-scale studies have shown that reduced renal function was independently

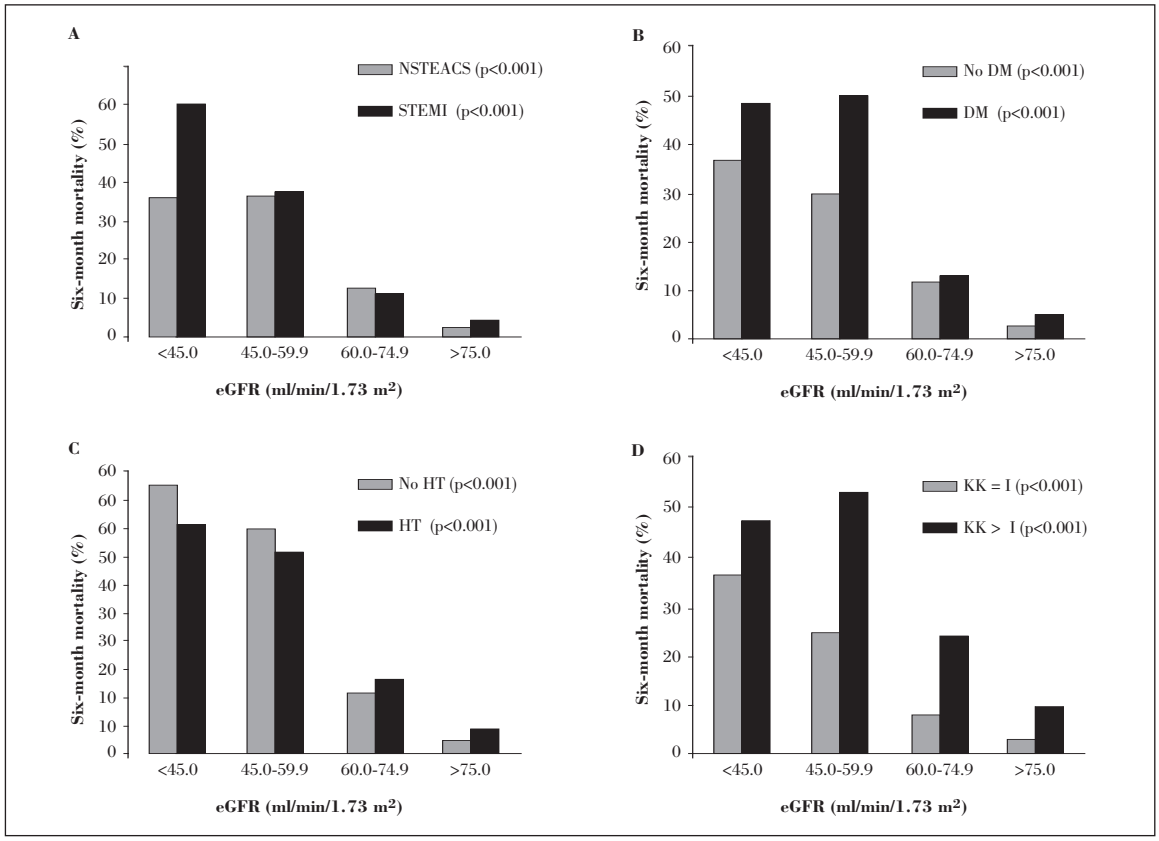

Figure 4. Overall six-month mortality rates according to estimated glomerular filtration rate category, stratified by type of acute coronary syndrome (A), history of diabetes mellitus (B) or hypertension (C), and Killip class on admission (D).

associated with increased risk of death and cardiovascular events [6, 9]. Our study documents the association of renal dysfunction with increased mortality, in a broad population of consecutive patients with ACS. Below 91 ml/min/1.73m², each 10-unit decrement in baseline estimated GFR was associated with a 29% increase in mortality at six-month follow-up. Assessment of renal function, however, is not used in the most widely used scores for early risk stratification on admission of patients with ACS [21, 22]. In a recent comparison of the prognostic value of three ACS risk scores [21-23], the best performance for one-year prognosis was achieved by the GRACE score, the only risk score including renal function determination (by means of serum creatinine level) in its composition [24].

The mechanisms by which renal dysfunction increases cardiovascular risk are poorly understood. Patients with renal dysfunction are at high risk partly because of the high prevalence of multiple risk factors, including older age, diabetes, hypertension, and previous myocardial infarction, as shown in *Table I*. In addition, these patients present with a less favorable clinical picture regarding Killip class. Still, in our study, even a mild reduction in estimated glomerular filtration rate was independently associated with increased mortality in multivariate analyses adjusting for the effect of several potentially confounding risk factors.

Proposed specific cardiovascular risk factors contributing to the vasculopathy induced by renal disease include hyperhomocysteinemia [25], elevated levels of lipoprotein (a) and oxidized low-density lipoproteins (LDL), endothelial dysfunction, diminished vascular nitric oxide production [26], and elevated uric acid levels [1]. It has also been proposed that reduced secretion of erythropoietin and insulin-like growth factor may also specifically contribute to an increased risk of thrombotic cardiovascular events by inhibiting vascular repair [27]. The chronic anemia and volume overload associated with severe renal dysfunction may also contribute to the increased vascular stiffness observed in these patients, which may be associated with higher cardiovascular mortality.

Furthermore, patients with mild to more severe renal impairment were less likely to receive guidelines-oriented therapeutic strategies, namely reperfusion therapy, beta-blockers, and percutaneous coronary revascularization procedures (*Table II*). These findings are in agreement with previous studies, which report that patients with chronic kidney disease receive less effective risk-factor modification and intervention (so-called "therapeutic nihilism") [6, 9, 28-30]. Potential reasons include hemodynamic and cardiovascular instability, and concern about worsening renal function and toxic effects of drugs related to reduced filtration [1, 6, 13, 28, 29]. In this study, patients with renal impairment were as likely as other patients to receive other risk-modifying cardiovascular medications, such as aspirin, angiotensin-converting enzyme (ACE) inhibitors, and statins. It was reported that patients with renal impairment have an increased risk of toxic effects of some of the therapeutic agents used in ACS (contrast agents, ACE inhibitors, glycoprotein IIb/IIIa inhibitors), and an increased risk of bleeding complications [8, 9]. Many cardiovascular trials have excluded patients with renal disease, limiting our knowledge of the efficacy and safety of cardiovascular medications and interventional strategies in these patients. However, it has been demonstrated that cardiovascular drugs and coronary interventional strategies can safely be administered to patients with renal insufficiency, when appropriately monitored, and yield similar benefits to those observed in the general population [6].

LIMITATIONS

This was an observational and non-randomized study, and as such, both identified and unidentified confounders may have influenced the outcomes. Another potential limitation of our study is that the measurement of creatinine, although performed at presentation, may have been influenced by the hemodynamic state of the patient and might not accurately reflect baseline renal function.

CONCLUSIONS

Baseline renal dysfunction, as assessed by estimated GFR, is a potent and easily identifiable determinant of outcome in patients with ACS. Mild to more severe renal impairment is independently associated with increased mortality after an ACS at six-month follow-up. This marker is readily obtained, is available to all hospitals, provides valuable prognostic information for immediate stratification, and should be determined in all patients with ACS. In agreement with previous studies, our data support the development and application of more aggressive strategies for preventing and treating ACS in patients with renal insufficiency, in order to optimize outcomes in this high-risk population.

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Address for reprints:

SÉRGIO NABAIS ARAÚJO
Hospital de S. Marcos, Serviço de Cardiologia
Largo Carlos Amarante
4701-965 Braga, PORTUGAL
Email: sergionnabais@gmail.com
Telefone: 00351933406200
Telefax: 00351253613334

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